(range 5.2-11384). Mean bone marrow plasma cell percentage was 18% (range 0-75%). Four pts (10.8%) had symptomatic multiple myeloma. Five pts (13.5%) required hemodialysis prior to ASCT. Tandem ASCT was performed in 5 pts. Induction treatment was instituted in 20 pts (54%), and was mainly based on bortezomib.
Four pts (10.8%) died before day +100 after ASCT due to cardiovascular events. Twenty three out of 27 evaluable pts (85%) achieved response to treatment, including 17 pts (63%) with CR and 5 pts (18.5%) with PR, whereas 4 patients (15%) had stable disease. Organ response was achieved by 13 pts (48%).
After a mean observation time of 4.2 years median OS was not reached, whereas median PFS was 4.06 years. Twelve out of 29 evaluable patients (41.4%) had disease progression after a median observation time of 2.74 years (range 0.9 – 5.7), and half of them (6 pts) died due to progressive disease after a median of 2.3 years post ASCT (range 1.1 – 6.4).
Longer PFS was observed in patients achieving hematologic CR (HR = 0.15; P = 0.007), hematologic PR (HR = 0.1356; P = 0.001), as well as organ response (HR = 0.3; P = 0.046). Higher risk of progression was seen in patients with heart involvement (HR = 3.77; P = 0.006). Factors adversely correlated with OS were heart involvement (HR = 10.7; P = 0.002), Mayo Stage > 2 (HR = 7.2; P = 0.003) and symptomatic involvement of more than two organs (HR = 8.8; P = 0.04).
Summary/Conclusion: Our data confirm that ASCT is feasible and efficacious in the treatment of AL amyloidosis. Heart involvement remains the main predictor of death. Prospective studies are warranted to better delineate the role of induction and melphalan dose.

PB2012 DELETIONS AND AMPLIFICATIONS OF THE IGH VARIABLE AND CONSTANT REGIONS: A NOVEL PROGNOSTIC PARAMETER IN PATIENTS WITH MULTIPLE MYELOMA

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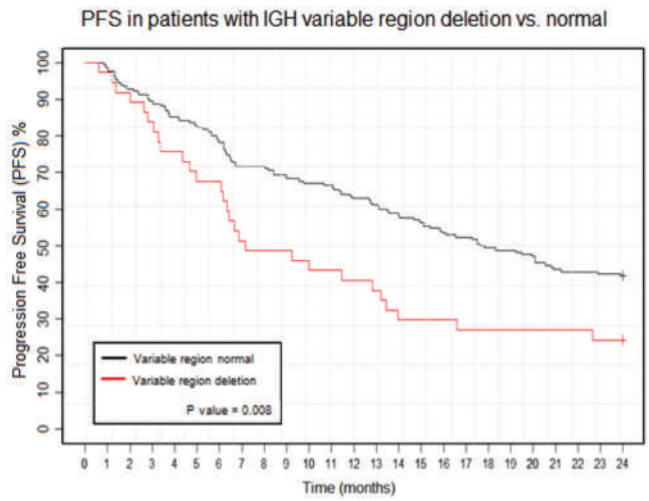
Background: Cytogenetic abnormalities are a recognized factor in the pathogenesis of multiple myeloma (MM). While chromosomal translocations involving the IGH gene have already been investigated and reported, the implications of deletions or amplifications in the IGH gene have only been examined in a few studies.
Aims: Study the prognostic and clinical implications of deletions or amplifications in the IGH gene among MM patients.
Methods: We conducted a retrospective analysis of 260 patients with MM from 4 Hematology units in Northern Israel. All patients had bone marrow samples sent to the Genetics laboratory of the Bnei Zion Hospital in Haifa, Israel between 2016 to 2018, for FISH analysis of separated CD-138 positive cells using Magnetic-activated Cell Sorting (MACS). IGH break apart probes were used to identify IGH abnormalities and statistical analysis of clinical and prognostic features comparing the different cytogenetic groups was performed.



Results: Deletions in the variable region of the IGH (IGHv) were found in 17.3% (n = 45) of patients. This finding correlated well with significantly worse PFS (after 2 years of follow up (p = 0.008)) and with worse response to 1st line treatment (p = 0.05). At 1 year of follow up the PFS was 51.1% in the IGHv deletion group, compared to 68.0% in patients without deletion (p = 0.049). However, OS was not significantly different in the two groups. PFS differences remained significant in subgroup analysis after separating patients by high and standard risk cytogenetics. In the standard risk group (n = 112, 26 with IGHv deletion) IGHv deletions showed a worse PFS curve (p = 0.046) (with age and sex adjusted HR of 2.0 (95% CI 1.0-3.2)). In the high-risk group (n = 108, 19 with IGHv deletion) the PFS curves were also worse ((p = 0.012), with median PFS of 6.7 and 14.9 in the IGHv deletion and IGHv non-deleted groups, respectively.
Constant region (IGHc) amplifications, were much less frequently encountered (6.15%, n = 16), but also demonstrated worse PFS at 2 years of follow up (p = 0.023). This difference remained valid in the High-Risk subgroup (p = 0.001, IGHc amplification 8/100), but not in standard risk patients. There was no significant difference in OS rates.
Summary/Conclusion: We found that in patients with MM deletion of IGH variable region and amplification in the IGH constant region are both associated with poor prognostic clinical features.

PB2013 DARA-VD VERSUS DARA-RD AS SALVAGE THERAPY FOR PATIENTS WITH MYELOMA. INITIAL FOLLOW-UP OF AN ITALIAN MULTICENTER RETROSPECTIVE CLINICAL EXPERIENCE BY RETE EMATOLOGICA PUGLIESE

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Background: Daratumumab is a CD38 monoclonal antibody approved in monotherapy or in combination with bortezomib and dexamethasone (Dara-Vd) or lenalidomide and dexamethasone (Dara-Rd) for the treatment of relapsed or refractory myeloma (rrMM).
Aims: We report here an initial multicenter retrospective analysis of 126 consecutive patients with rrMM treated with daratumumab in combination with bortezomib or lenalidomide as salvage therapy at 9 haematological centers in Puglia, conducted to evaluate the outcomes, as well as the toxicity profile of these combination in a daily practice setting outside clinical trials.
Methods: Of 126 patients, 122 were evaluable for response and toxicity. Forty-two patients (33%) (15 F and 27 M) received Dara-Vd and 84 patients (67%) (41 F and 43 M) with Dara-Rd; 74% of them had relapsed MM and 26% MM refractory to one or more previous treatment lines. The median age at diagnosis was 62 years (range 36-77) in the Vd-group, 66 years (range 32-83) in the Rd-group. The median time to initiation of daratumumab from diagnosis was 5 years (range 3-9) in the Vd-group, 3 years (range 1-10) in the Rd-group. Patients had received a median 2 prior lines of therapy (range 1-6) in the Vd-group, a median 1 prior course of therapy (range 1-4) in the Rd-group. Twenty patients (48%) in the Vd-group and 30 patients (37%) in the Rd-group had previously undergone single or tandem ASCT. In the Vd-group all patients were previously exposed to at least one proteasome inhibitor (91% of patients to bortezomib, 37% of patients to carfilzomib), in the Rd-group only 18% of patients was exposed to lenalidomide.
Results: The median number of administered cycles was 9 (range 1-23) in the VD-group and 8.5 (range 1-23) in the Rd-group. The ORR was 68.2% in the Vd-group (CR 4.8%, VGPR 12.2%, PR 51.2%) and 81.5% in the Rd-group (CR 21%, VGPR 35.8%, pr 24.7%). Median TTR was 2 months (range 1-6) in the Vd-group and 1.5 months (range 1-5) in the Rd-group. Median PFS was 10 months (range 8-16; 95% > CI) in the Vd-group; median PFS was not reached in the Rd-group (fig.1). Grade 3/4 neutropenia (37%) was the most common adverse event in the Rd-group, grade 3/4 thrombocytopenia (24%) was the most common adverse event in the

Vd-group. Seventeen (41%) patients in the Vd-group discontinued treatment due to relapse, 16 patients (19%) in the Rd-group because of haematological toxicity (4.5%), relapse (7.5%), death (6%) and the development of urological cancer (1%).
Summary/Conclusion: A higher rate of ORR (81.5% vs 68.2%) and very good partial response or better (responses > VGPR 56.8% vs 17%) was observed in the Dara-Rd group compared to Dara-Vd group. This difference could be due to the fact that: 1) in the Dara-Rd group the patients had received a lower number of prior antimyeloma therapies compared to Dara-Vd group; 2) the patients in the Dara-Rd group had a more indolent myeloma (median ISS 1) compared to the patients in the Dara-Vd group, who had a more advanced disease (median ISS 3); 3) in the Rd-group only 18% of patients was exposed to lenalidomide, in the Vd-group all patients were previously exposed to at least one proteasome inhibitor. Unfortunately, the interference of daratumumab with immunofixation and serum protein electrophoresis assays may lead to underestimation of CR.

PB2014 SECOND AUTOGRAFT OUTCOME IN RELAPSED MULTIPLE MYELOMA : A FRENCH MULTICENTRIC COHORT.

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Background: Despite recent breakthrough of novel therapies in multiple myeloma (MM), high dose chemotherapy (HDC) follow by autologous stem cell transplantation (ASCT) remain the standard of care as frontline therapy for patients up to 65-70 years. At relapse a second HDC follow by ASCT after re-induction therapy is a possible treatment option, especially for patients experencing long remission after first ASCT. However it is unclear whether second ASCT at relapse is still valuable in the era of novel agents.
Aims: Appreciate feasability, toxicity and response after a second ASCT in relapsed MM patients.
Methods: Between January 2007 and November 2019 in two french academic centers (St Louis and H. Mondor hospitals) we retrospectively analyzed outcomes of 48 relapsing MM patients treated by re-induction therapy follow by HDC and second ASCT. Were excluded patients who benefited of tandem ASCT, tandem allograft-autograft or rescue ASCT realized in refractory situations.
Results: Diagnosis of MM was made between January 1996 and January 2012. Patient's characteristics at diagnosis are listed in table 1. First line treatment included HDC followed by ASCT for all patients, median age at first ASCT was 53 years (32-65 y). Induction therapy before ASCT1 included triplet IMID's + IP's + Dexamethasone (VTD) in 35% patients, others Bortezomib-based regimen (PAD, Cy-BOR-Dex) in 31%, anthracyclin regimen (ie. VAD) in 21% and others IMID's-based regimen in 12%. Twenty-three patients received consolidations (48%) and only 4 patients received maintenance therapy. Median progression free survival (PFS) after ASCT1 (PFS1) was 47 months (4 - 104 m). At relapse, all patients received novel agents (IMID's and/or Bortezomib) as described in table 1. Overall response rate (ORR) before second HDC/ASCT was 93,75%, including complete response (CR) 18,75%, very good partial response (VGPR) 39,6%, and partial response (PR) 35,4%. Most patients (73 %) benefited from second ASCT at first relapse, 27 % patients at second relapse or more. Median age at second ASCT (ASCT2) was 59 years (44-70 y). HDC regimen were Melphalan 200 mg/m² in 85.1% and most patients received consolidation (91,7%) then maintenance (81,25%) therapy, mostly Lenalidomide. Toxicity of ASCT 2 was as expected and manageable, only 1 patient required ICU admission for severe sepsis and overall no death occurred at 3 months after ASCT2. Among the 38 patients not in CR before ASCT2, HDC improve response depth in 47,3% of them. Thus, after completion of ASCT2 and consolidation, more patients were in VGPR or better, 83,3% versus 58,35% before. With a median follow up of 23,5 months (2-134 m), the median estimated PFS was 33,5 months (6,6-133 m). There was no statistically significant difference in term of PFS between patients receiving or not maintenance therapy after ASCT2 (median PFS with maintenance 33,5 months (6,6-86 m), median PFS without maintenance, 43,59 months (14,9-133 m, p = 0,7).

Population	n = 48
Male / Female	45,8% (n = 22) / 54,2% (n = 26)
International staging system (ISS)	
1	25% (n = 12)
2	10,4% (n = 5)
3	4,2% (n = 2)
Unknown	60,4% (n = 29)
Cytogenetic	
No t(4;14) / No del(17p)	64,6% (n = 31)
t(4;14)	6,2% (n = 3)
del(17p)	0%
Others	4,2% (n = 2)
Unknown	25% (n = 12)
Re-induction therapy before ASCT2	
Triplet IMID's + IP's + Dexamethasone	77,1% (n = 37)
Triplet IP's + Dexamethasone + Alkylating agent (such as Melphalan or Cyclophosphamide)	10,4% (n = 5)
Others	12,5% (n = 6)
Response prior to ASCT2	
ORR	93,75% (n = 45)
CR	18,75% (n = 9)
VGPR	39,6% (n = 19)
PR	35,4% (n = 17)
SD	4,2% (n = 2)
Unknow	2,1% (n = 1)
Response after ASCT2 and consolidation (if completed)	
ORR	97,9% (n = 47)
CR	37,5% (n = 18)
VGPR	45,8% (n = 22)
PR	14,6% (n = 7)
Progression	2,1% (n = 1)
Maintenance therapy after ASCT2	
Yes	81,25% (n = 39)
Lenalidomide	n = 20
Others	n = 19
No	18,75% (n = 9)

Summary/Conclusion: For selected patients, a second HDC/ASCT is feasible without unexpected toxicity and may lead to high response rate and sustained remission with a median PFS of 33.5 months. Absence of difference in PFS between patients receiving or not maintenance make uncertain the need of such treatment after a second ASCT. More datas from more patients around others french centers are currently collected and may confirm or infirm this assumption.

PB2015 THE ROLE OF ABERRANT, COMPLEX KARYOTYPES, DOUBLE-HIT ABNORMALITIES AND AUTOLOGOUS STEM CELL TRANSPLANTATION IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA

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Background: Risk stratification in multiple myeloma is constantly updated due to the new information about the prognostic impact of genetic abnormalities and other factors. The division of patients into various risk groups based on the chromosomal markers is being utilized by many centers for select and optimize of therapeutic strategy. However, the role of complex karyotype, combination of genetic abnormalities, and autologous stem cell transplantation (autoSCT) remains unclear.
Aims: To determine the impact of genetic abnormalities and autoSCT overall and progression-free survival in patients with newly diagnosed multiple myeloma.
Methods: Metaphase cytogenetics on bone marrow samples was done by standard GTG-method. FISH analyses were performed according to the manufacturer's protocol for detection primary IgH translocations, 13q (13q14/13q34) deletion, 1p32/1q21 amplification/deletion, TP53/cen17 deletion (MetaSystems DNA probes). We additional searched the t(4;14), t(6;14), t(11;14), t(14;16) and t(14;20) in patients with IgH translocation. All 87 patient was treated by bortezomib-based programs (VD, CVD, VMP, PAD).
Results: The presence of an aberrant karyotype (combination of 2 non-high-risk anomalies), double hit (2 high-risk anomalies), and complex