

Abstract: PB1972

Title: ASC4START: A PHASE IIIB, OPEN-LABEL, RANDOMIZED STUDY OF ASCIMINIB VERSUS NILOTINIB IN PATIENTS WITH NEWLY DIAGNOSED PH+ CHRONIC MYELOGENOUS LEUKEMIA IN CHRONIC PHASE

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Session Title: Chronic myeloid leukemia - Clinical

Background:

Tyrosine kinase inhibitors (TKIs) have improved treatment outcomes for patients (pts) with newly diagnosed chronic myelogenous leukemia in chronic phase (CML-CP), transforming CML into a chronic disease requiring long-term treatment. However, new treatments are needed combining good efficacy and favorable safety. Asciminib is a first-in-class BCR::ABL1 inhibitor approved for pts with Philadelphia chromosome-positive (Ph+) CML-CP previously treated with ≥ 2 prior TKIs. Asciminib specifically targets the ABL myristoyl pocket (STAMP), which compared with the selectivity of second-generation (2G) TKIs can reduce off-target effects and improve tolerability yet maintain efficacy and reduce the probability of developing resistance. ASC4FIRST (NCT04971226) is investigating the efficacy and safety of asciminib vs investigator-selected TKI in pts with newly diagnosed Ph+ CML-CP, and further data in these pts may address patient-centric objectives, including pts remaining on treatment without permanent discontinuation due to adverse events (AEs).

Aims:

ASC4START (NCT05456191) will primarily evaluate the tolerability of asciminib vs the 2G TKI nilotinib in adults with newly diagnosed Ph+ CML-CP, as measured by the time to study treatment discontinuation due to adverse event (TTDAE), safety, efficacy, and quality of life (QoL) outcomes.

Methods:

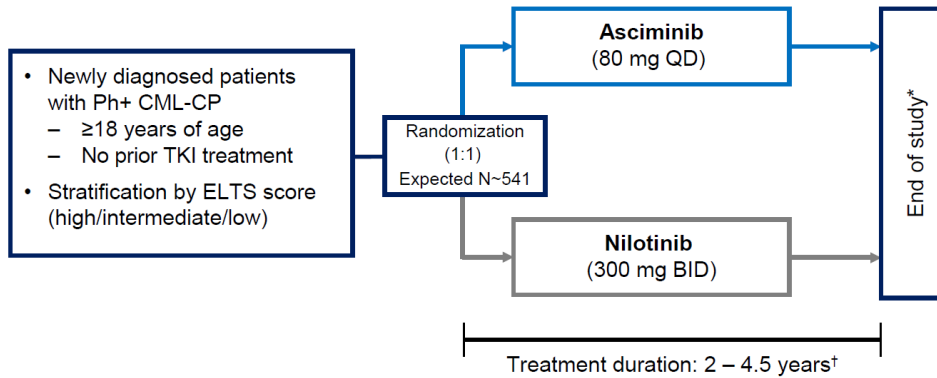
This is a phase IIIb, multi-center, open-label, randomized study in pts ≥ 18 years of age with newly diagnosed Ph+ CML-CP. The trial aims to enroll 541 pts with CML-CP diagnosed within 3 months of study entry and an Eastern Cooperative Oncology Group performance status ≤ 1 . Pts are excluded if they have received previous treatment for CML with any other anticancer agents (except hydroxyurea and/or anagrelide), have confirmed central nervous system infiltration, or have impaired cardiac function or abnormalities in cardiac repolarization. Pts are randomized 1:1 to asciminib 80 mg once daily or nilotinib 300 mg twice daily (both given orally under fasting conditions) with stratification based on European Treatment Outcome Study long-term survival (ELTS) score at diagnosis (high vs intermediate vs low) to achieve balance between the arms (Figure). The primary endpoint is TTDAE (time from the date of the first dose of study treatment to the date of discontinuation of study treatment due to an AE). Secondary endpoints include type, frequency and severity of AEs; dose modifications due to AE; changes in laboratory values outside pre-determined ranges; clinically notable ECG changes and other safety data; time to discontinuation due to lack of efficacy/treatment failure/disease progression/suboptimal response/death; major molecular response (MMR), MR⁴, MR^{4.5}, complete hematological response, and BCR::ABL1^{IS} $\leq 1\%$ at and by all scheduled data collection time points; duration of and time to first MMR, MR⁴, and MR^{4.5}; time to treatment failure; event-free survival, progression-free survival and overall survival; change from baseline in overall scores and individual scales of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaires QLQ-C30 and QLQ-CML24.

Results:

Recruitment was initiated in November 2022. As of 30 January 2023, 16 pts have been randomized and are receiving treatment (n=7 Germany, n=6 France, n=1 each Bulgaria, Czechia, and Slovakia), 13 more are in screening. Pts will be treated until approximately 64 discontinuations of either study treatment due to AEs are met. Treatment duration is expected to be 2–4.5 years for individual pts.

Summary/Conclusion:

The study is actively recruiting pts.



*Participants can be treated in the study until approximately 64 discontinuations due to adverse event are met. End of study is defined as when the necessary number of events has been reached and when end of treatment and the last assessments are completed.

†Expected treatment duration for individual patients.

CML-CP, chronic myelogenous leukemia in chronic phase; BID, twice daily; ELTS, European Treatment Outcome Study (EUTOS) long-term survival; N, approximate number of participants required to achieve 64 discontinuations due to adverse events; Ph+, Philadelphia chromosome-positive; QD, once daily; TKI, tyrosine kinase inhibitor.

Keywords: Phase III, Chronic myeloid leukemia, Clinical trial, Tyrosine kinase inhibitor