Asciminib in the Management of Chronic Myeloid Leukemia: Clinical Experience with a Novel STAMP Inhibitor in Japan

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The treatment landscape of chronic myeloid leukemia (CML) has dramatically evolved in the past 25 years with the development of tyrosine kinase inhibitors (TKIs), leading to excellent long-term survival for most patients. However, a substantial proportion of patients experience treatment failure, intolerance, or resistance to currently available TKIs, requiring switching of drugs, and in some cases, requiring a stem cell transplant. Therefore, a novel therapeutic approach with distinct mechanisms of action is anticipated.

Asciminib is the first-in-class STAMP (Specifically Targeting the ABL Myristoyl Pocket) inhibitor, with high selectivity for BCR-ABL1 inhibition through an allosteric mechanism, distinct from conventional ATP-competitive TKIs. This unique mode of action offers the potential to overcome resistance associated with kinase domain mutations and to improve tolerability in patients who are unable to continue prior TKI therapy.

Asciminib was first approved by the US FDA in 2021 for the treatment of Philadelphia (Ph) chromosome-positive CML in chronic phase (CP) who are intolerant or resistant to two or more previous lines of TKI therapy. This approval was followed by approval from the European Medicines Agency (EMA) in 2022 and from various other countries and regions across the globe for the same indication. In 2024, the US FDA granted accelerated approval for asciminib as a first-line treatment of choice for adult patients with CML-CP. Overall, asciminib is currently approved in more than sixty countries across the globe either as a first-line choice of treatment or against patients who are intolerant/resistant to other TKIs.
In this presentation, I will review the current treatment strategies for CML and discuss the emerging role of asciminib in clinical practice, with a particular focus on real-world experience in Japan. Asciminib was first approved in Japan in 2022 as a treatment option for third-line and beyond, and was later expanded to first-line use following data from the pivotal ASC4FIRST study in 2025. Therefore, while we have primarily used asciminib in patients with chronic-phase CML who had experienced failure or intolerance to multiple prior TKIs, including those with complex treatment histories, we are also expanding our experience with first-line use of the drug. Our clinical experience suggests that asciminib provides meaningful molecular responses in a substantial proportion of these patients, while maintaining a favorable safety profile.

Especially from a tolerability standpoint, asciminib has been generally well tolerated, with fewer off-target adverse events than ATP-competitive TKIs. Data from published reports will also be reviewed to ascertain the optimal positioning of asciminib in real-world clinical use. Case-based discussions will illustrate practical decision-making, adverse-event management, and treatment sequencing in routine practice.

Finally, I will discuss future perspectives on the positioning of asciminib in the CML treatment algorithm, including its potential role earlier in therapy, combination strategies, and implications for treatment-free remission. By sharing insights from Japanese real-world clinical practice, this presentation aims to provide practical guidance for hematologists managing patients with CML in the era of STAMP inhibition.