

## **Abstract: PB1948**

### **Title: ACALABRUTINIB IN THE TREATMENT OF RICHTER SYNDROME**

#### **Abstract Type: Publication Only**

#### **Session Title: Chronic lymphocytic leukemia and related disorders - Clinical**

#### **Background:**

Richter's syndrome is an aggressive histologic transformation of chronic lymphocytic leukemia, most commonly to diffuse large B-cell lymphoma, occurring in about 2-15% of patients with CLL. Outcomes for patients with RS are generally poor with median overall survival of 5.9–11.4 months and ongoing unmet clinical need for effective therapies. B-cell receptor signaling through Bruton tyrosine kinase is one of the essential growth pathways for CLL. Acalabrutinib is a highly selective, potent BTK inhibitor has shown significant efficacy in relapsed/refractory and untreated CLL.

#### **Aims:**

improving the outcomes of patients with RS

#### **Methods:**

We reported 5 cases of Richter syndrome treated with acalabrutinib in combination with immunochemotherapy in the period from June 2020 to February 2023. Table 1 shows the characteristics of 5 CLL pts who developed biopsy-proven DLBCL. The median time to transformation from CLL was 33,8 months (range 4-66 months). Determination of clonal association with CLL by blot hybridization was not available, but in 4 pts the p53 expression was studied by immunohistochemical method to determine the pathogenetic pathway of RS development and the PD-1 expression confirm the clonal association with CLL

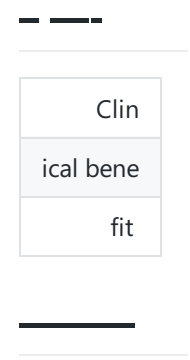
#### **Results:**

At the time of transformation, 2 pts were initially treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) with a suboptimal response, then acalabrutinib was added, 2 pts received 6 cycles of R-CHOP+ acalabrutinib and 1 patient - 5 cycles R-CVP + acalabrutinib. The overall response was 80% (1 pts had a CR and 2 PR), stabilization of the tumor process was achieved in 1 patient. The 3 pts with CR and PR are currently receiving acalabrutinib, 1 prs had progression of DLBCL after 15 months of acalabrutinib therapy and 1 pts died from Covid19- infection on the background of stabilization of the disease Acalabrutinib was well-tolerated; no patient required discontinuation as a result of adverse events.

**At the time of CLL diagnosis** (table1)

Patient	1	2	3	4	5
Age, y	75	28	64	34	65
Sex	M	F	M	F	M
Rai stage	II	II	II	II	II
CLL therapy	Rituximab monotherapy Efficacy - CR	none	FCG , 6 cycle Efficacy - CR	FCR 6 cycles Efficacy - CR;	none
Time from last CLL therapy to RS diagnosis months	66	45	48	4	6
Localization of the tumor	Peripheral, retroperitoneal LN, stomach	Peripheral LN, nasal sinuses, upper palate	Retroperitoneal LN, colon	Tumor of the tongue root	Oropharynx, right tonsil, peripheral and retroperitoneal LN
Subtype	GCB- type	Non-GCB	Non-GCB	Non-GCB	Non-GCB

**At the time of DLBCL diagnosis** (table 1- continuation)

Patient	1	2	3	4	5
Age, y	82	32	69	35	66
WBC ×10 <sup>9</sup> /L	5,53	6,23	10,25	0,84	30,27
Hemoglobin, g/dL	12,4	11,6	10,7	6,6	14,0
Platelet ×10 <sup>9</sup> /L	178,0	294,0	120,0	41,0	331,0
Bone marrow lymphocytes, %	21	44	17.2	8.2	55
<i>IGHV</i> mutation status	not possible to establish	Unmutated	Unmutated ( CLL1 subgroup)	not possible to establish	Unmutated
FISH	Normal	Normal	Normal	Normal	Deletion of 17p13/TP53
Mutation TP53	No mutations	No	No	No	Mutation p.R248W in exon 7
Mutation NOTCH1	-	Mutation c7544	No	No	Mutation c 7389
p53/PDL-1 expression	+/+	-	+++ / + ++	++ / ++	+++ / + ++
Related with CLL	De novo	unknown	clonally related	clonally related	clonally related
Duration of acalabrutinib therapy, months	27	20	15	9	10
Best response	PR	CR		Stable disease	PR
Status at most recent follow-up	Acalabrutinib therapy continues	Acalabrutinib therapy continues	Death from the progression of DLBCL	Death by COVID19	Acalabrutinib therapy continues

**Summary/Conclusion:**

Our experience suggests that acalabrutinib in combination with immunochemotherapy has potential as a novel therapeutic approach for patients with Richter syndrome.

**Keywords:** Chronic lymphocytic leukemia