were switched to a 2nd generation TKI (n=5) or to HU (n=3) for toxicity. Responses and outcomes are shown in the Table 1. Molecular responses (early molecular response, major molecular response, and deeper molecular response) were in the range reported for younger patients in prospective studies of treatment. Overall survival was poorer, because 19% of patients died in MMR or in CP without any evidence of progression, due to age−related complications, mainly cardiovascular and cerebrovascular.

Background: Since the introduction of TKI treatment in CML in the beginning of the current century, the expected survival of CML patients has increased substantially and is now close to the survival of the background population. Thus, the prevalence of CML has increased dramatically, and the number of patients in therapy, needing molecular monitoring increases accordingly. Whereas a large number of studies analyzes the outcome of CML cohorts, no prospective studies to our knowledge have focused on the distribution among the various TKIs and the molecular response.

Aims: The aim of this multicenter study was to measure the cross sectional molecular BCR-ABL1 response in CML patients in a demographic area and to analyze the molecular response across the different treatments available along with the distribution of treatment duration.

Methods: All hematological centers in Denmark and Iceland were invited to participate. The blood samples were then in two Risk groups, treated per CML patient after informed consent as part of a routine visit and shipped to central BCR-ABL1 analysis in the EUTOS MR4.5 certified laboratory in Vejle along with information on date of birth, gender, current treatment, dose, start date and line of treatment.

Results: Eight out of ten hematological centers in Denmark participated in the study as well as the Icelandic center. Five of the centers included more than 95% of their CML patients and in total 360 patients were included. One blood sample was lost during preparation, and of the remaining 359 samples 354 samples fulfilled the EUTOS quality criteria for Cross sectional Molecular Response (MR) scoring (=>24,000 GUSB copies per µgCR). In the MR scoring the patients were found to be 6.5% >MR2.0, 7.3% in MR2.0, 19% in MR3.0 (M4R), 17% in MR4.0 (of which 55/59 were BCR-ABL1 positive) and 50% in MR4.5 (of which 28/176 were BCR-ABL1 positive). Thus 150 pt (42%) were BCR-ABL1 negative and 47/194 (24.7%) indicating that the potential CML cure was high in this population, predominantly treated with imatinib. The average and median age of the patient group at sampling time was 58.7 years and 61.0 years, respectively, with a gender distribution of 57% males and 42% females. Of the 360 patients (95%) were in 1st line treatment, average duration 10.4 years (197/Imatinib, 4/Dasatinib, 12/Nilotinib and 1/NA); 97 pt (27%) were in 2nd line treatment, average duration 3.3 years (16/Imatinib, 47/Dasatinib, 28/Nilotinib, 5/TKI and/or interferon combinations and 1/Pause (BCR-ABL1 negative); 33 pt (9%) were in 3rd line treatment, average duration 2.6 years (3/Imatinib, 8/Dasatinib, 18/Nilotinib, 3/Bosutinib and 1/Pause (BCR-ABL1 negative); 10 pt (3%) were >3rd line treatment, average duration 1.1 year (1/Imatinib, 5/Dasatinib, 3/Nilotinib, 1/Ponatinib); 3 pt were transplanted; 1 BCR-ABL1 positive pt had been in treatment free remission for 12 years, and 2 pt lacked information on treatment line.

Summary/Conclusions: This study describes in the Danish and Icelandic CML patient population the present distribution of treatment, treatment line and duration combined with molecular response.

PB1832

SAFETY AND EFFICACY OF PONATINIB IN REAL WORLD CLINICAL PRACTICE. RESULTS FROM THE SPANISH COMPASSIONATE USE PROGRAM. A GELMC STUDY

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Background: Ponatinib is an oral TKI targeting BCR-ABL1 and other TKIs, which have been reported to have high rates of vascular complications when used in patients with CML. Although the drug is approved in some countries, there are currently no data from clinical trials on the real-world effectiveness and safety of ponatinib in CML patients. Therefore, we aimed to analyze the safety and efficacy of ponatinib in real-world clinical practice, focusing on patients treated in Spain.

Methods: This was an observational, multicenter, retrospective, real-world study conducted in Spain. The data were collected from patients treated with ponatinib at different centers in Spain. The study included patients with CML in chronic phase (CP) or accelerated phase (AP). The primary endpoint was the rate of treatment discontinuation due to adverse events (AEs) or lack of efficacy. The secondary endpoints were the proportion of patients achieving a major molecular response (MMR) or in CP without any evidence of progression, due to age−related complications, mainly cardiovascular and cerebrovascular.

Results: A total of 114 patients were included in the study, with a median follow-up of 13.5 months. The most common AEs were diarrhea, nausea, and vomiting. The discontinuation rate due to AEs was 16.1%. The MMR rate was 75.0% at 12 months.

Summary/Conclusions: Ponatinib showed a high efficacy in real-world clinical practice, with a high MMR rate and a moderate rate of treatment discontinuation due to AEs. However, more data are needed to fully understand the long-term safety and efficacy of ponatinib in patients with CML.
Aims: The purpose of this study is to provide safety and efficacy information from patients treated with ponatinib in real world clinical practice.

Methods: We have retrospectively collected data from 23 patients treated with ponatinib after resistance to previous treatment with tyrosine kinase inhibitors (TKIs). Molecular biology tests were done according to ELN guidelines and BCR-ABL/ABL is expressed as % IS. Clinical and comorbidities information (including CV risk factors) were collected before and during ponatinib treatment.

Results: Median age at diagnosis was 56 years (34-83). Most (70%) had CV risk factors and 20% had suffered a previous CV event. The percentage of low, intermediate and high-risk Sokal groups were 25%, 45% and 15%, respectively. Median time of TKIs exposure before ponatinib was 43 months. One patient was treated in accelerated phase (AP), while the rest were in first or second chronic phase (CP). Thirty seven (% ) of the patients had previously received 2 TKIs (masitinib, dasatinib, nilotinib, or bosutinib), and N (62%) had received ≥3 . At ponatinib start, 69% of patients had not achieved complete cytogenetic response (CCyR) while the rest were in CCyR (including 17% with major molecular response (MMR)). Sixty percent of the patients had one or more BCR-ABL I kinase domain mutations at the time of ponatinib start (45% had T315I mutation). Median follow-up was 29 months (3-53). Initial daily dose was 45, 30 and 15 mg in 85%, 5%, and 10% of patients, respectively. The initial dose was reduced in half of the patients, either due to side effects or to minimize the CV toxicity. In the last control, ponatinib daily dose was 45 mg, 30 mg and 15 mg in 65%, 10%, and 25% of the patients, respectively. Probabilities to obtain or maintain previous CCyR or MMR were 65% and 25%, respectively. Fifty eight percent of patients without CCyR at baseline achieved CCyR (17% achieving MMR), while 85% of patients with CCyR at baseline improved their molecular response. No differences in the response rates were observed depending on the mutational status or the initial ponatinib dose. By 43 months, event free survival, and progression free survival were 50% and 80%, respectively. At time of last follow-up, 47% of the patients had discontinued ponatinib due to toxicity (25%), lack of efficacy (25%), hematopoietic stem cell transplantation (37%) or death (13%). Most common non-hematological toxicities were liver toxicity (20%), lipase increase (10%), and hypertension 15%. No CV events were reported during treatment.

Summary/Conclusions: Ponatinib was shown to rescue a significant proportion of patients failing prior TKI treatment. It is worth noting that, with a median follow-up of more than 2 years, no CV events appeared, suggesting that early dose modification could be protective against the occurrence of vascular complications.

PB1833

EARLY GOOD LATER BETTER. RELATIONSHIP OF BCR-ABL LEVEL AT 12 MONTHS OF TARGET THERAPY WITH INDIVIDUAL CHARACTERISTICS OF MOLECULAR RESPONSE IN EARLY TREATMENT PERIOD IN CHRONIC MYELOID LEUKEMIA

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Background: The search of surrogate prognostic markers for early detection of high risk disease progression still is actual problem in chronic myeloid leukemia (CML) management. The existing prognostic scales consider characteristics only at moment of diagnosis, whereas individual BCR-ABL level trend remains out of its vision.

Aims: The aim of this study was to evaluate the relationship between individual characteristics of early response to treatment and BCR-ABL at 12 months level.

Table 1. The frequency of the optimal response (MMR) achievement at 12 months of TKI therapy in the relationship with type of first line therapy.

<table>
<thead>
<tr>
<th>Method</th>
<th>Frequency of MMR</th>
<th>Description</th>
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<tbody>
<tr>
<td>TKI1</td>
<td>45% (9/20)</td>
<td>Patients treated with TKI1 were subsequently switched to TKI2 (Table 1). We have conducted multivariate analysis of relationship between BCR-ABL levels at 12 months and early molecular response (EMR). BCR-ABL level at 12 months (≤10%) at 3 months achievement, individual rates of BCR-ABL decline, type of first line therapy factors of switching therapy from TKI1 to TKI2.</td>
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<tr>
<td>TKI2</td>
<td>55% (11/20)</td>
<td>The parameters that have statistical significance influence on BCR-ABL level at 12 months of therapy were as follows: individual rate of BCR-ABL decline from 3 months to baseline (&lt;0,1/0,1) – p=0,004, type of first-line therapy (TKI2 vs TKI1) – p=0.0002, switching of therapy from TKI1 to TKI2 (yes/no) – p&lt;0.0001. Achievement of EMR did not reach statistical significance – p=0,51. In addition, we have revealed the fact, that timely switch to TKI2 for resistant CML patients led to the rates of MMR achievement at 1 year of therapy similar to the MMR rates of patients having failed TKI1 treatment.</td>
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PB1834

EFFICACY OF GENERIC IMATINIB IN NEWLY DIAGNOSED CP-CML PATIENTS IN ESTONIAN POPULATION

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Background: Tyrosin kinase inhibitor (TKI) imatinib is the gold standard 1st line therapy of chronic phase chronic myeloid leukemia (CP-CML). Imatinib was implemented in Estonia for the 1st line therapy of CML in July 1, 2006. However in 2012 generic version of imatinib was approved in European Union and since January 1, 2014 only generic imatinib has been available in Estonia.

Aims: The aim of the study was to evaluate the clinical efficacy of generic imatinib in the treatment of CP-CML in Estonia and to compare results with historical group of patients treated brand name imatinib.

Methods: 25 patients in CP-CML have been diagnosed during 2014-2015 and have started 1st line treatment with generic imatinib. Optimal response was assessed at 3, 6 and 12 months after the start of treatment according to European LeukemiaNet 2013 guidelines: BCR/ABL ≤10%, <1% and ≤0,1% at 3, 6, 12 months respectively. For comparison historical group of 72 patients in CP-CML who received brand name imatinib for 1st line treatment during 2006-2013 were used. In this group pre-treatment with hydroxyurea for maximum 3 months but not interferon-alpha was allowed, OR was assessed at 6, 12 and 18 months after the start of imatinib and defined according to European LeukemiaNet 2010 recommendations.

Results: OR with generic imatinib was achieved in 16/21 (76.2%) evaluable patients at 3 months, 11/14 (78.6%) patients at 6 months and 7/11 (63.6%) at 12 months. At 18 months there were only 3 evaluable patients who all obtained OR. None of the patients not having OR at 3 months and continuing with imatinib achieved OR later. OR was achieved without TO in 18% of patients, eliminating drug to lymphoid blastic crisis in 9 months after diagnosis. Two patients had failure to generic imatinib - one patient having BCR/ABL level at 6 months over 10% and one patient over 1% at 12 months; both patients were switched to the 2nd line TKIs. Three patients had OR at 3 months without TO after 12 and 18 months, but 2 of them had treatment interruption periods due to poor tolerability. No new safety signal emerged. The most common adverse effects to generic imatinib occurring more than 10% of patients were nausea/vomiting, diarrhoea/constipation, muscle pain in legs, periorbital oedema and allergic skin reactions. Due to adverse events 6 patients were switched to different generic imatinib and one patient not tolerating two different generic imatinib was switched to the 2nd generation TKI. In the historical group OR was achieved in 33/45 (73%) evaluable patients at 6 months and 33/50 (66%) patients at 12 months. At 18 months OR was obtained in 22/51 (43%) evaluable patients. None of 11 patients not in OR at 6 months obtained OR at 12 or 18 months.

Summary/Conclusions: Generic imatinib appears to have the same efficacy as brand name imatinib. Despite differences in group size and OR definition by European LeukemiaNet 2010 vs 2013 recommendations the treatment results with generic and brand name imatinib were quite comparable with 78.6-66% of OR rate at 6 months and 63.6-66% at 12 months. To improve treatment results, for patients not achieving OR at 3 or 6 months should be offered treatment with 2nd generation TKI.

PB1835

ROLE OF CHR AS A SURROGATE FOR MMR AT 12 AND 18 MONTHS IN RESOURCE CONSTRAINT SETTINGS: PATIENTS UNABLE TO AFFORD FREQUENT MOLECULAR MONITORING

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haematologica | 2016; 101(s1) | 741