Real-World Safety Profile of Isocitrate Dehydrogenase (IDH)-1 Inhibitors: A Pharmacovigilance Comparison of Olutasidenib and Ivosidenib Utilizing the FDA Adverse Event Reporting System (FAERS)

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Introduction

- Ivosidenib was first approved for the treatment of relapsed or refractory (R/R) acute myeloid leukemia (AML) in July 2018.
- Another IDH-1 inhibitor, olutasidenib, was approved in December 2022 for the same indication.
- Comparisons of safety profiles between these agents may help guide their use in specific clinical scenarios.

Methods

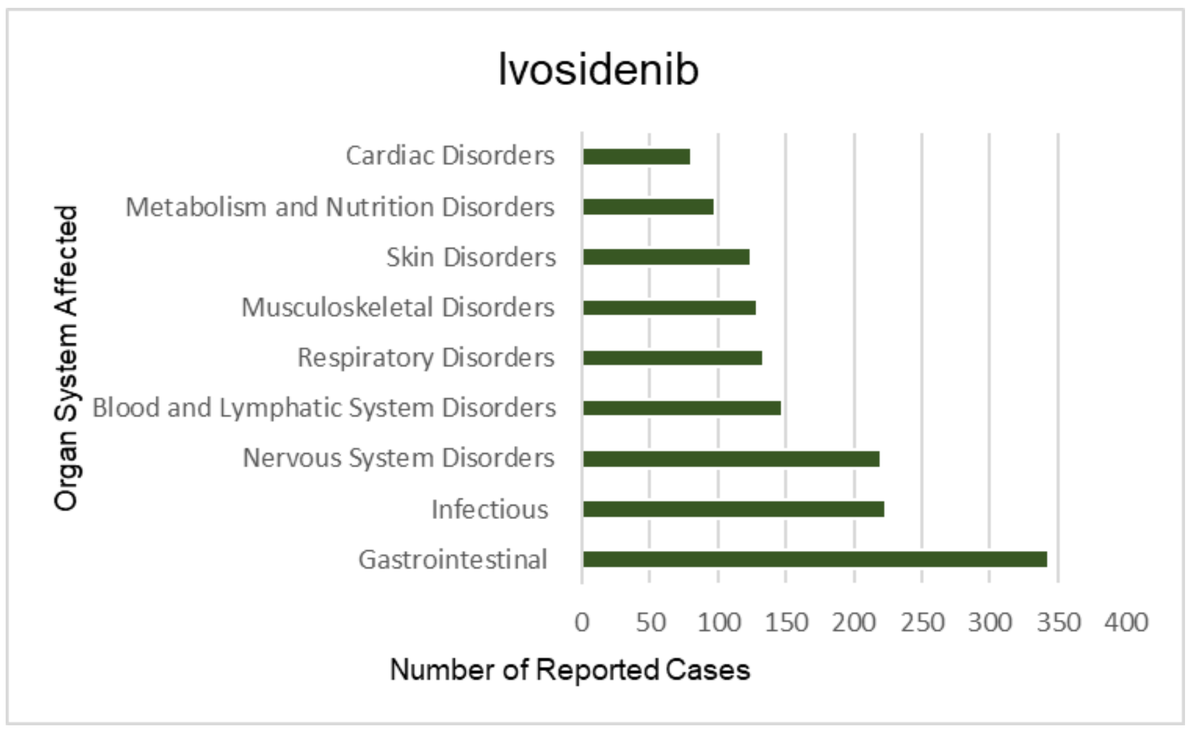
- We retrospectively queried real-world ivosidenib and olutasidenib-associated adverse events (AEs) reported to the FAERS database from the 2018 approval of ivosidenib until last submission on March 31, 2025.
- The FAERS database, which includes adverse event reports submitted to the FDA by manufacturers, consumers, and healthcare providers, was used to identify real-world adverse events associated with IDH1 inhibitors.
- Proportional reporting percentages were calculated by comparing drug-specific AEs to total reported AEs in the database.
- Descriptive analysis compared the most commonly reported AEs for each IDH1 inhibitor.

Results

- There were 1,555 ivosidenib-associated AEs and 163 olutasidenib-associated AEs reported to FAERS, with most of them (86%) from the US.
- For ivosidenib, the most commonly affected organ systems included gastrointestinal, infectious disease, and nervous system disorders. Of these AEs, 797 were considered serious (51%), with 441 (28%) hospitalizations, and 113 (7%) reported deaths.
- For olutasidenib, the most commonly affected organ systems included gastrointestinal, infectious disease, and nervous system disorders. Of these AEs, 97 were considered serious (59%), with 74 (45%) hospitalizations, and 24 (14%) reported deaths.

Results

- For ivosidenib, the commonly reported AEs, with associated proportionality reporting percentages and reporting odds ratios (ROR), included differentiation syndrome (10%, 1,063), febrile neutropenia (0.13%, 13.3), diarrhea (0.09%, 2.7), and fatigue (0.04%, 3.8).
- For olutasidenib, the commonly reported Aes, with associated proportionality reporting percentages and reporting odds ratios, included differentiation syndrome (0.8%, 797), febrile neutropenia (0.02%, 20.5), and constipation (0.01%,10.6).
- The proportion of severe AEs and distribution of organ systems involved did not differ between agents.



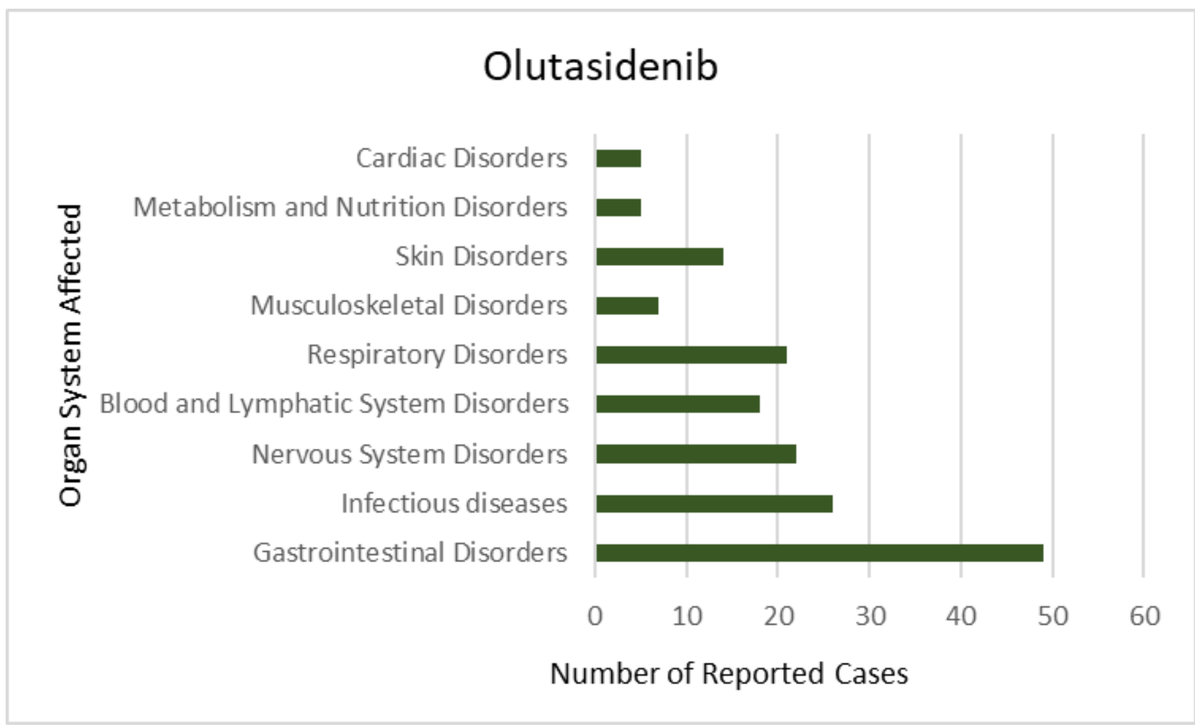


Figure 1 and 2: Number of cases of reported side effects associated with ivosidenib and olutasidenib and the corresponding affected organ systems.

Conclusion and Discussion

- The real - world safety profile for the recently approved olutasidenib was similar to the experience with ivosidenib.
- No new serious AEs have been reported with olutasidenib.
- Close monitoring for patients receiving these treatments is warranted, given the continued association with differentiation syndrome.
- For patients with disease progression on ivosidenib, olutasidenib may be an alternative with a similar real-world safety profile.

References

Venugopal S, Watts J. Olutasidenib: from bench to bedside. Blood Adv. 2023 Aug 22;7(16):4358-4365. doi: 10.1182/bloodadvances.2023009854. PMID: 37196640; PMCID: PMC10432604