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POSTER ABSTRACTS

632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Outcomes of Chronic Myeloid Leukemia Patients after Therapeutic Failure to Asciminib, a Multicenter Observational Study

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Introduction: Asciminib has recently entered the market as a promising option for patients with chronic myeloid leukemia (CML) and therapeutic failure to ³ 2 tyrosine kinase inhibitors (TKIs). It presents a relevant rate of therapeutic success thanks to its different mechanism of action, being the first in its class to produce an allosteric inhibition on the myristoylated pocket of ABL. However, a percentage of patients fail this drug due to intolerance or resistance. This group constitutes a highly polytreated population with few therapeutic options. The aim of this analysis is to determine the most frequent treatment strategies in this setting, as well as to ascertain the prognosis in this difficult to treat group.
Material and methods: a retrospective descriptive multicenter observational study was carried out. Eligible patients were those with a diagnosis of CML, >18 years and who had presented a therapeutic failure to asciminib, due to resistance or intolerance. Patients were selected from a cohort of 85 CML patients who received asciminib through a managed-access program.
Results: A total of 19 patients were recruited from 17 centers in Spain. Median age at the time of therapeutic failure to asciminib was 61.7 years. Median time from diagnosis to asciminib failure was 7.9 years (range 1.7-25.5), median number of previous lines was 5. 47% of patients had previously received ponatinib and 15.8% (3/19) had received an allogeneic hematopoietic stem cell transplantation (allo-HSCT) prior to asciminib. Median time on asciminib was 5.6 months (range 0.7- 40.9). 42% of patients (8/19) failed treatment due to intolerance and 58% (11/19) due to resistance. Four of them had progression to accelerated/blastic phase at the time of withdrawal. Of the intolerant patients, the most frequent reason for discontinuation was pancreatitis (50%, 4/8). The remaining causes were renal failure (1), pleural effusion (1), fatigue (1), and neurological symptoms (1).

Regarding the intolerant group, 2 patients did not require restart of treatment due to a sustained deep molecular response (MR). The rest (6/8) required treatment, which in all cases involved restarting a classic TKI that they had already received (2 imatinib, 2 dasatinib, 2 nilotinib). In 50% (3/6) dose reductions were used to control adverse events (AEs), which in 2/3 patients compromised efficacy. In another case, low-dose corticosteroid therapy was used for the management of pleural effusion, maintaining standard dose. Only 1/8 intolerant patients required an additional change of treatment, and all of them are still alive and without progression to advanced stages at the last follow-up.
Regarding the patients that required treatment change due to progression to advanced phases, one patient underwent allo-HSCT. The rest were not candidates due to age or clinical impairment (1 received dasatinib, 1 hydroxyurea (HU), 1 without treatment). Only the patient who underwent HSCT is alive more than one year after the procedure with a grade 5 MR. In the rest the median overall survival (OS) was less than 1 month. Of the remaining resistant patients, 4/7 (57%) received ponatinib (1 of 4 had received it previously), 1 imatinib, 1 allo-HSCT and the other patient received cytarabine + interferon + HU. Three of 7 patients required additional lines including change of TKI (asciminib, nilotinib, dasatinib) and other strategies (HU, busulfan, interferon, cytarabine). In terms of response, only the patient undergoing HSCT maintained a mayor MR (1/7). One patient maintained a complete cytogenetic response and the other 2 patients were unable to improve response despite treatment (maintaining worse response than CHR at the end of follow-up). Two patients died (1 acute myocardial infarction, 1 digestive neoplasia). With a median follow-up of 11.2 months, OS of the global cohort is 73%; 100% for intolerant patients, 71% for resistant patients and 25% for those in accelerated/blastic phase.
Conclusions: Patients who fail asciminib are a particularly difficult to manage group. In intolerant patients, dose reductions and symptomatic management of AEs may be an appropriate strategy. Resistant patients currently represent an unmet therapeutic need, with low cytogenetic and molecular response rates and poor survival with current strategies. Patients with progression to advanced phases have a dismal prognosis, HSCT may be the only option that provides long-term survival in this group.

Disclosures Pérez-Lamas: *Novartis:* Other: Travel grants; *Incyte:* Other: Travel grants. **García Gutiérrez:** *Incyte:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel grants, Research Funding; *Pfizer:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Travel grants, Research Funding; *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding.

	n=19
Baseline characteristics of patients with therapeutic failure to asciminib.	
Median age at asciminib failure, years (range)	61.7 (41.6 – 87.6)
Sex, n (%)	males 9 (47.4) females 10 (53.7)
Median time since diagnosis, years (range)	7.9 (1.7 – 25.6)
Sokal index at diagnosis, n (%)	
Low	6 (31.6)
Intermediate	6 (31.6)
High	6 (31.6)
Unknown	1 (0.05)
Phase at diagnosis, n (%)	
Chronic phase	18 (95)
Accelerated phase	1 (0.05)
Median of previous lines, no. (range)	5 (3-7)
imatinib, n (%)	16 (84.2)
dasatinib, n (%)	18 (94.7)
nilotinib, n (%)	13 (68.4)
bosutinib, n (%)	13 (68.4)
ponatinib, n (%)	9 (47.4)
Allogenic HSCT, n (%)	3 (15.8)
Median time on asciminib, months (range)	5.6 (0.7 – 40.9)
Disease status at asciminib initiation, n (%)	
Accelerated/blastic phase	2 (10.5)
Worse response than CHR	2 (10.5)
CHR	9 (47.4)
CCR	3 (15.8)
MMR	3 (15.8)
Reason for asciminib discontinuation, n (%)	
Resistance	11 (58)
Alert / suboptimal response*	0
Resistance*	7 (37)
Progression to accelerated/blastic phase*	4 (21)
Intolerance	8 (42)
Treatment after discontinuation	
Mean number of lines after asciminib, no. (range)	1.26 (0 - 4)
Intolerant to asciminib	0.87 (0 - 2)
Resistant to asciminib	1.54 (0 - 4)
Classic TKI, n (%)	
Imatinib	3 (15.8)
Dasatinib	4 (21.1)
Nilotinib	3 (15.8)
Bosutinib	0
Ponatinib	4 (21.1)
Asciminib, n (%)	1 (5.2)
Allogenic HSCT, n (%)	2 (10.5)
Other options, n (%)	
Cytarabine	1 (5.2)
Busulfan	1 (5.2)
Hydroxyurea	3 (15.8)
Interferon	2 (10.5)
Clinical trial	1 (5.2)

Table 1. Baseline characteristics of patients with therapeutic failure to asciminib and treatment after discontinuation.
HSCT: hematopoietic stem cell transplantation. CHR: complete hematologic response. CCR: complete cytogenetic response. MMR: major molecular response. TKI: tyrosine kinase inhibitor.
** Based on the European LeukemiaNet 2019 criteria.*

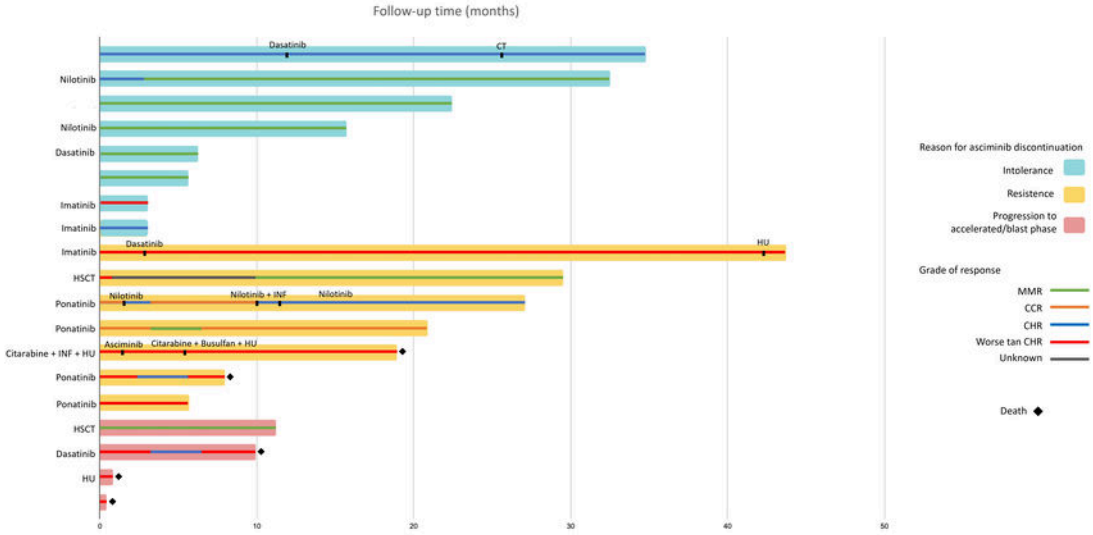

Figure 1. Swimmer-plot of patients after asciminib discontinuation.
Each bar represents a patient of the study.
HU: hydroxyurea; INF: interferon; HSCT: hematopoietic stem cell transplantation; MMR: major molecular response; CCR: complete cytogenetic response; CHR: complete hematologic response.

Figure 1

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