# **Table II.** Clinical trials designed to evaluate efficacy and tolerability of asciminib in chronic myeloid leukemia patients resistant/intolerant to ATP-competitive BCR-ABL1 tyrosine kinase inhibitors [48, 55–57]

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| **Trial title (study identifier)** | **Study population/design** | **Main objective** | **Relevant data** |
| A phase i, multi-center, open-label study of oral ABL001 in patients with chronic myelogenous leukemia (CML) or Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) (NCT02081378)\*(a dose-escalation study) | 141 pts with CP and 9 pts with accelerated-phase CML who had resistance to or unacceptable side effects from at least two previous ATP-competitive tyrosine kinase inhibitors (TKIs) | The primary objective was to determine the MTD or the recommended dose (or both) of asciminib | Identification of the MTD, as well as assessing the safety, pharmacokinetics and efficacy of asciminib |
| ASC2ESCALATE: A phase ii, multi-center, open-label, single-arm dose escalation study of asciminib monotherapy in 2nd line chronic phase chronic myelogenous leukemia (NCT05384587)\*(a dose escalation study) | Adult pts (aged ≥18 years) with CML-CP without the T315I mutation who experienced resistance (BCR::ABL1IS >1% with 6–12 months of 1L treatment or >10% with >12 months of 1st-line treatment) or intolerance (BCR::ABL1IS >0.1%) with ≥6 months of treatment with 1 prior ATP-competitive TKI are eligible. All pts will initiate treatment with asciminib 80 mg once a day. For pts not achieving BCR::ABL1IS <1% at 6 months, dose will be escalated to 200 mg once a day if pts do not have grade ≥3 toxicity or persistent grade 2 toxicity refractory to optimal management. In pts not achieving MMR at 12 months, either dose escalation from 80 to 200 mg once a day or from 200 mg once a day to 200 mg twice a day will occur or the pts will discontinue study treatment. Pts who achieve MMR at 12 months will continue asciminib at their current dose. Pts deriving clinical benefit from asciminib per investigator assessment may receive post-trial access | Percentage of participants who MMR (time frame: baseline up to 12 months)Secondary endpoints include:MMR rates by 3, 6, 18, and 24 monthsMR4.5 (BCR::ABL1IS ≤0.0032%) at 24 monthstime to and duration of MMRtime to treatment failure; and safety/tolerability | Ongoing trial (data not published yet) |
| A phase III, multi-center, open-label, randomized study of oral abl001 versus bosutinib in patients with chronic myelogenous leukemia in chronic phase (CML-CP), Previously treated with two or more tyrosine kinase inhibitors(ASCEMBL, NCT03106779)\* | Pts with CML-CP previously treated with ≥2 TKIs randomized (2:1) to receive third-line asciminib 40 mg twice a day vs. bosutinib 500 mg once a dayRandomization was stratified by MCyR status at baseline. Pts with documented treatment failure (specifically meeting the lack of efficacy criteria adapted from the 2013 ELN recommendations) while on bosutinib treatment were offered the option to switch to asciminib treatment within 96 weeks after the last pt was randomized to the study | Number of participants with MMR rate at 24 and 96 weeks | MMR rate:at 24 weeks: 25.5% vs. 13.2% (bosutinib)at 96 weeks: 37.6% vs. 15.8% (bosutinib) |
| A phase II, multi-center, open-label, randomized study of oral asciminib added to imatinib versus continued imatinib versus switch to nilotinib in patients with CML-CP who have been previously treated with Imatinib and have not achieved deep molecular response (ASC4MORE, NCT03578367)\* | Pts aged ≥18 years, have CML-CP, and have been treated with 1st-line IM for ≥12 months. Study entry requires patients to be receiving IM 400 mg once a day at randomization, have BCR-ABL1 transcript levels in the range of ≤1% to >0.01% on the IS, no prior achievement of MR4 (BCR-ABL1IS ≤0.01%) confirmed by two consecutive tests, and no prior treatment failure The study evaluates the efficacy of asciminib in two different doses (40 mg or 60 mg) in combination with IM 400 mg vs. continued IM vs. switch to nilotinib, vs. asciminib 80 mg single agent in subjects with CML-CP who have been previously treated with IM 1st-line therapy for at least one year and have not achieved DMR. 84 eligible subjects were randomized 1:1:1:1 to receive asciminib 60 mg once a day as add–on therapy to IM 400 mg once a day, or 40 mg once a day as add–on therapy to IM 400 mg once a day, or to continue IM 400 mg once a day, or to switch to nilotinib 300 mg twice a day | Molecular response (MR4.5) rate between asciminib + IM and IM alone (time frame: at 48 weeks) | At week 96, 19.0%, 19.0%, 4.8%, and 9.5% of pts in the 40-mg asciminib add–on, 60-mg asciminib add–on n, IM, and NIL arms, respectively, were in MR4.5  Cumulative MR4.5rates at week 96 were 28.6%, 28.6%, 9.5%, and 19.0%, respectively  Despite longer median durations of exposure with asciminib add–on, fewer pts experienced adverse evenst leading to discontinuation with asciminib 40 mg (4.8%) and 60 mg (14.3%) add–on vs. switching to NIL (33.3%). Rates of discontinuation with asciminib add–on did not increase with longer follow up compared to the primary analysis |

\*<https://clinicaltrials.gov/>; ATP — adenosine triphosphate; ELN — European LeukiemiaNet; IM — imatinib; IS — International Scale; MMR — major molecular response; MTD — maximum tolerated dose; NIL — nilotinib; pts — patients; TKI — tyrosine kinase inhibitors