FDA accelerates review of Novartis STAMP inhibitor asciminib (ABL001) for patients with chronic myeloid leukemia (CML)

Aug 25, 2021

Novartis today announced that the US Food and Drug Administration (FDA) accepted and granted Priority Review to the company's New Drug Application (NDA) for asciminib (ABL001) in chronic myeloid leukemia (CML), following its submission under the FDA's Real-Time Oncology Review (RTOR) program. Priority Review is granted to therapies that have the potential to provide significant improvements in the treatment, diagnosis or prevention of serious conditions, as determined by the FDA[1]. This designation could shorten the FDA review period to eight months compared to the 12 months under Standard Review[1].

- Priority Review granted based on positive data from the pivotal, Phase III ASCEMBL trial, where asciminib was compared to Bosulif® (bosutinib)* in patients with Philadelphia chromosome-positive CML in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine-kinase inhibitors (TKIs), and data from a Phase I trial that included patients with Ph+ CML-CP harboring the T315I mutation[2,3]
- Despite available treatments, many patients with CML remain at risk of disease progression, and sequential therapy with currently available TKIs may be associated with increased resistance and/or intolerance[4-10]
- Asciminib, a novel investigational therapy specifically targeting the ABL myristoyl pocket – also known as a STAMP inhibitor –, is in development across multiple treatment lines for CML[11-17]

Novartis has previously received Orphan Drug, Fast Track and two Breakthrough Therapy designations for asciminib. Breakthrough Therapy designations were granted for asciminib for the treatment of adult patients with Ph+ CML-CP previously treated with two or more TKIs, as well as adult patients with Ph+ CML-CP harboring the T315I mutation.

1. U.S. Food and Drug Administration (FDA). Priority Review. Available from: https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review.
2. Hochhaus A, et al. Efficacy and Safety Results from ASCEMBL, 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). Blood (2020) 136 (Supplement_2): LBA-4.
3. Cortes JE, et al. Asciminib, a First-in-Class STAMP Inhibitor, Provides Durable Molecular Response in Patients (pts) with Chronic Myeloid Leukemia (CML) Harboring the T315I Mutation: Primary Efficacy and Safety Results from a Phase 1 Trial. Oral presentation at: ASH Annual Meeting; Dec. 7, 2020.
4. 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
5. 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

6. 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
7. 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
8. Hochhaus A, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia*. 2020;34:966-984
9. 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.
10. 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.
11. Wylie AA, et al. The allosteric inhibitor ABL001 enables dual targeting of BCR–ABL1. *Nature*. 2017;543(7647):733-737
12. 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
13. Hughes TP, et al. Asciminib in Chronic Myeloid Leukemia after ABL Kinase Inhibitor Failure. *N Engl J Med*. 2019; 381(24):2315-2326
14. 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* (2016) 128 (22): 625.
15. 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
16. 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. EHA Library. 06/15/19; 267467; S884.
17. Cortes JE, et al. Combination Therapy Using Asciminib Plus Imatinib (IMA) in Patients (PTS) with Chronic Myeloid Leukemia (CML): Results from a Phase 1 Study. EHA Library. 06/15/19; 267466; S883.

List of links present in page

1. https://prod1.novartis.com/news/fda-accelerates-review-novartis-stamp-inhibitor-asciminib-abl001-patients-chronic-myeloid-leukemia-cml
2. https://www.novartis.com/news/media-releases/novartis-investigational-stamp-inhibitor-asciminib-abl001-shows-superior-mmr-rate-bosulif-chronic-myeloid-leukemia-trial
3. https://www.novartis.com/news/media-releases/novartis-receives-fda-breakthrough-therapy-designations-investigational-stamp-inhibitor-asciminib-abl001-chronic-myeloid-leukemia
4. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review