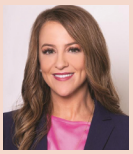
Oral Hypomethylating Agents for Myelodysplastic Syndromes: Highlights From SOHO 2020



Allyson Price, MPAS, PA-C, of The University of Texas MD Anderson Cancer Center, highlights implications for advanced practitioners from the presentation at the 2020 SOHO Annual Meeting by Guillermo Garcia-Manero, MD, also from MD Anderson Cancer Center, on the development of oral hypomethylating agents for myelodysplastic syndromes.

In this session, Dr. Garcia-Manero discussed three different trials examining the development and role of oral hypomethylating agents (HMA) for patients with myelodysplastic syndromes (MDS) and the differences in pharmacokinetics (PK) between the agents. He spoke on two studies that included the addition of cytidine deaminase inhibitors (CDIs) and one study with monotherapy.

The first trial was the ASCERTAIN study with ASTX727 (oral decitabine plus cytidine deaminase inhibitor), which led to U.S. Food & Drug Administration approval in 2020. The primary endpoints were equivalence of PK profile of 5-day decitabine IV with the oral agents (~99% ratio), showing the "almost identical profiles." The secondary endpoints looked at the complete response rates (~12%) and overall response rates (~65%), which were similar with rates for IV decitabine.

The next study Dr. Garcia-Manero discussed was an ongoing phase I study with ASTX030 (cedazuridine in combination with azacitidine). The study also looked at PK and pharmacodynamics (PD) outcomes. There were differences in the oral PK profile compared with the standard IV approach; however, the clinical activity seemed to be similar when comparing the response rate.

Key Points

- There was a recent FDA approval of oral combination decitabine and cedazuridine for the treatment of patients with MDS.
- Proper patient education and compliance is critical to achieve good outcomes from hypomethylating agents.

Dr. Garcia-Manero also discussed the phase III study with CC-486 (oral azacitidine without CDI). The study was terminated early due to toxicity but met its primary endpoint, which was improvement in transfusion of red blood cells (RBC). The study showed improvement of RBC transfusion dependency for 11.1 months with CC-486 compared with placebo for 5.0 months, with noted improvement in hemoglobin level from baseline compared with that seen with placebo. CC-486 improves survival in post-consolidation acute myeloid leukemia, but its role in MDS treatment is still unclear. Further investigation in MDS is warranted.

In conclusion, oral HMA and CDI show bioequivalent PK/PD profiles in comparison with IV HMAs. The study with CC-486 has a lower PK profile, but CC-486 still maintains clinical activity when compared with IV/SC azacitidine. There

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is still no established role for it in the MDS treatment landscape. The phase I trial with ASTX030 still needs to undergo evaluation of full toxicity profile and PK/PD profiles.

The Advanced Practitioner Perspective

Oral hypomethylating therapies can be of great benefit to our patients who spend a significant amount of time in the hospital receiving IV therapy. These oral therapies may mean patients do not need to have a peripherally inserted central catheter line or other line placement, which would improve their quality of life.

As advanced practitioners, we need to explain the clinical trial outcomes for IV vs. oral agents. Patients may be apprehensive about achieving similar outcomes and will need reassurance about the efficacy of oral therapies. Advanced practitioners must be diligent in monitoring oral therapies, stress the importance of compliance and adherence, and educate patients that discontinuation will lead to poorer outcomes. It is also important to look at the cost of these oral agents, as they can lead to financial toxicity.

There is potential to use these oral agents with other oral agents in combination therapy in the near future. Researchers still need to evaluate these medications in the post-transplant setting. Overall, these agents can lead to improved quality of life for patients with hematologic malignancies as they navigate their individualized treatments.

Disclosure

Ms. Price has no conflicts of interest to disclose.