

Novartis investigational STAMP inhibitor asciminib (ABL001) shows superior MMR rate to Bosulif®* in chronic myeloid leukemia trial

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- At 24 weeks, asciminib nearly doubled the major molecular response (MMR) rate compared to Bosulif® (bosutinib)*, in patients resistant to, or intolerant of, at least two prior tyrosine kinase inhibitor (TKI) therapies¹
- Despite advances in chronic myeloid leukemia (CML) care, many patients are at risk of disease progression, and sequential TKI therapy may be associated with increased resistance and intolerance²⁻⁷
- Data further reinforce the potential of asciminib to help patients with CML who suffer from intolerable side effects in later lines of therapy¹
- Data presented at ASH; submission to health authorities planned for first half of 2021

EAST HANOVER, N.J., Dec. 8, 2020 /PRNewswire/ -- Detailed results from the Phase III ASCSEMBL study demonstrate that, at 24 weeks, asciminib (ABL001) – a novel investigational treatment specifically targeting the ABL myristoyl pocket (STAMP) – nearly doubled the major molecular response (MMR) rate compared to Bosulif® (bosutinib)* (25.5% vs. 13.2%, respectively ([95% CI, 2.19-22.3]; 2-sided P=0.029) in patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine-kinase inhibitors (TKIs)¹. These data were presented today at a late-breaking abstracts session during the 62nd American Society of Hematology Annual Meeting & Exposition (ASH).

"These important comparative data are impressive, and they reinforce the critical role asciminib may play, if approved, in overcoming the treatment challenges we face in later treatment lines of chronic-phase CML," said Dr. Michael J. Mauro**, Member and Myeloproliferative Neoplasms Program Leader at Memorial Sloan Kettering Cancer Center and Professor at Weill Cornell Medicine. "While the advent and expansion of TKI therapies has resulted in tremendous progress for patients living with CML over the last decades, many of our patients in later treatment lines still face inadequate response, disease progression and intolerable side effects."

Despite the significant advances in the CML treatment landscape, many patients treated with two or more TKIs experience intolerance; for example, in an analysis of studies in patients who had previously failed two TKIs, up to 55% reported intolerance to treatment⁸⁻¹³. In addition, resistance rates for patients in later treatment lines remain high; and in the second-line setting, at least three out of five patients are unable to achieve MMR and up to 56% of patients do not achieve complete cytogenetic response (CCyR) within two years of follow-up^{5,13-18}. With few remaining treatment options, and no currently established standard-of-care in the third-line setting per treatment guidelines, patients who are resistant or intolerant to two or more TKIs are at a high risk of progression^{2-5,19-21}.

In the ASCSEMBL trial, 233 patients were randomized to receive asciminib 40 mg twice daily (n=157) or Bosulif 500 mg once a day (n=76)¹. Data showed that, at 24 weeks, more patients achieved a CCyR in the asciminib arm (40.8%) than in the Bosulif arm (24.2%); and deep molecular response (DMR) rates were higher for

patients in the asciminib arm than in the Bosulif arm – with 10.8% and 8.9% patients achieving MR⁴ and MR^{4.5} on asciminib, respectively, vs. 5.3% and 1.3% on Bosulif¹.

Grade ≥3 adverse events (AEs) occurred in 50.6% and 60.5% of patients treated with asciminib and Bosulif, respectively¹. Treatment discontinuation due to AEs in the asciminib arm was 5.8% compared to 21.1% for patients taking Bosulif¹. Similarly, AEs requiring dose interruption and/or dose adjustments were reported less frequently with asciminib than with Bosulif (37.8% vs. 60.5%, respectively)¹. At data cutoff, more patients were still on treatment in the asciminib arm vs. the Bosulif arm (61.8% vs. 30.3%, respectively)¹.

The most common grade ≥3 AEs (occurring in >10%) of patients treated with asciminib were thrombocytopenia (17.3%) and neutropenia (14.7%), while for Bosulif they were increased alanine aminotransferase (ALT) (14.5%), neutropenia (11.8%) and diarrhea (10.5%)¹. On-treatment deaths on the asciminib arm occurred in two (1.3%) patients (ischemic stroke and arterial embolism); there was one (1.3%) death on Bosulif (septic shock)¹. The most frequent AEs (all grades; ≥20%) were thrombocytopenia (28.8%) and neutropenia (21.8%) in the asciminib arm, compared to diarrhea (71.1%), nausea (46.1%), increased ALT (27.6%), vomiting (26.3%), rash (23.7%), increased aspartate aminotransferase (21.1%), neutropenia (21.1%) and thrombocytopenia (18.4%) in the Bosulif arm¹.

"Though some patients with CML may be told they have a 'good cancer' because of the wonderful advances in care that have been made over the years, this doesn't capture the full picture for everyone with the disease," said Greg Stephens, Executive Director and Founder of the US National CML Society. "The results of the ASCSEMBL study are very encouraging to the CML community, and help underscore the crucial need for additional treatment options to address real challenges that patients face."

Pre-clinical data suggests that asciminib has specificity for BCR-ABL²². Additional data accepted for online publication highlight that, as an investigational STAMP inhibitor, asciminib is designed to help overcome mutations on the ATP-binding site of BCR-ABL1, which may help address resistance in later treatment lines of CML and may potentially address off-target activity²².

"Novartis has been at the forefront of CML research for years – significantly changing the prognosis for patients. We are very proud to once again advance a potentially transformative medicine, a novel STAMP inhibitor, for those who do not adequately respond or are intolerant to currently available TKIs," said John Tsai, Head Global Drug Development and Chief Medical Officer, Novartis. "There is a clear need in later lines of therapy, and based on these results, we believe asciminib may become an important new development for patients. We look forward to sharing the data with regulatory authorities and moving forward with submissions worldwide."

The US Food and Drug Administration (FDA) has granted Fast Track designation for asciminib. Submission to the US and EU health authorities is planned for the first half of 2021.

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About asciminib (ABL001)

Asciminib (ABL001) is an investigational treatment specifically targeting the ABL myristoyl pocket (STAMP). As a STAMP inhibitor, asciminib may help address tyrosine-kinase inhibitor (TKI)-resistance and intolerance in later treatment lines of chronic myeloid leukemia (CML), and it is being studied in several clinical trials in

hopes of helping patients across multiple treatment lines of CML²³⁻³⁰.

About ASCEMBL

ASCSEMBL is a Phase III, multicenter, open-label, randomized study comparing the oral investigational treatment asciminib (ABL001) versus bosutinib in patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine-kinase inhibitors (TKIs)¹. Patients with failure or intolerance to the most recently administered TKI therapy were included in the trial¹.

About Novartis Commitment to CML

Our ongoing research in Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) has helped transform the disease from a fatal leukemia to a chronic condition in most patients. Novartis maintains an unwavering commitment to scientific innovation and access to care for patients worldwide. As an organization committed to patients, Novartis continues to reimagine CML care by pursuing ambitious goals with courage, passion and commitment for the global CML community.

* Bosulif is a registered trademark of Pfizer.

** Disclosure: Dr. Mauro has provided consulting services to Novartis.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs more than 15,000 people in the United States. For more information, please visit <https://www.novartis.us>.

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References

1. Hochhaus A, et al. Efficacy and Safety Results from ASCSEMBL, a Multicenter, Open-Label, Phase 3 Study of Asciminib, a First-in-Class STAMP Inhibitor, vs Bosutinib (BOS) in Patients (Pts) with Chronic Myeloid Leukemia in Chronic Phase (CML-CP) Previously Treated with ≥ 2 Tyrosine Kinase Inhibitors (TKIs). Oral presentation at: ASH Annual Meeting; Dec. 8, 2020.
2. Akard LP, et al. The "Hit Hard and Hit Early" Approach to the Treatment of Chronic Myeloid Leukemia: Implications of the Updated National Comprehensive Cancer Network Clinical Practice Guidelines for Routine Practice. *Clin Adv Hematol Oncol*. 2013;11(7):421-432
3. Cortes JE, et al. Long-term bosutinib for chronic phase chronic myeloid leukemia after failure of imatinib plus dasatinib and/or nilotinib. *Am J Hematol*. 2016;91(12):1206-1214
4. Cortes JE, et al. Ponatinib efficacy and safety in Philadelphia chromosome–positive leukemia: Final 5-year results of the phase 2 PACE trial. *Blood*. 2018;132(4):393-404
5. Garg RJ, et al. The use of nilotinib or dasatinib after failure to 2 prior tyrosine kinase inhibitors: long-term follow-up. *Blood*. 2009;114(20):4361-4368
6. Busque L, et al. Real-Life Analysis of CML Management Demonstrates that Second-Line Therapy is Frequently Used But is Prematurely Discontinued For Intolerance: Report on Behalf of the CML-MPN Quebec Research Group. Poster presented at: EHA Annual Meeting; June 13, 2015.
7. Hughes TP, et al. Asciminib in Heavily Pretreated Patients With Ph+ CML CP Sensitive to TKI Therapy. Poster presented at: EHA Annual Meeting; June 12, 2020.
8. Gleevec [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2020.
9. Tasigna [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2020
10. Sprycel [package insert]. Princeton, NJ: Bristol-Myers Squibb; December 2018.
11. Bosulif [package insert]. New York, NY; Pfizer Laboratories; July 2020.
12. Iclusig [package insert]. Cambridge, MA: Takeda Pharmaceutical Company; June 2020.
13. Ongoren S, et al. Third-line treatment with second-generation tyrosine kinase inhibitors (dasatinib or nilotinib) in patients with chronic myeloid leukemia after two prior TKIs: real-life data on a single center experience along with the review of the literature. *Hematology*. 2018; 23:4, 212-220.
14. Giles FJ, et al. Nilotinib is active in chronic and accelerated phase chronic myeloid leukemia following failure of imatinib and dasatinib therapy. *Leukemia*. 2010; 24(7):1299–1301.
15. Rossi RA, et al. Outcome of 82 chronic myeloid leukemia patients treated with nilotinib or dasatinib after failure of two prior tyrosine kinase inhibitors. *Haematologica*. 2013;98(3):399–403.
16. Kantarjian HM, et al. Nilotinib is effective in patients with chronic myeloid leukemia in chronic phase after imatinib resistance or intolerance: 24-month follow-up results. *Blood*. 2011;117(4):1141-1145.
17. Shah NP, et al. Potent, transient inhibition of BCR-ABL with dasatinib 100 mg daily achieves rapid and durable cytogenetic responses and high transformation-free survival rates in chronic phase chronic myeloid leukemia patients with resistance, suboptimal response or intolerance to imatinib. *Haematologica*. 2010;95:232-240.
18. Gambacorti-Passerini C., et al. Bosutinib efficacy and safety in chronic phase chronic myeloid leukemia after imatinib resistance or intolerance: Minimum 24-month follow-up. *Am J Hematol*. 2014;89:732-742.
19. Hochhaus A, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia*. 2020;34:966-984
20. Cortes JE., et al. Final 5-Year Study Results of DASISION: The Dasatinib Versus Imatinib Study in Treatment-Naïve Chronic Myeloid Leukemia Patients Trial. *J Clin Oncol*. 2016;34:2333-2340.
21. Steegmann JL., et al. European LeukemiaNet recommendations for the management and avoidance of adverse events of treatment in chronic myeloid leukaemia. *Leukemia*. 2016;30:1648-1671.
22. Schuld P., et al. Structural and Biochemical Studies Confirming the Mechanism of Action of Asciminib, an Agent Specifically Targeting the ABL Myristoyl Pocket (STAMP). *Blood*. 2020;136:34-35.

23. Wylie AA, et al. The allosteric inhibitor ABL001 enables dual targeting of BCR–ABL1. *Nature*. 2017;543(7647):733-737
24. Schoepfer J, et al. Discovery of Asciminib (ABL001), an Allosteric Inhibitor of the Tyrosine Kinase Activity of BCR-ABL1. *J Med Chem*. 2018;61(18):8120-8135
25. Hughes TP, et al. Asciminib in Chronic Myeloid Leukemia after ABL Kinase Inhibitor Failure. *N Engl J Med*. 2019; 381(24):2315-2326
26. Hughes TP, et al. Expanded Phase 1 Study of ABL001, a Potent, Allosteric Inhibitor of BCR-ABL, Reveals Significant and Durable Responses in Patients with CML-Chronic Phase with Failure of Prior TKI Therapy Blood. Poster presented at: ASH Annual Meeting & Exposition; Dec. 5, 2016.
27. Ottmann OG, et al. ABL001, a Potent, Allosteric Inhibitor of BCR-ABL, Exhibits Safety and Promising Single- Agent Activity in a Phase I Study of Patients with CML with Failure of Prior TKI Therapy. *Blood*. 2015;126(23):138
28. Mauro MJ, et al. Combination of Asciminib Plus Nilotinib (NIL) or Dasatinib (DAS) in Patients (PTS) with Chronic Myeloid Leukemia (CML): Results from a Phase 1 Study. Poster presented at: EHA Annual Meeting; June 15, 2019.
29. Cortes J, et al. Combination Therapy Using Asciminib Plus Imatinib (IMA) in Patients (PTS) with Chronic Myeloid Leukemia (CML): Results from a Phase 1 Study. Poster presented at: EHA Annual Meeting; June 15, 2019.
30. "Asciminib OR ABL001 Search Results." *ClinicalTrials.gov*, U.S. National Institutes of Health, 2020, www.clinicaltrials.gov/ct2/results?cond=&term=asciminib&cntry=&state=&city=&dist=.

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List of links present in page

1. <https://qa1.novartis.us/news/media-releases/novartis-investigational-stamp-inhibitor-asciminib-abl001-shows-superior-mmr-rate-bosulif-chronic-myeloid-leukemia-trial>
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