

What antiemetics were recommended or used in zolbetuximab trials?

**NK-1 and 5-HT<sub>3</sub> receptor antagonists, plus other prophylactic antiemetics, were recommended and given prior to the first zolbetuximab infusion in Phase 3 trials.**

The SPOTLIGHT and GLOW clinical trial protocols recommended the use of NK-1 and 5-HT<sub>3</sub> receptor antagonists, as well as other prophylactic antiemetics, per institutional standards of care and published guidelines, before zolbetuximab/placebo infusions.<sup>1,2</sup>

- Intravenous antiemetic premedication was recommended prior to zolbetuximab/placebo infusion while oral premedication was suggested ≥ 30 minutes before each study treatment.

Combined ad hoc exploratory analyses examined prophylactic antiemetic regimens used and incidence rates of nausea/vomiting on Cycle 1, Day 1 in SPOTLIGHT and GLOW.<sup>3</sup> Various combinations of antiemetics were administered before zolbetuximab/placebo infusions.

- 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

**Table 1. Use of prophylactic antiemetics and occurrence of nausea or vomiting on the day of the first zolbetuximab infusion<sup>a,3</sup>**

Use of prophylactic antiemetics, n (%)	n	With nausea	Without nausea	With vomiting	Without vomiting
<b>Any antiemetics</b>					
Yes	521	242	279	213	308
No	8	4	4	4	4
<b>Standard antiemetic regimens<sup>b</sup></b>					
<b>2-drug antiemetic regimens</b>					
NK-1 receptor antagonist + 5-HT <sub>3</sub> receptor antagonist	187	94 (50.3)	93 (49.7)	70 (37.4)	117 (62.6)
5-HT <sub>3</sub> receptor antagonist + steroid	93	42 (45.2)	51 (54.8)	45 (48.4)	48 (51.6)
<b>3-drug antiemetic regimens</b>					
NK-1 receptor antagonist+ 5-HT <sub>3</sub> receptor antagonist + steroid	97	38 (39.2)	59 (60.8)	24 (24.7)	73 (75.3)
<b>Other antiemetic regimens<sup>c</sup></b>					
	144	68 (47.2)	76 (52.8)	74 (51.4)	70 (48.6)

<sup>a</sup>Data represent the combined analysis of SPOTLIGHT and GLOW.

<sup>b</sup>Given that sample sizes beyond three-drug antiemetic regimens were small, various combinations of antiemetics not commonly used may not have been captured. Antiemetic regimens were excluded if not accurately documented as prophylactic or concomitant medication.

<sup>c</sup>Includes patients with less-common combinations of antiemetics as prophylactic or concomitant medications.

**Table 2. Use of prophylactic antiemetics and the occurrence of nausea or vomiting on the day of the first placebo infusion<sup>a,3</sup>**

Use of prophylactic antiemetics, n (%)	n	With nausea	Without nausea	With vomiting	Without vomiting
<b>Any antiemetics</b>					
Yes	522	62	460	16	506
No	4	0	4	0	4
<b>Standard antiemetic regimens<sup>b</sup></b>					
<b>2-drug antiemetic regimens</b>					
NK-1 receptor antagonist + 5-HT <sub>3</sub> receptor antagonist	201	35 (17.4)	166 (82.6)	8 (4.0)	193 (96.0)
5-HT <sub>3</sub> receptor antagonist + steroid	89	6 (6.7)	83 (93.3)	1 (1.1)	88 (98.9)
<b>3-drug antiemetic regimens</b>					
NK-1 receptor antagonist+ 5-HT <sub>3</sub> receptor antagonist + steroid	85	7 (8.2)	78 (91.8)	0	85 (100.0)
<b>Other antiemetic regimens<sup>c</sup></b>					
	147	14 (9.5)	133 (90.5)	7 (4.8)	140 (95.2)

<sup>a</sup>Data represent the combined analysis of SPOTLIGHT and GLOW.

<sup>b</sup>Given that sample sizes beyond three-drug antiemetic regimens were small, various combinations of antiemetics not commonly used may not have been captured. Antiemetic regimens were excluded if not accurately documented as prophylactic or concomitant medication.

<sup>c</sup>Includes patients with uncommon combinations of antiemetics as prophylactic or concomitant medications.

The prophylactic antiemetics given to  $\geq 5\%$  of patients may be accessed using the link below:<sup>4</sup>

- [Prophylactic antiemetics  \$\geq 5\%\$](#)

## References

1. Shah MA, Shitara K, Ajani JA, et al. Supplement to: Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial. *Nat Med.* 2023;29(8):2133-2141. Available at: <https://doi.org/10.1038/s41591-023-02465-7>.
2. Shitara K, Lordick F, Bang YJ, et al. Supplement to: Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. *Lancet.* 2023;401(10389):1655-1668. Available at: [https://doi.org/10.1016/s0140-6736\(23\)00620-7](https://doi.org/10.1016/s0140-6736(23)00620-7).
3. Shitara K, Smith E, Lordick F, et al. Impact and effective management of nausea/vomiting on patients treated with zolbetuximab + chemotherapy: insights from the phase III SPOTLIGHT and GLOW studies. *ESMO Open.* 2026;epub ahead of print105931. Available at: <https://doi.org/10.1016/j.esmoop.2025.105931>.
4. Data on File.