n=10/13; BP, n=29/3) and AEs in AP (n=16/5); death (n=6/0) and symptomatic deterioration (n=6/0) in BP.
Summary and Conclusions: Durable response was seen in ~50% AP responders (~25% BP responders at y1, for whom BOS may be bridge to transplant); toxicity was manageable with long-term treatment.

E1106

PATIENT CHARACTERISTICS AND ADVERSE EVENTS (AES) OF TYROSINE KINASE INHIBITORS (TKIS) FOR THE TREATMENT OF CHRONIC MYELOID LEUKEMIA (CML) IN REAL WORLD SETTINGS

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Background: The growing number of TKIs available for CML increases complexity in choosing therapy in non-research settings.
Aims: This study aims to determine patient (pt) characteristics & emergent AEs that might underlie treatment choices.
Methods: TKI treatment episodes for adult CML pts from 1/2008 - 7/2014 were identified in the MarketScan Commercial, Medicaid, and Medicare supplemental databases. Pts were required to have ≥6 mos of enrollment prior to each TKI episode and ≥1 pharmacy or medical claims for one of the TKIs on or after the first CML diagnosis date. Analyses were retrospective and descriptive. Charlson comorbidity index (CCI) and frequency of other key comorbid conditions prior to each TKI episode were used to characterize patient baseline status (BL). Corresponding treatment-emergent events were captured using the same diagnosis or treatment codes indicative of the conditions. Vascular occlusive (VO) conditions include one or more of the following: myocardial infarction, congestive heart failure (CHF), thrombotic events, acute coronary syndrome, peripheral vascular, cerebrovascular, or coronary artery diseases. Median duration of treatment was assessed using the Kaplan-Meier method.
Results: 4,166 TKI treatment episodes for CML were identified. Median follow up was 13 months. Imatinib (IM) was most commonly used 1st line, dasatinib (DAS) and nilotinib (NIL) 2nd line, and bosutinib (BOS) and ponatinib (PON) 3rd line. BOS pts had the most previous TKI episodes and were furthest from initial diagnosis. They were the oldest, had the highest CCI, the most histories of VO conditions, kidney diseases, and pleural effusion at baseline, but the lowest rates of serious emergent AEs and discontinuation. With younger age and lower CCI, PON pts had the highest incidences of treatment emergent VO events and fluid retention, with the shortest treatment duration and highest rates of discontinuation.

Table 1.

	IM n=1,898	DAS n=1,180	NIL n=953	BOS n=87	PON n=48
Age (median)	55	52	53	56	51.5
# Prior TKIs (mean)	0.8	1.2	1.2	2.4	2.0
Time since initial diagnosis (median mos)	9	10	11	25	18
CCI (mean)	5.5	5.0	5.4	6.2	5.4
BL /emergent AE (%)					
VO conditions	31/5	30/6	31/5	43/5	40/15
CHF	11/3	10/4	14/3	23/1	15/6
Dysrhythmias	19/4	18/6	24/9	39/5	35/8
Fluid retention	16/6	17/6	18/5	36/3	33/10
Renal diseases	13/4	11/4	16/3	20/3	19/6
Diabetes	24/6	24/4	23/5	23/2	25/4
Pleural effusion	7/3	10/8	14/4	33/1	29/2
COPD	22/4	22/6	23/3	26/2	23/0
Abdominal pain	32/7	36/7	37/9	45/2	46/10
Diarrhea	14/6	16/5	17/3	24/13	31/8
Treatment Duration (median mos)	16	17	15	13	5
Discontinuation (%)	27	19	24	15	29

Summary and Conclusions: BOS appeared to be associated with lower risks of serious AEs compared to other TKIs and suited to elderly pts with high orbidities. It will be important to confirm the findings with larger sample sizes.

E1107

THE EFFECT OF NILOTINIB IN CHRONIC MYELOID LEUKEMIA TREATMENT DOSE ON FERTILITY AND TERATOGENICITY IN A HEALTHY MOUSE MODEL

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Background: Chronic myeloid leukemia (CML) is a hematopoietic pluripotent stem cell disease where myeloid cells lead to uncontrolled proliferation. Current treatment of Ph (+) CML is based on the inhibition of tyrosine kinase inhibitors (TKI), especially second-generation drugs. Majority of CML patients are male and 46% of them are between 20 and 64 years of age. Therefore, it is conceivable that inhibition of c-kit or PDGFR by TKI may have deleterious effects on spermatogenesis or folliculogenesis, resulting in male or female subfertility. In the first part of this study we showed the suppression of folliculogenesis and prevention of spermatogenesis during the long-term nilotinib treatment.
Aims: The aim of this part of our study is to determine the effect of nilotinib on fertility and teratogenicity that is used routinely to treat CML.
Methods: Here we present the results of testicular and ovarian changes after nilotinib administration to five- week old male and female C57bl6 mice. Mice received 0.4 mg of nilotinib per day dissolved in the drinking water for 2 months. Control group received only drinking water. Treatment dose was determined according to the clinical studies regarding the plasma concentrations (20 mg/kg, orally).
Results: There were no differences in the fertility and live birth index, the sex ratio or the frequency of survival to the time of weaning and also no evidence of teratogenicity in the fetuses. Low birth weight fetuses were seen in the nilotinib receiving female group whether the interruption of the drug during the pregnancy. The pregnancy rates of the couples according to the case of the using nilotinib or not were shown in Table 1. The pregnancy rates were reduced to 75% in the case of male mice used nilotinib; to 60% in the case of female mice used nilotinib; and finally to 25% in the case of both female and male mice used nilotinib in the cohort.

Table 1. The pregnancy rates of the couples

Pregnancy Rate	Nilotinib Female (n=12)	Control Female (n=12)
Nilotinib Male (n=12)	25%	75%
Control Male (n=12)	60%	100%

Summary and Conclusions: Although our results indicate that mice achieved the pregnancy whether they used nilotinib, the pregnancy rates reduced significantly compared to the control group in the study, especially if both female and male mice used nilotinib together. According to limited information, the potential consequences of the drug on developing fetus is still matter of debate, all female mice have given birth to healthy baby in our study. In the third part of our ongoing study, we are investigating the long-term effect of nilotinib on baby mice.

E1108

DYNAMICS OF RESPONSE AND IMPACT OF SOKAL SCORE IN 3 MONTHS MOLECULAR "WARNING" CML PATIENTS. A RETROSPECTIVE STUDY OF GRUPPO TRIVENETO LMC

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Background: Response to TKI is considered the strongest predictor of long-term outcome in CML patients. As known, effective treatment overcomes the negative impact of most prognostic factors, including Sokal score. Different studies have demonstrated that early molecular response is strictly correlated with outcome: infact, missing the 10% BCR-ABL landmark at 3 months predicts inferior long-term survival.
Aims: We investigated the dynamics of 3 months molecular "warning" CML patients at 6 and 12 months landmarks; secondly, we sought to evaluate the impact of Sokal score in the context of this unfavourable group
Methods: A total of 51 patients with BCR-ABL levels >10% at 3 months were identified for the analysis from a cohort of 350 consecutive CML patients treated with front-line standard dose imatinib (400 mg daily). "Optimal", "warning" and "failure" responses were stated according to ELN2013 recommendations. Complete cytogenetic response (CCyR) was defined as 0% Ph+metaphases; major molecular response (MMR) was defined as BCR-ABL <0.1%IS. TTF was measured from the start of imatinib to the date of any of the following events: progression to accelerated or blastic phase, death for any cause at any time, primary or secondary hematologic, cytogenetic or molecular resistance leading to imatinib discontinuation. PFS was measured from the start of imatinib to the date of progression to accelerated or blastic phase or death for any cause at any time. Survival probabilities were estimated by the Kaplan-Meier method and compared by log rank test; differences among variables were evaluated