Abstract: PB1942

Title: PARTIAL RESPONSE WITH LYMPHOCYTOSIS (PR-L) IS NOT APPLICABLE FOR ACALABRUTINIB. AN ITALIAN MULTICENTER EXPERIENCE OF REAL LIFE.

Abstract Type: Publication Only

Session Title: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

Increased absolute lymphocyte count (ALC) characterizes chronic lymphocytic leukemia (CLL), and it is also observed in the first phase of treatment with Ibrutinib (IBR), the "first-in-class" Bruton's tyrosine kinase inhibitor (BTKi), independently of previous lines of treatment. The IBR induced lymphocytosis, which is due to a redistribution of lymphocytes from the neoplastic nodal compartment into the peripheral blood, is observed in 57% of patients treated in first line, and it is higher in IgHV mutated CLL. Prolonged lymphocytosis likely represents the persistence of a quiescent clone. This phenomenon is transient in most patients, resolving within 8 months, but can rarely persist over 12 months, without impact on survival. Despite lymphocytosis in IBR has been widely investigated, little is known about the presence and duration of lymphocytosis in patients treated with Acalabrutinib (Acala).

Aims:

The main purpose of this study is defining kinetics, timing, and impact of drug-induced lymphocytosis during treatment of CLL patients with Acala or IBR, to underline possible differences in terms of entity and duration of the lymphocytosis.

Methods:

In our retrospective study, we enrolled 181 patients (114 male and 67 female), treated in first line with BTKi monotherapy (111 IBR and 70 Acala), from 12 different Italian centers, with last follow up in January 2023. For each patient we collected data about the burden of disease at baseline (in terms of staging, adenopathy and splenomegaly), the biological features of the disease (cytogenetic aberrations and molecular mutations, IgHV mutational status) and the ALC at the baseline and at well-defined time-point (1-2- 3- 6- 9- 12 months) over an observational period of 1 year (Table 1).

Results:

We observed a median ALC increase after the beginning of therapy both in the IBR and in the Acala group. Median lymphocytosis was higher than baseline during the first months of treatment in both cohorts. A progressive decrease in median ALC occurred after the second month of treatment in both groups: at this time-point, median lymphocytes count was 70% of baseline in Acala cohort vs 81.5% in IBR cohort (p 0.049). From 6^{th} month to the end of the study, we found statistical differences in the ALC with higher counts in IBR. At 6^{th} months, median ALC was 5700/microL in Acala vs 10200/microL in IBR group, at 9^{th} 3800/microL vs 8070/microL and at 12^{th} 2600/microL vs 5150/microL (Table 1).

Summary/Conclusion:

Acala can determine, like IBR, an increase of ALC immediately after starting therapy. Therefore, lymphocytosis appears as a BTKi-class effect. Despite this, the kinetics of lymphocytosis are not overlapping when comparing the two drugs. From the 6^{th} month, the ALC reached almost-normal values in Acala group, with significantly statistical differences compared to IBR. These data suggest that the response criterion of PR-L may not be applicable for Acala.

Clinical and Biological characteristics and results 181 patients (last follow up January 2023)					
		All patients n=181	Ibrutinib arm n=111	Acalabrutinib arm N=70	P-value
Gender	**M, n (%)** **F, n (%)**	114 (63) 67 (37)	67(60) 44(40)	47(67) 23(33)	0.357
Rai Stadium	**A, n (%)** **B, n (%)** **C, n (%)**	24 (13) 79 (44) 78 (43)	18(16) 50(45) 43(39)	6(9) 29(41) 35(50)	0.193
Lymph nodes	**Absent** **< 5 cm** **5-10 cm** **> 10 cm**	10 90 40 22	6 55 22 13	4 35 19 9	0.933
Splenomegaly	**N**	110	66	44	0.965
FISH, n	**del 17p** **del 11q** **del 13q** **trisomy 12**	44 64 17 32	38 41 9 21	6 23 8 11	**< 0.001** 0.609 0.441 0.603
Molecular Biology, n	**TP53** **NOTCH1**	40 19	34 6	6 13	**0.002** **0.038**
IgVH mutational status, n	**Mutated** **unmutated**	64 82	43 44	21 38	0.175
Median ALC at different timepoints					
		All	**Ibrutinib arm**	**Acalabrutinib arm**	**P-value**
At baseline, Absolute/microL (normal range 1000-3000)		66120	63000	68815	0.909
1 month Absolute/microL % of baseline		68000 107	62995 113	78450 100	0.869 0.330
2 months Absolute/microL % of baseline		37015 80	36090 81	37960 70	0.363 **0.049**
3 months Absolute/microL % of baseline		23440 55	22390 53	24420 56	0.301 0.216
6 months Absolute/microL % of baseline		9000 26	10200 30	5700 17	**0.030** 0.064
9 months Absolute/microL % of baseline		6955 17	8070 21	3800 7	**0.016** 0.040
12 months Absolute/microL % of baseline		4240 11	5150 11	2600 8	**0.030** 0.187

Table 1: Clinical and Biological characteristics and results

Keywords: Bruton's tyrosine kinase inhibitor (BTKi), Absolute lymphocyte count, B-CLL