ions with genomic aberrations, e.g. TP53 with 17p- (p<.001), ATM with 11q- (p=.037), but there was no correlation between TP53mut and other recurrent mutations. Remarkably, 11 pretreated patients showed 2 to 4 TP53mut, while only a single untreated patient had two TP53mut. In the full trial cohort, none of the mutations had a significant impact on response, progression free survival (PFS) or overall survival (OS). Notably, in patients with 17p-, the incidence of TP53, SF3B1 and NOTCH1 mutations was similar in treatment naive (n=37) and pretreated (n=74) patients and the overall genomic landscape appeared not markedly different between those cohorts (Figure 1). These findings indicate that most genomic variants are present and are induced by fludarabine-based chemotherapy in 17p- CLL. Of note, in the 17p- front line cohort, there was a significant association of TP53 wild-type (hazard ratio 0.14; p=.02) and ATMmut status (hazard ratio 0.16; p=.04) with prolonged PFS. In contrast, within the refractory and 17p- relapsed subgroup, there was no significant association of any mutation with outcome. In the F-refractory cohort, when comparing the groups with (n=26) and without (n=21) 17p-, there was an association of ATMmut with absence of 17p- (p=.01), but no significant correlation to outcome.

Figure 1.

Summary/Conclusions: In conclusion, within the full trial cohort none of the recurrent mutations had an impact on outcome in the CLL2O trial. Fludarabine-based treatment does not appear to increase the overall complexity of the genomic landscape of 17p- CLL, but it might increase the number of intradividual TP53mut in a given tumor. TP53 is a prognostic factor in previously untreated, but not in pretreated and refractory patients enrolled within the CLL2O trial. Of note, in the F-refractory cohort 20/21 (95.2%) patients without 17p- and with TP53 wild-type had at least one other alteration such as 11q-, NOTCH1mut, ATMmut or SF3B1mut.

P595

IDEALALISIB IN COMBINATION WITH RITUXIMAB IN CHRONIC LYMPHOCYTIC LEUKEMIA AND TP53 ABERRATIONS

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Summary/Conclusions: This is the largest cohort reported to date for pts with CLL/SLL treated with IDELA+R, outside of clinical trials. Pts included in the EAP had similar demographic characteristics to those previously reported in clinical trials. 1 To date, available results indicate an acceptable profile of IDELA+R in the real-world setting for pts withTN CLL/SLL and 17p deletion/TP53m and for pts with R/R CLL/SLL.

Reference

P594

CHROMOSOME 8 ABNORMALITIES ARE ASSOCIATED WITH AN EVEN WORSE OUTCOME AND KARYOTYPE COMPLEXITY IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA AND TP53 ABERRATIONS

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Background: Idelalisib (IDEA) is a first-in-class selective PI3Kδ inhibitor approved in EU for use in combination with rituximab (R) for patients (pts) with relapsed CLL; or as first-line CLL treatment in the presence of del(17p) or TP53 mutation (TP53m) in pts unsuitable for chemo-immunotherapy. A post-authorisation, pre-national reimbursement early access program (EAP) was initiated for Australia, Belgium, Greece, Ireland, Spain and UK, for pts without other therapeutic options and who could not be included in an IDELA clinical trial.Pts with relapsed/refractory (R/R) CLL/SLL and treatment naive (TN) CLL/SLL with del(17p)/TP53m, were eligible for the CLL/SLL cohort. IDEA data outside clinical trials and in real-world settings is limited.

Aims: This analysis was to characterize baseline demographics of pts treated with IDELA+R in both TN CLL/SLL pts with del(17p)/TP53m and R/R CLL/SLL, outside of a clinical trial setting. Serious adverse events (SAE) reported are also presented.

Methods: The EAP enrolled pts from March 2015, analysis data-cut off was 15 January 2016. Available data were collected from de-identified pt registration data and SAE reports. This analysis summarizes baseline pt characteristics which were either mandatory or optional on the enrolment form. SAEs were reported whilst pts were on treatment. The proportion of missing data (unre- ported or unrecoverable) is also shown in the Table 1.

Results: Median follow up was 133 days (2-315). 170 pts with R/R CLL/SLL had documented prior treatment regimens (168 with specific treatment and 4 with number of lines only). Most commonly used prior therapies included anti-CD20 (85.6%), cyclophosphamide (69.3%), fludarabine (56.6%), bendamustine (43.3%) and prednisolone (40.0%). SAE data collected were consistent with previous clinical study SAE reporting with SAEs in 37/263 (14.1%) pts. SAEs included (3.0%) pneumonia, (2.7%) liver test elevations, (5.1%) neutropenia, (5 (1.9%) pneumonia, (4 (1.5%) skin reactions, (3 (1.1%) diarrhea and (3 (1.1%) febrile neutropenia.

Table 1.

<table>
<thead>
<tr>
<th>Baseline Demographic</th>
<th>Tn (n=144)</th>
<th>R/R (n=26)</th>
<th>Total (n=170)</th>
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</thead>
<tbody>
<tr>
<td>T (n=144)</td>
<td>1.06</td>
<td>0.82</td>
<td>1.07</td>
</tr>
<tr>
<td>R (n=26)</td>
<td>0.84</td>
<td>0.64</td>
<td>0.74</td>
</tr>
<tr>
<td>SAEs (n=170)</td>
<td>0.82</td>
<td>0.64</td>
<td>0.74</td>
</tr>
</tbody>
</table>

Summary/Conclusions: This is the largest cohort reported to date for pts with CLL/SLL treated with IDELA+R, outside of clinical trials. Pts included in the EAP had similar demographic characteristics to those previously reported in clinical trials. 1 To date, available results indicate an acceptable profile of IDELA+R in the real-world setting for pts withTN CLL/SLL and 17p deletion/TP53m and for pts with R/R CLL/SLL.

Reference
Methods: A total of 101 patients with TP53ab from 17 Spanish and Greek institutions were included in the study. 8p- and 8q+ were analyzed in peripheral blood samples by FISH using LPL (8p22) and MYC (8q24) probes (Abbott Molecular) in 75 and 101 cases, respectively. Clinical and cytogenetic data from patients with 8p- vs normal 8p (N-8p) and 8q+ vs normal 8q (N-8q) were compared.

Results: A total of 11/75 patients (14.7%) showed 8p- and 18/101 cases (17.8%) carried 8q+. In 6/75 patients (8%) both abnormalities were concomitant. As for the clinico-biological profile at diagnosis, 8p- and 8q+ cases displayed no differences regarding age, Hb/platelet/leucocyte values, as well as FISH detected abnormalities del(11q), del(13q) and trisomy 12 compared to cases with normal 8p (N-8p) and normal 8q (N-8q), respectively. However, cases with 8p- exhibited a higher incidence of B symptoms compared to N-8p cases (P=0.039). Interestingly, 8p- cases carried a higher number of 17p-deleted cells as well as a higher median number of chromosomal alterations detected by chromosomal banding analysis (CBA) (7 vs 3) and, therefore, a higher frequency of complex karyotypes (CK, defined as ≥3 structural/numerical aberrations) compared to N-8p cases (P=0.001, P=0.041 and P=0.006, respectively). Similarly, cases with 8q+ also showed a higher median number of chromosomal abnormalities (6.5 vs 2) and higher frequency of CK compared to N-8q cases (P=0.001 and P=0.002, respectively).

Ten-year survival analysis revealed a significant shorter overall survival (OS) for both 8p- and 8q+ (P=0.002 for 8p- vs N-8p, and P=0.007 for 8q+ vs N-8q). CK also had a negative impact on OS (P=0.018) (Figure 1). In multivariate analysis only CK retained independent significance (P=0.032, HR: 2.5).

Figure 1. Kaplan Meier plots for ten-year OS in patients carrying (A) 8p-, (B) 8q+ and (C) complex karyotype with 8q+ or N-8q.

Summary/Conclusions: 1. The prevalence of 8p- and 8q+ in this cohort of CLL patients with TP53ab was 14.7% and 17.8% respectively. 2. The detection of chromosome 8 abnormalities (8p- and/or 8q+) by FISH in patients with CLL and TP53ab is associated with karyotype complexity and further deteriorates outcome. 3. Genomic complexity assessed by CBA negatively impacts on survival even amongst patients with TP53ab. 4. Validation in large cohorts is required to elucidate if the observed dismal OS in CLL patients with 8p- and/or 8q+ is due to chromosome 8 alterations per se or by the genomic instability associated with complex karyotypes.


P596 OUTCOMES WITH SINGLE-AGENT IBRUTINIB BY PRIOR LINE OF THERAPY AND FOLLOWING IBRUTINIB DISCONTINUATION IN PATIENTS WITH CLL: ANALYSES FROM PHASE 3 STUDIES

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P597 SINGLE-AGENT IBRUTINIB VS STANDARD OF CARE FOR PATIENTS WITH RELAPSED/REFRACTORY (R/R) CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): AN ADJUSTED COMPARISON OF RESONATE™ WITH THE CLEARE DATABASE

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Background: The phase 3 RESONATE™ trial (NCT01578707) compared ibritinib (ibr) with ofatumumab (ofa) in patients (pts) with previously treated CLL and not eligible for purine analogue treatment. Ibr showed significantly improved progression-free survival (PFS; hazard ratio [HR]=0.22; 95% CI: 0.11-0.43; p<0.001) and 18-month overall survival (OS; adjusted for crossover) (HR=0.35 [0.16-0.75]) (Diels, ISPOR-EU 2015).

Aims: In the absence of a head-to-head comparison of single-agent ibr with other frequently used treatments, we investigated the relative efficacy of ibr vs physician choice in R/R CLL pts by comparing pt-level data from RESONATE™ with R/R pts in a real-world setting (the CLEARE database). The CLEARE database holds data on CLL pts from the Czech Republic, collected...