Poster #: 1907

XXI IWCLL International Workshop on CLL

Autoimmune cytopenias in patients with chronic lymphocytic leukemia receiving acalabrutinib treatment

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BACKGROUND

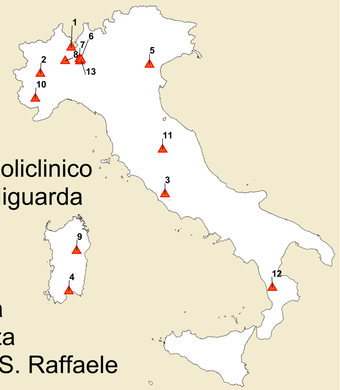
- Among autoimmune complications, autoimmune cytopenias (AIC) involve 5-9% of patients affected by chronic lymphocytic leukemia (CLL)[1]
- To date, the effects of acalabrutinib - a second-generation, covalent inhibitor of the BTK - on preexisting and treatment emergent AIC have not been fully investigated. In a few case reports, acalabrutinib has been successfully administered for the treatment of patients with immune thrombocytopenia (ITP) or pure red cell aplasia (PRCA)[2-3]

AIMS

- The aim of this study is to analyze the characteristics and outcome of preexisting AIC and the incidence, features and outcome of treatment-emergent AIC in patients with CLL receiving acalabrutinib monotherapy.

Figure 1. Italian centers involved in the study

1. Varese
2. Torino
3. Roma
4. Cagliari
5. Padova
6. Milano Policlinico
7. Milano Niguarda
8. Novara
9. Nuoro
10. Cuneo
11. Perugia
12. Cosenza
13. Milano S. Raffaele



METHODS

We retrospectively collected clinical and biological data from **consecutive patients diagnosed with CLL** and treated with **acalabrutinib** in 13 Italian centers (Figure 1).

RESULTS

- We collected data from **285 patients** with CLL (male/female ratio: 1.6) receiving **acalabrutinib monotherapy** (Table 1).
- The median follow-up for the entire cohort was 13 months
- **CLL outcome** → The overall response rate (**ORR**) was 90.9%, with 8.4% of complete response (**CR**) and 82.5% of partial response (**PR**).
- In the overall cohort, PFS and median OS were not reached.
- Preexisting AIC were reported in 20 patients (7%) (Figure 2)
  - → 11/20 (**55%**) AIHA
  - → 8/20 (**40%**) ITP
  - → 1/20 (**5%**) PRCA
- 95% of patient with pre-existing AIC received an AIC-directed treatment [i.e. corticosteroids (37%) or corticosteroids + rituximab (26%)].
- Acalabrutinib treatment: AIC distribution (information available for 19 patients at initiation and 18 patients following treatment) (Figure 3)
  - At initiation:
    - active in 42%
    - controlled in 37%
    - solved in 21%
  - Following treatment:
    - resolved in 61%
    - improved 6%
    - stable 33%
    - worsened 0%

4 patients (1.5%) developed treatment-emergent AIC, including 2 cases of ITP, 1 of AIHA, and 1 of autoimmune granulocytopenia (AIG) (Table 2)

Notably, patients with or without AIC (preexisting and treatment-emergent AIC) didn't differ significantly in terms of progression-free survival and overall survival.

Table 1. Characteristics of patients at the start of treatment with acalabrutinib

		Total sample
Total no of patient		285
Median age, y(range)		73 (44-93)
No. Of males		179 (63%)
Median lymphocyte count, *10^6L (range)		60000 (600-766810) [n=249]
Median hemoglobin, g/dL (range)		11.15 (9.5-12.8) [n=250]
Median platelet count *10^6L (range)		136000 (39-560000) [n=250]
Binet stage		285
	A	8 (3%)
	B	143 (50%)
	C	134 (47%)
Elevated lactate dehydrogenase		112 (40%) [n=282]
Median β2-microglobulin, mg/L(range)		4.2 (1.0-18.0) [n=205]
Unmutated IGHV		192 (71%) [n=271]
FISH abnormalities*		[n=271]
	del(13q)	61 (23%)
	Negative	90 (33%)
	Trisomy12	33 (12%)
	del(11q)	50 (18%)
	del(17p)	37 (14%)
Mutated TP53		36 (13%) [279]
No. Of treatment naive patients		219 (77%)
Median no. Of previous therapies (range)		0 (0-5)

Figure 2. History of AIC

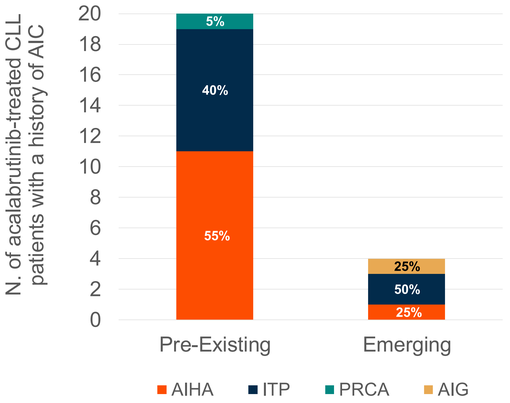


Figure 3. AIC distribution

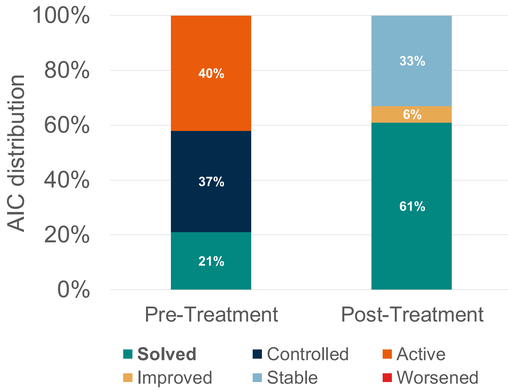


Table 2. Characteristics, management and outcome for patients with treatment-emergent AICs

Patient ID	AIC type	Age (y)	Sex	IGHV	FISH	TP53	No. of previous therapies	Time of occurrence*	Management	AIC outcome	Best CLL response
Cuneo-CN009	ITP	55	M	UM	del(13q)	WT	0	8 days	Acalabrutinib temporarily suspended; steroids, IVIG and Rituximab added; Acalabrutinib restarted at full dose	Active	PR
UCSC - 19	AG	75	M	NA	NA	NA	0	22 days	G-CSF	Resolved	CR
UCSC - 47	AIHA	71	F	UM	del(11q)	WT	0	24 days	Not treated	Controlled	SD
Nuoro - 03	ITP	50	M	UM	Negative	WT	0	453 days	Steroids Added	Resolved	PR

CONCLUSIONS

- Our retrospective analysis indicates that preexisting AIC can be effectively managed in the majority of patients with CLL treated with acalabrutinib. Similarly, treatment-emergent AIC were observed infrequently and were generally manageable. Notably, in this cohort and with the current follow up, the presence of AIC did not negatively impact treatment outcomes in patients receiving acalabrutinib.

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