Scemblix May Be a Better Option for Chronic Myeloid Leukemia

People treated with the targeted therapy had superior response rates and experienced fewer side effects than those who used older TKI drugs, but these benefits come at a higher cost.

June 6, 2024 By Liz Highleyman

Scemblix (asciminib) may be a more effective and better tolerated option for people with newly diagnosed chronic myeloid leukemia (CML) when compared against older tyrosine kinase inhibitor (TKI) targeted therapies, according to study results presented this week at the American Society of Clinical Oncology Annual Meeting (ASCO 2024).

“This randomized trial demonstrated that asciminib achieved a statistically superior efficacy when compared to all TKIs available for newly diagnosed patients with chronic phase CML. Importantly, safety and tolerability of asciminib was also excellent,” lead investigator Timothy Hughes, MD, of the University of Adelaide, said in an ASCO news release. “This combination of potency and safety may enable more patients to achieve treatment-free remission, the ultimate goal of CML therapy.”

More than 50 years ago, scientists discovered that a genetic alteration known as the Philadelphia chromosome can trigger the development of CML, which involves overproduction of abnormal white blood cells. In the 1990s, researchers found that Gleevec (imatinib), from Novartis, could block a protein produced by the abnormal gene. Approved in 2001, Gleevec was one of the first targeted therapies that work against cancers with specific genetic mutations, and it dramatically improved survival for people with this type of leukemia.

Since then, next-generation targeted therapies have been developed that may be more effective, but Gleevec is off patent, so it is much less expensive than new medications. Some people with CML respond well to TKIs, but nearly half eventually switch to another medication due to drug resistance or side effects. Most patients will need to stay on TKIs for many years—possibly for life—so safety, tolerability and cost are major concerns.

Hughes presented findings from the Phase III ASC4FIRST trial (NCT04971226), which compared Scemblix, also from Novartis, against older TKIs used as standard first-line treatment for CML. The results were also published in The New England Journal of Medicine.

Granted accelerated approval in 2021 for patients previously treated with at least two older TKIs,

Scemblix is the first “Specifically Target the ABL Myristoyl Pocket” (STAMP) drug, designed to bind to a specific structure on a protein produced by the abnormal gene.

The study included 405 adults with newly diagnosed Philadelphia chromosome-positive CML who had not previously used TKIs. Half were randomly assigned to receive Scemblix while the rest received another investigator-selected TKI. Within the latter group, half used Gleevec and half used a second-generation drug such as Bosulif (bosutinib), Sprycel (dasatinib) or Tasigna (nilotinib). About two thirds were men, half were white and 44% were Asian. The overall median age was 52 years, but younger patients were more often selected to receive second-generation TKIs because they could better tolerate more potent drugs.

After a median follow-up period of about 16 months, more people who received Scemblix were still on their assigned treatment than those who received Gleevec or a second-generation TKI (86%, 62% and 75%, respectively). The most common reasons for discontinuation were unsatisfactory therapeutic response or side effects.

At 48 weeks, the major molecular response (MMR) rate was significantly higher for Scemblix compared with any investigator-selected TKI (68% versus 49%) and for Scemblix compared with Gleevec in particular (69% versus 40%). Scemblix also had a somewhat higher MMR rate than second-generation TKIs (66% versus 58%), but this difference did not reach statistical significance. What’s more, Scemblix recipients were more likely than those in the comparison TKI group to experience a deep molecular response called MR4 (39% versus 21%) and an even deeper response known as MR5 (17% versus 9%), which could potentially lead to long-term remission off treatment.

Scemblix had more favorable safety and tolerability than Gleevec or second-generation TKIs, Hughes reported. Scemblix recipients had a lower rate of severe (Grade 3 or higher) adverse events (38%, 44% and 55%, respectively), less need for dose adjustments to manage side effects (30%, 39% and 53%) and half the rate of adverse events leading to treatment discontinuation (5%, 11% and 10%). The most common adverse events in the Scemblix group were low platelet counts and neutrophil counts (13% and 10%). Blood clots—a known potential TKI side effect—were rare in all groups (1%, 0% and 2%).

Scemblix “is the only agent to show a statistically significant superior efficacy and excellent safety and tolerability versus all current standard-of-care frontline treatment, with potential to be the therapy of choice for CML,” the researchers concluded.

These results have been submitted to the Food and Drug Administration for consideration of a first-line indication for Scemblix. The researchers will continue to follow the study participants to assess longer-term MMR, progression-free survival, treatment-free remission and overall survival.

Scemblix “is really poised to potentially change the management of first-line treatment of chronic myeloid leukemia,” Oreofe Odejide, MD, MPH, of Dana-Farber Cancer Institute, who was not involved with the study, said at an ASCO media briefing.

These findings suggest that Scemblix could be a better initial treatment choice for people with CML. Some clinicians, however, may want to start with a less expensive TKI and save Scemblix as a fallback option for patients who experience treatment failure on older drugs. Patients, on the other hand, may prefer to use a more effective and better tolerated medication from the outset.

“CML is a chronic condition, and the side effects of standard-of-care can be challenging for patients. They often affect their daily life and can lead to high rates of treatment switching,” Gerald Clements of the CML Advocates Network, said in a Novartis news release. “Effective care that can be tolerated long term is a key unmet need. By potentially bringing Scemblix to patients when they are first diagnosed, they may have an opportunity to be on a highly effective treatment while also maintaining their day-to-day from the start.”

Click here to read the study abstract.

Click here for more news about blood cancer.
Click here for more news from ASCO 2024.
