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Doctorate of Medicine (DM)

In

Clinical Haematology

By:

Dr.Venkatesh Shriganesh Ekbote MD

For the year: August 2014

Department of Clinical Haematology

Christian Medical College, Vellore.

Tamil Nadu, India.

Analysis of Management of Immune Thrombocytopenia: Retrospective Comparison of Efficacy of Dapsone and Azathioprine as Second Line Therapeutic Agents.

CERTIFICATE

This is to certify that this thesis titled "Analysis of Management of Immune Thrombocytopenia: Retrospective Comparison of Efficacy of Dapsone and Azathioprine as Second Line Therapeutic Agents", is a bonafide work of the candidate, Dr.Venkatesh Shriganesh Ekbote during the period from August 2011 to August 2014 in partial fulfilment, towards the award of degree of Doctorate of Medicine (Higher Specialty) in Clinical Haematology for the examinations to be conducted by the Dr.M.G.R Medical University in August 2014.

Dr. Biju George, MD, DM Clinical Hematology
(Thesis Guide)
Professor,
Department of Clinical Hematology
Christian Medical College, Vellore

Dr. Biju George, MD,DM,
Professor, Department of Haematology,
Christian Medical College,
VELLORE - 632 004,TN,INDIA.

Dr. Alok Srivastava, MD, FRACP, FRCPA, FRCP
Professor & Head of the Department,
Department of Clinical Haematology,
Christian Medical College, Vellore.

Dr. ALOK SRIVASTAVA, MD, FRACP, FRCPA, FRCP
Professor & Head,
Department of Haematology
Christian Medical College
VELLORE - 632 004, TN., INDIA.

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Analysis of Management of ITP: Single Centre Comparison of Efficacy of Dapsone and Azathioprine As Second Line agents
by 16115754 . D.m. Clinical Haematology VENKATESH SHRIGANESH EKBOTE . EKBOTESHRIGANESH

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Dr. Venkatesh Ekbote
PG Registrar
Department of Clinical Haematology
Christian Medical College
Vellore 632 004

Sub: **FLUID Research grant project NEW PROPOSAL:**
Analysis of management of immune thrombocytopenia: retrospective comparison between dapsone and azathioprine as second line agents.
Dr. Venkatesh Ekbote, PG Registrar, Clinical Haematology, Dr. Biju George, Dr. Alok Srivastava, Dr. Vikram Mathews, Dr. Auro Viswabandya, Dr. Aby Abraham, Dr. Rayaz Ahmed, Dr. Abhijeet Ganapule, Clinical Haematology.

Ref: IRB Min No: 8204 dated 13.02.2013

Dear Dr. Venkatesh Ekbote,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Analysis of management of immune thrombocytopenia: retrospective comparison between dapsone and azathioprine as second line agents." on February 13, 2013.

The Committees reviewed the following documents:

1. Format for application to IRB submission
2. Cvs of Drs. Venkatesh Ekbote,Biju George, Alok Srivastava, Dr. Vikram Mathews, Auro Viswabandya, Aby Abraham, Rayaz Ahmed, Abhijeet Ganapule.
3. A CD containing documents 1 – 2.

The following Institutional Review Board (Research & Ethics Committee) members were present at the meeting held on February 13, 2013 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

Dr. B J Prashantham, M.A, M. A., Dr. Min (Clinical)
Director, Christian Counselling Centre
Chairperson, Ethics Committee

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho
Chairperson, Research Committee & Principal

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Name	Qualification	Designation	Other Affiliations
Dr. Susanne Abraham	MBBS, MD	Professor, Dermatology, Venerlogy & Leprosy, CMC.	Internal, Clinician
Dr. Benjamin Perakath	MBBS, MS, FRCS	Professor, Surgery (Colorectal), CMC.	Internal, Clinician
Dr. Ranjith K Moorthy	MBBS MCh	Professor, Neurological Sciences, CMC	Internal, Clinician
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Dr. B J Prashantham, M.A, M. A., Dr. Min (Clinical)
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Chairperson, Research Committee & Principal

Dr. Nihal Thomas
MD,MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
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Dr. Nihal Thomas
MD,MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin)
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We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent. And on completion of the study you are expected to submit a copy of the final report.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr Nihal Thomas
MBBS MD MNAMS DNB (Endo) FRACP(Endo) FRCP(Edin)
Secretary (Ethics Committee)
Institutional Review Board

CC: Dr. Biju George, Department of Clinical Haematology, CMC

TEL : 0416 - 2284294, 2284202 FAX : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

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(In the name of God, Most Gracious; Most Merciful)

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CONTENTS

ABSTRACT:

TITLE: Analysis of Management of ITP: Single Centre Retrospective Comparison of Dapsone and Azathioprine as second line therapeutic agents

DEPARTMENT : Clinical Hematology, Christian Medical College, Vellore.

DEGREE AND SUBJECT : D.M. Clinical Hematology

NAME OF THE GUIDE : Dr. Biju George, Professor, Dept. of Clinical Hematology.

Aims and Objectives of the study: To assess efficacy of dapsone and azathioprine children and adults with steroid refractory or steroid dependent ITP and relapsed ITP treated in our institute.

Methodology: We included patients treated with either dapsone or azathioprine for steroid refractory/dependent or relapsed ITP during 5 year period (March 1st 2007 to March 1st 2012).

Results: Three hundred patients were included in the study; 104(34.7%) children & 196(65.3%) adults. Median ITP duration was 5 months (1-262). Overall response over median treatment duration of 10 months (1-61) was 58.6%, with equivalent response (58.8% and 58.5%) with dapsone and azathioprine respectively. In children with steroid refractory/dependent ITP, dapsone exhibited significantly better response than azathioprine (p=0.023). Median response duration was significantly longer with azathioprine-60 months (2-60) than with dapsone (p=0.015). Relapses on therapy was higher with dapsone than azathioprine (p=0.007). Response less than CR & steroid refractory/dependent ITP were significant predictors of relapse on therapy. There were no deaths and event free survival was significantly better with azathioprine.

Conclusion: Present study confirms comparable efficacy of dapsone and azathioprine, although azathioprine produced more durable responses than dapsone. The findings of our study need to be validated in prospective randomized control setting. **Keywords:** ITP, dapsone, azathioprine.

Introduction

Introduction:

Idiopathic thrombocytopenic purpura (ITP), also known as autoimmune thrombocytopenic purpura, is an entity characterized by isolated thrombocytopenia often occurring in the absence of identifiable and specific precipitants(1). It is an acquired disease that affects both children and adults and causes a transient or persistent decrease in platelet count. Depending upon the degree of thrombocytopenia it is associated with an increased risk of bleeding(2).

Definition and Nomenclature:

The definition and nomenclature of ITP has evolved since the first ever practice guideline was published in 1996 by the American Society of Hematologists(3) which used the acronym ITP for "idiopathic thrombocytopenic purpura", emphasizing that it is a diagnosis of exclusion with no specific criteria for diagnosis. Thus the earliest definition of ITP is an isolated thrombocytopenia with no clinically apparent associated conditions or other causes of thrombocytopenia. The other causes of thrombocytopenia that were addressed were: HIV infection, systemic lupus erythematosus, lymphoproliferative disorders, myelodysplasia, agammaglobulinemia or hypogammaglobulinemia, drug-induced thrombocytopenia, alloimmune thrombocytopenia and congenital hereditary or non-immune thrombocytopenia(3). Subsequently in 2003, the British Committee for Standards in Hematology (BCSH) brought out a similar definition(4). In addition, the definition used peripheral blood platelet count of less than 150 x $10^9/l$ as threshold for diagnosis. In the most recent guidelines published by 2009 International Working Group (IWG)(2), the panel of investigators decided to persist with the widely used acronym 'ITP' but instead of "idiopathic" in ITP, proposed use of "immune", to emphasize upon immune-mediated mechanism involved, and qualified it further by replacing "idiopathic" by "primary" to denote

the absence of any obvious initiating and/or underlying cause. Further the panel acknowledged that it is inappropriate to use the term 'pupura' since review of literature showed that in large proportion of cases, bleeding symptoms were absent. Thus the acronym ITP would expand henceforth to "**I**mmune **T**hrombocyto**P**enia" according the 2009 IWG guidelines(2).

In their guidelines, the IWG panel came to a consensus of using peripheral blood platelet count of less than 100 x $10^9/l$ as opposed to the previous cut off of less than 150 x $10^9/l$ to define individuals who can be considered thrombocytopenic. The recommendations cite the following considerations as basis: Stasi et al(5) showed that patients presenting with platelet count between 100 & 150x$10^9/l$ have very low (6.9%) risk of persistent platelet count less than 100 x $10^9/l$ over 10 years of follow-up(5); in ethnicities other than the Western, normal healthy individuals may have platelet counts ranging from 100 to 150x$10^9/l$. The present cutoff value of 100x$10^9/l$ is also based on the hypothesis this would reduce concern over mild "physiologic" thrombocytopenia associated with pregnancy.

The 2009 International Working Group(2) recognized that various trials evaluating patient characteristics, determine responses, and report clinical outcomes, used widely discrepant criteria of assessment(6). In their opinion, this heterogeneity had lead to uneven and therefore unreliable comparison, of the results of clinical trials or cohort description. In order to harmonize and standardize disease definitions for better application of practical guidelines, they proposed the following definitions(2).

Table 1 Summary of Recommendations : Adapted from 2009 IWG criteria(2):

Definitions Proposed by the International Working Group on ITP:(2)	
Primary ITP	It is defined as an "autoimmune disorder". There is isolated thrombocytopenia (peripheral blood platelet count <100 $x10^9$/L). Characteristically, other causes of isolated thrombocytopenia have to be excluded. Currently, there is lack of clinical or laboratory parameters for establishing diagnosis of ITP. ITP thus remains a diagnosis of exclusion.
Secondary ITP	All patients of ITP not satisfying criteria for primary ITP: The associated disease/disorder should be specified (SLE, Drug induced, pregnancy related, HIV associated) after the acronym of "secondary ITP".
Phases	**Newly diagnosed ITP:** ITP duration is within 3 months of diagnosis **Persistent ITP**: ITP duration is between 3 to 12 months of diagnosis. This is new category in present guidelines proposed to include ITP within 12 months of diagnosis since incidence of spontaneous remission is still significant. It includes patients who have not reached spontaneous remission or not maintaining complete response off therapy. **Chronic ITP:** Any ITP lasting beyond 12 months from diagnosis. **Severe ITP:** Any ITP with bleeding symptoms at onset of magnitude that in itself is an indication for treatment. Also includes bleeding requiring additional therapy with different platelet-enhancing agent or increased dose.

Review of Literature

Review of Literature:

Epidemiology and Natural History:

Adult chronic ITP has an incidence of 58–66 new cases per million population per year or nearly 5.8–6.6 per 100,000 in the US(7) with a similar incidence in the UK. This form of ITP affects mainly women of childbearing age (Male: Female-1:3)(8). Adult patients with ITP are more likely to manifest disease with a chronic course. Overall, approximately 15% of patients remit within 1 year after disease onset, but rare late remissions occur, even among patients who have failed splenectomy (9). Symptomatic bleeding is to a degree related to the platelet count, with literature suggesting that almost all major bleeding occurring with platelet counts < 30 $x10^9$/L. The risk of bleeding was analyzed in a pooled analysis of published clinical series comprising 1800 patients. Severe chronic ITP in adults was defined as platelet count < $30x10^9/L$ at least with 1 year after diagnosis, The annual incidence of fatal hemorrhage was 1.6-3.9 cases per 100 patient years, with a lower risk in patients < 40 years of age (0.4% per year) compared with patients > 60 years of age (13% per year)(9). Risk of nonfatal hemorrhage was estimated to be 3% per year in patients 40 years of age and 71% per year for patients > 60 years of age(9).

Childhood ITP has an incidence of between 4.0 and 5.3 per 100 000(10)(11). The peak age of presentation of ITP in children is between 5 and 6 years, with 70% of cases presenting between ages of 1 and 10 years. Approximately 50%-60% of children will have a febrile illness that preceded the discovery of thrombocytopenia(12). In a study of 863 children with newly diagnosed ITP[13]: a) none or mild bleeding manifestations in 77% patients, b).moderate bleeding occurred in 20%, and c).severe bleeding in 3%.[13] d).Life-threatening bleeding is rare and the estimated risk of intracranial hemorrhage is between 0.1% & 0.5% in newly diagnosed cases(13).

Approximately 65%-70% of children remit by 6 months and another 15%-20% by 12 months. The 5%-10% of children who develop chronic ITP tend to be older, are more often female and usually present with a higher platelet count(9).

Medical Management of ITP:

Goals of therapy(1)**:**

a) **In children:** For children with ITP, when treatment is given, it is initially aimed at rapidly increasing the platelet count to a safe level, then maintaining an adequate and safe count while awaiting as spontaneous remission(1).
b) **In adults:** For adults, most of whom will have chronic ITP, therapies are used to increase the platelet count to a safe level and/or to prevent further bleeding with minimal toxicities. Maintenance of platelet count> 30 x 10^9/L is considered an appropriate goal(1).

Table 2 : Options for Therapy: Adapted from International Consensus Report 2010 (14):

First line Therapy (Newly diagnosed ITP)	Corticosteroids: dexamethasone, methylprednisolone, prednis(ol)one Anti-D, IVIg
Second Line Therapy (Persistent/Chronic ITP)	**Surgical**: Splenectomy **Medical Therapy**: Cyclosporin A, Cyclophosphamide, Danazol, Dapsone, Mycophenolate mofetil, Vinca alkaloids Rituximab TPO receptor agonists

Treatment Options for patients who have failed first- and second-line therapies	**A: TPO receptor agonists;** Supported by adequate data. **B:** Campath-1H, Combination of first and second-line therapies, Combination chemotherapy, HSCT. The report acknowledges that category A is preferred over category B since data supporting the former is more substantial, whereas for the later, apart from inadequate supportive data, there is considerable toxicity associated with the later approach.

Steroids as First Line Therapy in Immune Thrombocytopenia(14)

Corticosteroids (prednisolone, methylprednisolone or dexamethasone) are the standard initial treatment[14]. Investigators have also noted that they may reduce bleeding independent of the platelet count rise by means of a direct effect on blood vessels. The frequency of complete remission (CR) after a course of first-line therapy with corticosteroids, noted across various studies, ranges from 10%-30% with daily oral prednisone. Additionally, investigators claim responses of as much as 60%-80% with high-dose, pulsed dexamethasone (HDD).(15)(16)(17) However, the latter remains to be confirmed in controlled trials, and currently available evidence does not establish the superiority of HDD. Patients are at risk of developing corticosteroid-related complications that vary with the dose and duration(14). Due to above reasons, it is not advisable to use multiple cycles of HDD to induce remission in patients who have failed a course of prednisone(18).

Second line Therapy for Cortecosteroid refractory or relapsed ITP(14)

The approach to treatment of steroid refractory and relapsed ITP hinges or two types of modalities of therapy:

a) Medical management: These included the following agents: anti-CD20 therapy, Dapsone, Azathioprine, Cyclophosphamide, Cyclosporine, Combination Therapy
b) Surgical Management: Splenectomy (Laparoscopic/Laparotomy).

The 2003 BCSH guideline(4) maintains that the wide variety of treatments available for second line therapy reflects their relative lack of efficacy. In their view, these agents should be used in non-urgent or 'semi-urgent' cases where there is a need to elevate the platelet count.

In 2010 the International consensus report for management of ITP guidelines(14), the goal of second-line therapy has been defined as the achievement of sustained increase of the platelet count that is considered hemostatic. The report lists more than 10 second line therapeutic options, including splenectomy, without indicating a preference. Azathioprine, danazol, cyclophosphamide, cyclosporine A, dapsone and mycophenolate mofetil have all shown limited efficacy in the treatment of ITP. No single agent induces un-maintained remission in >30% of refractory cases. This is particularly true in patients refractory to splenectomy(1).

There is paucity of evidence-based medicine on this topic as noted by various groups across detailed reviews(19). Both the American Society of Hematology(14) and the British Committee for Standards in Haematology General Haematology Task Force(4) have issued "practice guidelines." These are essentially a compilation of opinions from panels of experienced physicians who have agreed upon some but not all of the practices. Across all these reviews,

there are many unresolved issues and the investigators also agree that the approach to treatment to these cases will change in future as more and more data emerges to answer these question(20).

Dapsone and Azathioprine as Second Line Therapeutic Agents:

The 2003 BCSH guidelines(4) comment that in patients treated with dapsone, half of all patients with chronic ITP will show some response within 3 weeks, but it appears to be less effective in severe cases of ITP. They cite the series of 66 adults with chronic ITP that included patients with platelet counts < 50 $x10^9/l$ and treated them with dapsone at 75–100 mg orally(21). Responses were observed in 33 of 66 patients (50%), with a median duration of treatment required to achieve a response of 21 days. Sustained responses were observed in 19 patients(21). Treatment with azathioprine (2 mg/kg, usually up to a maximum of 150 mg/d) as single agent may also be considered and up to 25% of patients may have a sustained response. Azathioprine is slow-acting, and should be continued for up to 6 months before being deemed a failure(4).

The 2010 International consensus report for management of ITP(14) comments that dapsone as second-line therapy in doses of 75mg/day to 100mg/day, has moderate corticosteroid effects. The report notes that response may be observed in up to 50% of patients treated with dapsone.

The appropriate time to response is usually 3 weeks. Sustained response may be noted in up to two-thirds of responders to therapy. Guidelines have also noted that dapsone may delay splenectomy for up to 32 months in corticosteroid refractory patients but splenectomized patients have a low response rate (evidence level IIb)(14).

Regarding azathioprine the 2010 International Consensus report takes into account that despite few new data, this agent is still useful(14). Investigators have reported complete responses in 45% of 53 patients (40 splenectomized) treated with azathioprine (150 mg/day) for a median of 18 months(22). Although continued therapy is generally required, often a reduced dose suffices. Leukemia has only rarely been associated with azathioprine in other disorders but has not been described in ITP patients (evidence level III)(23)

The 2011 American Society of Hematology(24) evidence based practice guidelines note that in children with ITP unresponsive to steroids, the recommendation regarding second line agents steroid sparing agents is not possible due to lack of data on any single agent. The only exception to this is dapsone. In this regard, the guideline cites retrospective analysis of dapsone in chronic or persistent ITP that included 35 children from Christian Medical College Vellore(25), with a response rate of 66% and continuous complete response rate (platelet count > 50 x 10^9/L with or without dapsone) of 31%(25). The 2010 International consensus report(14) acknowledges that choice of second-line therapy in newly diagnosed patients who fail corticosteroids is controversial, as there are no comparative trials of treatment options in this setting. The 2011 evidence based practice guideline by American Society of Hematology(24) also acknowledges inadequate research in the area since 1996 guideline(3). It thus maintains that it is not possible for investigators to include formal evidence based recommendations for indications and timing of use of second line therapy for ITP.

Preliminary studies from Christian Medical College, Vellore in this context;

In 2005, Sharat Damodar et al(25)published data of 90 patients (55 adults and 35 children) of chronic ITP from Department Of Hematology ,Christian Medical College Vellore (platelet count of $<50 \times 10^9$/L). It primarily included patients with more than 6 months of duration of ITP that were treated with dapsone (at a dose of 1–2 mg/kg/d) as second line therapy. A response was observed in 57 (63.3%) patients with complete response (CR) of 48.9%. The mean time to response was 3.5 months (range 1–9). The average duration of treatment with dapsone in this cohort of patients was 10.4 months (range 4–14). Overall response rates of 65.7% and 61.8% were observed in children and adults respectively. Side effects requiring discontinuation of therapy were observed in three (2%) patients(25).

These results demonstrate that dapsone is an effective, inexpensive and well-tolerated treatment for chronic ITP, in both children and adults. Hence it could be considered for patients who fail steroid therapy(25).

Subsequently, in 2006 Rajsekhar et al (ISHTM Abstract 2006)(26) conducted a randomized control study comparing response of dapsone with azathioprine in patients with ITP who have failed steroids – defined as platelet counts $<30 \times 10^9$/l after one month of steroid therapy. A total of 103 adult patients with idiopathic thrombocytopenic purpura (ITP) who failed steroids were randomized to receive either azathioprine or dapsone. In all, 79 (76.7%) patients were available for evaluation of response of which 37 received azathioprine and 42 received dapsone[26]. Results of the study that was presented as abstract in ISHTM 2006 are outlined in TABLE 3.

Table 3: Comparison between Dapsone and Azathioprine as Second Line agents:

Parameter	Overall- (%) N=79/100	Azathioprine (%) (N= 37)	Dapsone (%) (N=42)	P value
Response	43 (53.8%)	21 (56.8%)	22 (52.4%)	0.69
Complete Response	23 (53.5%)	9 (24.3%)	14 (33.3%)	0.23
Partial Response	20 (46.5%)	NR	NR	NA
Time to Response	NR	NR	NR	NR
Response Duration	NR	NR	NR	NA
Relapse	12 (27.9%)	8	4	0.20
Re T/T- Dapsone (including NR)	17	NA	R – 8 (43.8%)	
ReT/T Azathioprine (Including NR)	9	R -- None	NA	
Total Response		30/59 (50.8%)	21/46 (45.7%)	0.60

The investigators Rajsekhar et al concluded that dapsone therapy is as effective as azathioprine in the treatment of chronic ITP but at a significantly lower cost(26).

In view of these observations and the fact that there is limited long term data on second line therapy in Indian patients with ITP, we intend study response to Dapsone and Azathioprine in patients diagnosed with relapsed or steroid refractory/dependent ITP therapy and in Department of Clinical Hematology Christian Medical College Vellore.

Aims and Objectives

Aims and Objectives:

To assess efficacy of Dapsone and Azathioprine in treatment of patients with relapsed ITP and ITP refractory to steroid therapy treated in Department Of Hematology.

Hypotheses:

1. The overall treatment outcome of children with ITP in India is similar to that reported in the international literature.
2. Using current treatment regimens, the outcome in the adults with ITP in India is similar to that as reported in literature.
3. In both children and adults, dapsone therapy is as effective and as well tolerated as azathioprine in the treatment of both steroid dependent/steroid refractory ITP and relapsed ITP.

Patients and Methodology

Study Design:

In this retrospective observational study, we compared efficacy of two second line agents, dapsone and azathioprine for treatment of patients with immune thrombocytopenia (ITP) who were either refractory to first line therapy (steroid therapy) or had relapse after achieving initial response. In order to identify patients with steroid refractory/dependent ITP or relapse of ITP, medical records of patients treated for ITP in Department of Hematology during the 5 year period between March 1st 2007 and March 1st 2012 were reviewed. Further analysis was done using data from medical records of patients who fulfilled inclusion criteria. Standard format of recording data was used for all patients included in the study. At the time of recording data, appropriate care was taken so that neither any direct or indirect identification of patient are mentioned.

This study was conducted over 1 year – from 1st February 2013 to 31st January 2014.

The study was approved by Institutional Review Board.

Patients:

Inclusion Criteria: All patients who underwent treatment in Department of Hematology during the five year period between March 1st 2007 and March 1st 2012 with either dapsone or azathioprine for steroid dependent/refractory ITP or relapsed ITP were included in the study:

1. ITP refractory to steroids was defined as ITP patients who continued to have platelet count <30,000/cumm at 1 month of treatment with 1mg/kg daily prednisolone

2. Steroid dependent ITP was defined as is ITP requiring treatment with corticosteroids repeatedly for two months to prevent bleeding or maintain platelet count >30,000/cumm, and

3. Relapsed ITP was defined as recurrence of low platelet count ($< 30 \times 10^9$/L) or a 2-fold or greater decrease in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.

For purpose of analysis, we combined 1. steroid refractory ITP and 2. steroid dependent ITP patients since the duration of ITP in both the subsets of patients is within 12 months of diagnosis(persistent ITP), when chances of spontaneous remissions are still significant(2).

Exclusion Criteria: Patients with ITP for whom data from medical records are not retrievable, were excluded from the study.

Method:

a) **Sample Size Calculation:** On review of comprehensive Hematology Database for cases of ITP diagnosed since 2007, there were more than 1200 cases in all. Assuming that approximately 50% of ITP patients fail to either show response or will have relapsed ITP and further, assuming 10% attrition rate at level of medical records, we decided to include at least 300 patients for retrospective analysis.

b) **All patients** with 1. Steroid refractory ITP, 2. Steroid Dependent ITP or 3. Steroid dependent ITP; who underwent treatment in Department of Hematology during recent 5 year period (March 1st 2007 to March 1st 2012) were identified by our comprehensive Hematology database.

c) Their medical records will be reviewed to gather the following data: age at diagnosis, gender, platelet count at diagnosis of ITP. Information regarding bleeding manifestations, both at time of diagnosis and at time of relapse or steroid failure, was recorded.

d) "Mild bleeding" will be defined as involving skin manifestations only (bruising and petechiae) without any mucosal bleeding(24).

e) Clinically important or major hemorrhage: defined as presence of 1 or more of the following occurring at any time during the course of ITP: (1) Intracranial hemorrhage, (2) epistaxis requiring cautery or nasal packing, (3) gross hematuria, or (4) other mucosal or cutaneous hemorrhage severe enough to cause a decline in patient's hemoglobin concentration to ≤10 g/dL or ≥2 g/dL below patient's baseline haemoglobin value(27).

Disease definitions: The disease definitions outlined in TABLE 4 are adapted from criteria laid down by International Working Group for Immune Thrombocytopenia(2).

Table 4: Definitions of disease(2)

Primary ITP	It is defined as an "autoimmune disorder". There is isolated thrombocytopenia (peripheral blood platelet count <100 $x10^9$/L). Characteristically, other causes of with isolated thrombocytopenia have to be excluded. Currently, there is lack of clinical or laboratory parameters for establishing diagnosis of ITP. ITP thus remains a diagnosis of exclusion.
Secondary ITP	All patients of ITP not satisfying criteria for primary ITP: The associated disease/disorder should be specified (SLE, Drug induced, pregnancy related, HIV associated) after the acronym of "secondary ITP".
ITP : Phases	**Newly diagnosed ITP:** ITP duration is within 3 months of diagnosis **Persistent ITP**: ITP duration is between 3 and 12 months of diagnosis. This is a new category in present guidelines proposed to include ITP within 12 months of diagnosis since incidence of spontaneous remission is still significant. It includes patients who have failed to reach spontaneous remission or are not maintaining complete response off therapy. **Chronic ITP:** Any ITP lasting beyond 12 months from diagnosis. **Severe ITP:** Any ITP with bleeding symptoms at onset of magnitude that in itself is an indication for treatment. Also includes bleeding requiring additional therapy with different platelet-enhancing agent or increased dose.

Dapsone and Azathioprine Therapy:

At our centre, dapsone and azathioprine are used as second line therapeutic agents for inducing response in steroid dependent/steroid refractory patients and also in relapsed ITP. The selection of particular therapeutic agent is based on physician preferences and affordability of the patient.

The initial dose of dapsone in children is 1.5mg/kg/d and that in the adult is 50mg per day for first 2 weeks. Patients are counseled regarding side-effects such as hemolytic anaemia, dermatitis and methemoglobinemia. They are electively re-assessed at the end of 1 week for intolerance. In patients without any intolerance to dapsone, the side effect profile and need for follow up for the same either with our centre or with a local physician is re-enforced at that visit. Patients are not tested for G6PD deficiency prior to initiation of therapy with dapsone. In case of compensated hemolysis, therapy is continued with bi-weekly monitoring of hemoglobin and bilirubin levels and a drop in hemoglobin>1g/dl is an indication to discontinue dapsone. Dermatitis, leucopenia hypersensitivity syndrome and methemoglobinemia are absolute indications for discontinuation of therapy. In absence of above, dose is increased to maximum dose of 2mg/kg/d in children and 100mg to 150mg in adults.

The initial dose of azathioprine therapy in children and adults is 1.5mg/kg/d. The patients are counseled regarding side effects such as cytopenia and dermatitis. Patients are re-assessed for the same at the end of 15 days. Thereafter the dose is increased over subsequent visits to reach a maximum dose of 2.5mg/kg./d.

Stable patients on treatment with dapsone or azathioprine are followed up at least once every three months for assessment of response. In patients achieving complete response, azathioprine was tapered and eventually stopped while dapsone therapy was stopped without prior tapering.

Primary Outcome: This included:

Overall response and complete response rates in ITP patients treated with dapsone and azathioprine as second line therapy therapy.

Secondary Outcome measures : These included:

1. Time to initial response, median dose for initial response, duration of response on therapy and comparative rates of relapse while on therapy.
2. Sustained response rates after stopping therapy, duration of sustained response and relapse rates after stopping second line therapeutic agents dapsone and azathioprine.
3. Comparison of overall survival and event free survival rates in patient who received dapsone and azathioprine.
4. Bleeding at diagnosis and at time of relapse or failure of steroid therapy in entire cohort.

Definition of Outcomes: In analysis of both arms, the assessment of response was based on recommendations of 2009 International Working Group Guidelines(2), as follows:

- **Complete response (CR)**: Patients were defined to be in CR when they achieved platelet count $\geq 100 \times 10^9$/L measured on 2 occasions at least 7 days apart and the absence of bleeding.
- **Response (R)**: Response to second line therapy was defined as achievement of platelet count $\geq 30 \times 10^9$/L or achievement of at least a 2-fold increase in platelet count from baseline measured on 2 occasions at least 7 days apart and in the absence of bleeding.
- **No response (NR)**: A platelet count $< 30 \times 10^9$/L or a less than 2-fold increase in platelet count from baseline or bleeding. Platelet count must be measured on 2 occasions more than a day apart.

- **Loss of complete response**: A platelet count < 100×10^9/L measured on 2 occasions more than a day apart and/or the presence of bleeding.
- **Loss of response**: A platelet count < 30×10^9/L or a less than 2-fold increase in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.
- **Time to response:** It was measured from start of treatment until the time that patient either achieved complete response or at least a response.
- **Duration of response:** The 2009 Guidelines by International Working Group on ITP defined duration of response in two ways. A) Time from complete response or response until loss of complete response or response. B) Duration of response can also be measured as the proportion of the cumulative time spent in complete response or response during the period under examination as well as the total time observed from which the proportion is derived.

Statistical Analysis:

Descriptive Statistics (mean, median and mode) were used for all variables. For dichotomous variables, the difference in proportions were assessed using Chi Square Test or Fisher's Exact Test. Difference in mean was assessed using T test or Mann Whitney "U" Test.

For purpose of analysis, it was decided to combine variables from steroid dependent ITP and steroid refractory ITP since the duration of ITP in both these categories was less than 12 months. There is evidence to suggest that there is still significant chance of remission during initial 12 months from time of diagnosis.

Children were defined as patients less than 15 years of age and adults were defined as 15 years or more in age, in accordance with previous study from our centre published by Damodar et al (25).

Overall survival was defined as time from initiating second line therapy to last follow up or death.

Event free survival was calculated from the time of initiation of second line therapy to time of last follow up or an event.

Events were defined as follows:

1. Death while on second line therapy,
2. Lack of response to second line therapy at 6 months,
3. Severe adverse effects of therapy necessitating discontinuation,
4. Relapse while on therapy, and
5. Relapse after stopping therapy.

Results

Results:

A total of 300 patients satisfied inclusion criteria. This included two patients who already had splenectomy for ITP elsewhere. Majority (98%) of patients included in study cohort had primary (ITP). Only 6 patients (2.0%) satisfied criteria for secondary ITP: it included two patients diagnosed with ITP associated with pregnancy, 3 patients with systemic lupus erythematosus and one patient with rheumatoid arthritis. Three patients (1.0%) with primary ITP had associated autoimmune hemolytic anaemia (Evan's Syndrome). The median age of entire cohort was 22 years (range 1-80 years). There were **104(34.7%)** children and **196(65.3%)** adults. The male to female ratio in the present cohort was **0.56:1.** Median platelet count at diagnosis was 12 x 10^9/l (range 10-56 x 10^9/l). There were 144 patients (48%) who had steroid refractory/dependent ITP and 156 patients had relapsed ITP in the present cohort of patients (TABLE 5A).

Table 5A: Comparative Patient Characteristics: Dapsone & Azathoiprine (N=300)

Characteristics	Total (%) N = 300	Dapsone (%) n = 170	Azathioprine (%) n = 130	P value
Children	104 (34.7)	64(37.7)	40(30.7)	**0.224**
Adults	196 (65.3)	106(62.3)	90(69.3)	**0.224**
Male:Female Ratio	0.56:1	0.68:1*	0.42:1*	**0.069***
Platelet<10x10^9/l at Diagnosis	129 (43.0)	74 (43.5)	55(42.3)	**0.906**
Platelet>10x10^9/l at Diagnosis	171(57.0)	96(56.5)	75(57.7)	
Median ITP Duration (months)	5 (1–262)	4(1-262)	6(1-146)	**0.149**

The adults included in the study had significantly lower male to female ratio (p=0.005) than adults. Median duration of was comparable between children and adults (TABLE 5B).

Table 5B: Comparative characteristics between children and adults (N = 300)

Characteristics	Total (%) N = 300	Children (%) n =104	Adults (%) n = 196	P value
Patients	300	104(34.7)	196(65.3)	---
Male : Female Ratio	0.56:1	0.89:1*	0.43:1*	**0.005***
Median Platelet Count at Diagnosis	12 x 10^9/l	12 x 10^9/l	12.5 x 10^9/l	0.112
Median ITP Duration	5(1-262)	5(1-64)	5.5(1-262)	0.346

Table 6: Comparative Indication of Second line Therapy For Entire Cohort (N=300):

Variable	Dapsone (%) n = 170	Azathioprine (%) n =130	P Value
Steroid Refractory/ Dependent ITP n = 144	90 (52.9)	54 (41.5)	0.062
Relapsed ITP n = 156	80 (47.1)	76 (58.5)	0.062

We observed that in present cohort of ITP patients, patients with steroid refractory/dependent ITP were more often treated with dapsone than azathioprine (TABLE 6). Patients with relapsed ITP were more often treated with azathioprine than dapsone. Thus, there were more steroid refractory/dependent ITP patients on dapsone therapy and more relapsed ITP patients on azathioprine in our study cohort, with trend towards significance (p=0.062).

On further subgroup analysis of children and adults treated with dapsone and azathioprine in the study cohort, the difference in treatment preference was found to be statistical significant only in adults (p=0.045) (TABLES 7A and 7B).

Table 7A: Comparative Indication of Second line Therapy in Children (N=104):

Variable	Dapsone (%) n = 64	Azathioprine (%) n = 40	P Value
Steroid Refractory/ Dependent ITP	33(51.6)	19(47.5)	0.840
Relapsed ITP	31(48.4)	21(52.5)	0.840

Table 7B: Comparative Indication of Second Line agents in Adults (N = 196):

Variable	Dapsone (%) n = 106	Azathioprine (%) n = 90	P Value
Steroid Refractory/ Dependent ITP	49 (46.2)	35 (38.9)	0.045
Relapsed ITP	57 (53.8)	55 (61.1)	0.045

Bleeding Manifestations:

Major Bleeding: In the present cohort of patients, at least one episode of major bleeding at diagnosis was documented in 44 **(14.7%)** of cases **(Table 8A)**. These included 9 patients **(3%)** who had intracranial hemorrhage at diagnosis and 34 patients**(11.3%)** who had mucosal bleeding (hematuria, menorrhagia, or recurrent gum bleeding) that caused decline in hemoglobin to <10g/dl or >2g/dl below the patient's baseline hemoglobin levels. One patient also had epistaxis

that required nasal packing. In contrast, only 16 patients **(5.3%)** had major episode of bleeding at the time of relapsed ITP or failed response to steroid. Only 1 patient had new onset intracranial hemorrhage at the time of relapse.

Table 8A: Bleeding Manifestations in Entire Cohort of Patients:

Characteristics		Total (%)	Dapsone (%)	Azathioprine (%)	P value
Bleeding at Diagnosis	Major	44 (14.6)	21(12.4)	23 (17.7)	0.066*
	Minor	252 (84)	149 (84.7)	103 (79.2)	
	None	4 (1.3)	0	4 (3.07)	
Bleeding at Steroid Failure* or Relapse	Major	16 (5.3)	7 (4.1)	9 (6.9)	0.544
	Minor	249 (83)	144 (84.7)	105 (80.8)	
	None	35 (11.7)	19 (11.2)	16 (12.3)	

* included Steroid refractory/dependent ITP.

Table 8B: Bleeding Manifestations in Children and Adults:

Characteristics		Total (%)	Children (%)	Adults (%)	P value
Bleeding at Diagnosis	Major	44 (14.7)	3 (2.9)	41 (20.91)	**0.001**
	Minor	252 (84)	100 (96.2)	152 (77.5)	
	None	4 (1.3)	1 (1)	3 (1.5)	
Bleeding at Steroid Failure* or Relapse	Major	16 (5.3)	1 (1)	15 (7.65)	0.106
	Minor	249 (83)	91 (87.5)	158 (80.6)	
	None	35 (11.7)	12 (11.5)	23 (11.7)	

* included Steroid refractory/dependent ITP.

Major hemorrhagic episodes in children (Table 8B) at diagnosis **(2.9%)** were significantly less among children than in adults - **(20.91%)** – **p=0.001**. None of the children included in the study had intracranial hemorrhage. All 10 patients with intracranial hemorrhage (9 patients at diagnosis and 1 additional patient at time of steroid failure) were adults. Thus 20.91% (41/196) adults had "severe ITP" compared to only 2.9% (3/104) in children. Although the same trend of bleeding manifestations was seen at time of steroid failure or at time of relapse of ITP, the difference was not statistically significant (Table 8B).

As compared to ITP at diagnosis, the proportion of "severe ITP" decreased from 14.7% to 5.3% in steroid refractory ITP/ dependent ITP and at relapse. The decrease in bleeding manifestations was seen both in children -2.9% to 1% and adults – from 20.9% to 7.65% (Table 8B).

Minor Bleeding: Majority of patients had minor episodes of bleeding in the form of petechial and purpuric rashes, both at diagnosis (84%) and at the time of relapse (83%). There were 4 patients that did not have bleeding manifestations at diagnosis. Further, the number of patients without any bleeding manifestations increased to 35 when it came to bleeding at time of relapse/steroid failure. Compared to adults (77.5%), significant majority of children (96.2%) had minor bleeding episodes at diagnosis (Table 8B). Although a similar trend of bleeding manifestations was seen at time of steroid failure, the difference was not statistically significant.

Primary Outcome: Response to Second Line Therapy: (TABLE 9A)

There were 170 patients who were treated with dapsone as second line therapy and 130 had received azathioprine as second line therapy. Of these, 2 patients had already undergone splenectomy for steroid refractory ITP before they received second line medical therapy. Overall response rate to second line medical therapy in the present cohort was **58.6%.** In all 124 patients (41.3%) failed to show response to either dapsone or azathioprine. The median time to response for entire cohort was 3 months (range 1-12 months). The time to initial response was identical for patients treated with both dapsone and azathioprine months (p=0.827). The median duration of treatment for entire cohort was 10 months (range 1–61 months).

Table 9A: Primary Outcome - Overall Comparison between Second Line Therapy.

Variables	Dapsone(%)	Azathioprine(%)	P value
Overall Response	100 (58.8)	76 (58.5)	1.000
Complete Response	78 (45.9)	60 (46.2)	1.000
Time To Response (months)	3 (1-12)	2.8 (1-11)	0.999
Dose Of Response: **Children**	1.5 (1-3 mg/kg/d)	2.0 (1-3 mg/kg/d)	---
Adults	100mg (50 -150mg)	2.0 (1-3 mg/kg/d)	---
Median T/t Duration (months)	10 (1-61)	10.5 (2-47)	0.857
Median Response Duration (months)	27 (5-74)	60 (2-60)	**0.015**

Overall response to dapsone therapy was **58.8%,** whereas it was **58.5%** in patients treated with azathioprine therapy **(p=1.000).** Both therapies showed comparable rates of complete response.

Patients who had steroid refractory/dependent ITP showed overall response rates of **55.6%,** comparable to response in patients with relapsed ITP **61.5% (p=0.348).** Patients with relapsed ITP achieved complete response rates of **50%** compared to steroid refractory ITP, who achieved complete response rates of **41.7% (p=0.165).**

In steroid refractory/dependent ITP dapsone showed overall response of **58.9%** which was comparable to **50%** response rate in patients treated with azathioprine (p=0.299). Similarly, complete response (CR) rate for dapsone **(44.4%)** was comparable to CR rate **(37%)** for azathioprine (p=0.383).

In patients treated for relapsed ITP, azathioprine showed overall response rate of 64.4% that was comparable to 58.8% overall response rate for dapsone (p=0.463). Similarly the complete response rate for azathioprine (52.6%) was comparable to that with dapsone (42.5%) (p=0.522).

The median duration of response to second line therapy was 35 months (2-74 months). Median duration of response was significantly more - 60 months (2 to 60 months) in patients treated with azathioprine therapy compared to patients on dapsone therapy where it was 27 months (5 to 74 months) **(p=0.015).**

Nature of Response: (Table 9B)

In the present retrospective analysis, median duration of treatment with dapsone was 10 months (range 1-61 months) and with azathioprine was 10.5 months (range 6-47months).

At a median time to initial response of 3 months (range 1-12 months), of 176 patients responding to therapy, 96(54.5%) showed complete response and 80(45.5%) patients showed “response”.

Of these 80 initial 'responders' 46(57.5%) patients went on to achieve complete response – platelet counts >100x10^9/l, whereas 34 patients (42.5%) remained in "response" – platelet count >30x10^9/l and absence of bleeding manifestations. Also, of the 96 patients who showed complete response to initial therapy, only 3 patients (3.125%) went on to lose their complete response while on therapy and proceeded to maintain only partial response thereafter.

In all there were 139(46.3%) patients who achieved CR and 37(12.3%) patients who achieved 'response' on second line therapy.

The median time to achieve complete response for entire cohort was 3 months with dapsone (range 1-15 months) and 5 months with azathioprine (range 1-12 months) (p=0.28). In the subset of patients with initial partial response who went on to achieve complete response, median time to achieve CR was a further of 4 months (range 1-20 months) from the time of initial response.

Table 9B: Nature of Response to Second line Agents In Present cohort of Patients:

Variables	CR	Response	NR
Number (%)	139 (46.3)	37 (12.3)	124 (41.3)
ITP Duration (months)	6 (1-210)	5.5 (1-85)	4 (1-262)
Time to Response (months)	2	3	NA
Median Duration of T/t (months)	16 (1-47)	13 (3-44)	6 (2-61)
Median Response Duration (months)	20 (1-76)	14.5 (3-86)	NA

Response to Second Line Therapy in Children: TABLE 10A

There were 104(34.7%) children in present cohort. Of these, 64 children (61.5%) were treated with dapsone and 40 children (38.46%) were treated with azathioprine. Fifty two children each had steroid refractory ITP and relapsed ITP. Overall response to both second line agents in children was 52.9%, with complete response of 45.2% of children. It was comparable to overall response and complete response rates in adults. Response in patients treated with dapsone was 59.3% whereas it was 42.5% in patients treated with azathioprine (p=0.062). The overall median duration of response in children was 28 months (6 to 64 months).

Table 10A: Comparative Data In Children – Second line therapy:

Variable	**Dapsone (64 children)**		**P value**	**Azathioprine (40 children)**		**P Value**
	Steroid Refractory or Dependent (n=33)	**Relapsed (n=31)**		**Steroid Refractory or Dependent (n=19)**	**Relapsed (n=21)**	
Overall Response	20 ***(60.6)***	18 ***(58.1)***	1.000	5 ***(26.3)***	12 ***(57.1)***	**0.062**
Complete Response	17 ***(51.5)***	16 ***(51.6)***	1.000	5 ***(26.3)***	8 ***(38.1)***	0.511

	Dapsone	**Azathioprine**	
Time to Response (months)	3 (1-7)	3 (1-10)	0.542
Median Dose to Response (mg/kg/d)	1.5 (1-3)	2.0 (1.5-3.0)	---
Mean Response Duration months	35.3*	44**	0.257

*(SE=4.526, 95% CI 26.474 – 44.215), **(SE=5.993, 95% CI 32.5 -55.992)

The median time to response and mean duration of response were similar to dapsone and azathioprine in children in the present cohort. Median response dose was comparable between dapsone and azathioprine. TABLE 10A outlines comparison of response to dapsone and azathioprine in children in the present cohort of ITP patients.

Children treated for steroid refractory/steroid dependent ITP showed overall response of 20/33 (60.6%) to dapsone, which was significantly better than azathioprine, with response rates of 5/19 (26.3) – (p=0.023). The CR rates also showed trend favoring dapsone (p = 0.090). In relapsed ITP the response to dapsone (58.1%) was comparable to azathioprine (57.1%).

The median duration of response was not reached in children treated with azathioprine, while it was 26 months (range 6-64 months) in children treated with dapsone (p=0.257). The mean duration of response was 35.3 months (SE=4.526, 95% CI 26.474 – 44.215) in children treated with dapsone, whereas it was 44.25 months (SE=5.993, 95% CI 32.5 -55.992) in children treated with azathioprine, although difference was not statistically significant (p=0.257).

Response to Second Line Therapy in Adults: TABLE 10B:

The present ITP cohort had 196 adults, 106(54.08%) of which received dapsone therapy and 90(45.91%) received azathioprine. Ninety two adults had steroid refractory ITP (46.93%), whereas 104 (53.06%) had relapsed ITP. The overall response rate in adults treated was 61.7%, with complete response rates of 47.95%. The overall median duration of response in adults to second line therapy was 33 months (2-74 months). Overall response in adults to dapsone was **59.6% (CR=42.5%)** comparable to response rate of **64.4% (CR=52.2%)** to azathioprine (p=0.376) (TABLE 10B).

Table 10B: Comparative Data In Adults – Second line therapy:

Variable	Dapsone N = 106 adults		P value	Azathioprine N = 90 adults		P Value
	Steroid Refractory or Dependent (n = 57)	**Relapsed (n=49)**		**Steroid Refractory or Dependent (n=35)**	**Relapsed (n=55)**	
Overall Response	33 ***(57.9)***	29 ***(62.9)***	1.000	22 ***(60)***	37 ***(67.3)***	0.820
Complete Response	23 ***(40.4)***	22 ***(44.9)***	0.696	15 ***(42.9)***	32 ***(58.2)***	0.196

	Dapsone	Azathioprine	
Median Time to Response	2 (1-12months)	2 months (1-11months)	0.957
Median Dose to Response	100mg (50-150)	2.0mg/kg (1-3mg/kg/d)	--
Median Response Duration	24 months(3-39months)	44 months (1-48months)	**0.037**

The median duration of response of 44 months (range 2-60 months) achieved with azathioprine was longer than that with dapsone – 24 months (range 5-74 months) – **p value = 0.037.**

Complete response to dapsone was achieved in 47/106 (44.33%), whereas it was 47/90 (52.2%) in adults treated with azathioprine (p value = 0.325). In relapsed ITP, azathioprine showed better overall response of 67.7%, compared to dapsone as for relapsed ITP (59.18%) (p=0.425).

Patients treated with azathioprine also included 6 secondary ITP patients, and 3 patients with Evan's syndrome. Seven patients (77.7%) of the 9 patients responded to azathioprine therapy, with complete response seen in 6 patients (66.6%). Of these, one patient relapsed while on therapy and another patient relapsed after stopping treatment.

Secondary Outcome: Relapse while on Therapy:

Of the 176 patients who showed response to second line therapy in present cohort of ITP patients, 166 were evaluable for secondary outcome. The remaining 10 patients were excluded due to inadequate follow up (< 6 months on therapy). Of the 166 patients, 49 patients **(28.5%)** relapsed while on therapy. Relapses **(38%)** were significantly higher in patients on dapsone therapy compared to azathioprine therapy **(18.9%) (p=0.007)**(Fisher's Exact Test). The median time to relapse was 14 months in case of both dapsone and azathioprine.

TABLE 11A shows comparative data for secondary outcome in present ITP cohort.

Variables	**Dapsone (%)**	**Azathioprine (%)**	**P value**
Relapses On Therapy: 49/166 (28.5%)	35/92 (38.0)	14/74 (18.9)	**0.007**
Relapse on stopping therapy : 18/46 (39%)	13/27 (48.1)	5/19 (26.3)	**0.075**
Sustained Response Off Therapy	14/27 (51.8)	14/19 (73.7)	0.165
Duration Of Response Off therapy (months)	12 (1-74)	11.2 (2-48)	0.451

Analysis for **predictors of relapse while on therapy** (TABLE 11B) showed that:

1. Achieving **anything less than complete response** to second line therapy was significantly associated with higher risk of relapse while on therapy (p = 0.030)

2. Primary **steroid refractory/steroid dependent ITP** was significantly associated with increased risk of relapse while on second line therapy. (p value =0.042).

Neither age (<15 or >15 years), gender nor platelet counts at diagnosis were predictive.

Table 11B: Analysis of Predictors of relapse while on Therapy:

Variables		No Relapse On Therapy (%)	Relapse on Therapy (%)	P value
Age at diagnosis	≤15 years	38 (32.8)	16 (32.7)	1.000
	> 15 years	78 (67.2)	33 (67.3)	
Platelet count at diagnosis	≤ 10,000	51 (44)	23 (46.9)	0.735
	>10,000	65 (56)	26 (53.1)	
Gender	Male	38 (32.8)	22 (44.9)	0.158
	Female	78 (67.2)	27 (55.1)	
Indication of Second Line Therapy	**Steroid Failure***	46 (39.7)	28 (57.1)	**0.042**
	Relapsed ITP	70 (60.3)	21 (42.9)	
Nature of Response	**CR**	105 (75.5)	34 (24.5)	**0.030**
	'Response'	18 (54.5)	15 (45.5)	

* includes steroid dependent and steroid refractory ITP

Secondary Outcome: Response and relapse rates after stopping second line therapy:

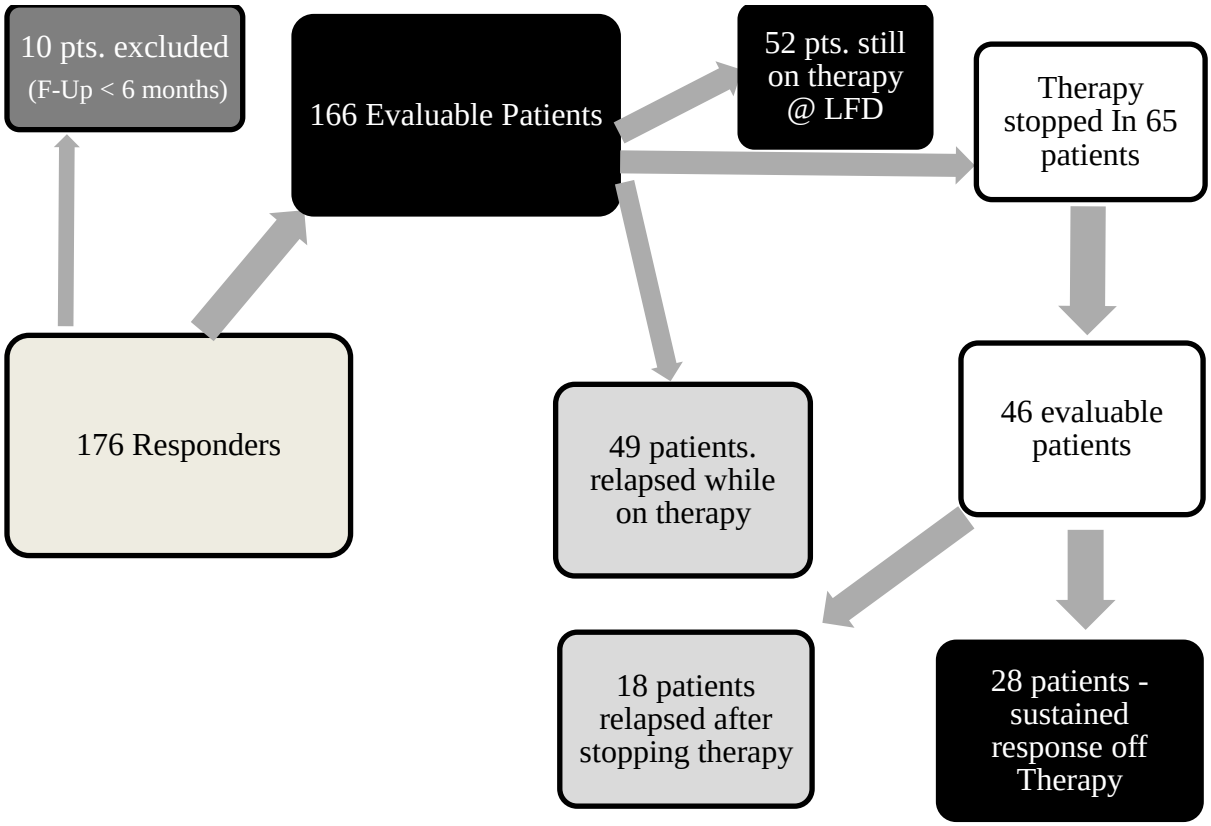
In addition, second line therapy was stopped in 65 of remaining 122 (53.3%) evaluable patients. Further analysis could only be carried out with 46 of 65 patients, since 19 patients, were lost to follow up after stopping therapy. Of the 46 evaluable patients off therapy, 27 (58.7%) patients were on dapsone and 19 (41.3%) patients were on azathioprine.

Overall, 28(61%) of 46 evaluable patients had sustained response off therapy. Thus, half of patients treated with dapsone - 14/27(51.8%) maintained response off therapy. Similarly, two-thirds of patients treated with azathioprine - 14/19(73.7%) maintained response after stopping therapy (p= 0.165).

The median duration of sustained response off therapy was 12 months (1-72 months) in dapsone group and was 11.2 months (2-48 months) in azathioprine group. Eighteen patients (39%) patients relapsed after stopping therapy. These included 13(48.1%) patients treated with dapsone and 5/19 (26.3%) patients in azathioprine (Table 11A).

Thus in all, 40% (67/166) of evaluable patients had relapse in present cohort of patients. Fifty two patients - 31% (51/166) are still on therapy and maintaining response at last follow up. There are also the additional 28 patients (16.4%) patient who maintained response for median of 12 months duration even after stopping of therapy. These are apart from 19 patients (11%) who had been advised to stop therapy at last follow up.

Figure 1: Secondary Outcome Measures in Responders in Present cohort of Patients:



Overall Survival And Event Free Survival:

There were no deaths in present cohort of patients with ITP. The estimated mean overall survival duration for the entire cohort was 24.5 months (S.E = 1.817, 95% CI: 20.89 – 28.01 months) and the estimated median overall survival time for the entire cohort was 14 months (S.E: 1.575, 95% CI: 10.87 – 17.127).

Event Free Survival: Three year estimated event free survival was 26.2% (±3.2%)

Figures 2(A) depicts Event Free Survival for entire cohort of patients.

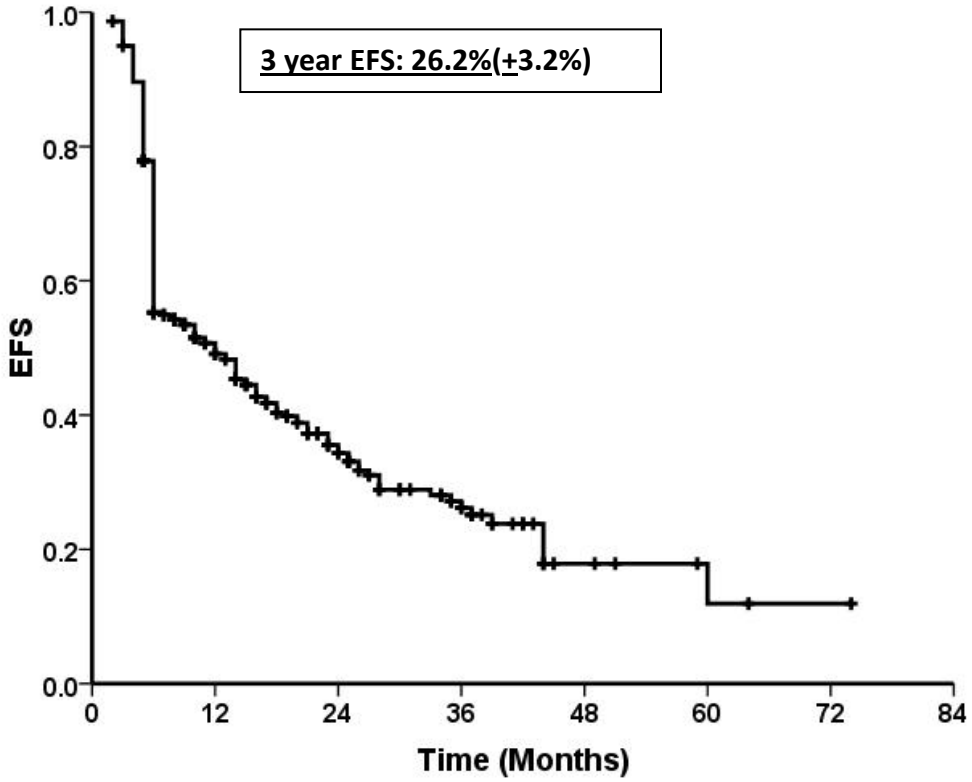


Figure 3(a): Kaplan Meier curves: event free survival for entire study cohort (N=300): Over median treatment duration of 10 months (range 1-61 months), estimated 3 year EFS of patients on second line therapy was 26.2% (±3.2%).

In patients treated with dapsone as second line therapy, estimated 3 year event free survival was 20.6% (± 3.9%). With with azathioprine, it was 35.2% (± 5.1%)

{X_2 = 1.996, df – 1, significance 0.158).

Figure 2(B) Comparative 3 year EFS (Dapsone and Azathioprine) For Entire Cohort:

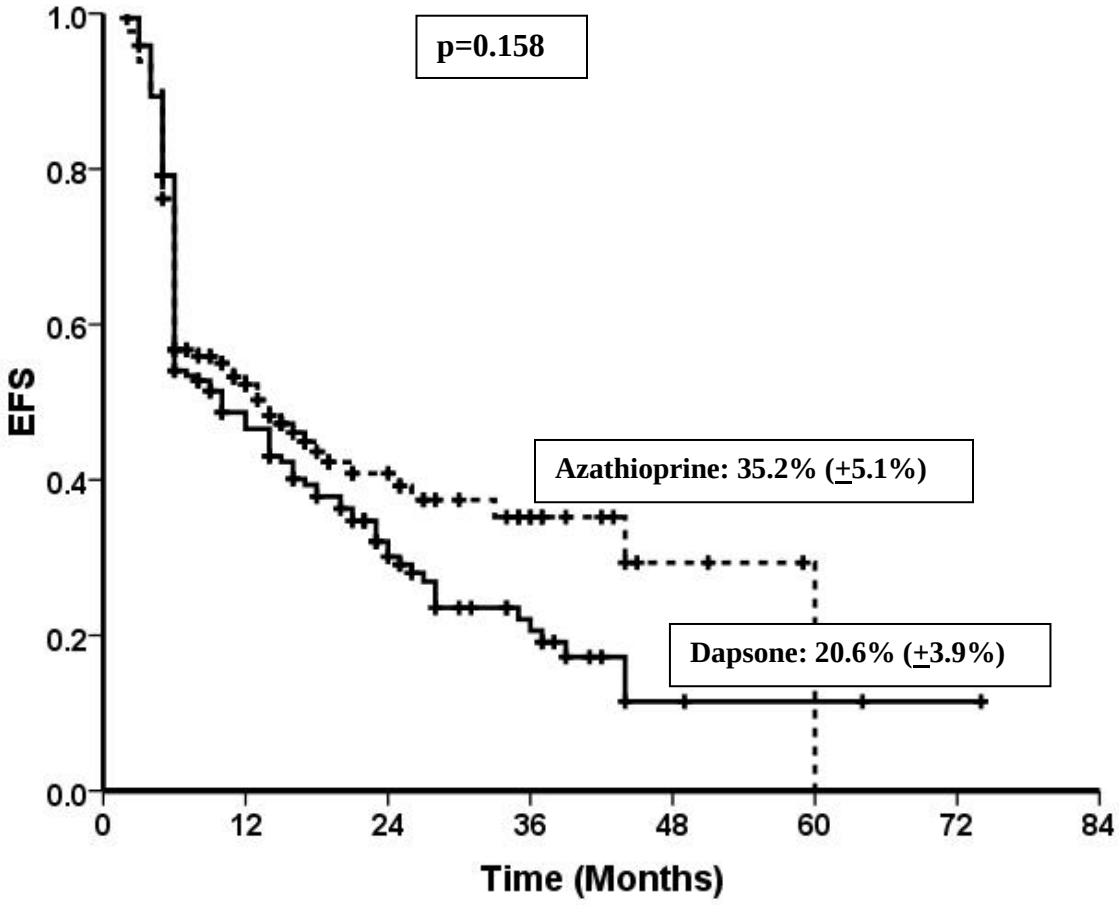


Figure 2(B): Kaplan Meier curves: event free survival comparison dapsone and azathioprine (N=300): Over median treatment duration of 10 months (range 1-61 months), estimated three year EFS was better in patients treated with azathioprine than dapsone, although difference was not statistically significant (p=0.158).

In the patients who responded to second line therapy, 3 year event free survival was significantly better - 48.7% (± 4.9%) than those who failed to respond to therapy where it was 0%.

{X_2 = 284.131, df – 1, significance <0.001).

Figure 3(A) shows EFS Comparison between Responders and Non-Responders.

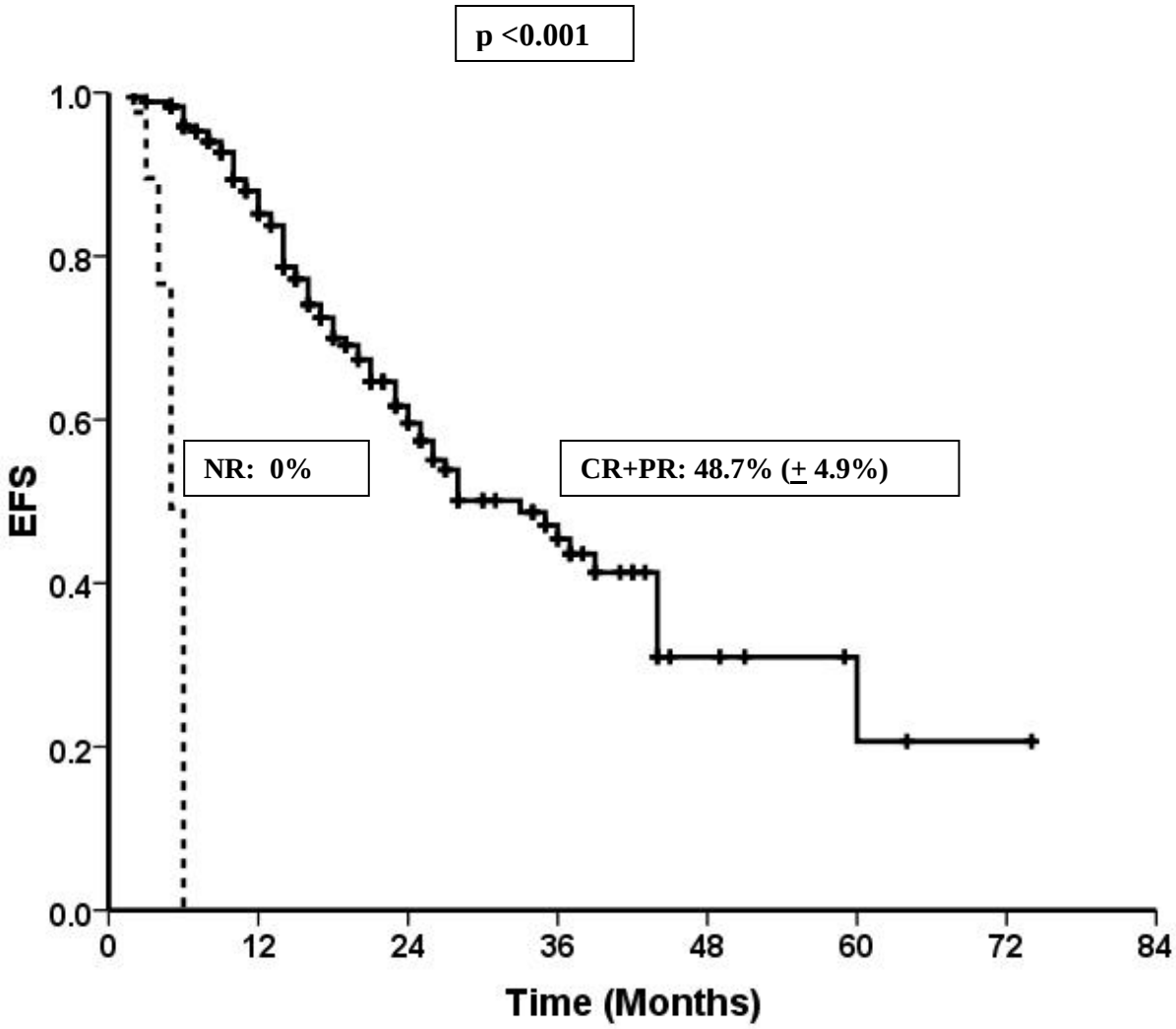


Figure 3(A): Kaplan Meier curves: event free survival comparison of responders and non-responders to second line therapy (N=300): Over median treatment duration of 10 months (range 1-61 months), estimated 3 year EFS of patients responding to second line therapy was significantly better (p<0.001) than patients who failed to respond to therapy.

Amongst patients who responded, estimated 3 years event free survival for azathioprine was significantly better - 61.0% (± 7.6%) than with dapsone – 36.1% (±6.4%).

{X_2 = 5.571, df – 1, significance - 0.018).

Figure 3(B): Estimated 3 year EFS Responders (CR+PR) : Dapsone versus Azathioprine

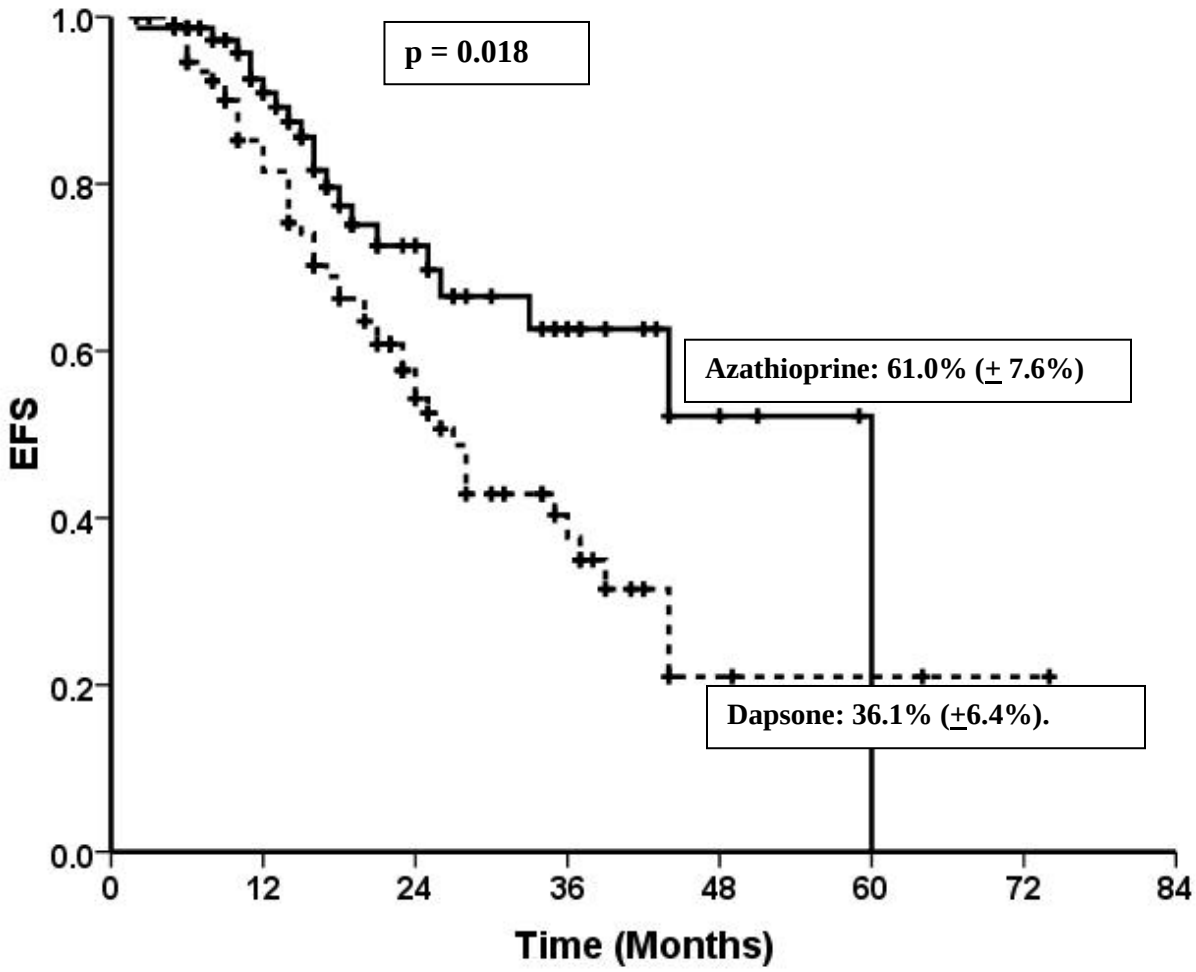


Figure 3(B): Kaplan Meier curves: event free survival comparison of dapsone and azathioprine in responders (N=176): Over median treatment duration of 10 months (range 1-61 months), estimated 3 year EFS of patients treated with azathioprine was significantly better (p=0.018) than patients treated with dapsone.

Third Line Therapy:

Data regarding various third line therapeutic agents was available in 150 (50%) of patients of the present cohort. These included 94 patients (62.66%) who had failed to respond to both second line therapeutic agents (dapsone and azathioprine), and 56 patients (37.1%) who had shown initial response to second line therapy. Of these patients, going 43 patients had relapse while on therapy. Another 9 patients had relapse after withdrawal of second line therapeutic agents. Additionally, 3 patients were changed over to third line therapy since they had achieved only partial response to second line therapeutic agents, 1 in dapsone arm & 2 in azathioprine arm. Also, 1 patient developed azathioprine induced dermatitis at 6 months of achieving response hence therapy was changed to dapsone therapy.

Table 12 shows various third line modalities of therapy & indications in the present cohort.

Third Line Therapy N = 150	**Dapsone (n=99)**		**Azathioprine (n=51)**		
	Non Response	Relapse / PR / Others	Non Response	Relapse / PR / Others	Total
Dapsone	1(1.9%)	10(19.6%)	26(51%)	14(27.45%)	51
Azathioprine	51(62.2%)	28(34.1%)	3(3.6%)	0	82
Splenectomy	4	1	4	0	9
***Others**	2	2	3	1	8

*Others includes: Dexa + Azathioprine, Dexa + Dapsone, Prednisolone+dapsone, Cyclophosmide-Vincristine-Prednisolone, Eltrombopag, Cycloporine, Mycophenolate.

Response to Dapsone and Azathioprine as "Third Line" Therapeutic Agents:

Patients who were treated with third line dapsone after failed response to azathioprine showed response rate of **45.8%.** In contrast, patients who received azathioprine as third line therapy after failing to respond to dapsone had response of **21.2%** (p = 0.168).

On re-challenging patients who had relapsed while on dapsone therapy, dapsone produced response in 7 out of 8 patients. Two of these patients subsequently relapsed, thus overall response rates to third line dapsone was **62.5%** in this group of patients. In contrast, only **30%** of patients who had relapse on therapy with azathioprine – showed response to re-treatment with azathioprine (p= 0.168**).** Table 13 shows comparative response rates between dapsone and azathioprine as third line therapeutic agents in the present cohort.

Table 13: Comparison Of Dapsone and Azathioprine as Third Line Agents:

Third Line Therapy	**Dapsone**			**Azathioprine**		
	Non Response	Relapse on therapy	Relapsed on stopping Therapy	Non Response	Relapse on Therapy + Side effects	Relapse on stopping therapy
Dapsone (48/51) P = 0.168	0/1	7*/8 (87.5%)	1/1	11/24 (45.8%)	6/9 + 1/1 (dermatitis)	2/3
Azathioprine (75/82) P = 1.000	10/47 (21.2%)	6/20 (30%) + 0/1 (R)	2/4	0/3	0	--

*2 of these patients relapsed. (R) – Patient with response that was less than CR.

Splenectomy:

In the present cohort, 41 of 298 patients eventually underwent splenectomy, subsequent to initiation of second line therapy. The analysis excluded the 2 patients who had already undergone splenectomy prior to being given second line medical therapy (dapsone or azathioprine) Table 14 shows splenectomy rates in various groups of patients in study cohort.

Table 14: Comparison between rates of Splenectomy in present cohort.

Splenectomy	**CR +PR**	**Non responders**	**P value**
Yes	10 (5.7%)	31 (25%)	<0.001
No	(164)	(93)	
Splenectomy	**Steroid Refractory/ Dependent ITP**	**Relapsed ITP**	**P value**
Yes	30 (21%)	11(7.1%)	<0.001
No	(113)	(144)	

In all, there were 10 patients who had initial response to second line therapy but either relapsed while on therapy (9 patients) or had relapse after stopping therapy 1 patient. The other 31 patients were the ones who had failed to show any response to second line therapeutic agents, dapsone and azathioprine. The failure to respond to second line therapy was significantly associated with increased incidence of splenectomy, exhibiting splenectomy sparing role of second line therapeutic agents (TABLE 14). In the present study we observed that patients who had steroid refractory or steroid dependent ITP had significantly higher rates splenectomy (21%) as compared to patients who received second line therapy for relapsed ITP, where splenectomy

rate was 7.1% (p=0.001). These findings suggest “splenectomy sparing” role of both second line therapeutic agents. Moreover, in those who eventually underwent splenectomy, we observed that median time to splenectomy in patients showing response to second line therapy was 26 months (13-47 months), which was significantly longer than median time to splenectomy of 14 months (3-65 months) in patients not responding to second line therapy (p=0.047). Over median post-splenectomy follow-up of 7 months (1-62 months), 83% (34/41) patients responded to splenectomy with complete response rate of 71%

Side Effect Profile: Dapsone:

Table 15A summarizes incidence of various side effects in patients on Dapsone Therapy:

Dapsone (Pts =170)	N	Percentage
Compensated Hemolysis	6 pts	3.5%
Dermatitis	2	1.1 %
Side Effect Requiring Discontinuation:		
Methemoglobinemia	1	0.5%
Agranulocytosis	1	0.5%
Dapsone Syndrome	2	1.1%
Uncompensated Hemolysis	1	0.5%
Overall Discontinuation	5	2.6%

In present cohort of patients, dapsone was found to be well tolerated. The most common side effect observed was compensated hemolysis (3.5%) as adjudged by presence of mild indirect hyperbilirubinemia, polychromasia, mild reticulocytosis, presence of “bite cells & blister cells” without significant fall in hemoglobin. Dapsone was continued without any further worsening of hemolysis. There were 2 patients who had self limiting dermatitis while on dapsone, which subsided with temporary discontinuation. Re-challenge with dapsone did not result in recurrence.

Significant side-effects (2.6%) that required stopping dapsone were: a) Dapsone Syndrome - Triad of fever with rashes and hepatitis was observed in 2 patients, b) Methemoglobinemia – occurred in 1 patient, c) Agranulocytosis seen in 1 patient, and d) Uncompensated hemolysis was seen in 1 patient.

Azathioprine Side effect Profile:

Azathioprine was well tolerated as second line therapy in present cohort of patients. The most common side effect was borderline uni-lineage cytopenia (Total WBC count <3000/cumm) that was observed in 6.1% of patients. Mean azathioprine dose in the 8 patients was 2.16mg/kg/day. Patients recovered baseline WBC counts after dose reduction. There were 2 patients (1.5%) who required discontinuation of azathioprine therapy on account of side effects; one patient had agranulocytosis and another patient had generalized erythroderma.

Table 15B summarizes the side effect profile of Azathioprine Therapy:

Azathioprine: (Pts = 130)	N	Percentage
Borderline Cytopenia	8	6.1%
Alopecia	2	1.5%
Dermatitis	2	1.5%
Side effects Requiring Discontinuation:		
Agranulocytosis	1	0.7%
Dermatitis	1	0.7%
Overall Discontinuation	2	1.5%

Discussion

Discussion:

The present study is a single centre retrospective analysis aimed at assessment of efficacy of two second line agents – dapsone and azathioprine in the treatment of steroid refractory/dependent ITP as well as relapsed ITP. Both children and adults were included in the study. Children were defined as patients between ages of 3 months to 15 years, and adults by an age of 15 years and above – in accordance with similar study published from our centre by Damodar et al(25). Standard definitions of ITP laid down by the International Working group on ITP (14) for steroid dependent ITP, steroid refractory ITP and relapsed ITP were used at the time of inclusion of patients in the study. Although the study aimed at assessing patients for response to dapsone and azathioprine as second line agents prior to splenectomy, two patients who had splenectomy prior to administration of dapsone or azathioprine were also included in the study. There were 106 children and 194 adults who satisfied the inclusion criteria of the present study. Majority of patients in the present study (98%) had primary ITP. Six patients (2%) had secondary ITP. There was female predominance in entire cohort - (M:F ratio 0.56:1), similar to that reported in various epidemiological studies across literature(8). The female predominance of ITP was more pronounced in adults (M:F ratio 0.42:1) than in children (M:F ratio 0.86:1). Similar findings are reported in prospective study conducted by Intercontinental Co-operative Thrombocytopenia study group(28). Kuhne et al has reported male:female ratio of 0.85:1 in children and 0.47:1 ratio in adults(28). The mean platelet count at diagnosis in children of our study was also similar (14.25 $x10^9$/l) between our study and that reported by ICIS study for children – which reported mean platelet counts of children of (18.1 $x10^9$/l). In adults, our study cohort had lower mean platelet counts - 12.5 $x10^9$/l at diagnosis, as compared to the ICIS study which reported mean platelet counts of 25.4$x10^9$/l for adults at diagnosis(28).

Investigators from All India Institute of Medical Sciences retrospectively analyzed 1230 patients of ITP diagnosed at their centre. These included both children and adults(29). The median age at diagnosis was reported as 19.6 years (range 0.9-80years) with slight female preponderance (51.1%). The median platelet count at diagnosis was $34 \pm 18.3 \times 10^9$/l. The patient population of our present study was also similar, with a median age of diagnosis at 22 years, showing female preponderance at 64%, although median platelet count at diagnosis was lower ($12 \pm 9.3 \times 10^9$/l). This is probably due to fact that analysis reported by Choudhary et al(29) was conducted in 2004, prior to International Working Group guidelines(2) that are in vogue only since 2009.

In the present cohort of study, there were 19 patients in the present study cohort who received treatment for ITP at platelet counts of $>30 \times 10^9$/l. Of these, 9 patients were treated at our centre prior to 2009. Five other patients had been diagnosed and treated elsewhere, before they were seen at our centre. One additional patient had significant bleeding in the form of menorrhagia causing anaemia that required blood transfusions.

Bleeding Manifestations:

Thus far, there is no consensus definition of significant bleeding in patients with ITP. In present study cohort, we used criteria reported previously by Medeiros et al (27), as presence of 1 or more of following occurring at any time during the course of ITP:

(1) Intracranial hemorrhage, (2) epistaxis requiring cautery or nasal packing, (3) gross hematuria, or

(4) other mucosal or cutaneous hemorrhage severe enough to cause a decline in patient's hemoglobin concentration to $\leq$10 g/dL or $\geq$2 g/dL below patient's baseline haemoglobin.

Minor bleeding was defined as involving skin manifestations only (bruising and petechiae) without any mucosal bleeding in accordance with the American Society of Hematology management guidelines(24). Using these criteria, 44 patients (14.7%) had at least one episode of major bleeding – thus satisfying criteria for "severe ITP". Major bleeding at diagnosis was seen significantly more in adults (20.91%) as compared to children (2.9%) – p = 0.001. In children, proportion of patients with minor bleeding was significantly higher (96.2%) compared to that in adults (77.5%).

Table 16: Bleeding at Diagnosis: Comparative Literature:

Bleeding at diagnosis In Children	ICIS Registry II (n =863)	Bolton-Maggs and Moon (n=427)	Present Study (n =300)
No or Mild	77%	76%	84%
Moderate	20%	21%	NR
Severe	3%	3%	2.9%

These results compare favorably with two other large scale prospective epidemiological studies(13)(30) that addressed the question of bleeding manifestations in childhood ITP at diagnosis. In both these studies, investigators categorized severity of bleeding into three categories – 1. none or mild – defined similar to that used in our study, 2. moderate bleeding – defined as more severe skin manifestations and more troublesome epistaxis and or menorrhagia, and 3. severe bleeding – again defined similar to used in our present study. Using the above severity scale, Bolton-Maggs and co-workers reported 3% incidence of major bleeding and 76% of no or minor bleeding manifestations at diagnosis in prospective analysis of 423 cases of childhood ITP(30).

Similarly, in the study on behalf of ICIS (13), investigators reported that 77% of children had no or mild bleeding manifestations and only 3% children had severe bleeding at diagnosis, findings that are virtually identical to those of our study. None of the children in our study cohort had intracranial hemorrhage, similar to only one patient (0.15%) in the ICIS prospective analysis and 0.6% incidence in subsequent study by the same group(28).

In order to maintain more objectivity in assessment of bleeding, our study did not use the more category of "moderate bleeding" that has definitions that are subjective. This accounts for the fact that there were more children (97.1%) with no or mild bleeding manifestations reported in our study, compared to 77% reported by Bolto-Maggs and Neunert and co-workers for ICIS. Thus, in part, our retrospective analysis supports the conclusion arrived at by the above studies that severe bleeding, in particular intracranial hemorrhage is uncommon in childhood ITP at diagnosis.

Bleeding manifestations at diagnosis were significantly higher in adults than in children in present study cohort. In contrast, the recently published prospective analysis by ICIS(28) reported higher bleeding rates in children (91%) than adults (69%) – ($p < 0.0001$) on comparing incidence of bleeding at any site. This observation was consistent both in treated and untreated group of patients in ICIS study(28). Also, in adults included in our study cohort incidence of intracranial hemorrhage at diagnosis was higher in patients (4.5%). Although the ICIS study(28) does not categorize bleeding manifestations according to severity, this difference in bleeding manifestations between our study and ICIS results could be due to the fact that mean platelet counts in our cohort of patients was less than 20 $x10^9$/l (12.5 $x10^9$/l) whereas in ICIS study it was more than 20 $x10^9$/l (25.4$x10^9$/l)(28).

Bleeding in relapsed and steroid refractory/dependent ITP:

In our study, majority of patients had mild bleeding, both at diagnosis **(84%)** and at in steroid refractory or relapsed ITP or **(83%).** Also, number of patients presenting with major bleeding manifestations declined significantly (14.7% to 5.3%) from time of diagnosis to when bleeding rates were analyzed for relapsed or steroid refractory ITP in the same cohort of patients. We observed no difference in incidence of bleeding in children and adults with diagnosis of steroid refractory/steroid dependent and relapsed ITP. The only prospective analysis which has addressed the question of bleeding in children with persistent ITP comes from ICIS group(31), which reported no intracranial hemorrhages in the study, a finding similar to our study. Investigators also summarized that the study was unable to arrive at predictors of subsequent bleeding due to infrequency of severe bleeding manifestations even at diagnosis. Thus, our study confirms the conclusion of the study(31) that ITP in children is a benign disease and is not associated with major hemorrhage even in patients with prolonged thrombocytopenia.

Response to Second Line Therapy:

Between the two agents, the patient characteristics are comparable between dapsone and azathioprine in most aspects. We acknowledge the fact that there are two major differences in patients treated with dapsone and azathioprine:

1. Patients with secondary ITP were treated only with azathioprine ($p = 0.002$) and

2. There are more steroid refractory patients in dapsone group and more relapsed patients were treated with azathioprine. The difference is statistically significantly in adults ($p=0.045$)

Overall response rates to second line medical therapy in the present cohort is 58.6%. Both dapsone and azathioprine showed comparable response rates as second line agents. In all, 125 patients (41.3%) failed to show response to either dapsone or azathioprine. These findings compare favorably with those reported in literature(14)(24). International consensus report 2010 on ITP (14) quotes response rate of up to 50% for dapsone – identical to 58.8% in the present study. The consensus report(14) also mentions that up to two-thirds patients treated with azathioprine show response – findings that are similar to overall response rates of 58.5% in to azathioprine in the present study that included patients with ITP refractory to steroid therapy or steroid dependent ITP and relapsed ITP.

The median time to response for the entire cohort of patients was 3 months. It was identical between dapsone (3 months) and azathioprine (2.8 months). The International consensus report(14) comments that response to azathioprine is slow and may take 3 to 6 months. In contrast, results of our study show that time to initial response was just 2.8 months in patients on azathioprine therapy. These findings compare favorably to the expected time to initial response (1 to 3 months) for azathioprine as per the American Society of Hematology evidence based guidelines(24). For dapsone, the time to initial response is quoted by International consensus report as 3 weeks – much lower than the 3 months noticed in our study. In a meta-analysis of patients treated with dapsone as second line agent, Rodrigo et al(32) reports a time to response between 3 weeks to 3 months.

Response to Second Line Therapy Dapsone in Adults:

There are no randomized control studies comparing efficacy of second line agents. Present study results compare favorably with all studies reviewed by Rodrigo et al(32) as outlined in (TABLE17). These included single arm prospective (Godeau et al, Hernandez et al, Zaja et al, Sharma et al) as well as retrospective studies (Audia et al, Damodar et al, Vancine-Califani et al).

Table 17: Dapsone As Second Line Therapy: Comparative response in Literature:

Author	Design	Pts	ITP Duration months	Overall RR	Time to response (months)	Duration (months)	Dose
Godeau	Prospective	66	52 (3-240)	50%	1	12	75-100mg
Hernandez	Prospective	15	29(12-131)	40%	1	NR	100mg
Le Louet	Prospective	19	NR	47%	NR	NR	100mg
Audia	Retrospective	40	40(2-249)	42%	1½	NR	100mg
Zaja	Prospective	20	46 (2-274)	55%	1	42	50 to 100mg
Damodar	Retrospective	90	24(6-132)	63.3%	3.5	12	1-2mg/kg
Vancine-Califani	Retrospective	52	5 (1-30)	44.3%	NR	21	100mg
Sharma	Prospective	46	NR	80%	NR	32	50-100mg
Present Study	Retrospective	**170**	**5 (1-262)**	**58.8%**	**3**	**27(5-74)**	**50-150mg**

The following are other notable comparisons:

1. Before International working group guidelines on response criteria (2) came into vogue, studies conducted prior to 2009 show lower overall response rates on account of response criteria that use higher platelet counts to define response. Godeau et al(21) defined complete response (CR) as platelet counts >150 x 10^9/l, and partial response as platelet counts >50x10^9/l. Although the overall response rates of 50% are similar to our study results, complete response rates (13/66) of 19.7% appear markedly less compared to complete response rates of 45.9% to dapsone (and azathioprine) in the present study, probably as a result of underestimation of CR rates in accordance to their response criteria. Le Louet et al(33) and Hernandez et al(34) using the criteria used by Godeau et al(21), have all reported similar response rates in their respective study population. In that respect, a previous study of 90 patients treated with dapsone from our centre by Damodar et al(25) that predates the 2009 guidelines, has reported response rates of 63.3% using response criteria similar to International working group 2009 guidelines(2).

2. On the other hand, Sharma et al (35) used 'disappearance of purpura and rise in platelet count > 40x10^9/l' as criteria of response. They have reported high response rates of 80% compared to 58.8% reported in our study. We speculate that it is probably again due to the subjectivity in the response criteria used by their study, compared to that stated by International Working Group(2), which require platelet counts to be > 30x10^9/l or at least a 2 fold rise from baseline platelet counts measured on 2 separate occasions at least 7 days apart – criteria that we used in our study.

3. Zaja et al(36) conducted prospective study of 20 patient unresponsive to or relapsing on treatment with combination of rituximab and dexamethasone. They have reported response rates of 55% using the International Working Group(2) criteria of response assessment, identical to

our study. Again, our retrospective analysis showed higher complete response rates to dapsone – 45.9% compared to 20% complete response rates to dapsone in their study. This is probably because responses in post splenectomy patients may be lower (14)(34). We had only 2 post-splenectomy patients in our study cohort. Both received dapsone therapy, and none of them achieved complete response.

4. The median duration of response was 27 months. This is lower from duration of response of 42 months, reported by Zaja et al(36) in their prospective analysis. This might be due to the fact that our study had higher incidence of relapse while patient was on treatment – 38% compared to 0% in study by Zaja et al(36).

5. In studies reviewed by Rodrigo et al(32), remarkably, there were very few relapses on therapy - 0% in study by Zaja et al(36) and 5% in study by Godeau et al(21) – compared to 38 % relapse rates on therapy with dapsone. Audia et al report relapse rates 37.5% in steroid refractory patients treated with dapsone – identical to our study findings**.** In our analysis, the steroid refractory/dependent ITP ($p=0.045$) and achievement of response less than CR ($p=0.030$), were significant predictors of relapse while on therapy.

6. In retrospective analysis of 52 patients of steroid refractory/steroid dependent ITP, investigators Vancine-Califani et al(37) reported an overall response rate of 44.2%. In our study, the overall response in steroid refractory/steroid dependent adult patients to dapsone is 58.9% with complete response rates of 44.4%, which compares favourably with that reported by Vancine-Califani et al (37) in their study.

Table 18: Dapsone: Secondary Outcome Measures across Various Studies in Literature:

Author	Design	Pts	Relapse on Therapy	Relapse on Stopping Therapy	Sustained Response OFF Therapy	Sustained Response Duration (months)	Splenectomy after Second Line Therapy
Godeau	Prospective	66	5%	92%	8%	NA	NR
Zaja	Prospective	20	0%	0%	50%	NA	NR
Damodar	Retrospective	90	NR	15.5%	50%	17	NR
Audia	Retrospective	40	37.5%	NR	NR	NR	NR
Vancine-Califani	Retrospective Primary-40, Secondary-12	40	NR	27.7%	83%	NR	Responders-0% NR - 68.9% (OR–0.01, 95%CI= 0.01 – 0.11)
Present Study	Retrospective (All primary)	170	37.5%	48.1%	51.82%	12(1-74)	Responders–5.7% NR – 25% (p <0.001)

Present study had 46 patients evaluable after stopping therapy. Twenty eight (61%) patients had sustained response off therapy for median duration of 1 year. With dapsone - 14/27(51.8%) maintained response off therapy. Similarly,with azathioprine - 14/19(73.7%) maintained response after stopping therapy (p=0.165). The results are comparable to sustained response rates reported in retrospective study by Vancine-Califani et al (37) and Damodar et al (25).

Response to Second Line Therapy Dapsone in Children:

There is scanty literature on response of dapsone as second line agent in children with ITP, partly because the persistent and chronic ITP is rarer in children than in adults(9)(32). In the 104 children included in present study cohort showed overall response of 52.88% with complete response rate of 45.2% - comparable to adults in study cohort. These responses are comparable to 65.7% overall response reported by Damodar et al(25) in a series of 35 children with chronic ITP and treated with dapsone at our centre. The complete response rates 48.5% were identical to our study. In another retrospective study by Meeker et al(38), 3 of 7 (43%) children responded.

The time to initial response of 3 months was also comparable to adults, and identical in both dapsone and azathioprine therapy. There were 52 patients with steroid dependent/steroid refractory ITP in present study. Therapy with dapsone has shown a significantly better overall response - 60.6%, than azathioprine - 26.3% (p=0.023). In this respect it proved to be a better steroid sparing agent in this subgroup of patients.

Response to Second Line therapy Azathioprine:

Patients treated with azathioprine as second line therapy had more number of patients who had relapsed ITP and lesser number of steroid refractory/steroid dependent ITP, than those treated with dapsone therapy, with a trend towards significance (p – 0.062). As opposed to patients treated with dapsone, patients on azathioprine therapy also included secondary ITP (6/130 - 4.6%) and Evans syndrome patients (2%) (p = 0.002).

Overall response to azathioprine was 58.5% with complete response in 46.2%. The response is similar to dapsone therapy. Median time to response and duration of response were also found to be similar to dapsone therapy, with equivalent responses in steroid refractory/steroid dependent

ITP and relapsed ITP in adults. The lower dose of response in dapsone therapy patients was found to be statistically significant. Children with steroid refractory ITP had inferior response to azathioprine as compared to dapsone ($p = 0.023$), whereas children with relapsed ITP showed no difference in response rates between dapsone and azathioprine.

Patients treated with azathioprine also included 6 secondary ITP patients, and 3 patients with Evan's syndrome. Seven patients (77.7%) of the 9 patients responded to azathioprine therapy, with complete response seen in 6 patients (66.6%). Of these, one patient relapsed while on therapy and another patient relapsed after stopping treatment.

Response rates in our study cohort compare favorably with response reported by other investigators (Table 19 and 20) with azathioprine for persistent and/or chronic refractory ITP.

Table 19: Comparison Of Azathioprine Therapy Response For ITP in Literature:

Author	Design	N	ITP Duration (months)	Response Rate	Time to response	Response Duration (months)	Dose to
Pizzuto	Retrospective Multicentre	41	NR (postsple-nectomy)	ORR 51% CR – 41%	NR	NR	2mg/kg
Quiquandon	Prospective	53	19 (6-350)	ORR - 64% CR - 45%	4.0 months	(7–180)	150mg
Present Study	Retrospective	130	6 (1-46)	ORR 57.7% CR - 46.9%	2.8 monhs (1-11)	60 (2-60)	2mg/kg

Table 20: Secondary Outcome In Patients on Azathioprine Therapy: Literature review

Author	Design	Pts	Relapse on Therapy	Relapse on Stopping Therapy	Sustained Response OFF Therapy	Sustained Response Duration	Splenectomy after Second Line Therapy
Quiquandon	Prospective	53	3/34 (8.8%)	5/34 (14.7%)	10/34 (29.4%)	7-182 months	NR
Present Study	Retrospective	130	14/73 (19.6%)	5/22 (22.3%)	17/22 77.3%	11.2 months	Responders – 5.7% NR – 25% (p <0.001)

Second Line Therapy: Splenectomy Sparing Effect:

We observed that failure to respond to second line therapy was significantly associated with increased incidence of splenectomy, exhibiting 'splenectomy sparing' role of second line therapeutic agents (TABLE 10). In the present study we observed that patients who had steroid refractory or steroid dependent ITP had significantly higher rates splenectomy (21%) as compared to patients who received second line therapy on account of relapsed ITP, where splenectomy rate was 7.1% (p=0.001). There was trend towards increased rates of splenectomy in patients treated with dapsone as second line therapy (p = 0.061), probably accounted for by:

a) Predominance of steroid refractory/steroid dependent ITP in dapsone therapy subgroup as compared to azathioprine therapy subgroup (p=0.069). This subset of patients has been shown to have significantly higher incidence of subsequently undergoing splenectomy in our analysis.

b) There were significantly more relapses in the dapsone group after while on therapy than in patients treated with azathioprine.

In a retrospective analysis of 40 primary ITP patients with steroid refractory/steroid dependent ITP treated with dapsone, investigators Vancine-Califani et al(37) noted that none of the patients who responded to dapsone required splenectomy, whereas 68.9% amongst non-responders required splenectomy. The relapse rates while on therapy was not reported in the study, whereas relapse on stopping therapy was 27.7%. Thus our results compare favorably with above study.

Dapsone and Azathioprine Side Effects: Review of Literature:

Dapsone was well tolerated in our study. There was only 2.6% chance of serious side effects requiring discontinuation of therapy. Similarly azathioprine was also well tolerated – with rates of discontinuation of only 1.5% on account of side effects.

Table 21A: Dapsone Side Effects: Literature Review

Author	Pts	Incidence of Hemolysis	Incidence of Methemo-globinemia	Incidence of Other Reactions	Serious side-effects requiring Discontinuation
Zaja	20	0	0	0	0
Godeau	66	2	1	6	9/66 (14%)
Hernandez	15	7	2	0	3/15 (20%)
Damodar	90	1	0	2	3/90 (3%)
Vancine- Califani	40	11	0	0	3/52 (6%)
Present Study	**170**	**6**	**1**	**5**	**5/170 (2.6%)**

Table 21B: Azathioprine Side Effects: Literature Review

Author	Pts	Borderline Cytopenia	Agranulo - cytosis	Dermatitis	Serious side-effects requiring Discontinuation
Quiquandon	53	7 (3%)	0	0	0
Present Study	130	8 (6%)	1	1	2/130 (1.5%)

Limitations of the Present Study:

The present retrospective analysis included ITP patients with median disease duration of 5 months (range 1-262 months). The indication of treatment with second line agent was predominantly steroid refractory/dependent ITP in patients treated with dapsone and relapsed ITP in patients treated with azathioprine, indicating a physician preference in our practice. This preference towards particular drug for particular indication – dapsone for steroid dependent or steroid refractory ITP and azathioprine use for relapsed ITP was statistically significant in adults. Apart from retrospective nature, this bias is a limitation of our study.

Another limitation of the study is that we had very few cases of secondary ITP (6/300) included in the study. Besides, all these cases were treated only with azathioprine. Hence it was not possible to make any comparisons of second line therapy efficacy in this group of patients. Due to the small number of patients of secondary ITP, we are also unable to draw any seperate conclusions in this category of patients. Hence, it was decided to include these in the analysis of entire cohort and thus we have not reported the outcome separately.

Conclusions

Conclusions:

The following are salient features of our study that allow for robust conclusions:

1. The high number of patients that we included in the study, with more than 100 patients in each arm and each subgroup. We also include more than 100 children in the study.
2. Use of response criteria as laid down by 2009 International Working Group on ITP. We have shown that these criteria are robust and objective even in retrospective study setting.
3. The response rates are comparable to contemporary literature for both agents.

The second line therapy with dapsone and azathioprine showed identical response rates with limited side effects. The response rates of dapsone and azathioprine and side effect profile are comparable with contemporary published literature.

Dapsone exhibited better response rates (overall response and complete response) than azathioprine in children treated for steroid dependent/steroid refractory ITP ($p=0.023$). In adults, azathioprine showed marginally better response rates than dapsone in relapsed ITP, but this was not statistically significant. Both these findings need confirmation in prospective setting.

Azathioprine produced significantly more durable response rates than dapsone; median response duration 60 months (range 2-60 months) for azathioprine and 27 months (range 5-74 months) for dapsone ($p=0.015$) with lower relapse rates while on therapy ($p=0.007$). The prolonged response was significant in adults ($p=0.037$) treated with azathioprine but not in children. These findings require to be validated in prospective randomized control trial setting.

An important finding of our study was higher relapse rates while on therapy. Steroid refractory/dependent ITP and any response less than complete response were significantly associated with relapse while on therapy. The bias towards treating steroid refractory/dependent ITP with dapsone that resulted in over-representation of these cases in dapsone arm, may explain the trend towards more relapses in the dapsone therapy patients when compared to azathioprine therapy patients. This finding requires confirmation in prospective randomized control setting.

Similarly, although the splenectomy sparing effect could be demonstrated in responders of second line therapy, this needs validation in prospective randomized control study. We also need to confirm in prospective setting the finding of significant association of steroid dependent-refractory ITP with increased incidence of splenectomy.

There were no deaths in present study cohort. This demonstrated that with our approach of using second line (and even third line) therapy for persistent and chronic ITP, we could reduce the rates of splenectomy without subjecting patients to increased mortality. In those who eventually underwent splenectomy the median time to splenectomy was significantly longer amongst responders- 26 months, compared to non-responders, thus showing that our approach helps delay splenectomy by at least 1 year duration. It remains to be assessed in the setting of prospective randomized control study for validation.

Finally our study confirmed that bleeding manifestations are rare in patients with persistent or chronic ITP. The bleeding manifestations in adults though were more in our study cohort than that reported in literature. We acknowledge that there is need to assess bleeding manifestations with objective criteria in a prospective setting in both children and adults with ITP, in order to arrive at a firm conclusion.

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Masterchart

sno	Hosp	Age	Gender	Date_of_Diag	Platelet_cc	Bleeding_a	Refract	Relapse	Date_of_R	Bleeding_@_Rel	Dose	Starting_Date	Time f	First_Response	Date_of_First	Time_to_response	DATECR	Time from	Time from	Response_	Response_	Response_	Response_	Response_	Starting_dc
1	270887D	1	Male	01-21-2009	4,000	Minor	Yes	No	9	Minor	Dapsone	03-03-2009	1	PR	07-14-2009	4	10-13-2009	3	4	NR	CR	NA	CR	CR	2.00
2	382268D	3	Male	12-12-2008	11,000	Minor	No	Yes	1/30/09	Minor	Dapsone	02-13-2009	2	CR	03-03-2009	1	03-03-2009	0	1	CR	CR	NA	CR	NA	2.00
3	389987D	28	Male	12-18-2008	14,000	Minor	Yes	No	9	Minor	Azathioprine	02-03-2009	2	CR	03-31-2009	2	03-31-2009	0	2	CR	CR	NA	NA	NA	2.00
4	286872D	18	Male	12-18-2008	14,000	Minor	Yes	No	9	Minor	Dapsone	01-13-2009	1	CR	03-15-2009	2	03-15-2009	0	2	CR	CR	NA	CR	NA	100.00
5	386077D	40	Female	01-01-2008	11,000	Other	No	Yes	1/18/09	Minor	Azathioprine	01-20-2009	13	NR	01-09-1900					NR	NR	NR	NA	NA	1.30
6	383477D	10	Male	04-16-2008	14,000	Minor	No	Yes	1/3/09	Minor	Dapsone	01-16-2009	9	PR	05-19-2009	4				NR	PR	PR	NA	NA	1.50
7	391090D	17	Female	01-16-2009	8,000	Other	No	Yes	3/6/09	Minor	Dapsone	03-06-2009	2	PR	06-30-2009	4	10-20-2009	4	4	NR	CR	NA	CR	CR	100.00
8	381518D	3	Male	12-27-2008	17,000	None	No	Yes	6/5/09	Minor	Azathioprine	06-05-2009	5	PR	09-11-2009	3	01-27-2010	5	8	PR	CR	CR	CR	CR	1.50
9	386758D	7	Female	12-01-2007	20,000	Minor	No	Yes	3/1/08	Minor	Dapsone	01-27-2009	14	CR	05-08-2009	3	05-08-2009	0	3	CR	CR	CR	NA	NA	2.00
10	395656D	53	Male	11-01-2007	5,000	Minor	No	Yes	11/1/08	Minor	Dapsone	02-13-2009	16	CR	05-12-2009	3	05-12-2009	0	3	CR	CR	CR	Relapse	NA	100.00
11	400171d	29	Female	02-03-2009	7,000	Minor	Yes	No	9	None	Dapsone	03-20-2009	2	NR	01-09-1900					NR	NR	NA	NA	NA	50.00
12	403330D	9	Male	03-01-2004	15,000	Minor	Yes	No	9	None	Dapsone	06-02-2009	64	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
13	409731D	17	Female	01-18-2009	4,000	Minor	Yes	No	9	Minor	Dapsone	02-17-2009	1	PR	10-07-2009	8	10-06-2009	3	8	NR	CR	CR	Relapse	CR	100.00
14	405384D	27	Female	01-01-2009	22,000	Minor	Yes	No	9	None	Dapsone	02-17-2009	2	PR	05-08-2009	3				NR	PR	Relapse	NR	NA	100.00
15	403332D	6	Female	01-24-2009	17,000	Minor	No	Yes	7/17/09	Minor	Dapsone	10-09-2009	9	PR	01-15-2010	3	11-30-2010	11	14	PR	PR	PR	NA	CR	1.50
16	410383D	5	Female	12-17-2008	5,000	Minor	No	Yes	2/16/09	Minor	Dapsone	02-20-2009	2	CR	05-19-2009	3	05-19-2009	0	3	CR	CR	CR	CR	Relapse	1.50
17	407779D	8	Male	01-25-2009	12,000	Other	Yes	No	9	Minor	Dapsone	03-27-2009	2	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
18	315301D	32	Female	09-16-2008	20,000	Other	Yes	No	9	Other	Azathioprine	03-03-2009	6	CR	07-14-2009	4	07-14-2009	0	4	NR	CR	NA	NA	NA	1.50
19	413579D	26	Male	01-01-2009	20,000	None	Yes	No	9	None	Azathioprine	03-03-2009	2	NR	01-09-1900					NR	NR	CR	CR	NA	2.00
20	421944D	26	Female	10-01-2008	20,000	Other	Yes	No	9	Other	Dapsone	03-24-2009	6	PR	04-01-2010	12				NR	NR	NA	PR	NA	100.00
21	415464D	5	Male	02-10-2009	4,000	Minor	Yes	No	9	Minor	Dapsone	03-13-2009	1	PR	05-29-2009	3				PR	PR	NA	Relapse	NR	1.50
22	422165D	19	Female	11-01-2008	25,000	Intracrania	Yes	No	9	Other	Dapsone	03-27-2009	5	NR	01-09-1900					NR	NR	NA	NA	NA	100.00
23	424284D	53	Male	03-20-2009	12,000	Minor	No	Yes	5/5/09	None	Azathioprine	05-05-2009	2	PR	06-05-2009	1	07-09-2009	1	2	CR	CR	CR	CR	NA	1.50
24	422912D	4	Male	09-01-2008	29,000	Minor	Yes	No	9	Minor	Dapsone	03-13-2009	6	CR	05-29-2009	3	05-29-2009	0	3	CR	CR	NA	Relapse	PR	1.50
25	417226D	38	Male	02-01-2009	15,000	Minor	Yes	No	9	Minor	Azathioprine	03-13-2009	1	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
26	423359D	33	Male	03-09-2009	14,000	Minor	Yes	No	9	Other	Dapsone	04-16-2009	1	NR	01-09-1900					NR	NR	NR	NA	NA	100.00
27	392297D	72	Female	01-21-2009	10,000	Intracrania	Yes	No	9	Other	Dapsone	04-03-2009	2	PR	05-08-2009	1	08-04-2009	3	4	CR	CR	PR	NA	PR	75.00
28	418506D	21	Female	01-21-2008	10,000	Minor	No	Yes	6/14/08	Minor	Azathioprine	06-20-2008	5	PR	11-27-2008	5	03-16-2009	4	9	NR	PR	CR	CR	NA	1.00
29	427871D	42	Female	01-19-2006	8,000	Intracrania	Yes	No	9	Minor	Dapsone	03-20-2009	39	PR	04-21-2009	1	07-20-2009	3	4	CR	CR	NA	PR	CR	100.00
30	427720D	20	Male	03-24-2009	8,000	Minor	No	Yes	2/1/09	Minor	Dapsone	08-04-2009	4	NR	01-09-1900					NR	NR	NR	NA	NA	100.00
31	427984D	28	Female	03-27-2009	5,000	Minor	Yes	No	9	Minor	Dapsone	05-15-2009	2	NR	01-09-1900					NR	NR	NA	NA	NA	100.00
32	436935D	5	Male	04-01-2009	3,000	Minor	Yes	No	9	Minor	Dapsone	05-08-2009	1	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
33	436593D	3	Female	04-01-2009	8,000	Minor	No	Yes	7/21/09	None	Dapsone	07-21-2009	4	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
34	422443D	9	Male	04-01-2007	10,000	Minor	No	Yes	3/20/09	None	Dapsone	03-20-2009	24	CR	06-19-2009	3	06-19-2009	0	3	CR	CR	Relapse	NR	NA	1.50
35	424586D	28	Male	01-01-2009	14,000	Minor	Yes	No	9	Minor	Dapsone	03-25-2009	3	PR	06-16-2009	3				PR	Relapse	NR	NR	NR	100.00
36	423049D	14	Female	01-03-2009	12,000	Minor	Yes	No	9	None	Azathioprine	04-24-2009	4	CR	07-03-2009	2	07-03-2009	0	2	CR	CR	NA	CR	CR	1.50
37	429535D	22	Female	10-01-2008	15,000	Minor	Yes	No	9	Other	Azathioprine	12-01-2008	2	NR	01-09-1900					NR	NR	CR	NA	CR	2.50
38	445240D	30	Male	06-27-2005	22,000	Minor	No	Yes	21/04/2009	Minor	Dapsone	04-21-2009	46	CR	07-03-2009	2	07-03-2009	0	2	CR	CR	CR	CR	CR	100.00
39	450408D	28	Female	03-27-2009	35,000	Minor	Yes	No	9	Minor	Dapsone	05-01-2009	1	CR	06-03-2009	1				PR	PR	NA	NA	NA	50.00
40	451205D	28	Female	02-24-2009	10,000	Minor	No	Yes	5/5/09	None	Dapsone	05-05-2009	2	CR	08-14-2009	3	08-14-2009	0	3	CR	CR	NA	CR	CR	100.00
41	449279D	32	Female	04-05-2009	3,000	Other	Yes	No	9	None	Dapsone	06-02-2009	2	CR	06-02-2009	0	06-02-2009	0	1	CR	CR	CR	CR	NA	100.00
42	453997D	50	Male	04-15-2009	1,000	Minor	Yes	No	9	Minor	Azathioprine	05-15-2009	1	PR	04-23-2010	11	06-07-2011	14	25	NR	NR	NR	PR	CR	1.80
43	456183D	34	Female	05-22-2009	13,000	Minor	Yes	No	9	Other	Dapsone	11-09-2009	6	CR	05-11-2010	6	05-11-2010	0	6	NR	CR	Relapse	NR	NR	100.00
44	468847D	5	Female	04-01-2008	8,000	Minor	No	Yes	18/04/2009	Minor	Azathioprine	06-12-2009	15	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
45	446318D	21	Female	03-01-2009	7,000	Other	No	Yes	8/10/12	Minor	Azathioprine	10-09-2012	44	CR	11-06-2012	1	11-06-2012	0	1	CR	CR	CR	CR	NA	1.50
46	469672D	45	Female	05-01-1996	12,000	Minor	No	Yes	3/5/09	Minor	Dapsone	06-30-2009	160	CR	08-25-2009	2	08-25-2009	0	2	CR	CR	NA	NA	NA	100.00
47	476714D	36	Female	03-01-2007	10,000	Minor	No	Yes	10/6/09	Minor	Dapsone	06-12-2009	28	CR	07-13-2009	1	07-13-2009	0	1	CR	CR	CR	CR	CR	100.00
48	174761D	48	Female	01-11-2006	12,000	Minor	Yes	No	9	Minor	Dapsone	01-22-2008	25	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
49	460115D	45	Female	07-10-2009	5,000	Other	Yes	No	9	Other	Azathioprine	08-11-2009	1	PR	09-20-2009	1	02-10-2010	5	6	NR	PR	CR	PR	PR	1.50
50	467358D	25	Male	04-01-2008	6,000	Minor	Yes	No	9	Minor	Dapsone	05-26-2009	14	CR	08-25-2009	3	08-25-2009	0	3	CR	CR	CR	Relapse	NR	100.00
51	471709D	6	Male	04-01-2009	28,000	Minor	Yes	No	9	Minor	Dapsone	06-12-2009	2	NR	01-09-1900					NR	NR	NR	NR	NR	2.50
52	488330D	13	Female	07-06-2009	12,000	Minor	Yes	No	9	Minor	Dapsone	07-31-2009	1	PR	09-04-2009	1	02-12-2010	5	7	CR	CR	CR	CR	CR	2.00
53	489009D	40	Female	07-17-2009	28,000	Minor	No	Yes	8/11/11	Minor	Azathioprine	11-08-2009	4	CR	01-10-2010	2	01-10-2010	0	2	CR	CR	CR	PR	NA	1.50
54	489958D	27	Female	06-05-2009	9,000	Other	Yes	No	9	Minor	Dapsone	07-14-2009	1	PR	08-18-2009	1				PR	PR	PR	Relapse	NR	100.00
55	227554F	40	Female	01-01-1993	15,000	Minor	No	Yes	15/06/2012	Minor	Dapsone	06-22-2012	237	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
56	490294D	42	Female	04-07-2009	15,000	Other	No	Yes	3/10/09	Minor	Azathioprine	10-30-2009	7	NR	01-09-1900					NR	NR	NA	NA	NA	1.00
57	501501D	25	Female	04-01-2008	10,000	Other	No	Yes	15/07/2009	Minor	Dapsone	08-04-2009	16	CR	09-15-2009	1	09-15-2009	0	1	CR	CR	NA	CR	Relapse	100.00
58	504523D	2	Female	04-13-2009	28,000	Minor	No	Yes	4/8/09	Minor	Dapsone	08-04-2009	4	NR	01-09-1900					NR	NR	NR	NR	NA	2.00
59	506883D	30	Female	08-07-2009	7,000	Minor	No	Yes	8/9/09	None	Azathioprine	09-08-2009	1	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
60	508414D	38	Female	04-08-2009	10,000	Minor	Yes	No	9	Minor	Dapsone	09-04-2009	5	CR	09-22-2009	1	09-22-2009	0	1	CR	CR	CR	CR	CR	100.00
61	512158D	12	Female	01-01-2009	10,000	Minor	Yes	No	9	Minor	Azathioprine	08-10-2009	7	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
62	512167D	23	Female	07-31-2009	15,000	Other	Yes	No	9	Other	Azathioprine	09-01-2009	1	PR	09-29-2009	1				PR	PR	NA	PR	Relapse	1.80
63	513818D	30	Male	04-08-2009	5,000	Other	Yes	No	9	Minor	Dapsone	08-21-2009	5	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
64	473552D	13	Female	06-01-2008	12,000	Minor	No	Yes	5/6/09	Minor	Dapsone	06-05-2009	12	CR	09-08-2009	3	09-08-2009	0	3	CR	PR	Relapse	PR	PR	1.50
65	522969D	12	Female	06-26-2004	12,000	Minor	No	Yes	15/09/2009	Minor	Azathioprine	10-23-2009	65	PR	11-24-2009	1				PR	PR	NA	NA	NA	2.00

66	520990D	5	Female	06-24-2008	26,000	Minor	No	Yes	10/8/09	Minor	Dapsone	08-10-2009	14	CR	09-08-2009	1	09-08-2009	0	1	CR	CR	CR	CR	NA	1.50
67	529139D	12	Male	07-01-2009	6,000	Minor	No	Yes	29/09/2009	Minor	Dapsone	09-20-2009	3	CR	01-08-2010	4	01-08-2010	0	4	CR	CR	NA	CR	CR	1.00
68	526235D	47	Female	07-24-2009	3,000	Other	Yes	No	9	Minor	Dapsone	08-28-2009	1	NR	01-09-1900					NR	NR	NR	CR	NA	100.00
69	533079D	13	Male	01-09-2009	3,000	Minor	Yes	No	9	Minor	Azathioprine	11-28-2009	11	PR	01-29-2010	2	11-26-2010	10	12	PR	CR	NA	Relapse	CR	1.50
70	542911D	11	Female	11-01-2007	7,000	Minor	No	Yes	25/09/2009	Minor	Azathioprine	09-25-2009	23	NR	01-09-1900					NR	NR	NR	PR	CR	2.00
71	551530D	21	Female	09-08-2009	12,000	Other	Yes	No	9	Minor	Dapsone	10-10-2009	1	NR	01-09-1900					NR	NR	NR	PR	NR	100.00
72	591232D	23	Female	11-29-2009	2,000	Other	No	Yes	7/2/10	Other	Azathioprine	02-07-2010	2	CR	03-09-2010	1	03-09-2010	0	1	NR	CR	CR	CR	NA	2.00
73	576872D	41	Female	06-27-2005	40,000	Minor	No	Yes	9/3/10	Minor	Azathioprine	03-09-2010	57	PR	08-31-2010	6				NR	PR	PR	PR	CR	1.50
74	581502D	58	Female	09-16-2009	12,000	Minor	No	Yes	29/12/2009	Minor	Azathioprine	12-29-2009	3	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
75	605490D	8	Male	12-19-2009	12,000	Minor	Yes	No	9	Minor	Azathioprine	02-02-2010	2	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
76	602635D	7	Female	07-01-2008	12,000	Minor	Yes	No	9	Minor	Dapsone	08-01-2008	1	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
77	603222D	23	Female	06-25-2003	7,000	Minor	No	Yes	15/12/2009	Minor	Azathioprine	12-15-2009	79	CR	01-22-2010	1	01-22-2010	0	1	CR	CR	CR	CR	CR	1.00
78	396890C	16	Female	08-01-2002	24,000	Minor	Yes	No	9	Minor	Dapsone	11-28-2003	16	PR	02-22-2004	3				PR	PR	PR	PR	PR	100.00
79	566617D	21	Female	10-23-2007	4,000	Other	Yes	No	9	Minor	Azathioprine	09-20-2009	23	NR	01-09-1900					NR	NR	NA	NA	NA	1.50
80	570820D	53	Female	04-20-2009	15,000	Minor	No	Yes	27/10/2009	Minor	Azathioprine	10-27-2009	6	NR	01-09-1900					NR	NR	NA	NA	NA	1.30
81	563327D	28	Male	06-01-2008	12,000	Minor	Yes	No	9	Minor	Dapsone	10-30-2009	17	NR	01-09-1900					NR	NR	NA	NA	NA	100.00
82	570984D	27	Male	09-01-2005	2,000	Minor	No	Yes	30/10/2009	Minor	Dapsone	11-03-2009	51	PR	02-12-2010	3				PR	Relapse	NR	NR	NA	100.00
83	577112D	38	Male	09-11-2009	8,000	Minor	Yes	No	9	Minor	Dapsone	01-08-2010	4	CR	06-11-2010	5	06-11-2010	0	5	NR	CR	CR	Relapse	CR	100.00
84	562095D	4	Male	08-01-2008	30,000	Minor	Yes	No	9	Minor	Dapsone	11-24-2009	16	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
85	614194D	38	Female	01-08-2010	5,000	Minor	No	Yes	30/03/2010	Minor	Azathioprine	03-30-2010	3	CR	09-24-2010	6	09-24-2010	0	6	NR	CR	CR	CR	CR	2.00
86	614923D	33	Female	04-01-2008	20,000	Minor	Yes	No	9	Minor	Dapsone	01-15-2010	22	PR	04-23-2010	3				PR	PR	Relapse	NR	NA	100.00
87	614587D	18	Female	09-01-2009	12,000	Minor	Yes	No	9	Minor	Dapsone	01-15-2010	5	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
88	178672D	35	Female	01-01-2000	20,000	Minor	No	Yes	30/01/2008	Minor	Dapsone	02-15-2008	99	PR	08-11-2008	6	11-06-2008	3	9	NR	PR	CR	CR	Relapse	100.00
89	622482D	1	Female	01-01-2010	7,000	Minor	No	Yes	19/02/2010	Minor	Dapsone	02-19-2010	2	PR	04-20-2010	2	05-20-2010	1	3	CR	CR	CR	CR	NA	1.30
90	623817D	25	Male	04-01-2006	16,000	Minor	No	Yes	29/01/2010	Minor	Dapsone	01-29-2010	47	CR	02-26-2010	1	02-26-2010	0	1	CR	CR	NA	NA	NA	100.00
91	624638D	28	Female	12-01-2009	25,000	Minor	Yes	No	9	Minor	Dapsone	01-29-2010	2	PR	03-10-2010	1				PR	PR	NA	NA	NA	100.00
92	609615D	8	Male	12-30-2009	10,000	Minor	Yes	No	9	Minor	Dapsone	01-29-2010	1	PR	04-27-2010	3	07-23-2010	3	6	PR	CR	CR	NA	CR	1.00
93	625203D	32	Male	01-01-2010	6,000	Minor	Yes	No	9	Minor	Dapsone	03-05-2010	2	CR	04-13-2010	1	04-13-2010	0	1	CR	CR	CR	CR	CR	100.00
94	625032D	33	Female	12-01-2009	5,000	Minor	Yes	No	9	Minor	Dapsone	02-03-2010	2	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
95	628004D	5	Female	08-01-2008	12,000	Minor	No	Yes	12/2/10	Minor	Dapsone	02-12-2010	19	CR	04-16-2010	2	04-16-2010	0	2	CR	CR	NA	Relapse	NA	2.00
96	630089D	18	Female	05-02-2010	7,000	Minor	No	Yes	18/06/2010	Minor	Azathioprine	07-02-2010	2	CR	08-03-2010	1	08-03-2010	0	1	CR	CR	CR	Relapse	CR	2.00
97	563678D	25	Female	09-17-2009	7,000	Minor	No	Yes	25/01/2010	Minor	Dapsone	01-29-2010	4	NR	01-09-1900					NR	NR	NA	NA	NA	100.00
98	638916D	28	Male	05-01-2009	10,000	Minor	Yes	No	9	Minor	Dapsone	03-26-2010	11	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
99	665562D	9	Male	01-01-2010	15,000	Minor	No	Yes	20/04/2010	Minor	Azathioprine	04-23-2010	4	PR	10-12-2010	6	06-30-2011	9	14	NR	PR	PR	PR	CR	1.50
100	678002D	34	Female	06-27-2005	19,000	Minor	No	Yes	3/8/10	Minor	Azathioprine	08-03-2010	62	PR	10-29-2010	3	02-15-2011	4	7	PR	CR	CR	CR	Relapse	1.50
101	686040D	2	Female	01-01-2010	12,000	Minor	No	Yes	30/04/2010	Minor	Dapsone	05-04-2010	4	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
102	690414D	5	Female	09-20-2009	10,000	Minor	No	Yes	5/4/10	Minor	Azathioprine	04-05-2010	7	NR	01-09-1900					NR	NR	NR	PR	PR	1.50
103	639226D	29	Female	02-08-2006	18,000	Minor	No	Yes	15/10/2010	Other	Dapsone	10-19-2010	57	NR	01-09-1900					NR	PR	PR	CR	NA	100.00
104	660077D	47	Female	01-18-2010	9,000	Minor	Yes	No	9	Minor	Dapsone	03-10-2010	2	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
105	669143D	25	Female	05-12-2010	12,000	Minor	Yes	No	9	Minor	Dapsone	06-22-2010	1	CR	07-21-2010	1	07-21-2010	0	1	CR	CR	NA	NA	NA	100.00
106	677658D	24	Female	06-01-2004	20,000	Minor	No	Yes	25/05/2010	Minor	Dapsone	06-08-2010	73	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
107	715761D	22	Female	06-01-2010	2,000	Minor	Yes	No	9	Minor	Dapsone	07-02-2010	1	CR	08-17-2010	2	08-17-2010	0	2	CR	CR	CR	CR	CR	75.00
108	700713D	52	Male	03-01-2010	11,000	Minor	Yes	No	9	Minor	Azathioprine	05-11-2010	2	NR	01-09-1900					NR	NR	NR	PR	PR	1.50
109	704000D	4	Female	06-01-2010	15,000	Minor	Yes	No	9	Minor	Azathioprine	07-01-2010	1	NR	01-09-1900					NR	NR	NR	NA	NA	1.30
110	729514D	39	Female	06-19-2010	8,000	Minor	Yes	No	9	Minor	Dapsone	07-21-2010	1	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
111	727200D	20	Female	12-01-2009	30,000	Minor	No	Yes	2/7/10	Minor	Dapsone	07-06-2010	7	PR	08-03-2010	1	09-27-2011	14	15	PR	PR	NA	CR	Relapse	100.00
112	724141D	33	Male	06-29-2010	4,000	Minor	Yes	No	9	Other	Dapsone	08-03-2010	1	NR	01-09-1900					NR	NR	NR	NR	CR	100.00
113	724146D	54	Female	06-28-2010	14,000	Minor	Yes	No	9	None	Dapsone	07-30-2010	1	CR	09-07-2010	1	09-07-2010	0	1	CR	CR	CR	NA	NA	100.00
114	738332D	5	Female	07-20-2010	9,000	Minor	Yes	No	9	Minor	Azathioprine	09-14-2010	2	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
115	719141D	18	Female	06-10-2010	4,000	Other	No	Yes	6/10/11	Minor	Dapsone	10-06-2011	16	CR	11-07-2011	1	11-07-2011	0	1	CR	CR	CR	CR	NA	100.00
116	741942D	6	Male	05-01-2010	16,000	Minor	Yes	No	9	Minor	Dapsone	07-23-2010	3	CR	08-23-2010	1	08-23-2010	0	1	CR	CR	NA	CR	CR	2.00
117	723806D	14	Male	06-01-2010	23,000	Minor	Yes	No	9	Minor	Dapsone	07-02-2010	1	PR	11-09-2010	4				PR	PR	Relapse	NR	NA	1.50
118	707237d	30	Female	03-01-2009	9,000	Minor	No	Yes	7/6/10	Minor	Azathioprine	07-06-2010	16	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
119	741241D	21	Female	02-01-2009	8,000	Minor	Yes	No	9	Minor	Azathioprine	10-19-2009	9	PR	02-11-2010	4	09-22-2011	20	23	NR	PR	CR	CR	CR	2.00
120	743773D	8	Female	05-01-2010	20,000	Minor	Yes	No	9	Minor	Dapsone	07-24-2010	3	CR	11-16-2010	4	11-16-2010	0	4	NR	CR	PR	CR	CR	1.50
121	749621D	49	Female	03-01-2010	5,000	Minor	Yes	No	9	Minor	Azathioprine	08-03-2010	5	PR	02-08-2011	6				NR	PR	Relapse	PR	PR	1.00
122	762296D	33	Female	08-01-2010	9,000	Minor	No	Yes	28/01/2011	Minor	Dapsone	01-28-2011	6	PR	02-25-2011	1				PR	Relapse	NR	NR	NA	100.00
123	762703D	3	Female	05-01-2010	20,000	Minor	Yes	No	9	None	Dapsone	08-24-2010	4	CR	09-24-2010	1	09-24-2010	0	1	CR	CR	CR	CR	NA	1.50
124	723910D	45	Female	12-01-2009	14,000	Minor	No	Yes	28/07/2010	Minor	Dapsone	07-30-2010	8	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
125	753057D	17	Female	08-01-2010	14,000	Minor	Yes	No	9	Minor	Azathioprine	09-10-2010	1	PR	10-08-2010	1	01-04-2011	3	4	CR	CR	CR	CR	CR	1.50
126	762785D	10	Female	08-01-2010	15,000	Minor	Yes	No	9	None	Dapsone	08-30-2010	1	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
127	738509D	6	Female	03-01-2010	30,000	Minor	No	Yes	20/08/2010	Minor	Dapsone	08-20-2010	6	PR	09-07-2010	1	10-05-2010	1	2	CR	CR	CR	CR	PR	1.50
128	779737D	34	Female	10-01-2010	15,000	Other	No	Yes	26/07/2011	Minor	Azathioprine	07-29-2011	10	CR	01-03-2012	5	01-03-2012	0	5	NR	CR	PR	CR	Relapse	1.50
129	770237D	38	Female	08-01-2010	4,000	Other	No	Yes	26/07/2011	Minor	Azathioprine	05-29-2011	10	PR	08-26-2011	3	05-08-2012	9		PR	PR	PR	CR	NA	1.50
130	000460D	29	Male	01-01-2007	32,000	Minor	No	Yes	19/06/2007	Minor	Dapsone	06-19-2007	6	CR	07-17-2007	1	07-17-2007	0	1	CR	CR	CR	CR	Relapse	100.00
131	805953D	35	Male	06-01-2010	14,000	Minor	No	Yes	2/10/10	Minor	Dapsone	11-09-2010	5	PR	12-07-2010	1				PR	Relapse	NR	CR	CR	100.00

132	832646D	27	Female	11-01-2009	16,000	Minor	No	Yes	11/2/10	Minor	Azathioprine	02-11-2011	16	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
133	396494F	26	Female	01-01-2013	8,000	Minor	Yes	No	9	Minor	Azathioprine	02-26-2013	2	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
134	828678D	13	Female	10-01-2010	5,000	Minor	Yes	No	9	Minor	Azathioprine	03-04-2011	5	CR	07-01-2011	4	07-01-2011	0	4	NR	CR	CR	CR	CR	1.50
135	845908D	39	Male	10-01-2010	25,000	Minor	Yes	No	9	Minor	Dapsone	12-17-2010	3	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
136	785849D	16	Female	05-01-2010	5,000	Minor	No	Yes	15/10/2010	Minor	Dapsone	10-26-2010	6	NR	01-09-1900					NR	NR	NR	NR	NR	75.00
137	788474D	35	Female	09-01-2010	19,000	Minor	No	Yes	9/11/10	Minor	Azathioprine	11-09-2010	2	NR	01-09-1900					NR	NR	PR	CR	CR	1.50
138	811449D	25	Male	06-01-2010	13,000	Minor	No	Yes	29/10/2010	None	Dapsone	10-29-2010	5	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
139	807280D	10	Female	01-01-2010	12,000	Minor	Yes	No	9	Minor	Dapsone	11-09-2010	10	CR	05-27-2011	7	05-27-2011	0	7	NR	CR	CR	CR	NA	1.50
140	801656D	27	Male	01-01-2004	4,000	Minor	No	Yes	8/10/10	Minor	Azathioprine	10-08-2010	82	CR	11-09-2010	1	11-09-2010	0	1	CR	CR	CR	CR	NA	1.50
141	503114A	30	Male	01-01-2005	10,000	Minor	No	Yes	2/8/10	Intracranial hem	Azathioprine	08-13-2010	68	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
142	754092D	43	Female	01-01-1993	26,000	Minor	No	Yes	10/8/10	Minor	Dapsone	08-17-2010	215	NR	01-09-1900					NR	NR	NR	NA	NA	100.00
143	750605D	2	Male	08-01-2010	15,000	Minor	No	Yes	14/12/2010	None	Dapsone	01-11-2011	5	PR	03-08-2011	2	12-28-2011	10	12	PR	PR	CR	CR	NA	1.50
144	812256D	65	Female	10-01-2010	12,000	Minor	No	Yes	29/04/2011	Minor	Dapsone	04-26-2011	7	CR	08-26-2011	4	08-26-2011	0	4	NR	CR	CR	Relapse	CR	100.00
145	913107D	20	Female	11-01-2010	10,000	Other	No	Yes	15/04/2011	Minor	Azathioprine	04-15-2011	6	CR	07-06-2011	3	07-06-2011	0	3	CR	CR	CR	CR	CR	1.50
146	036594D	34	Female	01-01-2012	10,000	Minor	Yes	No	9	None	Dapsone	03-02-2012	2	PR	06-05-2012	3	11-30-2012	6	9	PR	PR	CR	PR	NA	100.00
147	887624B	42	Male	05-01-2000	7,000	Minor	No	Yes	6/11/10	Minor	Azathioprine	01-07-2011	130	CR	02-01-2011	1	02-01-2011	0	1	CR	CR	CR	CR	CR	1.50
148	645591D	37	Male	06-01-2009	6,000	Other	No	Yes	2/3/10	Minor	Azathioprine	03-06-2010	9	CR	04-07-2010	1	04-07-2010	0	1	CR	CR	CR	CR	CR	1.50
149	894944D	31	Female	12-01-2010	10,000	Minor	No	Yes	18/03/2011	Minor	Azathioprine	03-18-2011	4	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
150	893349D	12	Female	12-01-2010	32,000	Minor	Yes	No	9	Minor	Azathioprine	03-15-2011	3	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
151	876086D	5	Female	03-01-2010	34,000	Minor	Yes	No	9	Minor	Azathioprine	02-04-2011	11	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
152	876665D	20	Female	01-01-2011	6,000	Minor	Yes	No	9	Minor	Dapsone	03-04-2011	2	NR	01-09-1900					NR	NR	NR	NA	NA	100.00
153	887616D	2	Female	10-01-2010	30,000	Minor	No	Yes	4/3/11	Minor	Azathioprine	03-04-2011	5	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
154	837756D	11	Male	09-01-2010	2,000	Minor	No	Yes	20/12/2010	Minor	Azathioprine	01-04-2011	4	NR	01-09-1900					NR	NR	NR	PR	PR	1.50
155	839790D	50	Male	01-27-2005	10,000	Minor	No	Yes	24/2/2011	Minor	Azathioprine	02-24-2011	74	CR	06-03-2011	3				NR	CR	PR	Relapse	NR	1.50
156	831684D	14	Female	09-01-2010	15,000	Other	Yes	No	9	Minor	Dapsone	12-21-2010	4	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
157	982308D	19	Male	05-24-2011	3,000	Minor	Yes	No	9	Minor	Dapsone	06-29-2011	1	PR	07-29-2011	1	08-28-2011	1	2	CR	CR	CR	CR	Relapse	100.00
158	983685D	40	Female	07-01-2011	6,000	Minor	Yes	No	9	Minor	Azathioprine	08-26-2011	2	PR	12-15-2011	4	03-08-2012	3	7	CR	CR	CR	CR	CR	1.50
159	976267D	42	Female	06-27-2005	5,000	Minor	No	Yes	10/10/11	Minor	Dapsone	10-10-2011	77	CR	06-15-2012	8	06-15-2012	0	8	NR	NR	CR	Relapse	NR	100.00
160	966868D	13	Female	06-01-2011	15,000	Minor	No	Yes	16/08/2011	Minor	Azathioprine	08-16-2011	3	PR	09-13-2011	1	06-29-2012	10	11	PR	PR	PR	CR	CR	1.50
161	948992D	27	Female	03-01-2011	15,000	Minor	No	Yes	5/5/12	Minor	Dapsone	05-18-2012	15	CR	07-23-2012	2	07-23-2012	0	2	CR	Relapse	CR	CR	NA	100.00
162	965503D	9	Female	06-01-2009	30,000	Minor	No	Yes	17/06/2011	Minor	Azathioprine	06-17-2011	25	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
163	957608D	35	Female	05-01-2011	5,000	Minor	Yes	No	9	Minor	Dapsone	06-01-2011	1	PR	07-15-2011	1				PR	PR	PR	PR	PR	100.00
164	891924D	36	Female	07-01-2010	35,000	Minor	No	Yes	25/02/2011	Minor	Dapsone	02-25-2011	8	NR	01-09-1900					NR	NR	NR	NR	NR	75.00
165	878510D	20	Female	02-01-2011	10,000	Minor	Yes	No	9	Minor	Dapsone	03-04-2011	1	NR	01-09-1900					NR	NR	CR	CR	NA	75.00
166	875179D	50	Male	09-01-2010	15,000	Minor	Yes	No	9	Minor	Azathioprine	02-11-2011	5	NR	01-09-1900					NR	NR	PR	PR	Relapse	1.50
167	992739D	18	Male	07-01-2011	3,000	Minor	Yes	No	9	Minor	Dapsone	08-23-2011	2	PR	09-20-2011	1	11-18-2011	2	3	CR	CR	CR	NA	NA	100.00
168	972642D	19	Female	04-01-2011	9,000	Minor	No	Yes	3/4/12	Minor	Azathioprine	04-03-2012	12	PR	06-29-2012	3	07-05-2013	12	15	PR	PR	NA	CR	NA	1.50
169	993073D	23	Male	07-01-2011	15,000	Minor	Yes	No	9	Minor	Dapsone	12-27-2011	6	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
170	987743D	7	Female	07-01-2011	18,000	Minor	No	Yes	10/1/12	Minor	Dapsone	01-10-2012	6	CR	04-13-2012	3	04-13-2012	0	3	CR	CR	NA	NA	NA	1.50
171	997196D	29	Female	07-01-2011	17,000	Minor	Yes	No	9	Minor	Azathioprine	08-05-2011	1	NR	01-09-1900					NR	NR	NA	NA	NA	1.50
172	974879D	2	Female	07-01-2011	7,000	Minor	Yes	No	9	Minor	Azathioprine	12-01-2011	5	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
173	968245D	27	Male	07-01-2011	3,000	Minor	Yes	No	9	Minor	Azathioprine	08-02-2011	1	NR	01-09-1900					NR	NR	NR	CR	CR	1.50
174	907224D	63	Female	03-01-2011	9,000	Intracranial	Yes	No	9	None	Dapsone	04-26-2011	2	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
175	795296D	32	Female	10-01-2010	8,000	Minor	Yes	No	9	Minor	Dapsone	11-04-2010	1	CR	02-08-2011	3	02-08-2011	0	3	CR	CR	Relapse	NR	NR	100.00
176	901294D	33	Male	03-01-2011	10,000	Minor	Yes	No	9	Minor	Dapsone	04-29-2011	2	CR	08-02-2011	3	08-02-2011	0	3	NR	CR	PR	CR	Relapse	100.00
177	902917D	27	Female	03-01-2011	35,000	Minor	Yes	No	9	Minor	Azathioprine	03-25-2011	1	CR	08-02-2011	4	08-02-2011	0	4	NR	NR	NR	NR	NA	1.50
178	911136D	58	Female	01-01-2013	7,000	Minor	No	Yes	22/03/2013	Minor	Azathioprine	03-22-2013	3	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
179	911843D	33	Male	03-01-2011	19,000	Minor	Yes	No	9	Minor	Azathioprine	05-17-2011	3	PR	06-17-2011	1	07-01-2011	0	2	CR	CR	CR	CR	NA	1.50
180	916437D	9	Male	04-27-2006	15,000	Minor	No	Yes	1/4/11	Minor	Dapsone	04-14-2011	60	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
181	916749D	62	Female	04-01-2010	7,000	Intracranial	No	Yes	1/4/11	Minor	Dapsone	04-12-2011	13	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
182	918567D	9	Male	03-01-2010	21,000	Minor	Yes	No	9	Minor	Azathioprine	04-05-2011	13	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
183	929985D	45	Female	03-01-2011	20,000	Minor	Yes	No	9	Minor	Azathioprine	04-19-2011	2	CR	06-10-2011	2	06-10-2011	0	2	CR	CR	CR	CR	CR	1.50
184	983742D	21	Female	07-01-2011	17,000	Minor	Yes	No	9	Minor	Dapsone	08-04-2011	1	NR	01-09-1900					NR	NR	NR	NR	PR	100.00
185	947089B	24	Female	08-01-2011	15,000	Minor	Yes	No	9	Minor	Azathioprine	10-18-2011	3	PR	11-18-2011	1				CR	PR	Relapse	PR	NA	1.50
186	017743F	50	Female	09-01-2008	5,000	Minor	No	Yes	24/01/2012	Minor	Azathioprine	01-24-2012	41	NR	01-09-1900					NR	PR	CR	CR	CR	1.00
187	047165F	7	Female	07-01-2011	25,000	Minor	Yes	No	9	Minor	Dapsone	10-07-2011	3	CR	05-01-2012	7				NR	CR	PR	NR	NR	1.50
188	041716F	27	Female	07-01-2011	20,000	Minor	No	Yes	10/1/12	None	Azathioprine	01-10-2012	6	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
189	094844F	37	Female	01-01-2012	10,000	Minor	No	Yes	12/7/12	Minor	Azathioprine	07-12-2012	6	NR	01-09-1900					NR	NR	NR	CR	NA	1.50
190	096193F	39	Female	01-01-2000	25,000	Minor	No	Yes	16/12/2011	Minor	Azathioprine	12-16-2011	146	PR	01-17-2012	1	06-11-2012	5	6	PR	PR	PR	CR	NA	1.50
191	089949F	18	Female	12-01-2011	6,000	Other	Yes	No	9	Minor	Dapsone	01-13-2012	1	CR	09-21-2012	8	09-21-2012	0	8	NR	NR	CR	CR	NA	100.00
192	072095F	22	Female	05-01-2011	10,000	Minor	No	Yes	14/02/2012	Minor	Azathioprine	02-14-2012	10	CR	03-16-2012	1	03-16-2012	0	1	CR	CR	CR	CR	NA	1.50
193	086134F	40	Male	11-01-2011	32,000	Minor	No	Yes	21/02/2012	Minor	Azathioprine	04-21-2012	6	PR	07-06-2012	3	09-28-2012	3	5	PR	CR	CR	Relapse	NA	1.50
194	043392F	12	Female	10-01-2011	8,000	Minor	Yes	No	9	Minor	Azathioprine	11-04-2011	1	NR	01-09-1900					NR	NR	NR	NR	NA	2.00
195	003575F	3	Male	11-01-2010	18,000	Minor	No	Yes	06/08 2011	Minor	Dapsone	08-12-2011	9	CR	09-16-2011	1	09-16-2011	0	1	CR	Relapse	NR	PR	NA	1.50
196	031122F	13	Female	10-24-2010	15,000	Minor	Yes	No	9	Minor	Azathioprine	09-16-2011	11	PR	02-10-2012	5	05-04-2012	3	8	NR	PR	CR	CR	Relapse	1.50
197	002121F	4	Male	05-01-2011	20,000	Minor	Yes	No	9	Minor	Dapsone	08-16-2011	4	CR	11-11-2011	3	11-11-2011	0	3	CR	Relapse	PR	CR	CR	1.50

198	034590f	75	Male	06-25-1994	50,000	Minor	No	Yes	17/09/2011	Minor	Dapsone	09-20-2011	210	PR	11-04-2011	2	02-14-2012	3	5	PR	PR	NA	NA	NA	100.00
199	025411F	28	Male	10-01-2009	22,000	Minor	No	Yes	6/9/11	Minor	Azathioprine	09-06-2011	24	NR	01-09-1900					NR	NR	NA	NA	NA	1.50
200	022605F	9	Female	12-01-2008	15,000	Minor	Yes	No	9	Minor	Azathioprine	10-04-2011	35	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
201	086834F	4	Male	06-01-2011	13,000	Minor	No	Yes	16/12/2011	Minor	Dapsone	12-16-2011	7	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
202	024875F	44	Male	03-01-2010	30,000	Minor	No	Yes	4/10/11	Minor	Dapsone	10-04-2011	19	PR	11-01-2011	1				PR	PR	PR	PR	NA	100.00
203	036330F	3	Male	02-01-2011	15,000	Minor	Yes	No	9	Minor	Azathioprine	10-25-2011	9	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
204	053058F	50	Female	07-01-2011	5,000	Minor	No	Yes	17/01/2012	Minor	Azathioprine	01-17-2012	7	PR	04-03-2012	3	06-26-2012	3	5	CR	CR	CR	CR	NA	2.00
205	052213F	41	Male	08-01-2010	4,000	Minor	No	Yes	18/10/2011	Minor	Azathioprine	10-19-2011	15	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
206	094490F	17	Female	12-01-2011	13,000	Epistaxis r	Yes	No	9	Minor	Dapsone	01-31-2012	2	PR	02-28-2012	1				PR	PR	PR	PR	NA	100.00
207	098684F	31	Female	12-23-2011	20,000	Other	Yes	No	9	Other	Azathioprine	01-27-2012	1	CR	03-23-2012	2	03-23-2012	0	2	CR	CR	CR	CR	NA	1.00
208	122899F	16	Female	06-27-2005	30,000	Minor	No	Yes	26/06/2012	Minor	Dapsone	06-20-2012	85	PR	09-21-2012	3				PR	PR	PR	PR	NA	100.00
209	124137F	17	Male	02-01-2012	12,000	Minor	Yes	No	9	Minor	Dapsone	02-24-2012	1	CR	06-05-2012	3	06-05-2012	0	3	NR	CR	CR	NA	NA	100.00
210	116505F	31	Male	12-01-2011	15,000	Minor	Yes	No	9	None	Azathioprine	02-10-2012	2	CR	03-13-2012	1	03-13-2012	0	1	CR	CR	CR	CR	NA	1.50
211	117332F	36	Female	06-01-2010	40,000	None	No	Yes	31/01/2012	None	Azathioprine	01-31-2012	20	PR	03-30-2012	2				PR	PR	PR	PR	NA	1.50
212	132241F	21	Female	01-01-2012	20,000	None	Yes	No	9	None	Azathioprine	02-07-2012	1	PR	03-02-2012	1				PR	Relapse	NR	NR	NR	1.00
213	129647F	45	Female	12-01-2011	12,000	Intracrania	Yes	No	9	None	Azathioprine	02-14-2013	15	PR	03-13-2013	1				PR	PR	PR	PR	NA	1.50
214	125718F	17	Female	02-01-2012	35,000	Other	Yes	No	9	None	Azathioprine	05-11-2013	16	NR	01-09-1900					NR	NR	NA	NR	NA	1.50
215	140570F	20	Female	01-01-2012	48,000	Minor	Yes	No	9	None	Azathioprine	02-21-2013	14	CR	03-23-2013	1	03-23-2013	0	1	CR	CR	PR	NA	NA	1.50
216	129797F	30	Female	02-01-2012	10,000	Minor	Yes	No	9	Minor	Azathioprine	02-24-2012	1	NR	01-09-1900					NR	NR	NR	CR	NA	1.50
217	154795F	35	Female	11-01-2011	9,000	Intracrania	Yes	No	9	Minor	Azathioprine	03-16-2012	5	PR	05-04-2012	2	09-07-2012	4	6	CR	CR	NA	NA	NA	1.50
218	144598F	28	Female	01-01-2012	12,000	Other	Yes	No	9	Minor	Azathioprine	03-20-2012	3	PR	06-14-2012	3				PR	PR	PR	PR	NA	1.50
219	147939F	38	Female	05-01-2009	9,000	Other	No	Yes	13/03/2012	Minor	Azathioprine	04-13-2012	36	CR	07-20-2012	3	07-20-2012	0	3	CR	CR	CR	CR	NA	1.50
220	159063F	2	Female	01-01-2012	9,000	Minor	No	Yes	8/5/12	Minor	Dapsone	05-08-2012	4	NR	01-09-1900					NR	NR	NR	NA	NA	1.50
221	168948F	10	Female	02-01-2012	10,000	Minor	No	Yes	24/04/2012	Minor	Azathioprine	05-01-2012	3	PR	08-03-2012	3				PR	PR	PR	PR	NA	1.50
222	291076F	2	Male	04-01-2012	12,000	Minor	No	Yes	08/02/2013	Minor	Azathioprine	02-08-2013	10	NR	01-09-1900					NR	NR	NR	NA	NA	2.00
223	139722F	11	Female	10-01-2010	40,000	Minor	No	Yes	27/03/2012	Minor	Azathioprine	03-30-2012	18	NR	01-09-1900					NR	PR	PR	Relapse	NA	1.50
224	175081F	58	Male	03-01-2012	10,000	Minor	Yes	No	9	Minor	Azathioprine	04-10-2012	1	NR	01-09-1900					NR	PR	CR	CR	NA	1.50
225	173367F	22	Female	04-01-2010	15,000	Intracrania	No	Yes	15/06/2012	Minor	Azathioprine	06-15-2012	27	CR	07-06-2012	1	07-06-2012	0	1	CR	CR	NA	NA	NA	1.50
226	183420F	3	Male	03-01-2012	12,000	Minor	Yes	No	9	Minor	Azathioprine	05-25-2012	3	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
227	122973F	32	Female	11-01-2011	5,000	Intracrania	No	Yes	31/01/2012	Minor	Azathioprine	01-31-2012	3	CR	04-23-2012	3	04-23-2012	0	3	CR	CR	NA	NA	NA	1.50
228	188965F	5	Male	05-01-2011	14,000	Minor	No	Yes	25/05/2012	Minor	Azathioprine	05-25-2012	13	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
229	178149F	32	Female	03-01-2012	5,000	Minor	Yes	No	9	Minor	Dapsone	05-04-2012	2	CR	07-31-2012	3	07-31-2012	0	3	CR	CR	NA	Relapse	NA	100.00
230	180007F	5	Female	04-01-2012	15,000	Minor	Yes	No	9	Minor	Azathioprine	06-15-2012	3	CR	11-20-2012	5	11-20-2012	0	5	NR	CR	CR	Relapse	NA	1.50
231	235925F	10	Female	05-01-2012	30,000	Minor	Yes	No	9	Minor	Azathioprine	06-26-2012	2	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
232	390133F	10	Male	03-01-2009	13,000	Minor	No	Yes	15/01/2013	Minor	Azathioprine	01-18-2013	47	PR	04-12-2013	3				PR	PR	PR	NA	NA	1.50
233	243066F	5	Male	03-01-2011	7,000	Minor	Yes	No	9	Minor	Dapsone	07-13-2012	17	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
234	198753F	48	Female	03-01-2012	34,000	Minor	No	Yes	24/08/2012	Minor	Azathioprine	08-24-2012	6	PR	09-25-2012	1	04-05-2013	6	7	PR	PR	PR	CR	NA	1.50
235	200873F	4	Male	08-01-2009	56,000	Minor	No	Yes	21/05/2012	Minor	Azathioprine	06-28-2012	35	CR	09-25-2012	3	09-25-2012	0	3	CR	CR	CR	CR	NA	1.50
236	206235f	21	Male	03-01-2000	32,000	Minor	No	Yes	18/05/2012	Minor	Dapsone	05-18-2012	149	PR	07-17-2012	2	10-09-2012	3	5	CR	CR	Relapse	PR	NA	100.00
237	199805F	36	Female	05-12-2012	4,000	Other	Yes	No	9	Other	Azathioprine	06-12-2012	1	CR	07-10-2012	1	07-10-2012	0	1	PR	PR	PR	Relapse	NA	1.50
238	201616f	18	Female	05-01-2010	19,000	Minor	No	Yes	15/05/2012	Minor	Dapsone	05-15-2012	25	CR	08-17-2012	3	08-17-2012	0	3	CR	CR	CR	CR	NA	100.00
239	190459F	18	Female	03-01-2012	22,000	Minor	No	Yes	22/05/2012	Minor	Azathioprine	09-18-2012	7	PR	12-11-2012	3				PR	PR	NA	PR	NA	2.50
240	199941F	11	Male	10-01-2011	19,000	Minor	No	Yes	12/05/2012	Minor	Dapsone	05-12-2012	7	NR	01-09-1900					NR	NR	NR	NR	NA	2.30
241	474777C	13	Male	04-30-2004	10,000	Minor	Yes	No	9	None	Dapsone	05-31-2004	1	CR	07-06-2004	1	07-06-2004	0	1	CR	CR	CR	CR	Relapse	1.50
242	433937C	1	Male	05-01-2002	30,000	Minor	No	Yes	February 2	Other	Azathioprine	05-07-2004	25	CR	08-10-2004	3	08-10-2004	0	3	CR	CR	CR	Relapse	CR	1.50
243	034777D	18	Female	06-01-2007	30,000	Minor	No	Yes	05/10/2007	Minor	Dapsone	07-05-2007	1	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
244	616549C	9	Female	03-01-2002	30,000	Minor	No	Yes	23/08/2005	Minor	Azathioprine	08-23-2005	42	CR	06-06-2006	10	06-06-2006	0	10	NR	NR	NR	CR	PR	1.50
245	625986C	10	Male	10-01-2004	21,000	Minor	No	Yes	19/04/2005	None	Azathioprine	04-19-2005	7	CR	05-24-2005	1	05-24-2005	0	1	CR	CR	CR	NA	NA	1.50
246	659581C	5	Female	06-01-2005	15,000	Minor	No	Yes	02/08/2005	Minor	Dapsone	08-02-2005	2	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
247	680715C	45	Female	09-08-2005	13,000	Minor	No	Yes	25/10/2005	None	Dapsone	10-25-2005	2	NR	01-09-1900					NR	PR	CR	NA	NA	100.00
248	690693C	20	Female	01-01-2003	13,000	Other	No	Yes	26/08/2005	Minor	Dapsone	08-27-2005	32	PR	09-30-2005	1	05-19-2006	8	9	CR	CR	CR	Relapse	Relapse	50.00
249	313299C	10	Male	05-01-2003	2,000	Minor	Yes	No	9	Minor	Dapsone	05-28-2004	13	CR	08-31-2004	3	08-31-2004	0	3	CR	CR	CR	CR	NA	1.50
250	434497C	14	Female	02-04-2004	8,000	Minor	No	Yes	01/02/2008	Minor	Dapsone	02-02-2008	49	NR	01-09-1900					NR	NR	NR	NR	NR	2.00
251	675900C	38	Male	03-01-2005	10,000	Minor	Yes	No	9	Minor	Azathioprine	07-29-2005	5	PR	10-25-2005	3				PR	PR	PR	Relapse	CR	1.50
252	410413C	45	Female	12-01-2003	5,000	Minor	No	Yes	14/09/2007	Minor	Dapsone	09-18-2007	46	PR	01-10-2008	4				NR	PR	PR	Relapse	PR	100.00
253	900582C	5	Male	09-01-2006	5,000	Minor	No	Yes	01/12/2006	Minor	Dapsone	12-01-2006	3	NR	01-09-1900					NR	NR	NR	NR	CR	1.50
254	095045D	19	Female	09-01-2007	12,000	Minor	No	Yes	22/2/2009	Minor	Azathioprine	02-24-2009	18	CR	05-19-2009	3	05-19-2009	0	3	CR	CR	NA	CR	NA	2.30
255	096379D	61	Male	06-01-2007	15,000	Minor	No	Yes	07/09/2007	Minor	Azathioprine	09-07-2007	3	CR	12-07-2007	3	12-07-2007	0	3	CR	CR	CR	CR	CR	1.50
256	081880D	3	Male	09-01-2007	8,000	Minor	Yes	No	9	None	Dapsone	11-13-2007	2	CR	05-30-2008	7	05-30-2008	0	7	NR	NR	CR	Relapse	NR	1.50
257	083998D	7	Female	11-01-2004	3,000	Other	Yes	No	9	Minor	Dapsone	08-17-2007	34	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
258	104189D	41	Female	03-01-2007	19,000	Minor	No	Yes	18/09/2007	Minor	Dapsone	09-18-2007	7	NR	01-09-1900					NR	NR	NR	CR	CR	100.00
259	105580D	5	Male	06-01-2007	15,000	Minor	No	Yes	29/9/2009	Minor	Dapsone	10-02-2009	28	CR	12-15-2009	2	12-15-2009	0	2	CR	CR	NA	CR	CR	1.50
260	105618D	20	Male	04-01-2005	20,000	Minor	No	Yes	23/11/2007	None	Azathioprine	11-23-2007	32	PR	01-11-2008	2	11-12-2008	10	12	PR	PR	NA	CR	CR	1.50
261	105987D	38	Female	09-01-2007	3,000	Other	No	Yes	11/03/2008	Minor	Azathioprine	03-11-2008	6	CR	07-25-2008	5	07-25-2008	0	5	NR	CR	CR	CR	CR	1.50
262	359596C	16	Female	09-01-2003	35,000	Minor	No	Yes	19/12/2003	Minor	Dapsone	12-19-2003	4	CR	01-27-2004	1	01-27-2004	0	1	CR	CR	CR	CR	CR	100.00
263	619910C	80	Female	10-01-2005	5,000	Minor	No	Yes	31/12/2007	None	Azathioprine	01-25-2008	28	CR	02-29-2008	1	02-29-2008	0	1	CR	CR	NA	NA	NA	1.00

264	150715D	12	Female	05-01-2007	12,000	Minor	No	Yes	14/12/2007	Minor	Dapsone	12-14-2007	8	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
265	153147D	28	Female	12-01-2007	4,000	Other	No	Yes	14/02/2008	None	Azathioprine	02-15-2008	3	CR	04-11-2008	2	04-11-2008	0	2	CR	CR	Relapse	CR	CR	1.50
266	161816D	7	Male	03-01-2005	4,000	Minor	Yes	No	9	Minor	Dapsone	01-08-2008	35	CR	02-08-2008	1	02-08-2008	0	1	CR	CR	CR	CR	CR	1.50
267	215005D	9	Male	04-01-2008	9,000	Minor	Yes	No	9	None	Dapsone	05-27-2008	2	NR	01-09-1900					NR	NR	NR	NR	CR	2.00
268	214816D	14	Male	12-01-2007	7,000	Minor	Yes	No	9	Minor	Dapsone	04-08-2008	4	PR	08-12-2008	4	11-09-2008	3	7	NR	PR	NA	CR	CR	1.50
269	208741d	5	Male	04-01-2008	25,000	Minor	No	Yes	25/11/2009	None	Dapsone	11-25-2009	20	NR	01-09-1900					NR	NR	NA	NA	NA	1.50
270	208794D	20	Female	01-01-2008	6,000	Minor	Yes	No	9	None	Azathioprine	03-28-2008	3	NR	01-09-1900					NR	NR	CR	CR	NA	1.50
271	206332D	8	Female	03-01-2008	7,000	Minor	No	Yes	14/5/2010	Minor	Dapsone	05-14-2010	27	CR	08-06-2010	3	08-06-2010	0	3	CR	CR	CR	CR	Relapse	1.50
272	202501D	28	Female	03-01-2008	6,000	Minor	No	Yes	13/10/2009	Minor	Dapsone	10-13-2009	20	CR	11-17-2009	1	11-17-2009	0	1	CR	CR	NA	NA	NA	100.00
273	202502D	30	Male	03-01-2006	15,000	Minor	No	Yes	03/02/2009	Minor	Azathioprine	02-03-2009	36	PR	05-01-2009	3	07-28-2009	3	6	CR	CR	PR	PR	PR	1.50
274	201429D	45	Female	03-01-2008	15,000	Minor	Yes	No	9	Minor	Dapsone	03-28-2008	1	NR	01-09-1900					NR	NR	NR	NA	NA	100.00
275	203501D	12	Female	02-01-2004	18,000	Minor	No	Yes	14/03/2008	Minor	Azathioprine	03-14-2008	50	CR	05-18-2008	2	05-18-2008	0	2	CR	CR	CR	CR	NA	1.50
276	232037D	24	Female	05-08-2008	5,000	Other	Yes	No	9	Minor	Dapsone	06-10-2008	1	NR	01-09-1900					NR	NR	NR	NR	CR	100.00
277	230700D	9	Female	04-01-2008	17,000	Minor	Yes	No	9	Minor	Dapsone	05-02-2008	1	CR	09-19-2008	5	09-19-2008	0	5	NR	CR	CR	CR	CR	1.50
278	235359D	18	Female	05-01-2008	13,000	Minor	No	Yes	05/08/2008	Minor	Dapsone	08-05-2008	3	NR	01-09-1900					NR	NR	CR	Relapse	NA	100.00
279	235113D	22	Male	04-01-2008	22,000	Minor	Yes	No	9	Minor	Dapsone	05-20-2008	2	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
280	515953B	23	Female	07-01-2008	16,000	Minor	No	Yes	24/04/2012	Minor	Azathioprine	05-29-2012	48	CR	06-12-2012	0	06-12-2012	0	0	CR	CR	CR	CR	NA	1.50
281	589125A	30	Male	11-01-1986	8,000	Minor	No	Yes	09/05/2008	Minor	Dapsone	05-09-2008	262	NR	01-09-1900					NR	CR	NR	NR	NR	100.00
282	235058D	4	Male	03-01-2007	28,000	Minor	No	Yes	13/05/2008	Minor	Dapsone	05-16-2008	15	PR	09-28-2008	5				NR	PR	PR	NA	NA	1.50
283	236543D	3	Female	04-01-2008	11,000	Minor	Yes	No	9	Minor	Dapsone	05-16-2008	2	PR	08-12-2008	3	08-11-2009	12	15	PR	PR	PR	PR	CR	1.50
284	240123D	3	Male	03-01-2008	12,000	Minor	Yes	No	9	Minor	Dapsone	05-27-2008	3	CR	08-12-2008	3	08-12-2008	0	3	CR	CR	NA	CR	CR	1.50
285	242168D	52	Male	03-01-2007	40,000	Minor	No	Yes	20/05/2008	Minor	Dapsone	05-20-2008	15	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
286	258498D	18	Male	12-01-2007	5,000	Minor	No	Yes	16/09/2008	Minor	Dapsone	09-16-2008	10	NR	01-09-1900					NR	NR	NR	NR	NR	100.00
287	267827d	30	Male	07-01-2008	5,000	Minor	No	Yes	08/08/2008	Minor	Dapsone	08-08-2008	1	NR	01-09-1900					NR	NR	NR	NA	NA	100.00
288	268591D	21	Female	04-01-2008	17,000	Minor	No	Yes	12/09/2008	Minor	Dapsone	09-12-2008	5	PR	12-09-2008	3				PR	CR	CR	NA	NA	100.00
289	257313D	8	Male	01-01-2008	4,000	Minor	No	Yes	20/06/2008	Minor	Azathioprine	06-20-2008	6	PR	03-17-2009	9				NR	NR	PR	PR	CR	1.50
290	266200D	74	Male	06-01-2008	10,000	Minor	Yes	No	9	Minor	Dapsone	06-27-2008	1	CR	09-23-2008	3	09-23-2008	0	3	CR	CR	CR	CR	CR	100.00
291	271112D	48	Male	06-01-2007	40,000	Minor	No	Yes	08/07/2008	Minor	Dapsone	07-08-2008	13	NR	01-09-1900					NR	NR	NR	NR	NA	100.00
292	274901D	45	Male	07-01-2007	22,000	Minor	No	Yes	07/05/2010	Minor	Dapsone	05-07-2010	35	PR	01-04-2011	8	06-24-2011	6	14	NR	PR	PR	CR	CR	100.00
293	274429D	7	Female	01-01-2008	10,000	Minor	Yes	No	9	Minor	Dapsone	09-09-2008	8	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
294	279795D	6	Female	06-01-2006	5,000	Minor	No	Yes	05/07/2008	Minor	Dapsone	07-08-2008	26	NR	01-09-1900					NR	NR	NA	NA	NA	1.00
295	279151D	37	Female	07-01-2008	6,000	Minor	Yes	No	9	Minor	Dapsone	09-02-2008	2	CR	11-05-2008	2	11-05-2008	0	2	CR	CR	NA	NA	NA	100.00
296	292586F	21	Female	06-01-2012	15,000	Minor	No	Yes	11/09/2012	Minor	Azathioprine	09-11-2012	3	NR	01-09-1900					NR	NR	NR	NR	NA	1.50
297	132145D	22	Male	11-01-2007	25,000	Minor	No	Yes	21/01/2008	Minor	Azathioprine	01-21-2008	3	NR	01-09-1900					NR	NR	NR	NR	NR	1.30
298	136777D	11	Male	04-01-2007	24,000	Minor	Yes	No	9	Minor	Dapsone	09-13-2007	6	NR	01-09-1900					NR	NR	CR	CR	CR	1.00
299	178298D	2	Female	08-01-2007	10,000	Minor	Yes	No	9	Minor	Azathioprine	09-22-2007	2	NR	01-09-1900					NR	NR	NR	NR	NR	1.50
300	177684D	49	Female	10-01-2004	14,000	Minor	No	Yes	01/02/200	Minor	Azathioprine	02-01-2008	41	PR	04-29-2008	3	09-29-2008	5	8	PR	CR	CR	CR	CR	1.5

Maximum_	mgkgday	Side_Effec	Refractory	Best_Resp	Duration_o	Relapse_w	THIRD_LIN	thirdlineres	THIRD_AG	Stopping_date_	stopdate	Time from	LFD	Best_susta	DURATION	Relapse_A	Splenecton	Splen date	Time from sta	Time from dat	PRESENT_	splenres	startingdate	LFUdate	osstatus
2.00		none	No	CR	30	No	NA		None	19/07/2011	07-19-2011	29	03-26-2013	CR	20	No	No				Remission		03-03-2009	03-26-2013	Alive/LFU
2.00		none	No	CR	18	No	NA		None	08/10/2011	08-10-2011	30	07-17-2012	PR	11	No	No				Persistent		02-13-2009	07-17-2012	Alive/LFU
2.00		none	No	CR	12	No	NA		none	Not known(Lost to followup)			08-17-2010	NA	NA	NA	No				Remission		02-03-2009	08-17-2010	Alive/LFU
100.00		none	No	CR	19	No	NA		none	04/15/2009	04-15-2009	3	11-22-2010	CR	19	No	No				Remission		01-13-2009	11-22-2010	Alive/LFU
1.50		none	Yes	NR	NA	NA	NA		None	NA			06-16-2009	NA	NA	NA	No				Chronic ITP		01-20-2009	06-16-2009	Alive/LFU
1.50		none	No	PR	9	No	NA		none	NA			11-17-2009	NA	NA	NA	No				Persistent		01-16-2009	11-17-2009	Alive/LFU
100.00		none	No	CR	39	No	NA		none	NA			07-31-2012	NA	NA	NA	No				Remission		03-06-2009	07-31-2012	Alive/LFU
1.50		none	No	CR	42	No	NA		none	08/17/2010	08-17-2010	15	09-02-2011	CR	12	No	No				Remission		06-05-2009	09-02-2011	Alive/LFU
2.00		none	No	CR	5	No	NA		none	NA			09-10-2009	NA	NA	NA	No				Remission		01-27-2009	09-10-2009	Alive/LFU
100.00		none	No	CR	9	No	Other	NA	none (Rest	02/15/2012	02-15-2012	37	07-10-2012	NR	NA	Yes	No				Remission		02-13-2009	07-10-2012	Alive/LFU
100.00		none	Yes	NR	NA	NA	AZA	NA	Azathioprir	08/25/2009	08-25-2009	5	08-25-2009	NA	NA	NA	No				Chronic ITP		03-20-2009	08-25-2009	Alive/LFU
1.50		none	Yes	NR	NA	NA	AZA	No	Azathioprir	18/06/2010	06-18-2010	13	01-17-2012	NR	NA	NA	Yes	11-01-12	32	0	Remission	CR	06-02-2009	01-17-2012	Alive/LFU
100.00		none	No	CR	9	No	NA		NA(ReRx [	Ist - 9/4/2010, II	04-09-2010	14	05-22-2013	CR	1	Yes	No				Remission		02-17-2009	05-22-2013	Alive/LFU
100.00		none	No	PR	9	Yes	DDS	No	Re- Daps. :	20/10/2009	10-20-2009	8	07-04-2011	NA	NA	NA	Yes	9999			Remission	CR	02-17-2009	07-04-2011	Alive/LFU
1.50		none	No	CR	21	No	NA		none	09/02/2010	09-02-2010	11	11-04-2011	CR	19	No	No				Remission		10-09-2009	11-04-2011	Alive/LFU
1.50		none(Reint	No	CR	12	No	DDS	No	Re- Daps.(	10/02/2010	02-10-2010	12	02-22-2013	CR	2	Yes	No				Remission		02-20-2009	02-22-2013	Alive/LFU
1.50		none	Yes	NR	NA	NA	AZA	No	AZA X 6 m	29/1/2010	01-29-2010	10	06-03-2011	NR	NA	NA	No				Chronic ITP		03-27-2009	06-03-2011	Alive/LFU
1.50		Cytopenia	No	CR	9	No	DDS	NA	Dapsonex :	10/07/2009	07-10-2009	4	09-29-2009	CR	3	No	No				Remission		03-03-2009	09-29-2009	Alive/LFU
2.00		none	Yes	NR	NA	NA	Splenect	Yes	(splenector	NA(20/1/12)	01-20-2010	11	05-04-2010	NA	NA	NA	Yes	21-09-09	7	8	Remission	CR	03-03-2009	05-04-2010	Alive/LFU
100.00		none	No	PR	6	Yes	AZA	No	Azoran(21/	21/09/2010	09-21-2010	18	12-13-2010	NA	NA	NA	No				Chronic ITP		03-24-2009	12-13-2010	Alive/LFU
1.50		none	No	PR	12	Yes	AZA	No	AZA X 3mt	NA(1/06/2012)	06-01-2012	39	06-01-2012	NR	NA	NA	No				Chronic ITP		03-13-2009	06-01-2012	Alive/LFU
100.00		none	Yes	NR	NA	NA	NA		none	NA			07-14-2009	NR	NA	NA	No				Chronic ITP		03-27-2009	07-14-2009	Alive/LFU
1.50		none	No	CR	9	No	NA		none	15/1/2010(9 mt	01-15-2010	9	03-28-2010	CR	2	No	No				Remission		05-05-2009	03-28-2010	Alive/LFU
1.50		mild compe	No	CR	9	Yes	DDS	Yes	Re - DDS)	20/4/2012	04-20-2012	38	07-06-2012	NR	NA	NA	No				Chronic ITP		03-13-2009	07-06-2012	Alive/LFU
2.30		cytopenia (	Yes	NR	NA	NA	DDS	NA	DDS(18/02	18/02/2011	02-18-2011	24	02-18-2011	NR	NA	NA	No				Chronic ITP		03-13-2009	02-18-2011	Alive/LFU
100.00		Dapsone -	Yes	NR	NA	NA	AZA	Yes	AZA X 3 M	09/06/2009	06-09-2009	2	11-10-2009	CR	2	NA	No				Remission		04-16-2009	11-10-2009	Alive/LFU
75.00		none	No	CR	12	No	NA		none	May-10	05-07-2010	13	04-13-2012	PR	24	No	No				Persistent		04-03-2009	04-13-2012	Alive/LFU
1.00		none	No	CR	7	No	NA		none	26/05/2009	05-26-2009	11	05-26-2009	NA	NA	NA	No				Remission		06-20-2008	05-26-2009	Alive/LFU
150.00	1.90	none	No	CR	34	No	NA		none	NA			01-03-2012	NA	NA	NA	No				Remission		03-20-2009	01-03-2012	Alive/LFU
100.00		none	Yes	NR	NA	NA	AZA	No	AZA(1/06/(	27/05/2011	05-27-2011	22	03-18-2013	NR	NA	NA	No				Persistent		08-04-2009	03-18-2013	Alive/LFU
100.00		none	Yes	NR	NA	NA	AZA	Yes	AZA(11/09	11/09/2009	09-11-2009	4	11-03-2009	NA	NA	NA	No				Persistent		05-15-2009	11-03-2009	Alive/LFU
2.00		none	Yes	NR	NA	NA	AZA	No	AZA(10/11	10/11/2009	11-10-2009	6	04-23-2013	NR	NA	NA	No				Chronic ITP		05-08-2009	04-23-2013	Alive/LFU
1.50		none	Yes	NR	NA	NA	AZA	No	AZA(14/05	October 2009(s	10-04-2009	3	03-26-2013	NR	NA	NA	No				Chronic ITP		07-21-2009	03-26-2013	Alive/LFU
1.50		none	No	CR	9	Yes	AZA	Yes	AZA(19/02	19/02/09	02-19-2010	11	03-26-2013	NA	NA	NA	No				Chronic ITP		03-20-2009	03-26-2013	Alive/LFU
125.00	2.00	none	No	PR	4	Yes	AZA	No	AZA- 6 mts	18/09/09	09-18-2009	6	08-17-2010	NA	NA	NA	Yes	16-04-10	13	4	Remission	CR	03-25-2009	08-17-2010	Alive/LFU
2.00		none	No	CR	24	No	NA		none	14/01/2011	01-14-2011	21	01-14-2011	NA	NA	NA	No				Remission		04-24-2009	01-14-2011	Alive/LFU
2.50		none	Yes	NR	NA	NA	DDS	Yes	DDS(30/06	30/06/2009	06-30-2009	7	11-18-2011	NA	NA	NA	No				Remission		12-01-2008	11-18-2011	Alive/LFU
100.00		none	No	CR	24	No	AZA	Yes	AZA AFTE	Jul-10	05-21-2010	13	05-24-2013	PR	12	Yes	No				Remission		04-21-2009	05-24-2013	Alive/LFU
50.00		none	No	PR	5	NA	NA		NA	9			09-29-2009	NA	NA	NA	No				Persistent		05-01-2009	09-29-2009	Alive/LFU
100.00		none	No	CR	24	No	AZA	No	AZA+Pred(	25/02/2011	02-25-2011	22	04-12-2013	NR	NA	Yes	No				Remission		05-05-2009	04-12-2013	Alive/LFU
100.00		none	No	CR	12	No	NA		none	NA			02-02-2010	NA	NA	NA	No				Remission		06-02-2009	02-02-2010	Alive/LFU
2.00		none	No	CR	24	No	NA		None	NA			06-07-2011	NA	NA	NA	No				Remission		05-15-2009	06-07-2011	Alive/LFU
100.00		none	No	CR	9	Yes	AZA	No	AZAX 2 ye	18/03/2011	03-18-2011	16	03-19-2013	NA	NA	NA	No				Chronic ITP		11-09-2009	03-19-2013	Alive/LFU
1.50		none	Yes	NR	NA	NA	DDS	No	DDSX1 yea	12/06/2009	12-06-2009	6	07-30-2010	NA	NA	NA	No				Chronic ITP		06-12-2009	07-30-2010	Alive/LFU
1.50		none	No	CR	12	No	NA		NA	01/09/1900			10-25-2013	NA	NA	NA	No				Remission		10-09-2012	10-25-2013	Alive/LFU
100.00		none	No	CR	4	NA	NA		NA	NA			11-13-2009	NA	NA	NA	No				Remission		06-30-2009	11-13-2009	Alive/LFU
100.00		none	No	CR	36	No	NA		none	27/7/2012	07-27-2012	38	07-27-2012	NA	NA	NA	No				Remission		06-12-2009	07-27-2012	Alive/LFU
100.00		none	Yes	NR	NA	NA	NA		None	19/06/2009	06-19-2009	17	09-23-2009	NR	NA	NA	Yes	15-09-09	20	0	Remission	CR	01-22-2008	09-23-2009	Alive/LFU
1.50		none	No	CR	48	No	NA		none	NA			04-30-2013	NA	NA	NA	No				Remission		08-11-2009	04-30-2013	Alive/LFU
100.00		none	No	CR	12	Yes	AZA	No	AZAX 1 ye	09/03/2010	03-09-2010	10	04-01-2011	NA	NA	NA	Yes	23-03-11	22	0	Remission	CR	05-26-2009	04-01-2011	Alive/LFU
2.50		none	Yes	NR	NA	NA	AZA	No	AZA X 1 ye	12/01/2010	01-12-2010	7	08-18-2012	NA	NA	NA	Yes	16-04-12	35	4	Remission	CR	06-12-2009	08-18-2012	Alive/LFU
2.00		none	No	CR	36	No	NA		None	12/11/2009	11-12-2009	3	10-05-2012	CR	12	No	No				Remission		07-31-2009	10-05-2012	Alive/LFU
1.50		none	No	CR	17	No	NA		none	NA			05-24-2013	NA	NA	NA	No				Remission		11-08-2009	05-24-2013	Alive/LFU
100.00		none	No	PR	11	Yes	AZA	No	AZAx6mts,	19/02/2010	02-19-2010	7	04-10-2013	NA	NA	NA	Yes	09-08-10	13	33	Chronic ITI	NR	07-14-2009	04-10-2013	Alive/LFU
100.00		none	Yes	NR	NA	NA	AZA	No	AZA X 6 M	22/02/2013	02-22-2013	8	07-05-2013	NA	NA	NA	Yes	03-07-13	13	0	Remission	CR	06-22-2012	07-05-2013	Alive/LFU
1.80		none	Yes	NR	NA	NA	NA		NONE	NA			05-24-2010	NA	NA	NA	No				Chronic ITP		10-30-2009	05-24-2010	Alive/LFU
100.00		none	No	CR	11	No	NA		NA	07/09/2010	07-09-2010	11	04-05-2013	CR	24	Yes	No				Remission		08-04-2009	04-05-2013	Alive/LFU
2.00		none	Yes	NR	NA	NA	AZA	No	AZA(3mts)	NA			01-08-2013	NA	NA	NA	No				Persistent		08-04-2009	01-08-2013	Alive/LFU
1.50		none	Yes	NR	NA	NA	NA		NA	NA			03-02-2010	NA	NA	NA	No				Chronic ITP		09-08-2009	03-02-2010	Alive/LFU
100.00		none	No	CR	24	No	NA		none	13/04/13	04-13-2013	44	04-13-2013	NA	NA	NA	No				Remission		09-04-2009	04-13-2013	Alive/LFU
2.00		none	Yes	NR	NA	No	DDS	No	DDS(09/04	09/04/2010	04-09-2010	8	04-09-2010	NA	NA	NA	No				Chronic ITP		08-10-2009	04-09-2010	Alive/LFU
1.80		none	No	PR	16	Yes	NA		none	Jan-11			05-17-2013	NA	NA	NA	No				Chronic ITP		09-01-2009	05-17-2013	Alive/LFU
100.00		none	Yes	NR	NA	NA	AZA	No	AZA(09/11	29/09/2011	09-29-2011	26	04-19-2013	NA	NA	NA	Yes	30-07-12	36	9	Remission	CR	08-21-2009	04-19-2013	Alive/LFU
2.00		none	No	CR	6	Yes	DDS	Yes	DDS X 1 Y	24/09/2010	09-24-2010	16	06-14-2011	NA	NA	NA	No				Persistent		06-05-2009	06-14-2011	Alive/LFU
2.80		DDS RASH	No	PR	5	No	NA		NONE	NA			03-30-2010	NA	NA	NA	No				Persistent		10-23-2009	03-30-2010	Alive/LFU

1.50		none	No	CR		15	No	NA		NONE	NA			01-21-2011	NA	NA		NA	No					Remission	08-10-2009	01-21-2011	Alive/LFU
1.00		none	No	CR		12	No	NA		none	17/09/2010	09-17-2010	12	07-17-2011	CR		12	No	No					Remission	09-20-2009	07-17-2011	Alive/LFU
100.00		Agranulocy	Yes	NR	NA		NA	AZA	No	AZAX9 mn	29/10/2009	10-29-2009	2	08-24-2010	NA	NA		NA	Yes	26-05-10	9	3	Remission	CR	08-28-2009	08-24-2010	Alive/LFU
2.00		Skin rash x	No	CR		24	Yes	NA		NA	04/10/2013	10-04-2013	47	10-04-2013	NA	NA		NA	No					Remission	11-28-2009	10-04-2013	Alive/LFU
2.50		none	Yes	NR	NA		NA	DDS	Yes	DDSX 1 1/	20/04/2010	04-20-2010	7	05-25-2012	NA	NA		NA	No					Chronic ITP	09-25-2009	05-25-2012	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZAX 9 mt	13/07/2010	07-13-2010	9	04-12-2013	NR	NA		NA	Yes	28-03-11	18	25	Chronic ITI	NR	10-10-2009	04-12-2013	Alive/LFU
2.00		Borderline	No	CR		12	No	NA		none	NA			03-22-2011	NA	NA		NA	No					Remission	02-07-2010	03-22-2011	Alive/LFU
2.50		Borderline	No	PR		6	No	DDS	Yes	DDS X 1 Y	13/05/2011	05-13-2011	14	01-25-2012	NA	NA		NA	No					Remission	03-09-2010	01-25-2012	Alive/LFU
1.50		none	Yes	NR	NA		NA	DDS	No	DDS x 1 ye	13/04/2010	04-13-2010	4	02-29-2012	NR	NA		NA	No					Chronic ITP	12-29-2009	02-29-2012	Alive/LFU
1.50		none	Yes	NR	NA		NA	DDS	No	DDS X 3 m	30/08/2011	08-30-2011	19	11-01-2011	NA	NA		NA	No					Chronic ITP	02-02-2010	11-01-2011	Alive/LFU
1.50		none	Yes	NR	NA		NA	AZA	No	AZA X 1 ye	22/1/2010	01-22-2010	18	12-24-2010	NA	NA		NA	No					Chronic ITP	08-01-2008	12-24-2010	Alive/LFU
2.50		none	No	CR		36	No	NA		None	NA			12-13-2012	NA	NA		NA	No					Remission	12-15-2009	12-13-2012	Alive/LFU
100.00		none	No	PR		3	No	NA		none	20/02/2004	02-20-2004	3	01-05-2010	PR		72	NA	NA					Persistent	NA	11-28-2003	01-05-2010	Alive/LFU
2.00		none	Yes	NR	NA		NA	NA		none	NA(lost to f/up)			03-09-2010	NA	NA		NA	No					Persistent		09-20-2009	03-09-2010	Alive/LFU
1.50		none	Yes	NR	NA		NA	NA		none	9			03-09-2010	NA	NA		NA	No					Chronic ITP		10-27-2009	03-09-2010	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	NA	AZA X 1 m	30/03/2010	03-30-2010	5	04-13-2010	NA	NA		NA	No					Chronic ITP		10-30-2009	04-13-2010	Alive/LFU
100.00		none	No	PR		3	Yes	AZA	NA	AZA X 1 m	12/02/2010	11-02-2010	12	11-02-2010	NR	NA		NA	No					Chronic ITP		11-03-2009	11-02-2010	Alive/LFU
100.00		none	No	CR		6	Yes	AZA	Yes	Aza x1 yR-	01/03/2011	03-01-2011	14	06-04-2013	NA	NA		NA	No					Remission		01-08-2010	06-04-2013	Alive/LFU
3.00		DDS Hemo	Yes	NR	NA		NA	AZA	Yes	AZA X 2 1/	02/07/2010	07-02-2010	7	05-30-2013	NA	NA		NA	No					Persistent		11-24-2009	05-30-2013	Alive/LFU
2.00		none	No	CR		36	No	NA		NA	11/06/2013	06-11-2013	39	06-11-2013	NA	NA		NA	No					Persistent		03-30-2010	06-11-2013	Alive/LFU
100.00		subclinical	No	PR		3	Yes	AZA	No	AZA X 1 yr	20/07/2010	07-20-2010	6	06-28-2011	NA	NA		NA	No					Chronic ITP		01-15-2010	06-28-2011	Alive/LFU
100.00		none	Yes	NR	NA		NA	Splenect	No	Splenecton	05/04/2010	05-04-2010	4	04-26-2012	NA	NA		NA	Yes	05-04-10	3	25	Chronic ITI	NR	01-15-2010	04-26-2012	Alive/LFU
100.00		none	No	CR		12	No	DDS	Yes	Re Rx DDS	11/09/2009	09-11-2011	43	12-03-2013	CR		6	Yes	No					Persistent		02-15-2008	12-03-2013	Alive/LFU
2.50		none	No	CR		12	No	NA		none	17/05/2011	05-17-2011	15	10-04-2011	CR		6	No	No					Remission		02-19-2010	10-04-2011	Alive/LFU
100.00		none	No	CR		5	No	NA		none	NA			06-22-2010	NA	NA		NA	No					Remission		01-29-2010	06-22-2010	Alive/LFU
100.00		none	No	PR		4	No	NA		none	NA			06-28-2010	NA	NA		NA	No					Persistent		01-29-2010	06-28-2010	Alive/LFU
2.00		none	No	CR		6	Yes	AZA	No	ct DDS-CR	29/05/2012	05-29-2012	28	02-26-2013	NR	NA		NA	Yes	19-11-12	34	3	Remission	CR	01-29-2010	02-26-2013	Alive/LFU
100.00		none	No	CR		24	No	NA		none	30/03/2012	03-30-2012	25	06-28-2012	CR		3	No	No					Remission		03-05-2010	06-28-2012	Alive/LFU
100.00		Hemolysis	Yes	NR	NA		NA	AZA	No	AZA X 9 m	NA			02-11-2011	NA	NA		NA	No					Chronic ITP		02-03-2010	02-11-2011	Alive/LFU
2.00		none	No	CR		10	Yes	AZA	Yes	AZA X 6 m	11/02/2011	02-11-2011	12	08-05-2011	NA	NA		NA	No					Remission		02-12-2010	08-05-2011	Alive/LFU
2.00		none	No	CR		12	No	NA		none	07/06/2010	06-07-2011	11	03-26-2013	CR		2	Yes	No					Remission		07-02-2010	03-26-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	NA	AZA @ LF	14/05/2010	05-14-2010	4	05-14-2010	NA	NA		NA	No					Chronic ITP		01-29-2010	05-14-2010	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 6mt	NA			12-21-2010	NA	NA		NA	No					Chronic ITP		03-26-2010	12-21-2010	Alive/LFU
2.50		none	No	CR		30	No	NA		NA	05/03/2013	03-05-2013	35	03-05-2013	NA	NA		NA	No					Remission		04-23-2010	03-05-2013	Alive/LFU
1.50		none	No	CR		16	No	NA		none	24/02/2012	02-24-2012	19	07-05-2013	CR		7	Yes	No					Remission		08-03-2010	07-05-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	AZA	Yes	AZA X 2 1/	07/09/2010	09-07-2010	4	07-02-2013	NA	NA		NA	No					Persistent		05-04-2010	07-02-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	DDS	Yes	DDS X 1/2	18/01/2011	01-18-2011	10	05-28-2013	NA	NA		NA	No					Chronic ITP		04-05-2010	05-28-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	Other	Yes	DEX+AZAI	25/01/2011	01-25-2011	3	08-21-2011	NA	NA		NA	No					Remission		10-19-2010	08-21-2011	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 1 yr	01/06/2010	10-08-2010	7	05-17-2011	NA	NA		NA	No					Chronic ITP		03-10-2010	05-17-2011	Alive/LFU
100.00		DAPSONE	No	CR		5	No	NA		NA	21/07/2010	07-21-2010	1	09-16-2010	CR		2	No	No					Remission		06-22-2010	09-16-2010	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 6mt	14/09/2010	09-14-2010	3	04-05-2011	NA	NA		NA	No					Chronic ITP		06-08-2010	04-05-2011	Alive/LFU
75.00		none	No	CR		24	No	NA		NA	11/05/2012	05-11-2012	23	05-11-2012	NA	NA		NA	No					Remission		07-02-2010	05-11-2012	Alive/LFU
1.50		none	Yes	NR	NA		NA	DDS	Yes	DDS X 1 Y	03/09/2010	09-03-2010	4	10-01-2013	NA	NA		NA	No					Remission		05-11-2010	10-01-2013	Alive/LFU
2.50		none	Yes	NR	NA		NA	NA		NA	NA			09-14-2010	NA	NA		NA	No					Chronic ITP		07-01-2010	09-14-2010	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	Yes	AZA X 21 r	09/11/2010	11-09-2010	4	06-25-2013	NR	NA		NA	No					Chronic ITP		07-21-2010	06-25-2013	Alive/LFU
150.00	3.00	none	No	CR		12	Yes	AZA	NA	AZA @ LF	16/03/2012	03-16-2012	21	03-16-2012	NR	NA		NA	No					Chronic ITP		07-06-2010	03-16-2012	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	Yes	AZA @ 6 n	14/12/2010	12-14-2010	4	04-12-2012	NA	NA		NA	Yes	06-10-11	14	6	Persistent	PR	08-03-2010	04-12-2012	Alive/LFU
100.00		none	No	CR		6	No	NA		NA	NA			05-10-2011	NA	NA		NA	No					Remission		07-30-2010	05-10-2011	Alive/LFU
1.50		none	Yes	NR	NA		NA	DDS	No	DDS - NR	09/02/2011	02-09-2011	5	09-21-2012	NA	NA		NA	No					Chronic ITP		09-14-2010	09-21-2012	Alive/LFU
100.00		none	No	CR		24	No	NA		NA	NA			11-21-2012	NA	NA		NA	No					Remission		10-06-2011	11-21-2012	Alive/LFU
2.00		none	No	CR		24	No	NA		NA	01/06/2012	06-01-2012	23	06-01-2012	NA	NA		NA	No					Remission		07-23-2010	06-01-2012	Alive/LFU
2.00		none	No	PR		5	Yes	AZA	No	AZA X 6 m	17/06/2011	06-17-2011	12	01-02-2012	NR	NA		NA	No					Chronic ITP		07-02-2010	01-02-2012	Alive/LFU
3.00		none	Yes	NR	NA		NA	NA		NA	NA			01-03-2012	NA	NA		NA	No					Chronic ITP		07-06-2010	01-03-2012	Alive/LFU
2.50		none	No	CR		24	No	NA		NA	26/03/2013	03-26-2013	42	03-26-2013	NA	NA		NA	No					Remission		10-19-2009	03-26-2013	Alive/LFU
2.50		none	No	CR		24	No	NA		NA	07/05/2013	05-07-2013	34	05-07-2013	NA	NA		NA	No					Remission		07-24-2010	05-07-2013	Alive/LFU
2.00		none	No	PR		18	No	NA		NA	NA			08-20-2013	NA	NA		NA	No					Persistent		08-03-2010	08-20-2013	Alive/LFU
100.00		none	No	PR		4	Yes	AZA	No	AZA X 6 m	24/05/2011	05-24-2011	4	09-23-2011	NR	NA		NA	No					Chronic ITP		01-28-2011	09-23-2011	Alive/LFU
1.50		none	No	CR		12	No	NA		NA	16/12/2011	12-16-2011	16	12-16-2011	NA	NA		NA	No					Remission		08-24-2010	12-16-2011	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	aZA X 1 ye	18/03/2011	03-18-2011	8	05-29-2012	NA	NA		NA	No					Chronic ITP		07-30-2010	05-29-2012	Alive/LFU
1.50		none	No	CR		24	No	NA		na	30/10/2012	10-30-2012	26	08-20-2013	CR		12	No	No					Remission		09-10-2010	08-20-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	AZA	No	AZA X 6 m	11/03/2011	03-11-2011	6	09-02-2011	NA	NA		No	No					Chronic ITP		08-30-2010	09-02-2011	Alive/LFU
1.50		none	No	CR		18	No	AZA	No	AZAX 4 Mo	26/06/2012	06-26-2012	23	07-09-2013	NA	NA		NA	No					Chronic ITP		08-20-2010	07-09-2013	Alive/LFU
2.50		none	No	CR		12	Yes	NA		NA	NA			07-05-2013	NA	NA		NA	No					Chronic ITP		07-29-2011	07-05-2013	Alive/LFU
2.00		none	No	CR		9	No	NA		na	na			08-03-2012	NA	NA		NA	No					Remission		05-29-2011	08-03-2012	Alive/LFU
100.00		none	No	CR		9	No	NA		NA	04/03/2008	03-04-2008	9	10-22-2013	CR		18	Yes	No					Persistent		06-19-2007	10-22-2013	Alive/LFU
100.00		none	No	PR		6	Yes	AZA	No	AZA X 6 m	31/05/2011	05-31-2011	7	06-25-2013	NA	NA		NA	No					Remission		11-09-2010	06-25-2013	Alive/LFU

2.50		none	Yes	NR	NA		NA	NA		NA	26/08/2011	08-26-2011	7	08-26-2011	NA	NA		NA	No					Chronic ITP	02-11-2011	08-26-2011	Alive/LFU
2.50		none	Yes	NR	NA		NA	NA		NA	01/09/1900			10-25-2013	NA	NA		NA	No					Chronic ITP	02-26-2013	10-25-2013	Alive/LFU
2.50		hair loss	No	CR		24	No	NA		NA	18/09/2012	09-18-2012	19	05-31-2013	CR		6	No	No					Remission	03-04-2011	05-31-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 6 M	13/05/2011	05-13-2011	5	11-18-2011	NA	NA		NA	No					Chronic ITP	12-17-2010	11-18-2011	Alive/LFU
75.00	1.50	none	Yes	NR	NA		NA	AZA	No	AZA X 6 M	01/05/2012	05-01-2012	18	01-15-2013	NA	NA		NA	No					Chronic ITP	10-26-2010	01-15-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	DDS	Yes	DDS X 2 Y	08/04/2011	04-08-2011	5	07-05-2013	NA	NA		NA	No					Remission	11-09-2010	07-05-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	Other	No	CYCLOSP	27/05/2011	05-27-2011	7	10-07-2011	NA	NA		NA	No					Chronic ITP	10-29-2010	10-07-2011	Alive/LFU
1.50		none	No	CR		18	No	NA		NA	27/06/2011	06-27-2011	8	06-27-2011	NA	NA		NA	No					Chronic ITP	11-09-2010	06-27-2011	Alive/LFU
1.50		none	No	CR		27	No	DDS	No	DDS @ RL	04/01/2013	04-01-2013	30	07-05-2013	NR	NA		Yes	No					Remission	10-08-2010	07-05-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	Other	No	Eltrombopa	21/01/2011	01-21-2011	5	08-13-2013	NA	NA		NA	No					Chronic ITP	08-13-2010	08-13-2013	Alive/LFU
150.00	2.50	Meth-hemc	Yes	NR	NA		NA	NA		NA	05/04/2011	05-04-2011	9	11-08-2011	NA	NA		NA	NA					Chronic ITI	NA	08-17-2010	11-08-2011	Alive/LFU
1.50		none	No	CR		18	No	NA		NA	07/10/2012	07-10-2012	18	11-06-2012	CR		3	NA	No					Remission		01-11-2011	11-06-2012	Alive/LFU
100.00		none	No	CR		8	Yes	DDS	Yes	ReRx DDS	NA			10-08-2013	NA	NA		NA	No					Remission		04-26-2011	10-08-2013	Alive/LFU
1.50		none	No	CR		24	No	NA		NA	04/10/2013	04-10-2013	24	10-04-2013	NA	NA		NA	No					Remission		04-15-2011	10-04-2013	Alive/LFU
100.00		none	No	CR		15	No	NA		NA	11/05/2013	05-11-2013	15	10-11-2013	PR		5	Yes	No					Chronic ITP		03-02-2012	10-11-2013	Alive/LFU
2.50		Grade I cyt	No	CR		18	No	NA		NA	12/04/2013	04-12-2013	28	10-11-2013	CR		6	No	No					Remission		01-07-2011	10-11-2013	Alive/LFU
2.00		none	No	CR		24	No	NA		NA	01/07/2011	07-01-2011	16	10-14-2013	CR		28	No	No					Remission		03-06-2010	10-14-2013	Alive/LFU
2.50		none	Yes	NR	NA		NA	AZA	No	dds x 2 wk	NA			10-12-2012	NA	NA		NA	No					Chronic ITP		03-18-2011	10-12-2012	Alive/LFU
2.00		Grade I cyt	Yes	NR	NA		NA	Other	No	Mycept x 6	20/09/2011	09-20-2011	6	07-20-2012	NA	NA		NA	No					Chronic ITP		03-15-2011	07-20-2012	Alive/LFU
2.50		none	Yes	NR	NA		NA	DDS	No	DDS X 6 m	08/07/2011	07-08-2011	5	12-04-2012	NA	NA		NA	No					Chronic ITP		02-04-2011	12-04-2012	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 3 M	02/08/2011	08-02-2011	5	10-04-2012	NA	NA		NA	No					Chronic ITP		03-04-2011	10-04-2012	Alive/LFU
2.00		none	Yes	NR	NA		NA	DDS	No	DDS X 5 m	29/07/2011	07-29-2011	5	12-23-2011	NA	NA		NA	No					Chronic ITP		03-04-2011	12-23-2011	Alive/LFU
2.50		none	Yes	NR	NA		NA	DDS	Yes	DDS X 1 1/	17/1/2012	01-17-2012	13	08-09-2013	NA	NA		NA	No					Persistent		01-04-2011	08-09-2013	Alive/LFU
2.50		none	No	PR		5	Yes	DDS	Yes	DDS X 1 1/	25/12/2011	12-25-2011	10	08-30-2013	NA	NA		NA	No					Chronic ITP		02-24-2011	08-30-2013	Alive/LFU
2.00		none	Yes	NR	NA		NA	AZA	No	AZA X 1 YI	17/05/2011	05-17-2011	5	09-30-2013	NA	NA		NA	Yes	08-08-12	20	14	Chronic ITI	NR	12-21-2010	09-30-2013	Alive/LFU
100.00		none	No	CR		12	Yes	DDS	Yes	Re Rx DDS	21/06/2013(AZ/	06-21-2013	24	10-15-2013	NA	NA		NA	No					Remission		06-29-2011	10-15-2013	Alive/LFU
2.50		none	No	CR		24	No	NA		NA	NA			08-16-2013	NA	NA		NA	No					Remission		08-26-2011	08-16-2013	Alive/LFU
100.00		none	No	CR		4	Yes	AZA	No	AZA X 6 m	NA			10-25-2013	NA	NA		NA	No					Chronic ITP		10-10-2011	10-25-2013	Alive/LFU
1.50		none	No	CR		12	No	NA		NA	21/12/12	12-21-2012	16	09-03-2013	CR		9	No	No					Remission		08-16-2011	09-03-2013	Alive/LFU
150.00	2.50	NONE	No	CR		3	Yes	AZA	Yes	AZA X 6 r	25/01/2013	01-25-2013	8	07-23-2013	NA	NA		NA	No					Remission		05-18-2012	07-23-2013	Alive/LFU
2.50		none	Yes	NR	NA		NA	DDS	Yes	DDS X 9 m	04/08/2012	04-08-2012	10	10-04-2013	NA	NA		NA	No					Chronic ITP		06-17-2011	10-04-2013	Alive/LFU
150.00	1.70	none	No	PR		22	No	NA		NA	NA			07-19-2013	NA	NA		NA	No					Persistent		06-01-2011	07-19-2013	Alive/LFU
150.00	2.00	none	Yes	NR	NA		NA	NA		NA	NA			07-24-2013	NA	NA		NA	No					Remission		02-25-2011	07-24-2013	Alive/LFU
150.00	2.00	none	Yes	NR	NA		NA	AZA	No	AZA X 1 YI	27/08/2013	08-27-2013	30	08-27-2013	NA	NA		NA	No					Remission		03-04-2011	08-27-2013	Alive/LFU
2.00		none	Yes	NR	NA		NA	DDS	Yes	DDS X 1 Y	06/05/2011	05-06-2011	3	07-16-2013	NA	NA		NA	Yes	07-07-13	29	0	Remission	CR	02-11-2011	07-16-2013	Alive/LFU
100.00		none	No	CR		9	No	NA		NA	NA			05-06-2012	NA	NA		NA	No					Remission		08-23-2011	05-06-2012	Alive/LFU
2.00		none	No	CR		12	No	NA		NA	NA			07-07-2013	NA	NA		NA	No					Remission		04-03-2012	07-07-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA x 9 m	01/05/2012	05-01-2012	4	03-26-2013	NA	NA		NA	No					Chronic ITP		12-27-2011	03-26-2013	Alive/LFU
1.50		none	No	CR		3	No	NA		NA	NA			07-10-2012	NA	NA		NA	No					Remission		01-10-2012	07-10-2012	Alive/LFU
2.50		none	Yes	NR	NA		NA	NA		NA	NA			12-20-2011	NA	NA		NA	No					Chronic ITP		08-05-2011	12-20-2011	Alive/LFU
1.50		none	Yes	NR	NA		NA	DDS	No	DDS X 1 Y	20/03/2012	03-20-2012	4	07-05-2013	NA	NA		NA	No					Chronic ITP		12-01-2011	07-05-2013	Alive/LFU
2.50		none	Yes	NR	NA		NA	Splenect	No	Post splen	NA			03-15-2013	NA	NA		NA	Yes	15-05-12	10	10	Remission	CR	08-02-2011	03-15-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 1 1/	02/12/2011	12-02-2011	7	08-30-2013	NA	NA		NA	No					Chronic ITP		04-26-2011	08-30-2013	Alive/LFU
100.00		DDS Induc	No	CR		6	Yes	AZA	No	AZAX 6 mt	05/06/2011	06-05-2011	7	09-27-2013	NA	NA		NA	Yes	03-06-13	31	4	Persistent	PR	11-04-2010	09-27-2013	Alive/LFU
125.00	2.00	none	No	CR		12	Yes	AZA	Yes	AZAX 1 ye	16/10/2012	10-16-2012	18	07-19-2013	NA	NA		NA	No					Remission		04-29-2011	07-19-2013	Alive/LFU
1.50		none	No	CR		8	Yes	DDS	No	DDS X 1 m	01/05/2012	01-05-2012	10	09-25-2012	NA	NA		NA	No					Chronic ITP		03-25-2011	09-25-2012	Alive/LFU
2.50		none	Yes	NR	NA		NA	Other	No	Added Puls	NA			08-23-2013	NA	NA		NA	No					Chronic ITP		03-22-2013	08-23-2013	Alive/LFU
2.00		none	No	CR		12	No	NA		na	na			03-16-2012	NA	NA		NA	No					Chronic ITP		05-17-2011	03-16-2012	Alive/LFU
2.00		none	Yes	NR	NA		NA	AZA	No	AZA X 6 m	09/09/2011	09-09-2011	5	03-13-2012	NA	NA		NA	No					Chronic ITP		04-14-2011	03-13-2012	Alive/LFU
150.00	3.00	none	Yes	NR	NA		NA	NA		NA	NA			07-12-2012	NA	NA		NA	No					Chronic ITP		04-12-2011	07-12-2012	Alive/LFU
1.50		none	Yes	NR	NA		NA	AZA	No	AZA X 1 ye	09/08/2011	09-08-2011	5	06-19-2012	NA	NA		NA	No					Chronic ITP		04-05-2011	06-19-2012	Alive/LFU
2.50		none	No	CR		18	No	NA		NA	22/01/2013	01-22-2013	21	08-19-2013	CR		8	No	No					Remission		04-19-2011	08-19-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 6 m	13/01/2012	01-13-2012	5	04-23-2013	NA	NA		NA	Yes	01-10-12	14	7	Persistent	PR	08-04-2011	04-23-2013	Alive/LFU
2.50		none	No	PR		7	Yes	DDS	Yes	dds X 4 mr	19/06/2012	06-19-2012	8	10-09-2012	NA	NA		NA	No					Remission		10-18-2011	10-09-2012	Alive/LFU
2.00		none	Yes	NR	NA		NA	DDS	Yes	DDS X 1 1/	24/03/2011	03-24-2012	2	08-16-2013	NA	NA		NA	No					Remission		01-24-2012	08-16-2013	Alive/LFU
1.50		Hemolysis	No	PR		2	No	AZA	No	AZA X 1 YI	01/05/2012	07-27-2012	10	07-26-2013	NA	NA		NA	No					Chronic ITP		10-07-2011	07-26-2013	Alive/LFU
1.50		NONE	Yes	NR	NA		NA	NA		NA	NA			10-01-2012	NA	NA		NA	Yes	23-11-12	11	5	Remission	CR	01-10-2012	04-26-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	Splenect	No	Splenecton	02/10/2012	10-02-2012	3	08-30-2013	NA	NA		NA	Yes	06-02-13	7	7	Remission	CR	07-12-2012	08-30-2013	Alive/LFU
2.50		none	No	CR		18	No	NA		NA	NA			07-09-2013	NA	NA		NA	No					Remission		12-16-2011	07-09-2013	Alive/LFU
100.00		none	No	CR		18	No	NA		NA	NA			09-20-2013	NA	NA		NA	No					Remission		01-13-2012	09-20-2013	Alive/LFU
1.50		none	No	CR		18	No	NA		NA	NA			08-23-2013	NA	NA		NA	No					Remission		02-14-2012	08-23-2013	Alive/LFU
2.00		none	No	CR		6	Yes	NA		NA(ReRx /	NA			09-27-2013	NA	NA		NA	No					Remission		04-21-2012	09-27-2013	Alive/LFU
2.50		none	Yes	NR	NA		NA	Splenect	No	Splenecton	NA			07-09-2013	NA	NA		NA	Yes	07-01-13	14	6	Chronic ITI	NR	11-04-2011	07-09-2013	Alive/LFU
2.00		none	No	CR		4	Yes	AZA	Yes	AZA X 1 YI	09/12/2011	12-09-2011	4	12-28-2012	NA	NA		NA	No					Persistent		08-12-2011	12-28-2012	Alive/LFU
2.50		none	No	CR		18	Yes	DDS	NA	DDS @ LF	04/10/2013	10-04-2013	25	12-06-2013	NA	NA		NA	No					Chronic ITP		09-16-2011	12-06-2013	Alive/LFU
1.50		none	No	CR		3	Yes	NA		NA	9			10-04-2013	NA	NA		NA	No					Remission		08-16-2011	10-04-2013	Alive/LFU

100.00	none	No	CR		5	No	NA		NA	9			02-14-2012	NA	NA	NA	No				Persistent	09-20-2011	02-14-2012	Alive/LFU
2.50	none	Yes	NR	NA		NA	NA		NA	9			02-16-2012	NA	NA	NA	No				Chronic ITP	09-06-2011	02-16-2012	Alive/LFU
1.50	none	Yes	NR	NA		NA	NA		NA	9			09-04-2012	NA	NA	NA	No				Chronic ITP	10-04-2011	09-04-2012	Alive/LFU
1.50	none	Yes	NR	NA		NA	AZA	No	AZA X 9 m	04/01/2013	01-04-2013	13	10-01-2013	NA	NA	NA	No				Chronic ITP	12-16-2011	10-01-2013	Alive/LFU
100.00	none	No	PR		18	No	NA		NA	9			10-01-2013	NA	NA	NA	No				Chronic ITP	10-04-2011	10-01-2013	Alive/LFU
2.00	none	Yes	NR	NA		NA	NA		NA	9			09-10-2012	NA	NA	NA	No				Chronic ITP	10-25-2011	09-10-2012	Alive/LFU
2.50	none	No	CR		18	No	NA		NA	9			06-20-2013	NA	NA	NA	No				Remission	01-17-2012	06-20-2013	Alive/LFU
2.50	none	Yes	NR	NA		NA	NA		NA	9			08-17-2012	NA	NA	NA	No				Chronic ITP	10-19-2011	08-17-2012	Alive/LFU
100.00	none	No	PR		18	Yes	NA		NA	9			10-15-2013	NA	NA	NA	No				Chronic ITP	01-31-2012	10-15-2013	Alive/LFU
1.00	none	No	CR		18	No	NA		NA	9			10-27-2013	NA	NA	NA	No				Remission	01-27-2012	10-27-2013	Alive/LFU
100.00	none	No	PR		12	No	NA		NA	NA			10-08-2013	NA	NA	NA	No				Persistent	06-20-2012	10-08-2013	Alive/LFU
100.00	none	No	CR		5	No	NA		NA	NA			08-03-2012	NA	NA	NA	No				Remission	02-24-2012	08-03-2012	Alive/LFU
1.50	none	No	CR		12	No	NA		na	na			05-10-2013	NA	NA	NA	No				Remission	02-10-2012	05-10-2013	Alive/LFU
2.00	none	No	PR		1	No	NA		NA	NA			07-02-2013	NA	NA	NA	No				Persistent	01-31-2012	07-02-2013	Alive/LFU
2.00	none	No	PR		3	Yes	DDS	No	DDS X 5 m	26/03/2013	03-26-2013	14	08-13-2013	NA	NA	NA	Yes	18-09-13	20	1	Remission CR	02-07-2012	10-11-2013	Alive/LFU
1.50	Grade 1 cy	No	PR		1	No	NA		NA	NA			08-30-2013	NA	NA	NA	No				Persistent	02-14-2013	08-30-2013	Alive/LFU
2.50	Grade 1 cy	Yes	NR	NA		NA	DDS	No	DDS X 1 y	04/09/2012	09-04-2012	-8	08-23-2013	NA	NA	NA	No				Chronic ITP	05-11-2013	08-23-2013	Alive/LFU
1.50	none	No	CR		7	No	NA		NA	NA			10-04-2013	NA	NA	NA	No				Remission	02-21-2013	10-04-2013	Alive/LFU
2.50	none	Yes	NR	NA		NA	DDS	Yes	DDS X 1 y	10/07/2012	07-10-2012	5	07-06-2013	NA	NA	NA	No				Remission	02-24-2012	07-06-2013	Alive/LFU
2.50	none	No	CR		5	No	NA		NA	NA			09-11-2012	NA	NA	NA	No				Remission	03-16-2012	09-11-2012	Alive/LFU
2.50	None	No	PR		12	No	NA		NA	NA			06-07-2013	NA	NA	NA	No				Persistent	03-20-2012	06-07-2013	Alive/LFU
1.50	none	No	CR		12	No	NA		NA	NA			10-01-2013	NA	NA	NA	No				Remission	04-13-2012	10-01-2013	Alive/LFU
1.50	NONE	Yes	NR	NA		NA	AZA	NA	AZA @LFI	14/09/2012	09-14-2012	4	09-14-2012	NA	NA	NA	No				Chronic ITP	05-08-2012	09-14-2012	Alive/LFU
1.50	none	No	PR		12	No	NA		NA	NA			07-12-2013	NA	NA	NA	No				Chronic ITP	05-01-2012	07-12-2013	Alive/LFU
2.00	none	Yes	NR	NA		NA	NA		NA	9			10-29-2013	NA	NA	NA	No				Chronic ITP	02-08-2013	10-29-2013	Alive/LFU
1.50	none	Yes	NR	NA		No	DDS	No	DDS X 9 m	14/06/2012	06-14-2012	3	02-12-2013	NA	NA	NA	No				Chronic ITP	03-30-2012	02-12-2013	Alive/LFU
1.50	none	Yes	NR	NA		NA	DDS	Yes	DDS X 1 Y	20/07/2012	07-20-2012	3	09-27-2013	NA	NA	NA	No				Remission	04-10-2012	09-27-2013	Alive/LFU
1.50	none	No	CR		6	No	NA		NA	NA			12-11-2012	NA	NA	NA	No				Remission	06-15-2012	12-11-2012	Alive/LFU
3.00	none	Yes	NR	NA		NA	NA		NA	NA			09-30-2013	NA	NA	NA	No				Chronic ITP	05-25-2012	09-30-2013	Alive/LFU
2.00	none	No	CR		3	No	NA		NA	NA			07-23-2012	NA	NA	NA	No				Remission	01-31-2012	07-23-2012	Alive/LFU
2.50	none	Yes	NR	NA		NA	DDS	No	DDS X 9 m	02/10/2012	10-02-2012	4	09-24-2013	NA	NA	NA	Yes	27-07-13	14	2	Remission CR	05-25-2012	09-24-2013	Alive/LFU
100.00	none	No	CR		14	Yes	AZA	NA	AZA @LFI	06/09/2013	09-06-2013	16	10-04-2013	NA	NA	NA	No				Chronic ITP	05-04-2012	10-04-2013	Alive/LFU
2.50	none	No	CR		12	Yes	DDS	Yes	DDS+Pred	06/09/2013	09-06-2013	15	10-04-2013	NA	NA	NA	No				Persistent	06-15-2012	10-04-2013	Alive/LFU
1.50	none	Yes	NR	NA		NA	DDS	No	DDS X 6 m	11/27/2012	11-27-2012	5	04-10-2013	NA	NA	NA	Yes	22-07-13	13	2	Remission CR	06-26-2012	10-04-2013	Alive/LFU
1.50	none	No	PR		6	No	NA		NA	NA			10-01-2013	NA	NA	NA	No				Persistent	01-18-2013	10-01-2013	Alive/LFU
2.00	none	Yes	NR	NA		NA	AZA	No	aza x 6 mt	05/04/2013	04-05-2013	9	07-12-2013	NA	NA	NA	No				Chronic ITP	07-13-2012	07-12-2013	Alive/LFU
2.00	none	No	CR		11	No	NA		NA	NA			08-02-2013	NA	NA	NA	No				Remission	08-24-2012	08-02-2013	Alive/LFU
1.50	none	No	CR		9	No	NA		NA	05/02/2013	05-03-2013	10	05-03-2013	CR		3	No				Remission	06-28-2012	05-03-2013	Alive/LFU
100.00	none	No	CR		7	Yes	NA		NA (Contin	NA			07-26-2013	NA	NA	NA	No				Persistent	05-18-2012	07-26-2013	Alive/LFU
2.50	none	No	CR		9	Yes	DDS	Yes	DDS + PR	17/05/2013	05-17-2013	11	09-20-2013	NA	NA	NA	No				Persistent	06-12-2012	09-20-2013	Alive/LFU
100.00	none	No	CR		12	No	NA		NA	NA			07-05-2013	NA	NA	NA	No				Remission	05-15-2012	07-05-2013	Alive/LFU
2.50	none	No	PR		9	No	NA		NA	NA			09-06-2013	NA	NA	NA	No				Persistent	09-18-2012	09-06-2013	Alive/LFU
2.30	none	Yes	NR	NA		NA	AZA	No	aza x 6 mt	14/08/2012	08-14-2012	3	06-07-2013	NA	NA	NA	No				Chronic ITP	05-12-2012	06-07-2013	Alive/LFU
1.50	none	No	CR		4	Yes	Other	No	Predni + D.	24/07/2006	07-24-2006	26	10-09-2009	NR	NA	NA	Yes	24-07-06	26	39	Remission CR	05-31-2004	10-09-2009	Alive/LFU
1.50	none	No	CR		12	Yes	DDS	Yes	DAPSONE	AZO - 08/11/20	08-11-2005	15	09-10-2007	NR	NA	NA	No				Remission	05-07-2004	09-10-2007	Alive/LFU
100.00	none	Yes	NR	NA		NA	AZA	Yes	AZAX9mnt	19/06/2009	06-19-2009	24	10-22-2013	NA	NA	NA	No				Remission	07-05-2007	10-22-2013	Alive/LFU
3.00	none	No	CR		18	No	NA		none	08/01/2008	01-08-2008	29	08-29-2008	CR		8	No				Remission	08-23-2005	08-29-2008	Alive/LFU
1.50	Dapsone ir	No	CR		5	No	NA		none	18/11/2005	11-18-2005	7	01-20-2006	CR		3	No				Remission	04-19-2005	01-20-2006	Alive/LFU
2.50	none	Yes	NR	NA		NA	AZA	Yes	azathioprin	DDS-21/3/06 , /	03-21-2006	8	07-06-2010	NA	NA	NA	No				Remission	08-02-2005	07-06-2010	Alive/LFU
100.00	none	Yes	NR	NA		NA	AZA	Yes	azathioprin	DDS-24/1/06 , /	01-24-2006	3	06-26-2007	NA	NA	NA	No				Remission	10-25-2005	06-26-2007	Alive/LFU
100.00	none	No	CR		24	Yes	DDS	Yes	ReRX DDS	20/4/2006,	04-20-2006	8	10-24-2008	NA	NA	NA	No				Persistent	08-27-2005	10-24-2008	Alive/LFU
2.00	none	No	CR		16	No	AZA	Yes	Azoran(Ma	14/6/2005	06-14-2005	13	01-16-2007	CR		16	Yes				Remission	05-28-2004	01-16-2007	Alive/LFU
2.00	none	Yes	NR	NA		NA	AZA	No	AZA X 6 m	22/05/2009	05-22-2009	16	03-12-2010	NA	NA	NA	No				Chronic ITP	02-02-2008	03-12-2010	Alive/LFU
2.00	none	No	PR		12	Yes	DDS	No	DDS X 1 y	03/02/2007	02-03-2007	18	11-20-2012	NA	NA	NA	Yes	23-04-08	33	56	Remission CR	07-29-2005	11-20-2012	Alive/LFU
100.00	none	No	PR		6	Yes	DDS	Yes	ReRX DDS	10/05/2011	05-10-2011	44	05-10-2011	NR	NA	NA	No				Chronic ITP	09-18-2007	05-10-2011	Alive/LFU
1.50	none	Yes	NR	NA		No	AZA	No	AZA X 9 M	05/10/2007	05-10-2007	5	08-13-2013	NA	NA	NA	Yes	23-07-08	20	62	Remission CR	12-01-2006	08-13-2013	Alive/LFU
2.30	none	No	CR		12	No	NA		NA	NA			07-06-2010	NA	NA	NA	No				Remission	02-24-2009	07-06-2010	Alive/LFU
1.50	none	No	CR		24	No	NA		NA	11/12/2009	12-11-2009	28	08-06-2010	PR		9	No				Persistent	09-07-2007	08-06-2010	Alive/LFU
1.50	none	No	CR		4	Yes	AZA	No	AZA X 1 1/	07/12/2008	12-07-2008	13	07-07-2012	NA	NA	NA	No				Persistent	11-13-2007	07-07-2012	Alive/LFU
1.50	NONE	Yes	NR	NA		NA	AZA	No	AZA X 8 m	19/02/2008	02-19-2008	6	10-28-2008	NA	NA	NA	No				Chronic ITP	08-17-2007	10-28-2008	Alive/LFU
100.00	none	Yes	NR	NA		NA	NA		NA	14/03/2008	03-14-2008	6	05-29-2012	NR	NA	NA	Yes	15-04-08	7	50	Remission CR	09-18-2007	05-29-2012	Alive/LFU
1.50	NONE	No	CR		24	No	NA		none	29/07/2011	07-29-2011	22	07-29-2011	NA	NA	NA	No				Remission	10-02-2009	07-29-2011	Alive/LFU
1.50	none	No	CR		24	No	NA		NA	16/09/2010	09-16-2010	34	06-14-2013	PR		24	Yes				Remission	11-23-2007	06-14-2013	Alive/LFU
1.50	alopecia	No	CR		12	Yes	DDS	Yes	DDS X 5 m	17/07/2009	07-17-2009	16	08-24-2012	NA	NA	NA	No				Remission	03-11-2008	08-24-2012	Alive/LFU
100.00	none	No	CR		12	No	NA		NA	19/11/2004	11-19-2004	11	08-03-2007	CR		36	Yes				Remission	12-19-2003	08-03-2007	Alive/LFU
1.50	AZA derma	No	CR		6	No	DDS	Yes	DDS x 2 y	11/03/2008	03-11-2008	2	07-08-2011	CR		48	No				Remission	01-25-2008	07-08-2011	Alive/LFU

2.00		none	Yes	NR	NA		NA	NA		NA	11/09/2012	09-11-2012	58	06-04-2013	NA	NA	NA	Yes	30-04-13	65	1	Remission	CR	12-14-2007	06-04-2013	Alive/LFU
2.00		Grade I Cy	No	CR		9	Yes	Other	Yes	Pred x 2 ye	08/08/2008	08-08-2008	6	02-14-2013	NA	NA	NA	No				Remission		02-15-2008	02-14-2013	Alive/LFU
2.00		none	No	CR		24	No	Splenect	Yes	Splenecton	21/08/2009	08-21-2009	20	10-11-2013	CR		1	Yes	Yes	10-11-11	47	23	Remission	CR	01-08-2008	10-11-2013	Alive/LFU
3.00		none	Yes	NR	NA		NA	AZA	No	AZA X 6 m	13/04/2009	04-13-2009	11	07-27-2012	NA	NA	NA	Yes	17-06-09	13	38	Remission	CR	05-27-2008	07-27-2012	Alive/LFU
2.00		none	No	CR		12	No	NA		NA	21/10/2011	10-21-2011	43	07-12-2013	CR		21	No	No			Remission		04-08-2008	07-12-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	NA		NA	NA			03-30-2010	NA	NA	NA	No				Chronic	ITP	11-25-2009	03-30-2010	Alive/LFU
1.50		none	Yes	NR	NA		NA	NA		NA	03/01/2009	01-03-2009	9	05-01-2009	NA	NA	NA	Yes	06-01-09	9	4	Remission	CR	03-28-2008	05-01-2009	Alive/LFU
1.50		none	No	CR		21	Yes	DDS	Yes	CT RX DD:	NA			07-02-2013	NA	NA	NA	No				Remission		05-14-2010	07-02-2013	Alive/LFU
100.00		none	No	CR		5	No	NA		NA	NA			12-08-2009	NA	NA	NA	No				Remission		10-13-2009	12-08-2009	Alive/LFU
1.50		none	No	PR		24	No	NA		NA	NA			04-09-2013	NA	NA	NA	No				Remission		02-03-2009	04-09-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	NA		NA	NA			10-24-2008	NA	NA	NA	No				Chronic	ITP	03-28-2008	10-24-2008	Alive/LFU
1.50		none	No	CR		10	No	NA		na	NA			03-14-2009	NA	NA	NA	No				Remission		03-14-2008	03-14-2009	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 6 m	28/04/2009	04-28-2009	11	01-10-2012	NA	NA	NA	Yes	09-10-09	16	27	Remission	CR	06-10-2008	01-10-2012	Alive/LFU
2.00		none	No	CR		24	No	NA		NA	23/03/2010	03-23-2010	23	01-04-2013	CR		18	Yes	No			Persistent		05-02-2008	01-04-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	Yes	AZA X 6 m	27/01/2009	01-27-2009	6	06-26-2009	NA	NA	NA	No				Chronic	ITP	08-05-2008	06-26-2009	Alive/LFU
125.00	1.60	Dermatitis	Yes	NR	NA		NA	AZA	No	AZA X 2 ye	27/03/2009	03-27-2009	10	12-21-2012	NA	NA	NA	Yes	01-08-11	39	17	Persistent	PR	05-20-2008	12-21-2012	Alive/LFU
1.50		none	No	CR		12	No	NA		NA	NA			09-20-2013	NA	NA	NA	No				Remission		05-29-2012	09-20-2013	Alive/LFU
100.00		none	Yes	NR	NA		NA	DDS	NA	DDS @ LF	26/08/2008	08-26-2008	4	06-12-2012	NA	NA	NA	Yes	30-07-08	3	47	Chronic	ITI NR	05-09-2008	06-12-2012	Alive/LFU
1.50		none	No	PR		5	No	NA		NA	27/02/2009	02-27-2009	10	02-27-2009	NA	NA	NA	No				Chronic	ITP	05-16-2008	02-27-2009	Alive/LFU
1.50		none	No	CR		24	No	NA		NA	NA			10-19-2010	NA	NA	NA	No				Remission		05-16-2008	10-19-2010	Alive/LFU
2.00		none	No	CR		24	No	NA		NA	14/06/2009	06-14-2009	13	12-14-2010	CR		18	No	No			Remission		05-27-2008	12-14-2010	Alive/LFU
100.00		none	Yes	NR	NA		No	Splenect	Yes	CR (POST	30/05/2013	05-30-2013	61	06-06-2013	NA	NA	NA	Yes	30-05-13	61	0	Remission	CR	05-20-2008	06-06-2013	Alive/LFU
100.00		none	Yes	NR	NA		No	Splenect	No	SPLENEC	15/07/2009	07-15-2009	10	02-07-2012	NA	NA	NA	Yes	20-07-09	10	31	Chronic	ITI NR	09-16-2008	02-07-2012	Alive/LFU
100.00		none	Yes	NR	NA		NA	NA		NA	NA			03-17-2009	NA	NA	NA	No				Chronic	ITP	08-08-2008	03-17-2009	Alive/LFU
100.00		none	No	PR		6	No	NA		NA	NA			03-06-2009	NA	NA	NA	No				Remission		09-12-2008	03-06-2009	Alive/LFU
2.00		none	No	PR		3	No	DDS	Yes	DDS X 1 Y	12/06/2009	06-12-2009	12	05-03-2013	NA	NA	NA	No				Remission		06-20-2008	05-03-2013	Alive/LFU
100.00		none	No	CR		24	No	NA		NA	NA			07-13-2010	NA	NA	NA	No				Remission		06-27-2008	07-13-2010	Alive/LFU
100.00		none	Yes	NR	NA		NA	AZA	No	AZA X 6 M	06/01/2009	01-06-2009	6	05-05-2009	NA	NA	NA	No				Chronic	ITP	07-08-2008	05-05-2009	Alive/LFU
100.00		none	No	CR		24	No	NA		none	NA			05-21-2013	NA	NA	NA	No				Remission		05-07-2010	05-21-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	NA		NA	06/03/2009	03-06-2009	6	06-16-2009	NA	NA	NA	No				Chronic	ITP	09-09-2008	06-16-2009	Alive/LFU
1.50		none	Yes	NR	NA		NA	NA		NA	NA			12-03-2008	NA	NA	NA	No				Chronic	ITP	07-08-2008	12-03-2008	Alive/LFU
100.00		none	No	CR		4	NA	NA		NA	NA			02-05-2009	NA	NA	NA	No				Remission		09-02-2008	02-05-2009	Alive/LFU
2.00		none	Yes	NR	NA		NA	NA		NA	9			10-29-2013	NA	NA	NA	No				Chronic	ITP	09-11-2012	10-29-2013	Alive/LFU
1.50		none	Yes	NR	NA		NA	AZA	No	AZANX 1 Y	06/01/2009	01-06-2009	12	09-23-2012	NA	NA	NA	Yes	9999			Persistent	PR	01-21-2008	09-23-2012	Alive/LFU
2.00		none	Yes	NR	NA		NA	Splenect	No	SPLENEC	03/03/2008	03-03-2008	6	04-08-2011	NA	NA	NA	Yes	25-02-08	6	38	Remission	CR	09-13-2007	04-08-2011	Alive/LFU
2.50		none	Yes	NR	NA		NA	DDS	No	DDS X 3 M	10/07/2010	07-10-2010	34	07-03-2012	NA	NA	NA	No				Chronic	ITP	09-22-2007	07-03-2012	Alive/LFU
2		none	No	CR		31	No	NA		NA	01/08/2010	01-08-2010	24	09-12-2011	NR	NA	Yes	No				Persistent		02-01-2008	09-12-2011	Alive/LFU

ostimem	efsdate	efsstatus	efstimem	Time from 1st response to relapse/response date (months)
49		No event	49	45
42		No event	42	41
19		No event	19	17
23		No event	23	21
5	06-16-2009	event	5	
10		No event	10	6
41		No event	41	38
27		No event	27	24
8		No event	8	4
41	02-15-2012	event	37	39
5	08-25-2009	event	5	
32	12-01-2009	event	6	
52	04-30-2010	event	15	44
29	06-30-2010	event	17	26
25		No event	25	22
49	04-09-2010	event	14	11
27	08-04-2009	event	4	
7		No event	7	3
14	09-08-2009	event	6	
21	09-20-2010	event	18	9
39	05-14-2010	event	14	37
4	07-14-2009	event	4	
11		No event	11	10
40	03-12-2010	event	12	38
24	07-01-2009	event	4	
7	07-19-2009	event	3	
37		No event	37	36
11		No event	11	6
34		No event	34	33
44	01-01-2010	event	5	
6	11-03-2009	event	6	
48	11-17-2009	event	6	
45	10-04-2009	event	3	
49	12-18-2009	event	9	46
17	09-18-2009	event	6	14
21		No event	21	19
36	05-15-2009	event	6	
50	08-12-2011	event	28	43
5		No event	5	4
48	03-25-2011	event	23	45
8		No event	8	8
25		No event	25	14
41	01-04-2011	event	14	35
14	12-10-2009	event	6	
13		No event	13	12
5		No event	5	3
38		No event	38	37
20	06-19-2008	event	5	
45		No event	45	44
23	03-09-2010	event	10	19
39	12-02-2009	event	6	
39		No event	39	38
43		No event	43	41
46	05-18-2010	event	10	44
13	11-23-2012	event	5	
7	03-24-2010	event	5	
45	06-20-2012	event	35	43
42	01-01-2010	event	5	
6	03-02-2010	event	6	
44		No event	44	43
8	01-11-2010	event	5	
45	01-21-2011	event	17	44
45	01-04-2010	event	5	
25	03-30-2010	event	10	21
5		No event	5	4

18		No event	18	17
22		No event	22	19
12	10-27-2009	event	2	
47	11-19-2010	event	12	45
32	03-20-2010	event	6	
43	04-16-2010	event	6	
14		No event	14	13
23	05-13-2011	event	14	17
26	06-08-2010	event	5	
21	07-19-2010	event	6	
29	01-28-2009	event	6	
36		No event	36	35
74		No event	74	71
6	03-09-2010	event	6	
4	03-09-2010	event	4	
6	04-13-2010	event	6	
12	05-11-2010	event	6	9
41	03-01-2011	event	14	36
43	06-02-2010	event	6	
39		No event	39	33
18	05-24-2011	event	16	14
28	07-08-2010	event	6	
71	05-15-2010	event	27	65
20		No event	20	18
5		No event	5	4
5		No event	5	4
37	05-29-2012	event	28	35
28		No event	28	27
12	08-10-2010	event	6	
18	02-11-2011	event	12	16
33	08-05-2011	event	13	32
4	05-14-2010	event	4	
9	09-23-2010	event	6	
35		No event	35	29
36	09-28-2012	event	26	33
39	11-02-2010	event	6	
38	09-22-2010	event	6	
10	01-24-2011	event	3	
14	08-31-2010	event	6	
3		No event	3	2
10	12-11-2010	event	6	
23		No event	23	21
41	09-03-2010	event	4	
3	09-14-2010	event	3	
36	01-31-2011	event	6	
21	03-16-2012	event	21	20
21	12-03-2010	event	4	
9		No event	9	8
25	03-25-2011	event	6	
14		No event	14	13
23		No event	23	22
18	06-16-2011	event	12	14
18	12-14-2010	event	5	
42		No event	42	38
34		No event	34	30
37		No event	37	31
8	09-23-2011	event	8	7
16		No event	16	15
22	10-28-2010	event	3	
36		No event	36	35
12	03-11-2011	event	6	
35	06-26-2012	event	23	35
24	04-19-2013	event	21	18
14		No event	14	11
77	10-13-2009	event	28	76
32	08-23-2011	event	10	31

7	07-26-2011	event	6	
8	08-27-2013	event	6	
27		No event	27	23
11	05-13-2011	event	5	
27	04-29-2011	event	6	
32	04-15-2011	event	5	
11	03-27-2011	event	5	
8		No event	8	1
33	07-05-2013	event	33	32
37	01-21-2011	event	5	
15	01-01-2011	event	5	
22		No event	22	20
30	06-20-2012	event	14	26
30		No event	30	27
20	10-11-2013	event	20	18
34		No event	34	33
44		No event	44	43
19	09-14-2011	event	6	
16	09-22-2011	event	6	
22	08-12-2011	event	6	
19	09-08-2011	event	6	
10	08-15-2011	event	5	
32	06-03-2011	event	5	
31	01-17-2012	event	11	27
34	05-17-2011	event	5	
28	06-18-2013	event	24	27
24		No event	24	20
25	03-30-2013	event	18	17
25		No event	25	24
14	10-08-2012	event	5	12
28	12-20-2011	event	6	
26		No event	26	25
29	08-16-2011	event	6	
30	07-08-2011	event	4	
30	08-01-2011	event	6	
9		No event	9	8
15		No event	15	12
15	05-01-2012	event	4	
6		No event	6	3
5	12-20-2011	event	5	
19	04-17-2012	event	5	
20	01-24-2012	event	6	
29	11-04-2011	event	6	
35	06-04-2011	event	7	32
27	04-27-2013	event	24	24
18	05-01-2012	event	13	14
5	08-23-2013	event	5	
10		No event	10	9
11	10-06-2011	event	6	
15	07-12-2011	event	3	
15	09-06-2011	event	5	
28		No event	28	27
21	02-09-2012	event	6	
12	06-18-2012	event	8	11
19	03-23-2012	event	2	
22		No event	22	15
16	06-29-2012	event	6	
14	01-08-2013	event	6	
19		No event	19	18
21		No event	21	12
19		No event	19	18
17	06-18-2013	event	14	15
20	04-03-2012	event	5	
17	02-07-2012	event	6	16
27	10-04-2013	event	25	22
26	02-02-2012	event	6	23

5		No event	5	3
5	02-16-2012	event	5	
11	03-18-2012	event	6	
22	06-15-2012	event	6	
24		No event	24	23
11	04-25-2012	event	6	
17		No event	17	15
10	04-13-2012	event	6	
21	10-01-2013	event	20	20
21		No event	21	19
16		No event	16	13
5		No event	5	2
15		No event	15	14
17		No event	17	15
20	08-24-2013	event	19	18
7		No event	7	6
3	08-23-2013	event	3	
8		No event	8	7
17	07-09-2012	event	5	
6		No event	6	4
15		No event	15	12
18		No event	18	15
4	09-14-2012	event	4	
15		No event	15	11
9	08-02-2013	event	6	
11	06-22-2012	event	3	
18	07-20-2012	event	3	
6		No event	6	5
16	11-30-2012	event	6	
6		No event	6	3
16	11-28-2012	event	6	
17	09-06-2013	event	16	14
16	09-06-2013	event	15	11
16	11-27-2012	event	5	
9		No event	9	6
12	01-03-2013	event	6	
11		No event	11	10
10		No event	10	7
14	02-05-2013	event	9	12
16	09-21-2012	event	3	15
14		No event	14	11
12		No event	12	9
13	11-09-2012	event	6	
65	07-18-2006	event	26	64
41	11-08-2005	event	18	38
77	01-04-2008	event	6	
37		No event	37	27
9		No event	9	8
60	12-16-2005	event	5	
20	01-24-2006	event	3	
38	08-21-2008	event	36	37
32	06-02-2006	event	25	29
26	07-11-2008	event	5	
89	06-13-2006	event	11	86
44	05-07-2011	event	44	41
82	05-15-2007	event	6	
17		No event	17	14
35		No event	35	32
57	02-26-2009	event	16	9
15	02-18-2008	event	6	
57	03-14-2008	event	6	
22		No event	22	20
68	10-23-2012	event	60	58
54	07-17-2009	event	16	12
44	08-03-2007	event	44	43
42	03-11-2008	event	2	0

67	03-28-2008	event	4	
61	12-18-2008	event	10	8
70	09-29-2009	event	21	20
51	11-16-2008	event	6	
64		No event	64	60
4	03-30-2010	event	4	
13	08-26-2008	event	5	
38	04-03-2012	event	23	35
2		No event	2	1
51		No event	51	48
7	09-10-2008	event	6	
12		No event	12	10
44	11-11-2008	event	5	
57	07-22-2011	event	39	52
11	02-03-2009	event	6	
56	09-24-2008	event	4	
16		No event	16	16
50	08-26-2008	event	4	
10		No event	10	5
30		No event	30	27
31		No event	31	28
61	11-17-2008	event	6	
41	02-23-2009	event	5	
7	02-17-2009	event	6	
6		No event	6	3
59		No event	59	50
25		No event	25	22
10	01-12-2009	event	6	
37		No event	37	29
9	03-06-2009	event	6	
5	12-03-2008	event	5	
5		No event	5	3
14	01-21-2013	event	4	
57	04-04-2008	event	2	
43	02-14-2008	event	5	
58	02-03-2008	event	4	
44	09-12-2011	event	44	41