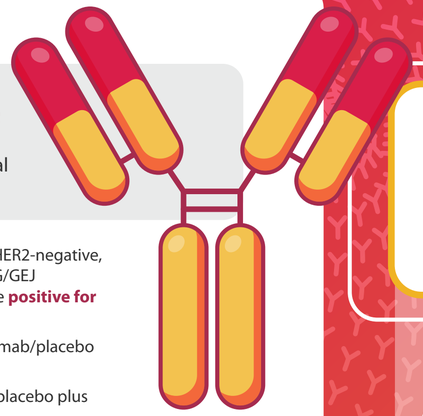
Nausea and vomiting with zolbetuximab: EXPERIENCE and MANAGEMENT

Please see the full publication for further details

BACKGROUND



The IgG1 **monoclonal antibody zolbetuximab** targets **CLDN18.2** and has been investigated in two global Phase 3 randomized clinical trials: **SPOTLIGHT** and **GLOW**[1,2]

- **Key inclusion criteria:** Adults with HER2-negative, locally advanced unresectable or mG/GEJ adenocarcinoma whose tumors were **positive for CLDN18.2**[1,2a]
  - **SPOTLIGHT**: First-line zolbetuximab/placebo plus mFOLFOX6, n = 565[1]
  - **GLOW**: First-line zolbetuximab/placebo plus CAPOX, n = 507[2]
- **Key findings:** Zolbetuximab plus mFOLFOX6/CAPOX significantly **prolonged PFS and OS** versus placebo plus mFOLFOX6/CAPOX[1,2]

INCIDENCE OF NAUSEA AND VOMITING

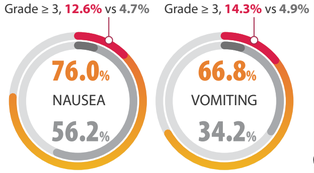
Experience with zolbetuximab

Nausea and vomiting were the **most common AEs** in zolbetuximab treatment arms[4,5]

Nausea and/or vomiting led to early **treatment discontinuation**[b] for some patients[4]

The median time to first occurrence of nausea and/or vomiting was **< 1 hour** after starting the first zolbetuximab infusion[4]

POOLED ANALYSIS[5]



Zolbetuximab + mFOLFOX6/CAPOX
Placebo + mFOLFOX6/CAPOX

Guidance

A need for **evidence-based consensus guidelines** was identified[3]

An international Delphi panel of 15 experts reached **consensus** on **prevention** and **management** of nausea and vomiting in patients treated with first-line zolbetuximab + chemotherapy[3]

EXPERIENCE IN CLINICAL TRIALS

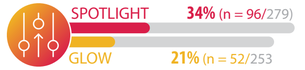
Prophylactic antiemetics were recommended per **institutional care and guidelines**[1,2]

The most common **combinations of prophylactic antiemetics** during the first zolbetuximab infusion were[4]:

- 5-HT3 + NK-1
- 5-HT3 + NK-1 + others
- 5-HT3 + NK-1 + steroids

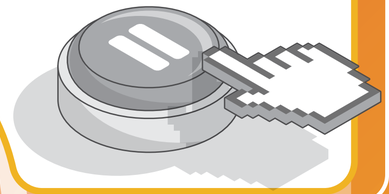
Some patients required **infusion modifications** due to AEs[4]

Modification due to an AE in first infusion[4]



Incidence of nausea and vomiting was **highest during** the **first** zolbetuximab cycle and then decreased[4]

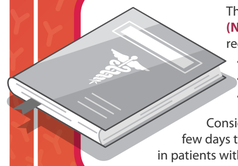
Infusion interruptions were most common during the **first zolbetuximab infusion** and decreased in subsequent infusions[4]



Prophylaxis

The **National Comprehensive Cancer Network® (NCCN®) recommended** high-emetic-risk regimens were endorsed[6]:

- NK-1 + 5-HT3 + dexamethasone + olanzapine
- NK-1 + 5-HT3 + dexamethasone
- 5-HT3 + dexamethasone + olanzapine



Consider a **PPI or histamine-2 receptor blocker** a few days to a week before administering zolbetuximab in patients with an intact stomach

During infusions

Patients with vomiting:
Stop zolbetuximab infusion for **30–60 mins**; if symptoms improve, **restart at a slower rate**.
IV hydration may be appropriate in some circumstances

Patients with only nausea:
First infusion: Consider **no modifications**, or stop the infusion for **30–60 mins** and restart at same rate if symptoms improve. After the first hour, additionally consider **slowing** the infusion without stopping

Plan for next infusions

1. **Adjust infusions and antiemetic regimens** based on patients' symptoms during previous infusions
2. Patients may tolerate **titration of infusion rate** back to 100%, or maximum tolerated rate
3. **Monitor** for recurrent symptoms and administer rescue antiemetics as needed
4. Patients with only nausea in second or subsequent infusion: Consider first **slowing infusion** without stopping; if ineffective, **stop and then restart** at same or a slower rate
5. **Permanently discontinuing zolbetuximab** due to nausea and/or vomiting without modifying infusion rate and/or escalating nausea and vomiting treatment **is not recommended**

CONSENSUS-BASED GUIDELINES[3]

Please contact your local Astellas medical expert for more information

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Footnotes
[a] Moderate-to-strong staining in ≥ 75% of tumor cells.
[b] Within 9 weeks of randomization.

Abbreviations
5-HT3, serotonin receptor blocker; AE, adverse event; CAPOX, capecitabine and oxaliplatin; CLDN18.2, claudin 18.2; HER2, human epidermal growth factor receptor 2; IgG1, immunoglobulin G1; mFOLFOX6, modified FOLFOX6 (folinic acid, fluorouracil, and oxaliplatin); mG/GEJ, metastatic gastric/gastroesophageal junction; NCCN, National Comprehensive Cancer Network; NK-1, neurokinin-1 receptor blocker; OS, overall survival; PFS, progression-free survival; PPI, proton pump inhibitor.

References
1. Shitara K, et al. *Lancet*. 2023;401(10389):1655–1668. 2. Shah MA, et al. *Nat Med*. 2023;29(8):2133–2141. 3. Klempner SK, et al. *ESMO Gastrointest Oncol*. 2025;7: Epub ahead of print. 4. Shitara K, et al. Presented at ASCO Gastrointestinal Cancers Symposium 2024. Abstract 372. 5. Shitara K, et al. *N Engl J Med*. 2024;391(12):1159-1162 and supplement. 6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.2.2024.

MA-MM-14151 | March 2025

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