Occurrence and Evolution of Autoimmune Cytopenias in Chronic Lymphocytic Leukemia Patients treated with Venetoclax: a study of the French Innovative Leukemia Organization (FILO)

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iwCLL

Introduction

Autoimmune cytopenias (AICs) are a common complication in chronic lymphocytic leukemia (CLL) occurring in about 5 to 15% of cases, however their impact on survival is still controversial. Some drugs like fludarabine or ibrutinib are known to trigger AICs, but there is poor evidence regarding the role of venetoclax (VEN) in those events. Some authors have reported successful treatment of AIC with VEN, while some cases of emerging AICs were reported in VEN associated trials. Furthermore, its frequent use with anti-CD20 agents might represent a confounding factor to assess its impact on AIC

Objective

Evaluate the outcome of AICs in CLL patients treated with VEN.

These are the results of a retrospective multicenter study of the FILO

Materiel and methods

We retrospectively collected in all the FILO centers the cases of CLL patients who presented any kind of AICs [autoimmune hemolytic anemia (AIHA), autoimmune thrombocytopenia (AIT), autoimmune erythroblastopenia (AIEB), aplastic anemia (AA), EVANS syndrome (ES) or autoimmune neutropenia (AIN) before or after treatment with VEN. Response criteria were used as already published (Michallet et al, Leuk Lymphoma 2011). Regarding CLL response by itself, iwCLL criteria were used except for bone marrow biopsy criteria, then we defined complete response (CR) as clinical CR.

Results

Patient Characteristics

Eighteen patients were included from 13 FILO centers in France

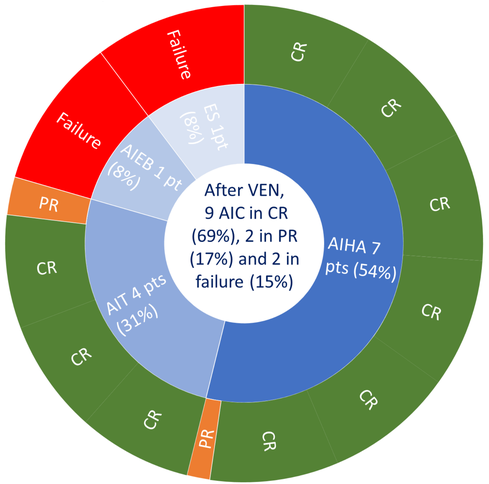
	N=18
Median age (years, range)	81 (65-90)
Hierarchical cytogenetics (FISH) classification	
Del(17p)	6 (33)
Del(11q)	4 (22)
Trisomy 12	0
Normal	5 (28)
Del(13q)	1 (6)
Other	2(11)
Mutated *TP53*	
Yes	5 (28)
No	9 (50)
Unknown	4 (22)
IGHV gene mutation status	
Unmutated	10 (56)
Unknown	8(44)
Complex karyotype	
Yes	7 (39)
No	11 (61)
Number of previous lines	2(1-8)
Patients with Previous event of AIC	14(78)
AHAI	9 (50)
TAI	6 (33)
EB	2 (11)
EVANS syndrome	1 (6)
Median Number of AIC events	1,5 (1-10)

Traitement with VEN = 18 patients

Active AIC at VEN initiation = 13 pts (72%)

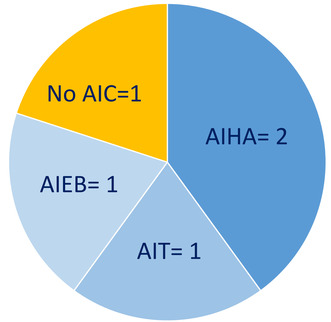
No AIC at VEN initiation = 5 pts (28%)

Responses of AIC under VEN treatment



Regarding the CLL, 8 out of 13 achieved clinical CR (61 %), 4 (31%) in PR and one (8%) in progression. There seemed to be a correlation between the response of the CLL and the AIC: all patients who achieve a CR of the CLL were also in CR regarding the AIC. In the same way, the 2 patients in failure regarding the AIC were in progression and PR of the CLL.

Development of AIC after introduction of VEN



AIC occurred at 2.9 months in median (1.9-4.3) after initiation of the treatment. VEN was definitely stopped for all 4 patients with AIC at D0 of the AIC for 2 patients, D1 and D38 for the 2 others.

Conclusion

VEN can be both the cause or the treatment of AICs associated with CLL.

When introduced while an AIC is active, it results in CR of the AIC in a majority of the cases and seems to be correlated with the response of the CLL.

It is more difficult to conclude about the AIC triggered by VEN in this retrospective setting, because VEN was stopped quasi immediately after AIC and never reintroduced.

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