oncology exchange
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Introducing VYLOY® (zolbetuximab-clzb): A New Treatment Option for Your Patients with Advanced* HER2-Negative G/GEJ Cancer

The first-in-class FDA approved claudin 18.2-targeted monoclonal antibody in combination with chemotherapy* for the treatment of advanced† HER2-negative, CLDN18.2-positive gastric/gastroesophageal junction (G/GEJ) cancer

*Fluoropyrimidine- and platinum-containing chemotherapy.
† Locally advanced unresectable or metastatic.

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Agenda

1. Impact and unmet needs in advanced G/GEJ cancer
2. Introducing VYLOY
3. Clinical evidence for VYLOY in advanced* G/GEJ cancer
4. Administering VYLOY
5. Summary

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*Locally advanced unresectable or metastatic.

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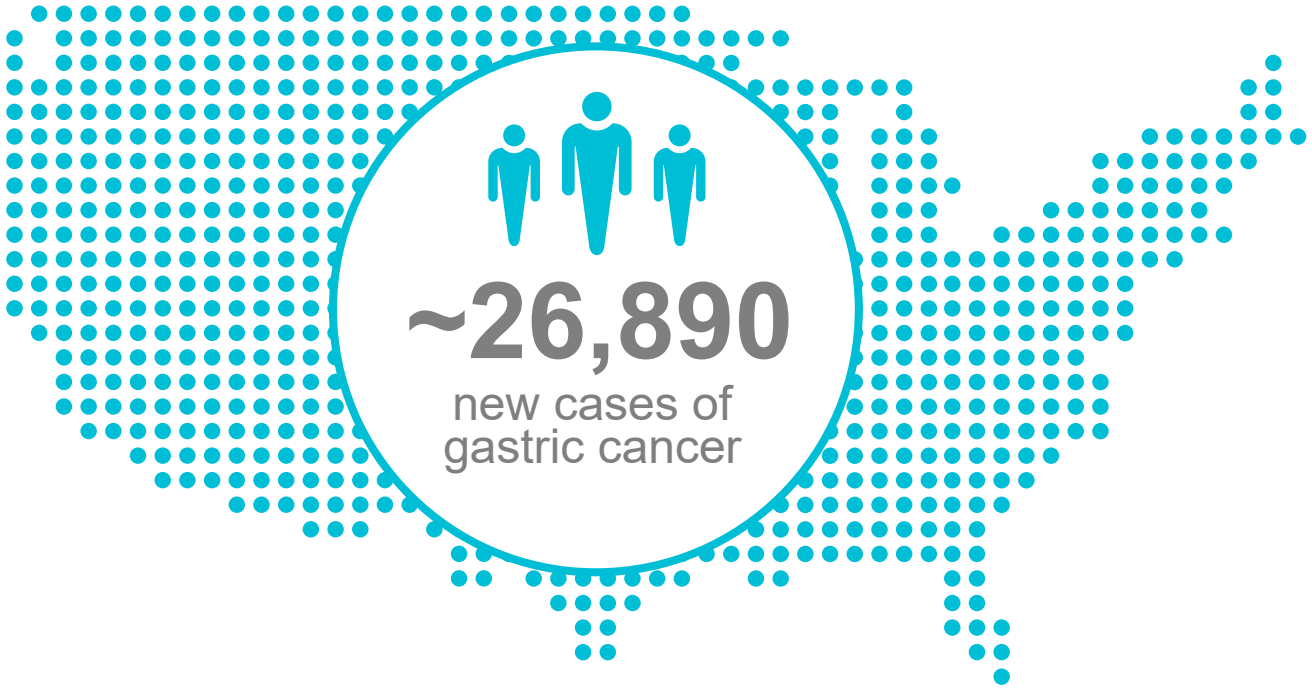
Impact and unmet needs in advanced* G/GEJ cancer

*Locally advanced unresectable or metastatic.

In 2024, an estimated 26,890 new cases of gastric cancer (61% advanced* stage) were diagnosed in the US[1,2†]



In the US, over 95% of gastric cancers are adenocarcinomas, which are typically classified based on anatomic location (cardia/proximal or non-cardia/distal) and histologic type (diffuse or intestinal).[3]

Gastric cancer and GEJ cancer are **often diagnosed at advanced stages** due to a lack of screening programs in the US. As a result, these patients will likely have a poor prognosis.[3,4]

Esophageal cancers may be classified based on histological type (squamous cell carcinoma or adenocarcinoma) and/or anatomic location. The Siewert classification specifies if the tumor is type I or II (typically treated according to esophageal/GEJ cancer guidelines) or type III (typically treated according to gastric cancer guidelines).[4]

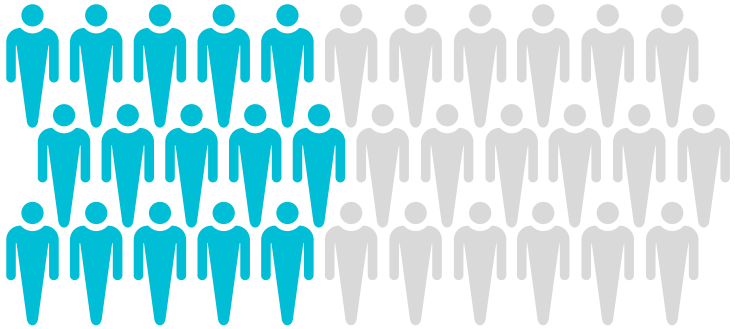
*Locally advanced (stages II and III) and metastatic (stage IV) G/GEJ cancer per tumor-node-metastasis (TNM) staging classification as described in NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).[3,4]
†Diagnosis estimate for the US in 2024 for esophageal cancer: ~22,370 new cases (71% advanced stage). SEER data do not have a separate classification for GEJ apart from esophageal cancer; therefore, true GEJ projections are unknown.[5]
G/GEJ=gastric/gastroesophageal junction; **NCCN**=National Comprehensive Cancer Network; **SEER**=Surveillance, Epidemiology, and End Results Program; **TNM**=tumor-node-metastasis.

References: 1. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: stomach cancer. Accessed April 26, 2024. https://seer.cancer.gov/statfacts/html/stomach.html. **2.** American Cancer Society. *Cancer Facts & Figures 2024*. Accessed March 7, 2024. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2024/2024-cancer-facts-and-figures-acs.pdfs 2024. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed March 7, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **4.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed August 15, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **5.** National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: esophageal cancer. Accessed May 10, 2024. https://seer.cancer.gov/statfacts/html/esoph.html.

Impact of G/GEJ cancer

In the US, patients with advanced disease at diagnosis will likely have a **poor outcome,[1,2] and fewer than 50% will receive second-line therapy for mG/GEJ cancer[3]***

<50%
RECEIVE SECOND-LINE THERAPY



68
MEDIAN AGE AT DIAGNOSIS

Gastric cancer is most frequently diagnosed among people aged 65-74 years, with a **median age at diagnosis of 68 years[4]**

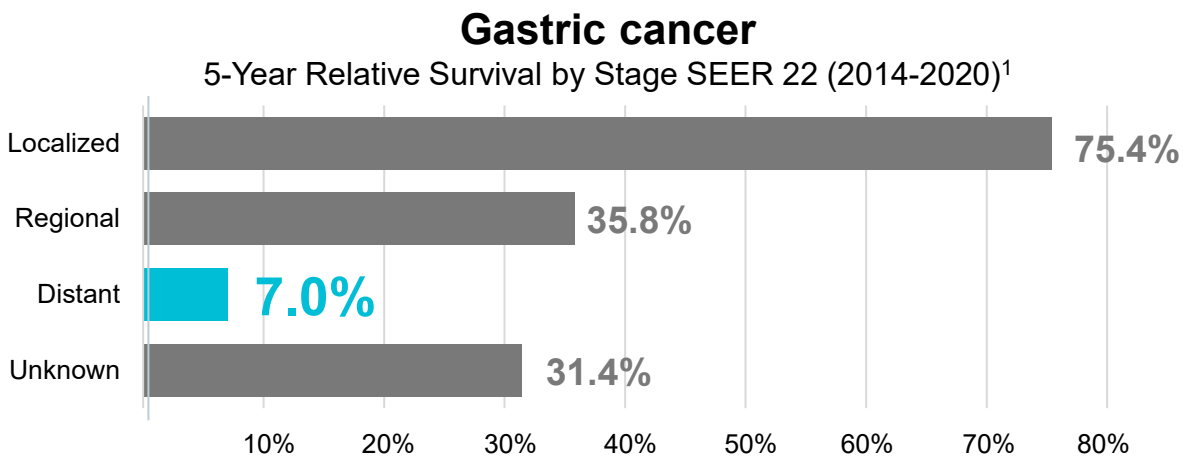
Men are nearly **twice as likely** as women to be diagnosed with gastric cancer[4]

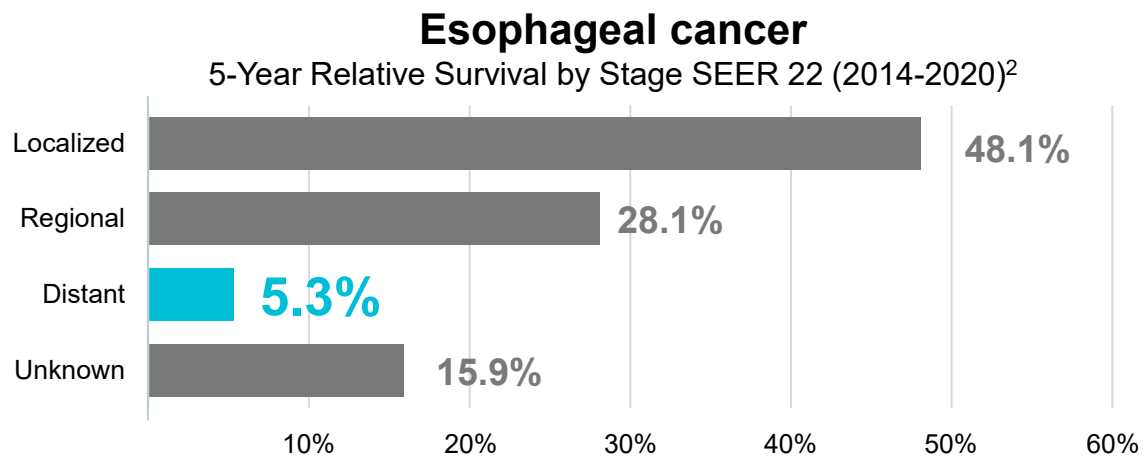
*Data from a retrospective analysis of electronic medical records of 3850 eligible patients with G/GEJ/esophageal adenocarcinoma who underwent first-line therapy and were alive at 45 days after completion of first-line therapy.[3]

mG/GEJ=metastatic gastric/gastro-esophageal junction; **G/GEJ**=gastric/gastroesophageal junction.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed August 12, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed July 30, 26, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **3.** Barzi A, et al. *Cancer Control*. (Epub) 05-06-2019. **4.** National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: stomach cancer. https://seer.cancer.gov/statfacts/html/stomach.html. Accessed September 25, 2024.

5-year relative survival by stage (SEER 22, 2014-2020)[1,2]





Patients diagnosed with mG/GEJ* have an especially poor prognosis[1,2]

*True GEJ projections are difficult to locate: SEER data do not have a separate classification for GEJ apart from esophageal cancer.[2]
mG/GEJ=metastatic gastric/gastro-esophageal junction; **SEER**=Surveillance, Epidemiology, and End Results Program.
References: 1. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: stomach cancer. https://seer.cancer.gov/statfacts/html/stomach.html. Accessed September 25, 2024. **2.** National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: esophageal cancer. https://seer.cancer.gov/statfacts/html/esoph.html. Accessed September 25, 2024.

Biomarker testing should be performed in patients with gastric/GEJ cancer

The NCCN Guidelines® for Gastric Cancer and Esophageal/Esophagogastric Junction Cancer recommendations for biomarker testing include[1,2]:

- HER2
- PD-L1
- MSI/MMR
- NTRK fusion
- RET
- BRAF V600E
- TMB

BRAF=v-raf murine sarcoma viral oncogene homolog B1; **GEJ**=gastroesophageal junction; **HER2**=human epidermal growth factor 2; **MMR**=mismatch repair; **MSI**=microsatellite instability; **NCCN**=National Comprehensive Cancer Network; **NTRK**=neurotrophic tyrosine receptor kinase; **PD-L1**=programmed death ligand 1; **RET**=rearranged during transfection; **TMB**=tumor mutational burden.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed August 12, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed July 30, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org.

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INDICATION

VYLOY, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adults with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors are claudin (CLDN) 18.2 positive as determined by an FDA-approved test

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WARNINGS AND PRECAUTIONS:

Hypersensitivity reactions, including serious anaphylaxis reactions, and serious and fatal infusion-related reactions (IRR) have been reported in clinical studies when VYLOY has been administered. **Any grade hypersensitivity reactions**, including anaphylactic reactions, occurring with VYLOY in combination with mFOLFOX6 or CAPOX was 18%. **Severe (Grade 3 or 4) hypersensitivity reactions**, including anaphylactic reactions, occurred in 2% of patients. Seven patients (1.3%) permanently discontinued VYLOY for hypersensitivity reactions, including two patients (0.4%) who permanently discontinued VYLOY due to anaphylactic reactions. Seventeen (3.2%) patients required dose interruption, and three patients (0.6%) required infusion rate reduction due to hypersensitivity reactions. **All grade IRRs** occurred in 3.2% in patients administered VYLOY in combination with mFOLFOX6 or CAPOX. Severe (Grade 3) IRRs occurred in 2 (0.4%) patients who received VYLOY. An IRR led to permanent discontinuation of VYLOY in 2 (0.4%) patients and dose interruption in 7 (1.3%) patients. The infusion rate was reduced for VYLOY for 2 (0.4%) patients due to an IRR. Monitor patients during infusion with VYLOY and for 2 hours after completion of infusion or longer if clinically indicated, for hypersensitivity reactions with symptoms and signs that are highly suggestive of anaphylaxis (urticaria, repetitive cough, wheeze and throat tightness/change in voice). Monitor patients for signs and symptoms of IRRs including nausea, vomiting, abdominal pain, salivary hypersecretion, pyrexia, chest discomfort, chills, back pain, cough and hypertension. If a severe or life-threatening hypersensitivity or IRR reaction occurs, discontinue VYLOY permanently, treat symptoms according to standard medical care, and monitor until symptoms resolve. For any Grade 2 hypersensitivity or IRR, interrupt the VYLOY infusion until Grade ≤1, then resume at a reduced infusion rate for the remaining infusion. Follow Grade 2 management for Grade 3 infusion-related nausea and vomiting. Premedicate the patient with antihistamines for the subsequent infusions, and closely monitor the patient for symptoms and signs of a hypersensitivity reaction. The infusion rate may be gradually increased as tolerated.

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CAPOX=capecitabine/oxaliplatin; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen.

Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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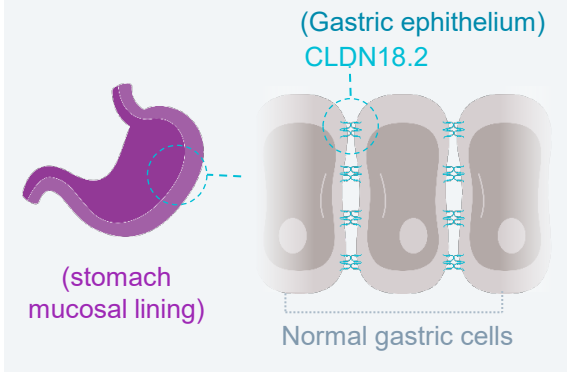
Claudin 18.2 (CLDN18.2) offers a new therapeutic target in gastric tumors*

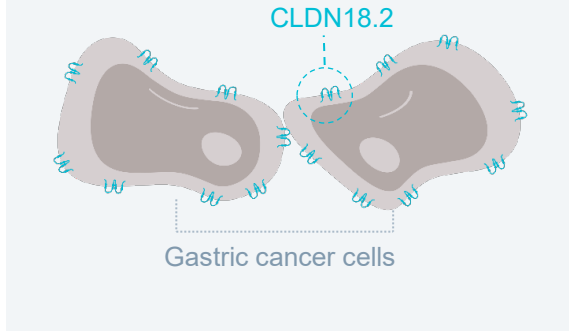
CLDN18.2 is typically confined within healthy gastric mucosa; however, it may become exposed, and thus more accessible to VYLOY as tumors develop[1,2]

CONFINED IN HEALTHY TISSUE



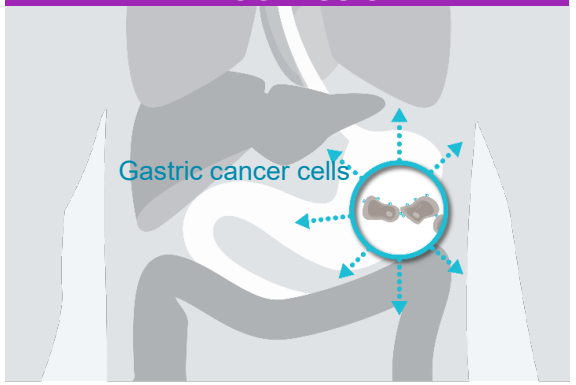
In normal gastric mucosa, CLDN18.2 is typically buried within tight junctions.[1,2] As a component of tight junctions, claudins are involved in the regulation of permeability, barrier function, and polarity of epithelial layers[3-5]

RETAINED AND EXPOSED IN MALIGNANT TRANSFORMATION



CLDN18.2 is often retained during malignant transformation of gastric tissue. CLDN18.2 may be more exposed and accessible to antibodies when cell polarity disruptions and structure loss occur[1,2,6]

MAINTAINED IN METASTATIC PROGRESSION



CLDN18.2 may also be expressed in lymph node metastases of gastric adenocarcinoma as well as other distant metastatic sites[1,7-9]

- Claudins are found throughout the body, but CLDN18.2 is the dominant CLDN18 isoform in gastric tissue[1,10]
- **VYLOY specifically targets CLDN18.2[11]**

*Advanced G/GEJ adenocarcinoma.
CLDN=claudin; **G/GEJ**=gastric/gastro-esophageal junction.

References: 1. Sahin U, et al. *Clin Cancer Res*. 2008;14(23):7624-7634. **2.** Sahin U, et al. *Eur J Cancer*. 2018;100:17-26. **3.** Turner JR, et al. *Semin Cell Dev Biol*. 2014;36:204-212. **4.** Tsukita S, et al. *Trends Biochem Sci*. 2019;44(2):141-152. **5.** Hu YJ, et al. *Mol Biol Rep*. 2013;40(11):6123-6142. **6.** Lamouille S, et al. *Nat Rev Mol Cell Biol*. 2014;15(3):178-196. **7.** Pellino A, et al. *J Pers Med*. 2021;11(11):1095. **8.** Coati I, et al. *Br J Cancer*. 2019;121(3):257-263. **9.** Rohde C, et al. *Jpn J Clin Oncol*. 2019;49(9):870-876. **10.** Niimi T, et al. *Mol Cell Biol*. 2001;21(21):7380-7390. **11.** VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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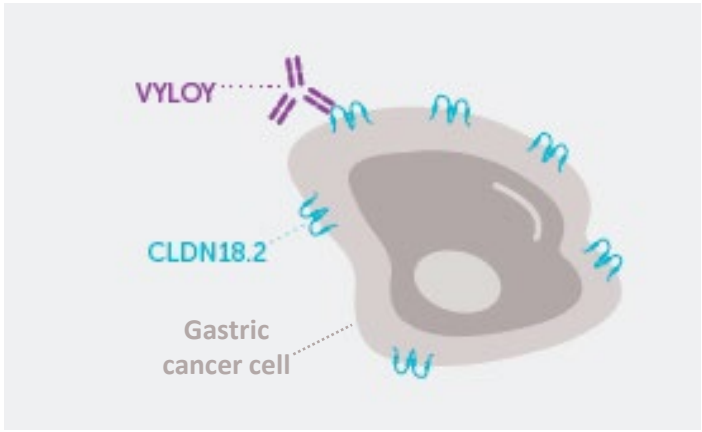
VYLOY is a CLDN18.2-directed cytolytic antibody that mediates cytotoxic immune system mechanisms: ADCC and CDC[1,2]

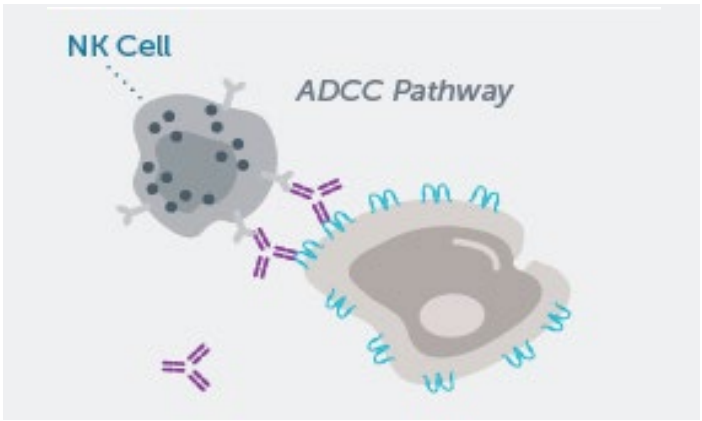
In preclinical studies, VYLOY:

CLDN18.2 DIRECTED



VYLOY is a CLDN18.2-directed cytolytic antibody that selectively binds to cells that express CLDN18.2, where cytotoxic immune responses are activated[1,2]

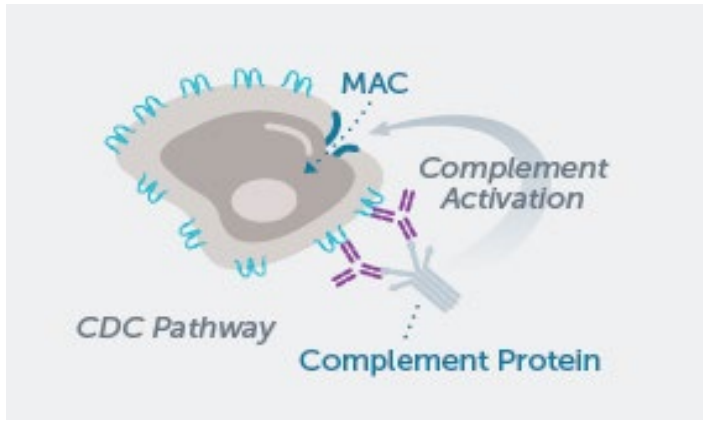
ADCC: ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY



VYLOY depletes CLDN18.2+ cells via ADCC[1]

- ADCC: Effector cells, such as natural killer cells, recognize antibody-targeted tumor cells and release cytotoxic molecules for lysis[3]

CDC: COMPLEMENT-DEPENDENT TOXICITY



VYLOY also depletes CLDN18.2+ cells via CDC[1]

- CDC: In addition, complement proteins gather to assemble a membrane attack complex (MAC), which forms pores that lyse targeted tumor cells[3]

VYLOY + chemotherapy had increased antitumor activity in CLDN18.2-expressing mouse tumor models compared to VYLOY or chemotherapy alone.[1]

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ADCC=antibody-dependent cellular cytotoxicity; **CDC**=complement-dependent toxicity; **CLDN**=claudin; **MAC**=membrane attack complex; **NK**=natural killer.

References: 1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Sahin U, et al. *Eur J Cancer*. 2018;100:17-26. **3.** Hendriks D, et al. *Int Rev Cell Mol Biol*. 2017;331:289-383.

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Testing for claudin 18.2 helps reveal which patients may be candidates for VYLOY + chemo* as first-line therapy[1]

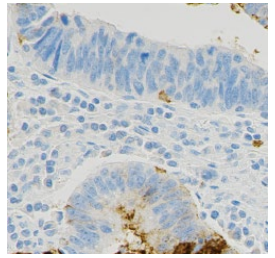
According to estimates from 2 global Phase 3 studies:

38% of patients with advanced† G/GEJ cancer are CLDN18.2+‡ and may be candidates for VYLOY + chemo[1-3*]

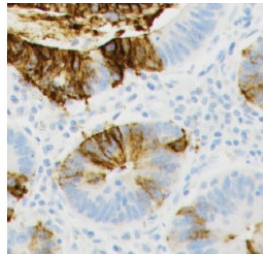
- The clinical cutoff for VYLOY is ≥75% of viable tumor cells demonstrating moderate-to-strong membranous CLDN18 staining by IHC[1,4§]
- Testing for CLDN18.2 status can be ordered alongside HER2 and other biomarkers[2,3,5,6]
- A companion diagnostic to determine CLDN18.2 status is available: VENTANA CLDN18 (43-14A) RxDx assay[1,4]

Evaluating CLDN18.2 Status[7]

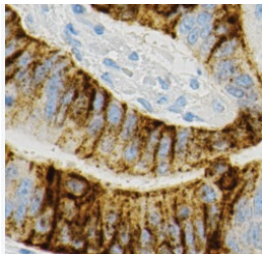
MEMBRANOUS STAINING INTENSITY AND PERCENTAGE OF VIABLE TUMOR CELLS STAINED



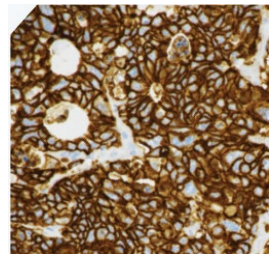
No Staining



Weak Staining



Moderate Staining



Strong Staining

*Fluoropyrimidine- and platinum-containing chemotherapy.[1]
†Locally advanced unresectable or metastatic.
‡CLDN18.2+ (claudin 18.2 positive) is defined as ≥75% of tumor cells demonstrating moderate to strong membranous CLDN18 staining by IHC.[2,3]
§Test results of the VENTANA CLDN18 (43-14A) RxDx assay should be interpreted by a qualified pathologist in conjunction with histological examination, relevant clinical information, and proper controls.[1,4]
CLDN=claudin; **G/GEJ**=gastric/gastro-esophageal junction; **HER2**=human epidermal growth factor receptor 2; **IHC**=immunohistochemistry.

References: 1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Shitara K, et al. *Lancet*. 2023;401(10389):1655-1668. **3.** Shah MA, et al. *Nat Med*. 2023;29(8):2133-2141. **4.** VENTANA CLDN18 (43-14A) assay. Package insert. Tucson, AZ: Ventana Medical Systems, Inc; 2023. **5.** Abrahao-Machado LF, et al. *World J Gastroenterol*. 2016;22(19):4619-4625. **6.** Fuchs CS, et al. *Gastric Cancer*. 2022;25(1):197-206. **7.** VENTANA CLDN18 (43-14A) RxDx Assay Interpretation Guide for Gastric Adenocarcinoma Including Gastroesophageal Junction (GEJ). Tuscon, AZ: 2023.

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CLDN18.2 is one of the most highly prevalent biomarkers for advanced G/GEJ adenocarcinoma[1-11]

Biomarker prevalence estimates from select studies are reported below. Prevalence data can vary among studies due to tumor heterogeneity, differences in patient population, clinical trial methodology, and diagnostic assays used.[1-11]

CLDN18.2[1,2] (positive)*†	**PD-L1**[3-7] (variable due to multiple factors)‡	**HER2**[8-10] (positive)	**MSI**[6,7,11] (MSI-high)§
38%	**CPS ≥1: 67-82%** **CPS ≥5: 29-60%** **CPS ≥10: 16-49%**	**14-22%**	**3-7%**

*CLDN18.2 positivity defined as ≥75% of tumor cells demonstrating moderate to strong membranous CLDN18 IHC staining.[1,2,12]
†Data from 2 global randomized Phase 3 studies: SPOTLIGHT, which included 2403 assessable patients, of which 922 were CLDN18.2 positive; and GLOW, which included 2104 assessable patients, of which 808 were CLDN18.2 positive.[1,2]
‡CPS thresholds are still being explored. Data are from randomized controlled trials and real-world retrospective medical records studies.[3-7]
§MSI-high prevalence varies by stage of disease. Data shown are from patients with advanced disease.[6,7,11]
CLDN=claudin; **CPS**=combined positive score; **G/GEJ**=gastric/gastro-esophageal junction; **HER2**=human epidermal growth factor receptor 2; **IHC**=immunohistochemistry; **MSI**=microsatellite instability; **PD-L1**=programmed death-ligand 1.

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.** Mehta R, et al. *Curr Oncol.* 2023;30(2):1869-1881. **4.** Schoemig-Markiefka B, et al. *Gastric Cancer.* 2021;24(5):1115-1122. **5.** Fuchs CS, et al. *Gastric Cancer.* 2022;25(1):197-206. **6.** Shitara K, et al. *Nature.* 2022;603(7903):942-948. **7.** Rha SY, et al. ESMO Virtual Plenary 2023. VP1-2023. **8.** Van Cutsem E, et al. *Gastric Cancer.* 2015;18(3):476-484. **9.** Janjigian YY, et al. *Ann Oncol.* 2012;23(10):2656-2662. **10.** Kim WH, et al. *Appl Immunohistochem Mol Morphol.* 2016;26(4):239-245. **11.** Chao J, et al. *JAMA Oncol.* 2021;7(6):895-902. **12.** VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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SELECT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS:

Severe Nausea and Vomiting. VYLOY is emetogenic. Nausea and vomiting occurred more often during the first cycle of treatment. **All grade nausea and vomiting** occurred in 82% and 67% respectively of patients treated with VYLOY in combination with mFOLFOX6 and 69% and 66% in combination with CAPOX, respectively. **Severe (Grade 3) nausea** occurred in 16% and 9% of patients treated with VYLOY in combination with mFOLFOX6 or CAPOX respectively. **Severe (Grade 3) vomiting** occurred in 16% and 12% of patients treated with VYLOY in combination with mFOLFOX6 or CAPOX. Nausea led to permanent discontinuation of VYLOY in combination with mFOLFOX6 or CAPOX in 18 (3.4%) patients and dose interruption in 147 (28%) patients. Vomiting led to permanent discontinuation of VYLOY in combination with mFOLFOX6 or CAPOX in 20 (3.8%) patients and dose interruption in 150 (28%) patients. Pretreat with antiemetics prior to each infusion of VYLOY. Manage patients during and after infusion with antiemetics or fluid replacement. Interrupt the infusion, or permanently discontinue VYLOY based on severity.

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CAPOX=capecitabine/oxaliplatin; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen.

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Clinical studies of VYLOY + chemotherapy in advanced* G/GEJ cancer

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*Locally advanced unresectable or metastatic.

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VYLOY was studied with standard chemotherapy options in two Phase 3 trials

SPOTLIGHT and GLOW: two international, multicenter, double-blind, randomized, controlled Phase 3 trials involving 1072 patients[1-3]

SPOTLIGHT

VYLOY + mFOLFOX6*†
(n=283)

Placebo + mFOLFOX6†‡
(n=282)

GLOW

VYLOY + CAPOX*§
(n=254)

Placebo + CAPOX‡§
(n=253)

*VYLOY was administered at a loading dose of 800 mg/m^2 IV on Cycle 1 Day 1 followed by 600 mg/m^2 IV every 3 weeks.[1-3]
†Patients received 12 treatments of mFOLFOX6 for 4 cycles (42 days) on Days 1, 15, and 29. After 12 mFOLFOX6 treatments, patients continued to receive fluorouracil (5-FU) and folinic acid at the investigator's discretion until the patient met study treatment discontinuation criteria.[1,2]
‡Placebo was administered on Cycle 1 Day 1 and every 3 weeks thereafter.[1-3]
§Patients received CAPOX (capecitabine/oxaliplatin) treatment until IRC confirmed disease progression or a total of 8 treatments (approximately 21 days). Oxaliplatin was administered on Day 1 of each cycle, whereas capecitabine was taken twice daily on Days 1 through 14. After a maximum of 8 treatments of oxaliplatin, patients could continue to receive capecitabine twice daily on Days 1 through 14 of each cycle at the investigator's discretion until the patient met study treatment discontinuation criteria.[1,3]
CAPOX=capecitabine plus oxaliplatin; **IV**=intravenous; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen.
References: 1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Shitara K, et al. *Lancet.* 2023;401(10389):1655-1668. **3.** Shah MA, et al. *Nat Med.* 2023;29(8):2133-2141.

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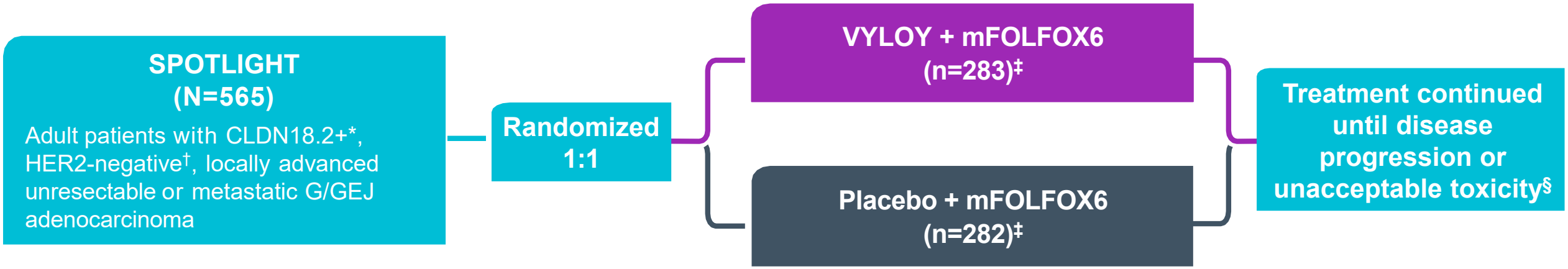
In the SPOTLIGHT Phase 3 trial, VYLOY + mFOLFOX6 was evaluated against mFOLFOX6 alone[1,2]

VYLOY is a first-in-class CLDN18.2-targeted therapy studied with mFOLFOX6 in a double-blind, randomized, global, multicenter Phase 3 study[1,2]



*Claudin 18.2+ is defined as ≥75% of tumor cells demonstrating moderate to strong membranous CLDN18 staining by IHC.[2]
†HER2-negative tumor as determined by local or central testing.[2]
‡Patients were randomized 1:1 to receive VYLOY in combination with mFOLFOX6 (n=283) or placebo in combination with mFOLFOX6 (n=282). VYLOY was administered intravenously at a loading dose of 800 mg/m^2 (Day 1 of Cycle 1) followed by subsequent doses of 600 mg/m^2 every 3 weeks in combination with up to 12 treatments (4 cycles) of mFOLFOX6 (oxaliplatin 85 mg/m^2, folinic acid (leucovorin or local equivalent) 400 mg/m^2, fluorouracil 400 mg/m^2 given as a bolus and fluorouracil 2400 mg/m^2 given as a continuous infusion) administered on Days 1, 15, and 29 of a 42-day cycle. After 12 treatments, patients were allowed to continue treatment with VYLOY, 5-fluorouracil, and folinic acid (leucovorin or local equivalent) at the discretion of the investigator, until progression of disease or unacceptable toxicity.[1]
§Treatment continued until RECIST v1.1–defined progression of disease as determined by an independent review committee.[1]
CLDN=claudin; **G/GEJ**=gastric/gastro-esophageal junction; **HER2**=human epidermal growth factor receptor 2; **IHC**=immunohistochemistry; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen; **RECIST**=Response Evaluation Criteria in Solid Tumors.

References: 1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Shitara K, et al. *Lancet.* 2023;401(10389):1655-1668.

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Participant eligibility, study population, and trial endpoints

ELIGIBILITY CRITERIA[1]*

- CLDN18.2+, HER2-negative, previously untreated adult patients
- Radiological evaluable disease per RECIST v1.1
- ECOG performance status 0 or 1
- Adequate organ function

SELECT EXCLUSION CRITERIA[1]*

- Received prior treatment for locally advanced unresectable or metastatic G/GEJ adenocarcinoma

STUDY POPULATION:

Median age was 61 (range: 20-86). 62% were male. Racial groups: 48% White, 34% Asian, 3.0% American Indian or Alaska, 1.2% Black or African American, 4.1% other, 9% race unknown or missing; 78% non-Hispanic or Latino, 13% Hispanic or Latino, and 10% ethnicity missing. 98% had ECOG performance status of 0 or 1. 76% had gastric cancer, 24% had GEJ cancer, 84% were metastatic, 16% were locally advanced, and 29% had prior gastrectomy. Subsequent anticancer therapy: 135 (48%) patients in the VYLOY + mFOLFOX6 arm and 148 (53%) patients in the placebo + mFOLFOX6 arm.[2] Lauren classification: 35% diffuse, 24% intestinal, 8% mixed, 16% unknown, 16% other, and 1% missing.[1]

MAJOR ENDPOINT[1,2]	ADDITIONAL EFFICACY ENDPOINTS[1,2]
Progression-Free Survival (PFS)†	Overall Survival (OS) Objective Response Rate (ORR)† Duration of Response (DOR)†

*Does not include all patient inclusion and exclusion criteria for the SPOTLIGHT trial.[1]
†PFS, ORR, and DOR were assessed per RECIST v1.1 by IRC.[2]
CLDN=claudin; **DOR**=duration of response; **ECOG**=Eastern Cooperative Oncology Group; **G/GEJ**=gastric/gastro-esophageal junction; **HER2**=human epidermal growth factor receptor 2; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen; **ORR**=objective response rate; **OS**=overall survival; **PFS**=progression-free survival; **RECIST**=Response Evaluation Criteria in Solid Tumors.

References: 1. Shitara K, et al. *Lancet.* 2023;401(10389):1655-1668. **2.** VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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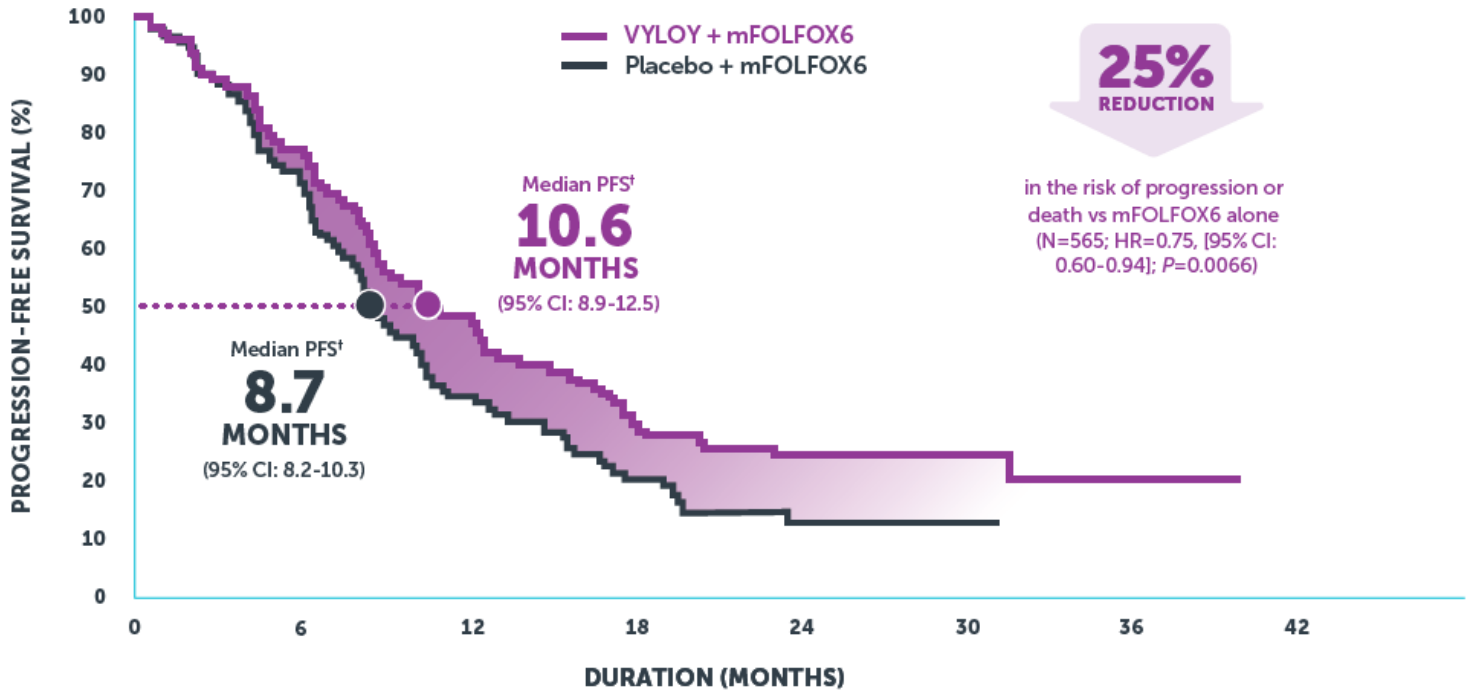
VYLOY + mFOLFOX6 significantly improved progression-free survival vs mFOLFOX6 alone

PROGRESSION-FREE SURVIVAL (MAJOR ENDPOINT)*



PATIENTS AT RISK								
VYLOY + mFOLFOX6	283	187	78	33	12	7	2	0
Placebo + mFOLFOX6	282	168	56	19	8	2	0	0

In SPOTLIGHT:

Median PFS was 10.6 months vs 8.7 months with mFOLFOX6 alone (HR=0.75 [95% CI: 0.60-0.94]; *P*=0.0066)

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*PFS was assessed per RECIST v1.1 by IRC.
†Based on Kaplan-Meier estimate.
CI=confidence interval; **HR**=hazard ratio; **IRC**=independent review committee; **ITT**=intent to treat; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen; **PFS**=progression-free survival; **RECIST**=Response Evaluation Criteria in Solid Tumors.
Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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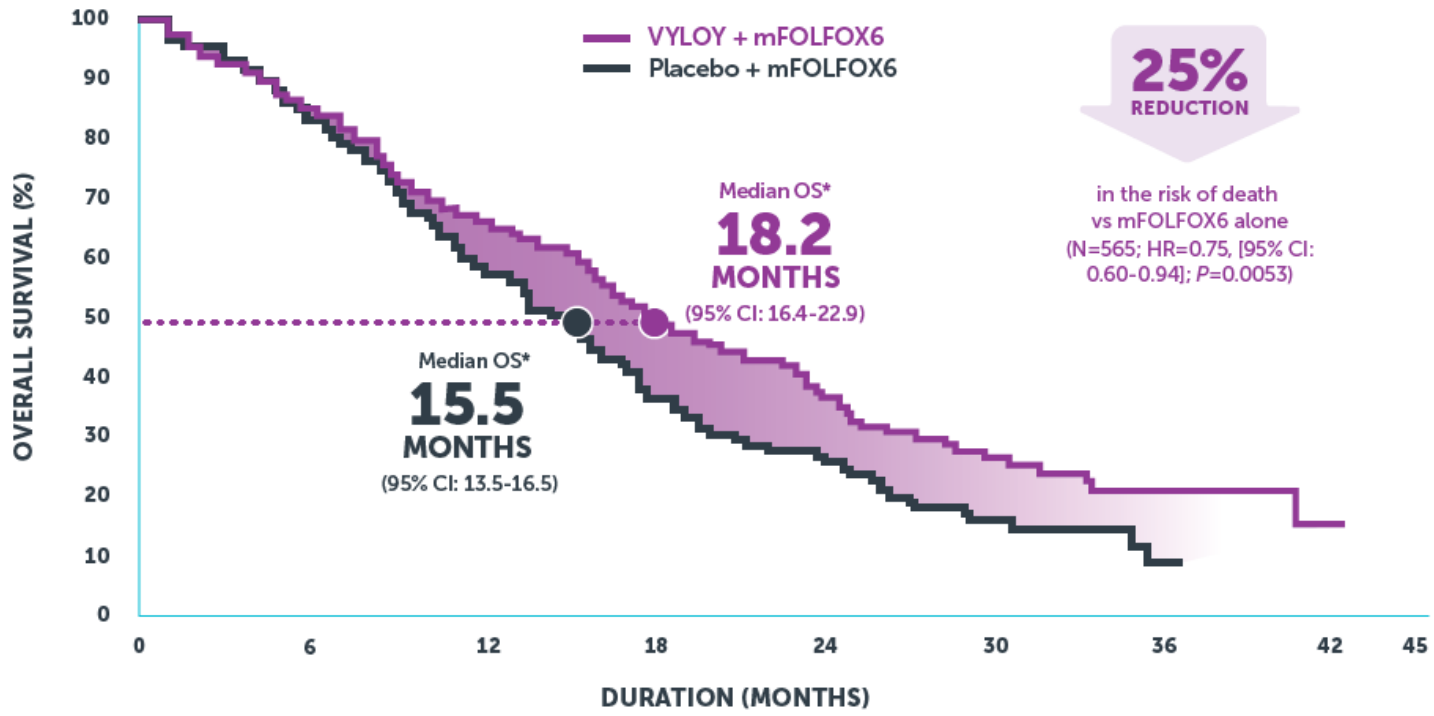
Overall survival significantly improved with VYLOY + mFOLFOX6 vs mFOLFOX6 alone

OVERALL SURVIVAL (ADDITIONAL ENDPOINT)



PATIENTS AT RISK									
VYLOY + mFOLFOX6	283	233	146	83	49	23	9	1	0
Placebo + mFOLFOX6	282	224	139	64	34	15	2	0	0

In SPOTLIGHT:

Median OS was 18.2 months with VYLOY + mFOLFOX6 vs 15.5 months with mFOLFOX6 alone (HR=0.75 [95% CI: 0.60-0.94]; *P*=0.0053)

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*Based on Kaplan-Meier estimate.
CI=confidence interval; **HR**=hazard ratio; **ITT**=intent to treat; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen; **OS**=overall survival.
Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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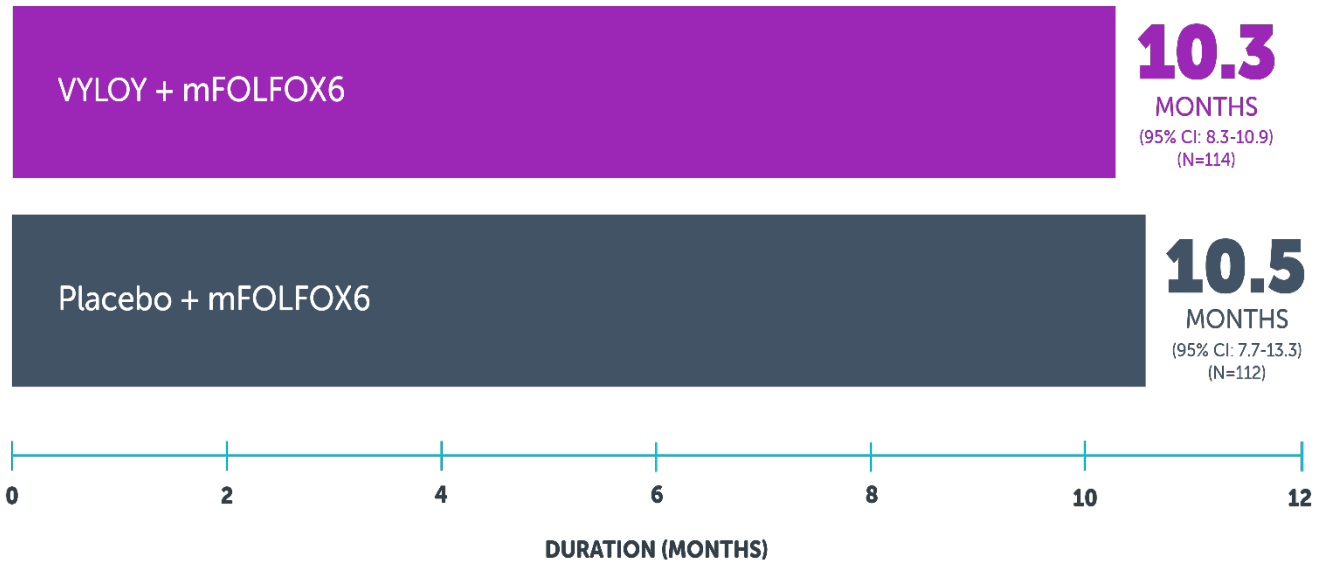
Response rates

OBJECTIVE RESPONSE RATE (ADDITIONAL ENDPOINT)*†

VYLOY + mFOLFOX6	Placebo + mFOLFOX6
40.3%	**39.7%**
(95% CI: 34.5-46.3)	(95% CI: 34.0-45.7)
ORR	ORR

MEDIAN DURATION OF RESPONSE (ADDITIONAL ENDPOINT)†



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*ORR was based on binomial distribution (Clopper-Pearson).
†ORR and DOR was assessed per RECIST v1.1 by IRC.
CI=confidence interval; **DOR**=duration of response; **IRC**=independent review committee; **ITT**=intent to treat; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen; **ORR**=objective response rate; **RECIST**=Response Evaluation Criteria in Solid Tumors.
Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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ADVERSE REACTIONS:

Most common adverse reactions (≥15%): Nausea, vomiting, fatigue, decreased appetite, diarrhea, peripheral sensory neuropathy, abdominal pain, constipation, decreased weight, hypersensitivity reactions, and pyrexia.

Most common laboratory abnormalities (≥15%): Decreased neutrophil count, decreased leucocyte count, decreased albumin, increased creatinine, decreased hemoglobin, increased glucose, decreased lymphocyte count, increased aspartate aminotransferase, decreased platelets, increased alkaline phosphatase, increased alanine aminotransferase, decreased glucose, decreased sodium, increased phosphate, decreased potassium, and decreased magnesium.

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Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

SELECT SAFETY INFORMATION

ADVERSE REACTIONS

SPOTLIGHT Study: 279 patients with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive who received at least one dose of VYLOY in combination with mFOLFOX6

Serious adverse reactions occurred in 45% of patients treated with VYLOY in combination with mFOLFOX6; the **most common serious adverse reactions** (≥2%) were vomiting (8%), nausea (7%), neutropenia (2.9%), febrile neutropenia (2.9%), diarrhea (2.9%), intestinal obstruction (3.2%), pyrexia (2.5%), pneumonia (2.5%), respiratory failure (2.2%), pulmonary embolism (2.2%), decreased appetite (2.1%) and sepsis (2.0%). **Fatal adverse reactions** occurred in 5% of patients who received VYLOY in combination with mFOLFOX6 including sepsis (1.4%), pneumonia (1.1%), respiratory failure (1.1%), intestinal obstruction (0.7%), acute hepatic failure (0.4%), acute myocardial infarction (0.4%), death (0.4%), disseminated intravascular coagulation (0.4%), encephalopathy (0.4%), and upper gastrointestinal hemorrhage (0.4%). Permanent discontinuation of VYLOY due to an adverse reaction occurred in 20% of patients; the **most common adverse reactions leading to discontinuation** (≥2%) were nausea and vomiting. Dosage interruptions of VYLOY due to an adverse reaction occurred in 75% of patients; the **most common adverse reactions leading to dose interruption** (≥5%) were nausea, vomiting, neutropenia, abdominal pain, fatigue, and hypertension.

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CLDN=claudin; **G/GEJ**=gastric/gastro-esophageal junction; **HER2**=human epidermal growth factor receptor 2; **mFOLFOX6**=modified folinic acid, fluorouracil, and oxaliplatin regimen.

Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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ADVERSE REACTIONS

GLOW Study: 254 patients with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive who received at least one dose of VYLOY in combination with CAPOX

Serious adverse reactions occurred in 47% of patients treated with VYLOY in combination with CAPOX; the **most common serious adverse reactions** (≥2%) were vomiting (6%), nausea (4.3%), decreased appetite (3.9%), decreased platelet count (3.1%), upper gastrointestinal hemorrhage (2.8%), diarrhea (2.8%), pneumonia (2.4%), pulmonary embolism (2.3%), and pyrexia (2.0%). **Fatal adverse reactions** occurred in 8% of patients who received VYLOY in combination with CAPOX including sepsis (1.2%), pneumonia (0.4%), death (0.8%), upper gastrointestinal hemorrhage (0.8%), cerebral hemorrhage (0.8%), abdominal infection (0.4%), acute respiratory distress syndrome (0.4%), cardio-respiratory arrest (0.4%), decreased platelet count (0.4%), disseminated intravascular coagulation (0.4%), dyspnea (0.4%), gastric perforation (0.4%), hemorrhagic ascites (0.4%), procedural complication (0.4%), sudden death (0.4%), and syncope (0.4%). Permanent discontinuation of VYLOY due to an adverse reaction occurred in 19% of patients; the **most common adverse reaction leading to discontinuation** (≥2%) was vomiting. Dosage interruption of VYLOY due to an adverse reaction occurred in 55% of patients; the **most common adverse reactions leading to dose interruption** (≥2%) were nausea, vomiting, neutropenia, thrombocytopenia, anemia, fatigue, infusion-related reaction, and abdominal pain.

SPECIFIC POPULATIONS

Lactation Advise lactating women not to breastfeed during treatment with VYLOY and for 8 months after the last dose.

CAPOX=capecitabine plus oxaliplatin; **CLDN**=claudin; **G/GEJ**=gastric/gastro-esophageal junction; **HER2**=human epidermal growth factor receptor 2.

Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

Exploratory analysis: Progression-free survival at 12 and 24 months

LIMITATIONS: The results below are from exploratory analyses that were not prespecified within the SPOTLIGHT protocol and were not statistically powered to detect differences between treatment arms, and therefore no conclusions can be drawn. These results are provided only as descriptive clinical information.

PFS rate estimates at 12 and 24 months*

DURATION	VYLOY + mFOLFOX6	Placebo + mFOLFOX6
At 12 months	**49% (95% CI, 42-55)**	**35% (95% CI, 28-42)**
At 24 months	**24% (95% CI, 17-32)**	**15% (95% CI, 9-22)**

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*Based on Kaplan-Meier estimate.
mFOLFOX6=modified folinic acid, fluorouracil, and oxaliplatin regimen; **PFS**=progression-free survival.
Reference: Shitara K, et al. *Lancet.* 2023;401(10389):1655-1668.

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Exploratory analysis: Overall survival at 12 and 24 months

LIMITATIONS: The results below are from exploratory analyses that were not prespecified within the SPOTLIGHT protocol and were not statistically powered to detect differences between treatment arms, and therefore no conclusions can be drawn. These results are provided only as descriptive clinical information.

Estimated OS at 12 and 24 months

DURATION	VYLOY + mFOLFOX6	Placebo + mFOLFOX6
At 12 months	**68% (95% CI, 61-73)**	**60% (95% CI, 54-66)**
At 24 months	**39% (95% CI, 32-46)**	**28% (95% CI, 22-35)**

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mFOLFOX6=modified folinic acid, fluorouracil, and oxaliplatin regimen; **OS**=overall survival.
Reference: Shitara K, et al. *Lancet.* 2023;401(10389):1655-1668.

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Adverse events reported in ≥15% of patients treated with VYLOY with a difference between arms of ≥5% compared to placebo

ADVERSE REACTION		VYLOY + mFOLFOX6 (n=279)		Placebo + mFOLFOX6 (n=278)	
		All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Gastrointestinal disorders	Nausea	82	16	61	7
	Vomiting	67	16	36	6
Metabolism and nutrition disorders	Decreased appetite	47	6	34	3.2
General disorders and administration site conditions	Peripheral edema	18	0.7	9	0

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mFOLFOX6=modified folinic acid, fluorouracil, and oxaliplatin regimen.
Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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VYLOY safety profile

- Serious adverse reactions occurred in 45% of patients treated with VYLOY in combination with mFOLFOX6; the most common serious adverse reactions (≥2%) were vomiting (8%), nausea (7%), neutropenia (2.9%), febrile neutropenia (2.9%), diarrhea (2.9%), intestinal obstruction (3.2%), pyrexia (2.5%), pneumonia (2.5%), respiratory failure (2.2%), pulmonary embolism (2.2%), decreased appetite (2.1%) and sepsis (2.0%).
- Fatal adverse reactions occurred in 5% of patients who received VYLOY in combination with mFOLFOX6 including sepsis (1.4%), pneumonia (1.1%), respiratory failure (1.1%), intestinal obstruction (0.7%), acute hepatic failure (0.4%), acute myocardial infarction (0.4%), death (0.4%), disseminated intravascular coagulation (0.4%), encephalopathy (0.4%), and upper gastrointestinal hemorrhage (0.4%)
- Permanent discontinuation of VYLOY due to an adverse reaction occurred in 20% of patients; the most common adverse reactions leading to discontinuation (≥2%) were nausea and vomiting
- Dosage interruptions of VYLOY due to an adverse reaction occurred in 75% of patients; the most common adverse reactions leading to dose interruption (≥5%) were nausea, vomiting, neutropenia, abdominal pain, fatigue, and hypertension
- Median duration of exposure to VYLOY in combination with mFOLFOX6 was 6.2 months (range: 1 day to 40.9 months)

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mFOLFOX6=modified folinic acid, fluorouracil, and oxaliplatin regimen.

Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

Laboratory abnormalities (≥15%) in SPOTLIGHT with a difference between arms of ≥5% compared to placebo

LABORATORY ABNORMALITY	VYLOY + mFOLFOX6*		Placebo + mFOLFOX6*	
	All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Albumin decreased	78	4.4	47	1.1
Potassium decreased	28	11	21	6
Glucose decreased	45	0.4	35	0.4
Sodium decreased	29	5	21	2.9

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*The denominator used to calculate the rate varied from 271 to 272 based on the number of patients with a baseline value and at least one post-treatment value.
mFOLFOX6=modified folinic acid, fluorouracil, and oxaliplatin regimen.
Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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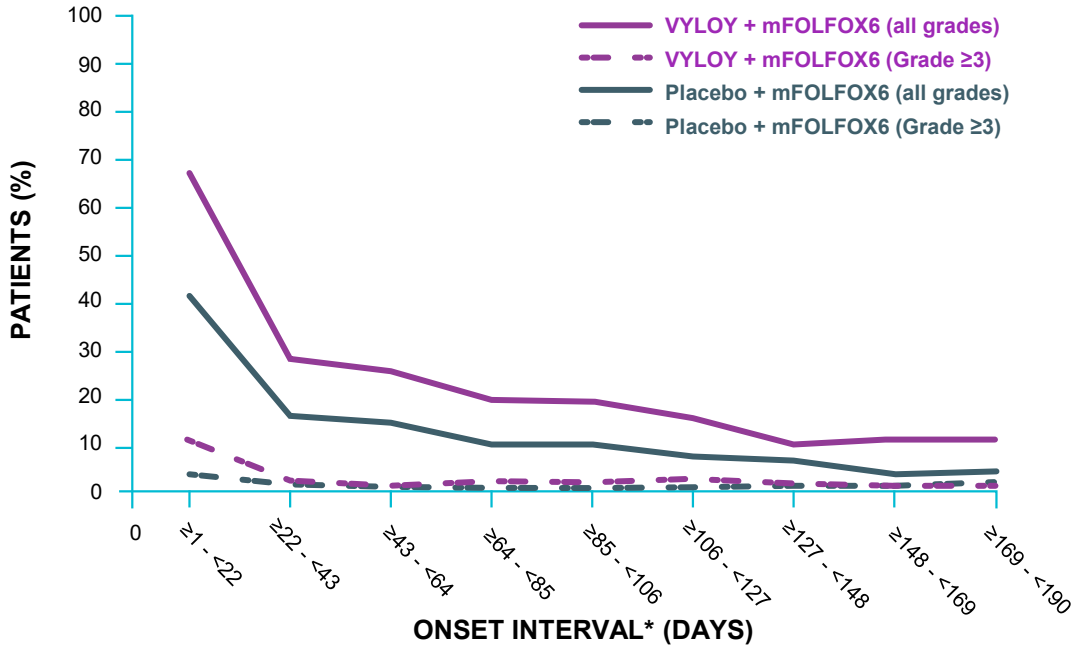
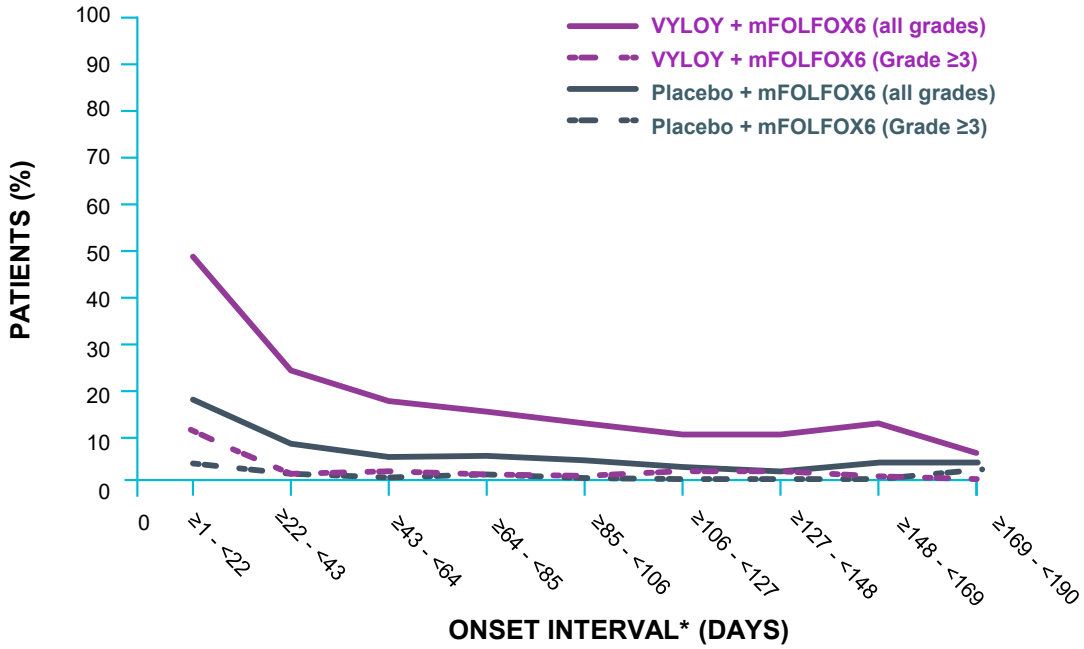
Nausea and vomiting occurred more often during the first cycle of treatment[1]

Nausea: All occurrence in SPOTLIGHT (SAS)[2]



Vomiting: All occurrence in SPOTLIGHT (SAS)[2]



Nausea and vomiting have been confirmed as important identified risks. Adverse events, graded according to National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03, were monitored throughout the trial and for 90 days after treatment discontinuation. Adverse event preferred terms were defined according to the Medical Dictionary for Regulatory Activities terminology version 25.0. Grade 4 nausea is not defined in Common Terminology Criteria for Adverse Events v4.03 and was determined and managed at investigator discretion. These data are not generalizable and cannot be used to predict adverse event outcomes. These data are from the safety analysis set (SAS) in a Phase 3, global, randomized, multicenter trial (VYLOY + mFOLFOX6: n=279; Placebo + mFOLFOX6: n=278). The results presented are provided only as descriptive clinical information.[3]

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*The onset day in the onset interval was defined as the date of onset minus the date of the first dose plus one.
mFOLFOX6=modified folinic acid, fluorouracil, and oxaliplatin regimen.
References: 1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Supplement to: Shitara K, et al. *Lancet.* 2023;401(10389):1655-1668. **3.** Shitara K, et al. *Lancet.* 2023;401(10389):1655-1668.

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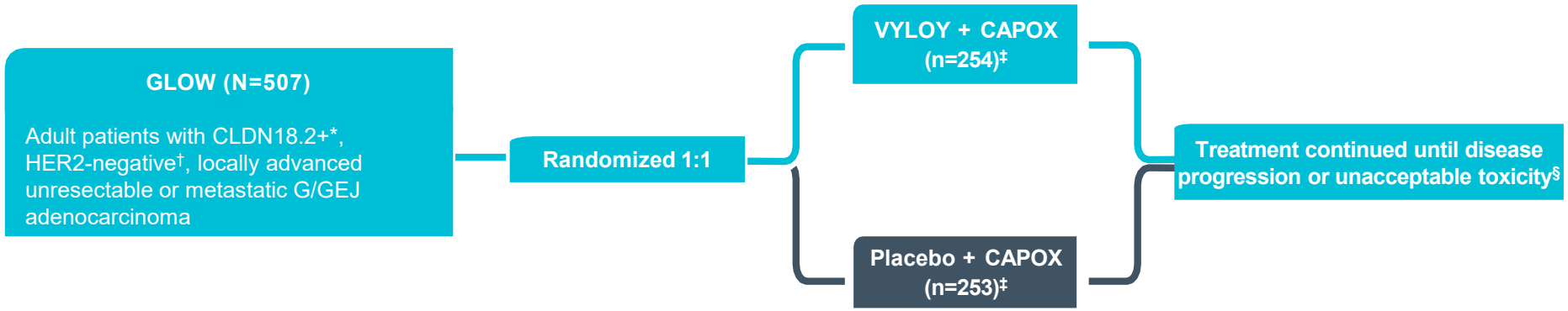
In the GLOW Phase 3 trial, VYLOY + CAPOX was evaluated against CAPOX alone[1,2]

VYLOY is a first-in-class CLDN18.2-targeted therapy studied with CAPOX in a double-blind, randomized, global, multicenter Phase 3 study[1,2]



ELIGIBILITY CRITERIA[1¶]

- CLDN18.2+, HER2-negative, previously untreated adult patients
- Radiological evaluable disease per RECIST v1.1
- ECOG performance status 0 or 1
- Adequate organ function

SELECT EXCLUSION CRITERIA[1¶]

- Received prior treatment for locally advanced unresectable or metastatic G/GEJ adenocarcinoma

STUDY POPULATION:

Median age was 60 (range: 21-83 years). 62% were male. 62% were Asian, 36% White, 1.4% race missing; 95% non-Hispanic or Latino, 3.4% Hispanic or Latino, and 1.4% ethnicity missing. 99% had ECOG performance status of 0 or 1. 84% had primary gastric cancer, 16% had primary GEJ cancer, 88% were metastatic, 12% were locally advanced, and 27% had prior gastrectomy.[2] Lauren classification: 37% diffuse, 15% intestinal, 8% mixed, 28% unknown, 12% other, and 1% missing.[1]

*CLDN18.2+ (claudin 18.2 positive) is defined as ≥75% of tumor cells demonstrating moderate to strong membranous CLDN18 staining by IHC.[2]
†HER2- tumor as determined by local or central testing.[2]
‡Patients were randomized 1:1 to receive VYLOY in combination with CAPOX (n=254) or placebo in combination with CAPOX (n=253). VYLOY was administered intravenously at a loading dose of 800 mg/m^2 (Day 1 of Cycle 1) followed by a subsequent dose of 600 mg/m^2 every 3 weeks in combination with up to 8 treatments (8 cycles) of CAPOX administered on Day 1 (oxaliplatin 130 mg/m^2) and on Days 1 to 14 (capecitabine 1000 mg/m^2) of a 21-day cycle. After 8 treatments of oxaliplatin, patients were allowed to continue treatment of VYLOY and capecitabine at the discretion of the investigator, until progression of disease or unacceptable toxicity.[1]
§Treatment continued until RECIST v1.1–defined progression of disease as determined by an IRC.[1]
¶Does not include all patient inclusion and exclusion criteria for the GLOW trial.[1]
CAPOX=capecitabine plus oxaliplatin; **CLDN**=claudin; **ECOG**=Eastern Cooperative Oncology Group; **G/GEJ**=gastric/gastro-esophageal junction; **HER2**=human epidermal growth factor receptor 2; **IHC**=immunohistochemistry; **IRC**=independent review committee; **RECIST**=Response Evaluation Criteria in Solid Tumors.

References: 1. Shah MA, et al. *Nat Med*. 2023;29(8):2133-2141. **2.** VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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GLOW trial major and additional endpoints

	GLOW (N=507)[1,2]
mPFS*†‡	31% reduction in risk of progression or death vs chemotherapy alone (HR=0.69 [95% CI: 0.54-0.87]; *P*=0.0007)
	1.4-month improvement (8.2 months [95% CI, 7.5-8.8] vs 6.8 months [95% CI, 6.1-8.1] with chemotherapy alone)
mOS‡§	23% reduction in risk of death vs chemotherapy alone (HR=0.77 [95% CI: 0.62-0.97]; *P*=0.0118)
	2.2-month improvement (14.4 months [95% CI, 12.3-16.5] vs 12.2 months [95% CI, 10.3-13.7] with chemotherapy alone)
ORR†§¶	32.3% (95% CI: 26.6-38.4) vs 31.2% (95% CI: 25.6-37.3) with chemotherapy alone
mDOR†§	8.3 months (95% CI: 6.3-11.4; N=82) vs 6.2 months (95% CI: 6.0-7.6; N=79) with chemotherapy alone

*Major endpoint.[1,2]
†PFS, ORR, and DOR were assessed per RECIST v1.1 by IRC.[1]
‡Based on Kaplan-Meier estimate.[1]
§Additional efficacy endpoints.[1,2]
¶ORR based on binomial distribution (Clopper-Pearson).[1]
CI=confidence interval; **DOR**=duration of response; **HR**=hazard ratio; **IRC**=independent review committee; **mDOR**=median duration of response; **mOS**=median overall survival; **mPFS**=median progression-free survival; **ORR**=objective response rate; **PFS**=progression-free survival.
References: 1. VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Shah MA, et al. *Nat Med*. 2023;29(8):2133-2141.

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SELECT SAFETY INFORMATION

ADVERSE REACTIONS

GLOW Study: 254 patients with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive who received at least one dose of VYLOY in combination with CAPOX

Serious adverse reactions occurred in 47% of patients treated with VYLOY in combination with CAPOX; the **most common serious adverse reactions** (≥2%) were vomiting (6%), nausea (4.3%), decreased appetite (3.9%), decreased platelet count (3.1%), upper gastrointestinal hemorrhage (2.8%), diarrhea (2.8%), pneumonia (2.4%), pulmonary embolism (2.3%), and pyrexia (2.0%). **Fatal adverse reactions** occurred in 8% of patients who received VYLOY in combination with CAPOX including sepsis (1.2%), pneumonia (0.4%), death (0.8%), upper gastrointestinal hemorrhage (0.8%), cerebral hemorrhage (0.8%), abdominal infection (0.4%), acute respiratory distress syndrome (0.4%), cardio-respiratory arrest (0.4%), decreased platelet count (0.4%), disseminated intravascular coagulation (0.4%), dyspnea (0.4%), gastric perforation (0.4%), hemorrhagic ascites (0.4%), procedural complication (0.4%), sudden death (0.4%), and syncope (0.4%). Permanent discontinuation of VYLOY due to an adverse reaction occurred in 19% of patients; the **most common adverse reaction leading to discontinuation** (≥2%) was vomiting. Dosage interruption of VYLOY due to an adverse reaction occurred in 55% of patients; the **most common adverse reactions leading to dose interruption** (≥2%) were nausea, vomiting, neutropenia, thrombocytopenia, anemia, fatigue, infusion-related reaction, and abdominal pain.

SPECIFIC POPULATIONS

Lactation Advise lactating women not to breastfeed during treatment with VYLOY and for 8 months after the last dose.

CAPOX=capecitabine plus oxaliplatin; **CLDN**=claudin; **G/GEJ**=gastric/gastro-esophageal junction; **HER2**=human epidermal growth factor receptor 2.

Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

Administering VYLOY

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VYLOY can be administered every 2 or 3 weeks aligning with selected chemo dosing schedule

PRIOR TO ADMINISTRATION

If a patient is experiencing nausea and/or vomiting, symptoms should be resolved to Grade ≤1 before the first infusion

PREMEDICATION

Prior to each VYLOY infusion, premedicate patients with a combination of antiemetics (e.g., NK-1 receptor blockers and/or 5-HT3 receptor blockers, as well as other drugs as indicated) for the prevention of nausea and vomiting

VYLOY DOSING*

First dose:

800 mg/m^2 intravenously

Subsequent doses:

600 mg/m^2 intravenously every 3 weeks

or

400 mg/m^2 intravenously every 2 weeks

BSA

Recommended VYLOY dosage for each patient is based on body surface area

VYLOY ADMINISTRATION

If VYLOY + chemotherapy† are administered on the same day, VYLOY must be administered first

RECOMMENDED DURATION OF TREATMENT IS UNTIL DISEASE PROGRESSION OR UNACCEPTABLE TOXICITY

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*Administer VYLOY in combination with fluoropyrimidine- and platinum-containing chemotherapy.

†Fluoropyrimidine- and platinum-containing chemotherapy.

5-HT3=5-hydroxytryptamine; **BSA**=body surface area; **NK-1**=neurokinin-1.

Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

Recommended VYLOY dosage and infusion rates

VYLOY Dose		Initial Infusion Rate (first 30-60 minutes)	Subsequent Infusion Rate
First dose	800 mg/m^2	100 mg/m^2/hr	200-265 mg/m^2/hr
Subsequent doses	600 mg/m^2 every 3 weeks or 400 mg/m^2 every 2 weeks	75 mg/m^2/hr or 50 mg/m^2/hr	150-265 mg/m^2/hr or 100-200 mg/m^2/hr

- In the absence of adverse reactions after 30-60 minutes, the infusion rate can be increased to the subsequent infusion rate as tolerated
- Recommended VYLOY dosage for each patient is based on body surface area
- For the **first VYLOY dose**, the estimated minimum infusion time is **approximately 3.5 hours**. Total infusion time will depend on dose interruptions or infusion rate reductions
- For **subsequent VYLOY doses**, the estimated minimum infusion time is **approximately 2.5 hours**. Total infusion time will depend on dose interruptions or infusion rate reductions
- If the infusion time exceeds the recommended storage time (6 hours from end of preparation of infusion solution at room temperature, 15°C to 30°C [59°F to 86°F]), the infusion bag must be discarded and a new infusion bag prepared to continue the infusion.

Dose modifications

No dose reduction for VYLOY is recommended. Adverse reactions for VYLOY are managed by reducing the infusion rate, interruption of the infusion, withholding the dose, and/or permanently discontinuing VYLOY as described in the full Prescribing Information.

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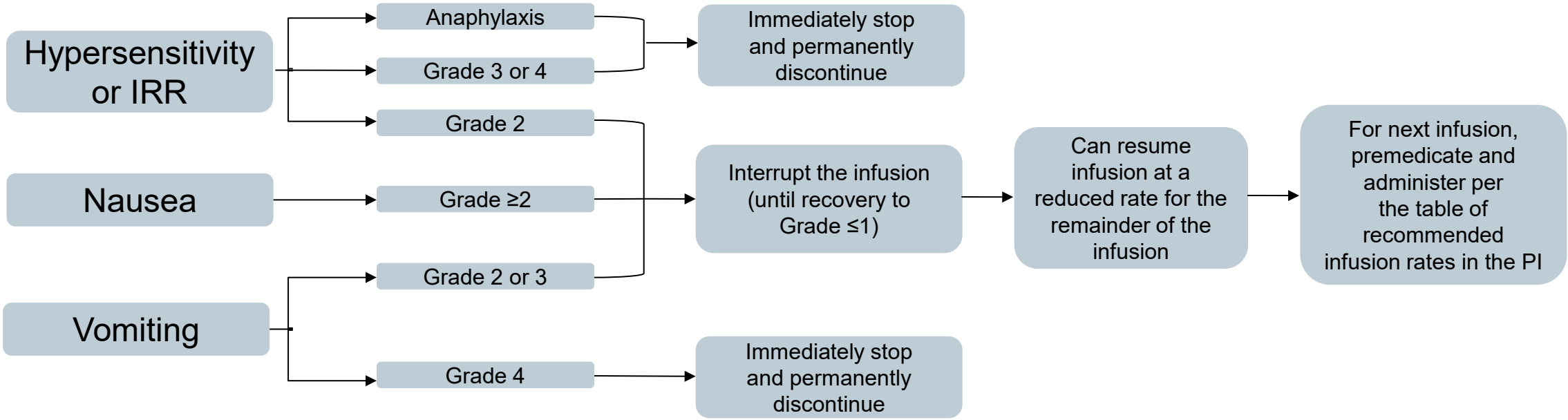
Recommended dose modifications for VYLOY adverse reactions

No dose reduction for VYLOY is recommended.

Adverse reactions for VYLOY are managed by reducing the infusion rate, withholding the dose, interrupting (pausing) infusion, and/or discontinuing treatment as outlined below.



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Toxicity is graded per National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. The CTCAE does not have a Grade 4 classification for nausea.
IRR=infusion-related reaction; **PI**=prescribing information.
Reference: VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc.

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Summary

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Summary

- CLDN18.2 is a biomarker with expression that is often retained and becomes exposed throughout malignant transformation in cases of advanced G/GEJ cancer[1-9]
- VYLOY, a first-in-class monoclonal antibody that targets CLDN18.2, has been studied in two Phase 3 trials involving 1072 patients with locally advanced unresectable or metastatic G/GEJ cancer[10-12]

	SPOTLIGHT (N=565)[10,11]	GLOW (N=507)[10,12]
mPFS	25% reduction in risk of progression or death vs chemotherapy alone (HR=0.75 [95% CI: 0.60-0.94]; *P*=0.0066)	31% reduction in risk of progression or death vs chemotherapy alone (HR=0.69 [95% CI: 0.54-0.87]; *P*=0.0007)
	1.9-month improvement (10.6 months [95% CI, 8.9-12.5] vs 8.7 months [95% CI, 8.2-10.3] with chemotherapy alone)	1.4-month improvement (8.2 months [95% CI, 7.5-8.8] vs 6.8 months [95% CI, 6.1-8.1] with chemotherapy alone)
mOS	25% reduction in risk of death vs chemotherapy alone (HR=0.75 [95% CI: 0.60-0.94]; *P*=0.0053)	23% reduction in risk of death vs chemotherapy alone (HR=0.77 [95% CI: 0.62-0.97]; *P*=0.0118)
	2.7-month improvement (18.2 months [95% CI, 16.4-22.9] vs 15.5 months [95% CI, 13.5-16.5] with chemotherapy alone)	2.2-month improvement (14.4 months [95% CI, 12.3-16.5] vs 12.2 months [95% CI, 10.3-13.7] with chemotherapy alone)

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CI=confidence interval; **CLDN**=claudin; **G/GEJ**=gastric/gastro-esophageal junction; **HR**=hazard ratio; **mOS**=median overall survival; **mPFS**=median progression-free survival.

References: 1. Sahin U, et al. *Clin Cancer Res*. 2008;14(23):7624-7634. **2.** Sahin U, et al. *Eur J Cancer*. 2018;100:17-26. **3.** Turner JR, et al. *Semin Cell Dev Biol*. 2014;36:204-212. **4.** Tsukita S, et al. *Trends Biochem Sci*. 2019;44(2):141-152. **5.** Hu YJ, et al. *Mol Biol Rep*. 2013;40(11):6123-6142. **6.** Lamouille S, et al. *Nat Rev Mol Cell Biol*. 2014;15(3):178-196. **7.** Pellino A, et al. *J Pers Med*. 2021;11(11):1095. **8.** Coati I, et al. *Br J Cancer*. 2019;121(3):257-263. **9.** Rohde C, et al. *Jpn J Clin Oncol*. 2019;49(9):870-876. **10.** VYLOY [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **11.** Shitara K, et al. *Lancet*. 2023;401(10389):1655-1668. **12.** Shah MA, et al. *Nat Med*. 2023;29(8):2133-2141.

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Summary: Warnings and precautions

- Hypersensitivity reactions including serious anaphylaxis reactions and serious and fatal infusion-related reactions have occurred. Monitor patients during and for at least 2 hours after infusion with VYLOY. Interrupt, slow the rate of infusion or permanently discontinue VYLOY based on severity and type of reaction. Premedicate with antihistamines for subsequent infusions after a hypersensitivity reaction.
- Severe nausea and vomiting: Premedicate patients with antiemetics prior to each infusion. Interrupt or permanently discontinue VYLOY based on the severity of the nausea and/or vomiting. Manage patients during and after infusion with antiemetics or fluid replacement.

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VYLOY Support Solutions™: Helping patients access VYLOY

VYLOY Support Solutions offers support and financial assistance to help patients overcome challenges to accessing VYLOY after a prescribing decision has been made.

Enroll your patients in VYLOY Support Solutions so they have access to the full range of support.

Access support

VYLOY Support Solutions offers help to patients to access their prescribed treatment. Contact VYLOY Support Solutions for:

Coding and billing information*
Benefits investigation
Prior authorization information†
Denial appeal information†

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*Information and materials provided by VYLOY Support Solutions are to assist providers, but the responsibility to determine coverage, reimbursement, and appropriate coding for a particular patient and/or procedure remains at all times with the provider.
†The healthcare provider remains responsible for populating all clinical information.

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Financial assistance

VYLOY Savings Program*: Patients may be eligible for one of the VYLOY Support Solutions financial assistance programs, depending on the type of insurance they have

Co-pay assistance: Patients who have private commercial insurance and are not insured by any federal or state healthcare program may be eligible for the VYLOY Co-pay Assistance Program,† which allows eligible patients to pay as little as $5 per dose

Astellas Patient Assistance Program: Eligible patients without insurance coverage for VYLOY may receive VYLOY at no cost‡

Financial assistance information: VYLOY Support Solutions can provide information about other resources that may be able to help patients with Medicare/Medicaid

*Information and materials provided by VYLOY Support Solutions are to assist providers, but the responsibility to determine coverage, reimbursement, and appropriate coding for a particular patient and/or procedure remains at all times with the provider.

†By enrolling in the VYLOY Co-pay Assistance Program ("Program"), the patient acknowledges that they currently meet the eligibility criteria and will comply with the following terms and conditions: The Program is for eligible patients with commercial prescription insurance for VYLOY® (zolbetuximab-clzb) and is good for use only with a valid prescription for VYLOY. The Program has an annual maximum co-pay assistance limit of $25,000 per calendar year. After the annual maximum on co-pay assistance is reached, patient will be responsible for the remaining monthly out-of-pocket costs for VYLOY. The Program is not valid for patients whose prescription claims are reimbursed, in whole or in part, by any state or federal government program, including, but not limited to, Medicaid, Medicare, Medigap, Department of Defense (DoD), Veterans Affairs (VA), TRICARE, Puerto Rico Government Insurance, or any state patient or pharmaceutical assistance program. Patients who move from commercial insurance to federal or state prescription health insurance will no longer be eligible, and agree to notify the Program of any such change. This offer is not valid for cash paying patients. Patients agree not to seek reimbursement from any health insurance or third party for all or any part of the benefit received by the patient through the Program. This offer is not conditioned on any past, present, or future purchase of VYLOY. This offer is not transferrable, has no cash value, and cannot be combined with any other offer, free trial, prescription savings card, or discount (including any program offered by a third-party payer or pharmacy benefit manager, or an agent of either, that adjusts patient cost-sharing obligations, through arrangements that may be referred to as "accumulator" or "maximizer" programs). The full value of the Program benefits is intended to pass entirely to the eligible patient. The benefit available under this Program is valid only for the patient's out-of-pocket medication costs for VYLOY. The benefit is not valid for any other out-of-pocket costs such as medication administration charges or other healthcare provider services. No other individual or entity (including, without limitation, third-party payers, pharmacy benefit managers, or the agents of either) is entitled to receive any benefit, discount, or other amount in connection with this Program. This offer is not health insurance and is only valid for patients in the 50 United States, Washington DC, and Puerto Rico. This Program is void where prohibited by law. No membership fees. Certain rules and restrictions apply. Astellas reserves the right to revoke, rescind, or amend this offer without notice for any reason (including to ensure that the offer is utilized solely for the patient's benefit).

‡Subject to eligibility. Program terms and conditions apply. Void where prohibited by law.

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Patient and caregiver support

Patient Connect is a program that helps connect patients and caregivers to resources that can provide emotional, logistical, and informational support to assist in managing daily life while being treated with VYLOY

TO LEARN MORE ABOUT ACCESS AND REIMBURSEMENT SUPPORT, CONNECT WITH VYLOY SUPPORT SOLUTIONS™

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Questions?

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Clinical Session