What antiemetics are recommended with zolbetuximab?

Premedicate patients with a combination of antiemetics (e.g., NK-1 and/or 5-HT3 receptor antagonists, as well as other drugs as indicated).

Modified Delphi Panel Consensus Guidance recommends using one of the following high-emetic risk regimens for nausea and vomiting prophylaxis before the first zolbetuximab infusion:[1]

- NK-1 receptor antagonist + 5-HT3 receptor antagonist + dexamethasone + olanzapine.
- NK-1 receptor antagonist + 5-HT3 receptor antagonist + dexamethasone.
- 5-HT3 receptor antagonist + dexamethasone + olanzapine.

Oral or intravenous antiemetics may used based on individual patient needs.[1] For patients with an intact stomach, the panel also recommends considering an H2 receptor antagonist or PPI to prevent dyspepsia, which can mimic nausea. Start these a few days to one week before zolbetuximab treatment for maximal mucosal protection.

Ad hoc exploratory analyses of antiemetic usage in the zolbetuximab Phase 3 trials suggest that multi-class antiemetic prophylaxis (≥ 3 classes, including steroids) may reduce nausea and vomiting on Cycle 1, Day 1.[2]

Additional information

Modified Delphi Panel Consensus Guidance[1]

It may be necessary to escalate the antiemetic regimen in the second and subsequent infusions.

- If a patient has experienced only nausea (no vomiting) with the previous zolbetuximab infusion, with the next infusion, either: make no change to the previous antiemetic regimen or escalate the antiemetic regimen from the previous infusion.
- If a patient has experienced vomiting with the previous zolbetuximab infusion, with the next infusion, escalate the antiemetic regimen from the previous infusion.

Zolbetuximab should not be discontinued permanently without first attempting to modify or temporarily interrupt the infusion and/or without providing additional treatment for nausea and vomiting in the absence of hypersensitivity reactions or infusion-related reactions.

A complete overview of the Consensus Guidance can be accessed using the link below.

- The Modified Delphi Panel Consensus Guidance

Phase 3 clinical trials: SPOTLIGHT and GLOW[3,4]

Ad hoc exploratory analyses examined prophylactic antiemetic regimens used and incidence rates of nausea/vomiting on Cycle 1, Day 1 in SPOTLIGHT and GLOW.[2]

- Various combinations of antiemetics were given prophylactically prior to the first zolbetuximab infusion.
- Using a 3-drug prophylactic antiemetic regimen before zolbetuximab, 75.3% (73/97) of patients did not experience vomiting, and 60.8% (59/97) of patients did not experience nausea.
- Using a 2-drug prophylactic antiemetic regimen before zolbetuximab, 58.9% (165/280) of patients did not experience vomiting and 51.4% (144/280) did not experience nausea.
- Patients who received steroids as part of a 2- or 3-drug antiemetic regimen had lower rates of nausea and vomiting, and an ad hoc analysis found that patients treated with zolbetuximab + steroids had numerically higher PFS and OS compared to those who received zolbetuximab without steroids.

Additional information can be accessed using the link below.

- Antiemetic recommendations and usage in the zolbetuximab Phase 3 trials

Real-world evidence

Three real-world studies describe protocols for managing nausea and vomiting with prophylactic antiemetics.

- Shimozaki et al. developed a protocol for managing zolbetuximab-induced gastrointestinal toxicity and included administration of mandatory NK-1 receptor antagonist, H1 antagonist, H2 antagonist, 5-HT3 receptor antagonist, dexamethasone, and optional olanzapine given over three to five days.[5]
- The protocol developed by Narita et al. for zolbetuximab-induced gastrointestinal toxicity included mandatory NK-1 receptor antagonist, 5-HT3 receptor antagonist, dexamethasone, chlorpheniramine, vonoprazan, rebamipide and optional olanzapine administered over six days.[6]
- Yakuwa et al.'s protocol for zolbetuximab administration included premedication given over two to four days with oral diphenhydramine hydrochloride and olanzapine and intravenous fosnetupitant, palonosetron, and dexamethasone. In patients with severe anxiety, alprazolam or lorazepam was optional.[7]

Brief summaries of these studies can be accessed using the link below.

- Real-world evidence on incidence and management of nausea and vomiting

References

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