Abstract: P410

Title: ASCIMINIB FOR RELAPSED OR REFRACTORY PHILADELPHIA POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA (PH+ ALL) AND LYMPHOID BLAST CRISIS CHRONIC MYELOGENOUS LEUKEMIA (LBC-CML).

Abstract Type: Poster Presentation

Topic: Acute lymphoblastic leukemia - Clinical

Background:

The combination of tyrosine kinase inhibitors (TKIs) with conventional chemotherapy has greatly improved the prognosis of Philadelphia positive acute lymphoblastic leukemias (Ph+ ALL). However, 20-30% of patients experience relapse, often due to BCR::ABL1 TK domain mutations. Asciminib, a novel STAMP (Specifically Targeting the ABL Myristoyl Pocket) inhibitor of BCR::ABL1, showed promising activity against various ABL1 kinase domain mutations (ABL1 TKD), including the T315I gatekeeper mutation.

Aims:

Limited data are available on the use of asciminib of in Ph+ ALL/lymphoid blast crisis chronic myelogenous leukemia (LBC-CML) after conventional TKI failure. We decided to retrospectively analyse the efficacy of asciminib (ASC) used in compassionate and named access programs in French centers from the GRAALL group.

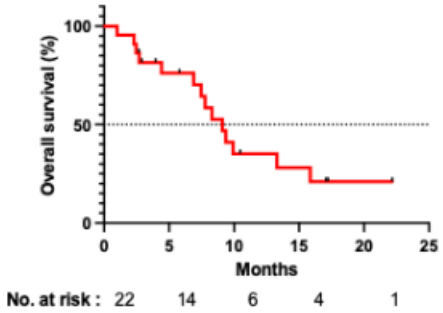
Methods:

Patients treated with ASC alone or in combination for relapsed/refractory Ph+ ALL or LBC-CML in the context of compassionate use or named access program were eligible. Patient data were manually collected from electronic or paper records. Complete molecular remission was defined as BCR::ABL1 in blood < 0,01% or bone marrow IgTCR <10-5.

Results:

From February 2020 to February 2024, 22 patients including 18 Ph+ ALL and 4 LBC-CML were registered. Median age was 58 years (19-83) and sex ratio was 1.0. At the time of ASC initiation, 9 patients were in 3rd line of therapy and 7 patients were in 4th or subsequent line of therapy. Six patients had relapsed post allogenic transplantation. Three patients had refractory disease (14%) and central nervous system involvement was recorded in 24% of cases. A median of three TKIs were used prior to ASC (IQR 2-3). At the time of analysis, median follow-up from ASC initiation was 7.6 months (CI95% 5.2-10.0) and median duration of ASC based therapy was 5.1 months (CI95% 3.0-7.1). Mutations of ABL1 TK domain were analyzed in 19 out of 22 patients before treatment with ASC. Mutations in ABL1 were detected in 14 patients (73.7%) including T315I in 7 patients, E255V/K in 2 patients, and compound mutation (T315I and E255V) in 3 patients. ASC was administered as monotherapy in 48% of cases. 5 patients (23%) were treated with a combination of ASC and chemotherapy, including 2 patients treated intensively and 3 patients who received low-intensity chemotherapy. ASC was combined with immunotherapy in 3 patients, and with other TKI in 2 patients (Ponatinib and Dasatinib). ASC daily doses ranged from 40 mg twice daily in 3 patients (17%) to 200 mg twice daily in the others (80%). Eighteen patients achieved complete hematologic remission (81.8 %). Only one patient presented with refractory disease. A complete molecular remission was observed in 10 of the responding patients (10/18). Survival analysis showed a median overall survival (OS) of 9.1 months (figure 1). Median OS for patients treated with ASC as a monotherapy or in combination were comparable. Out of the 14 deaths, 11 were due to relapse and 3 to uncontrolled infection. Two patients underwent allogeneic transplantation after treatment with ASC and two others received CAR T cells treatment.

Figure 1: Overall survival after Asciminib treatment



Summary/Conclusion:

We report the first real life cohort of patient treated with ASC for R/R Ph+ ALL/LBC-ALL in France. Our data suggest that ASC, alone or in combination, induced a high rate of complete remission in patients previously exposed to several line of therapy and despite the presence BCR::ABL1 TK domain mutations. The sensitivity to ASC translated in a median OS of 9.1 months without signal for limiting toxicities with the limitation of the retrospective nature of our study.

Keywords: Asciminib, Acute lymphoblastic leukemia