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POSTER ABSTRACTS

632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Sustained Efficacy and Safety with Asciminib (ASC) after Almost 4 Years of Median Follow-up from Ascembl, a Phase 3 Study of ASC Vs Bosutinib (BOS) in Patients (Pts) with Chronic Myeloid Leukemia in Chronic Phase (CML-CP) after ≥2 Prior Tyrosine Kinase Inhibitors (TKIs): An End of Study Treatment (EOS Tx) Update, Including Results from Switch Population

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INTRODUCTION CML requires chronic therapy, emphasizing the need for Txs that are characterized by high, durable efficacy and a low adverse event (AE) burden. ASC, the first BCR::ABL1 inhibitor Specifically Targeting the ABL Myristoyl Pocket (STAMP), demonstrated significantly superior efficacy and better safety/tolerability compared with BOS in pts with CML-CP who received ≥2 prior TKIs in the phase 3 ASCEMBL study. Major molecular response (MMR) rate was 25.5% with ASC vs 13.2% with BOS at wk 24, meeting the primary objective, and 37.6% vs 15.8% at wk 96, meeting the key secondary objective.

Despite the longer duration of exposure to ASC, safety/tolerability remained consistently better with ASC vs BOS, with fewer all-grade and grade ≥3 AEs and AEs leading to Tx discontinuation observed.
After a median follow-up of 3.7 y, we report EOS Tx results from ASCEMBL (cutoff: March 22, 2023). We also report the first available data from pts who experienced Tx failure on BOS and switched to ASC.

METHODS Adults (aged ≥18 y) with CML-CP after ≥2 prior TKIs, with intolerance or lack of efficacy per 2013 ELN recommendations were randomized 2:1 to receive either ASC 40 mg twice daily or BOS 500 mg once daily. Pts who met Tx failure criteria per 2013 ELN while on BOS could switch to ASC and were analyzed separately. Pts who discontinued BOS due to intolerance could not switch. EOS will occur 5 y from when the last enrolled pt received first Tx dose.

RESULTS A total of 233 pts were randomized to ASC (n=157) or BOS (n=76). The most common reason for discontinuation was lack of efficacy in 40 (25.5%) pts on ASC and 28 (36.8%) on BOS. At the time of EOS Tx cutoff, Tx with ASC and BOS was ongoing in 77 (49.4%) and 8 (10.5%) pts, respectively; pts deriving benefit from study Tx at EOS TX, per investigator assessment, continued receiving posttrial access.
MMR rate at wk 156 continued to be higher with ASC (33.8%) than with BOS (10.5%) (Figure 1). The difference after adjusting for baseline (BL) major cytogenetic response was 23.2%(95% CI, 13.1%-33.2%; 2-sided $P<.001$). The *BCR::ABL1* ^{IS} ≤1% rate at wk 156 in pts without this level of response at BL also continued to be higher with ASC (43.0%) than with BOS (11.1%).
Despite the longer median duration (range) of exposure to ASC (156.0 [0.1-256.3] wk) vs BOS (30.5 [1.0-239.3] wk), safety/tolerability of ASC continued to be better compared with BOS and were consistent with previous analyses. Two new pts had AEs leading to Tx discontinuation since the wk 96 cutoff (1 pt on ASC reported pregnancy; 1 pt on BOS reported diarrhea), and rates remained lower with ASC vs BOS (8.3% vs 27.6%). The most frequent (≥10%) grade ≥3 AEs with ASC vs BOS were thrombocytopenia (22.4% vs 9.2%), neutropenia (18.6% vs 14.5%), diarrhea (0% vs 10.5%), and increased alanine aminotransferase (0.6% vs 14.5%). Most AEs occurred within the first 6 months (Figure 2). Exposure-adjusted incidence rates of arterial occlusive events (AOEs) with ASC decreased since the wk 96 cutoff, from 3.0 to 2.2 per 100 pt-y, and no new AOEs occurred with ASC, indicating that the risk of AOEs did not increase over time. Among pts who discontinued Tx due to lack of efficacy or disease progression, no new mutations occurred since the wk 96 cutoff.
Of 28 pts who discontinued BOS for lack of efficacy, 25 switched to ASC. Almost all switch pts (96%) had BL *BCR::ABL1* ^{IS} >10% prior to switch. No switch pts achieved MMR at or by wk 48 post switch. However, at wk 48, 24% achieved *BCR::ABL1* ^{IS} ≤10% and 8% achieved *BCR::ABL1* ^{IS} ≤1%. The safety profile of ASC in switch pts was consistent with that in pts receiving ASC in the randomized period. Most frequent (≥10%) grade ≥3 AEs were neutropenia (32.0%) and thrombocytopenia (24.0%). AEs leading to Tx discontinuation occurred in 8.0% of switch pts.

CONCLUSIONS With almost 4 y of follow-up in ASCEMBL, ASC continued to show greater efficacy and better safety/tolerability than BOS in pts with CML-CP after ≥2 prior TKIs. The robust safety profile of ASC was sustained through each analysis in ASCEMBL (wk 24, wk 96, and EOS Tx), confirming that pts receiving ASC can maintain a high level of response and continue Tx without experiencing late-emerging AEs. Results in the switch population support the use of ASC early in the Tx paradigm. ASCEMBL EOS Tx results continue to strongly support ASC as the therapy of choice for pts with suboptimal responses and/or intolerance to ≥2 prior TKIs, allowing more pts to remain on Tx and achieve their Tx goals without needing to switch.

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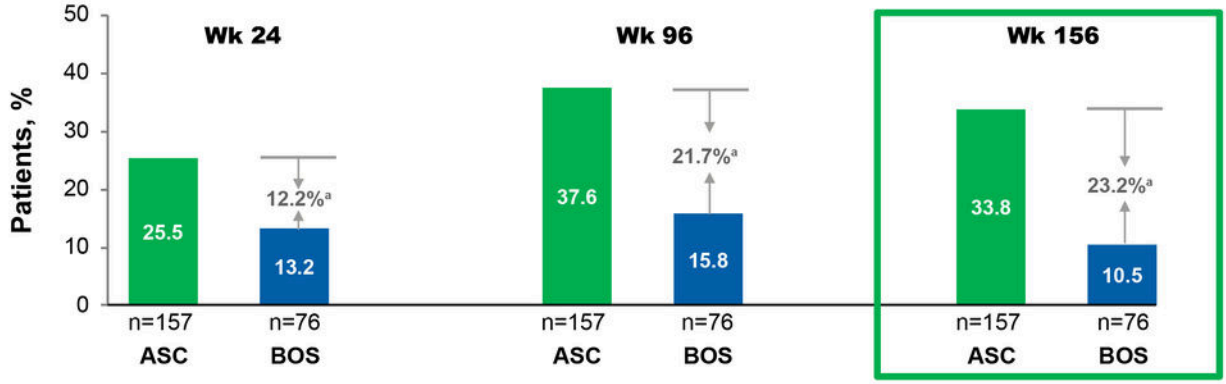
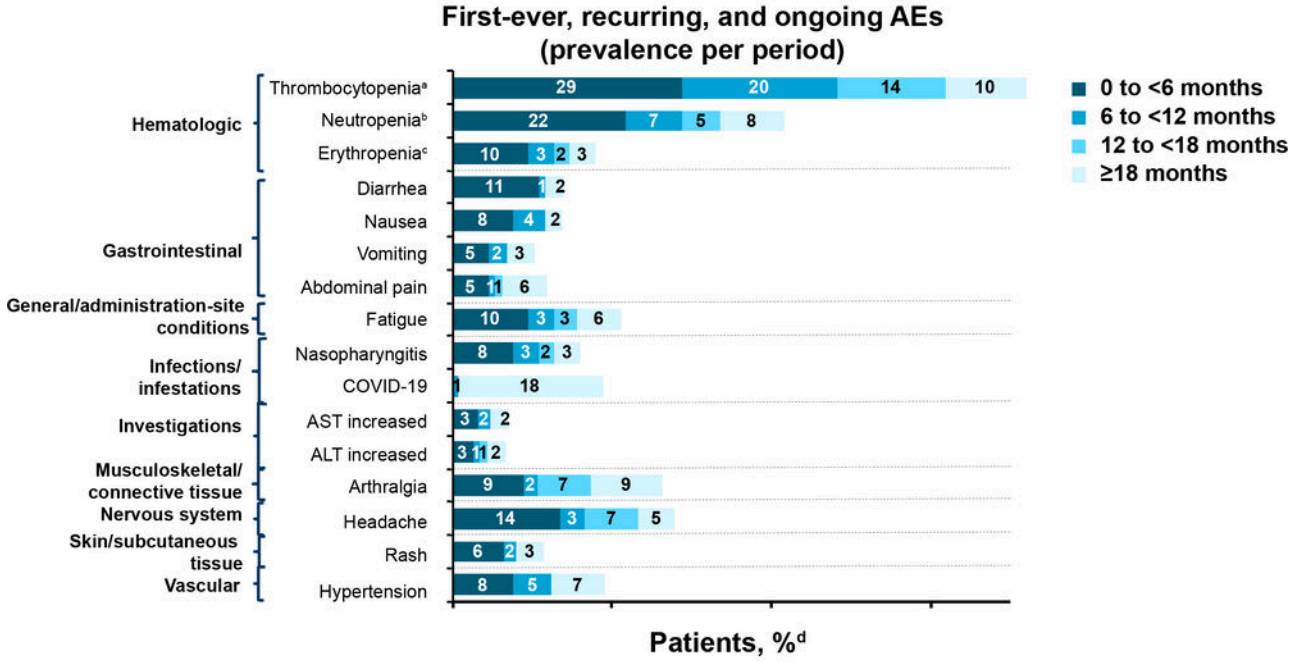
Figure 1. MMR rate at wk 24, wk 96, and wk 156



ASC, asciminib; BOS, bosutinib; MCyR, major cytogenetic response; MMR, major molecular response.
[a] MMR rate difference between arms after adjusting for baseline MCyR: 12.24% (95% CI, 2.19%-22.30%; 2-sided P=.029) at wk 24; 21.74% (95% CI, 10.53%-32.95%; 2-sided P=.001) at wk 96; and 23.16% (95% CI, 13.14%-33.18%; 2-sided P<.001) at wk 156.

Figure 2. Prevalence of all-grade AEs over time



AE, adverse event; ALT, alanine aminotransferase, AST, aspartate aminotransferase.
[a] Includes thrombocytopenia and platelet count decreased. [b] Includes neutropenia and neutrophil count decreased. [c] Includes anemia and normocytic anemia. [d] A patient with multiple occurrences of an AE is counted only once in that period. Percentages were rounded to zero decimal places. The denominator is the number of patients ongoing at the beginning of each period.

Figure 1

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