## METODS

### Study Design and Objectives

- **Patients with CLDN18.2+/HER2− (ie, locally advanced unresectable or metastatic G/GEJ adenocarcinoma; NCT03653070)** is being conducted in ~500 adult patients from ~130 centers globally.

### Study Treatment Period

| Cycle 1-8 | Zolbetuximab or placebo + CAPOX |
| **Cycle 9+** | Zolbetuximab or placebo + capecitabine + oxaliplatin (CAPOX) |

<table>
<thead>
<tr>
<th>Treatment Discontinuation Criteria (Met)</th>
<th>Follow-up visit</th>
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<td>30-day follow-up visit</td>
<td>90-day follow-up visit</td>
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**Post-Treatment Follow-Up Period**

- **FEC/CAPOX** will be evaluated; **FEC** will be administered as indicated for progression per IRC on Day 1 of each 21-day cycle; **CAPOX** will be administered on Day 1 of each 21-day cycle for up to eight cycles; **FEC** will be re-administered every 21 days if progression is noted after completion of eight cycles or earlier for patients who are continued on treatment following disease stabilization.

### Pharmacokinetics

- **Sampling for pharmacokinetics and immunogenicity will occur on Day 1 of Cycles 1-3 (every 3 weeks), as well as Day 1 of Cycles 5, 9, 13, and 17, and 30 and 90 days post zolbetuximab/ placebo treatment.**

### Safety

- **Adverse events of special interest will be collected; these include nausea, vomiting, abdominal pain, anemia, neutropenia, and hypersensitivity/infection-related reactions.**

### Quality of Life (HRQoL)

- **Patients will complete HRQoL assessments at screening, every 3 weeks during study treatment, at study treatment discontinuation, and 30 and 90 days post zolbetuximab/placebo treatment.**

### Immunogenicity

- **Immunogenicity will be evaluated through the measurement of antibodies to zolbetuximab and the presence of CAPOX-specific antibodies.**

### Adverse Events

- **Adverse events will be summarized; these include nausea, vomiting, abdominal pain, anemia, neutropenia, and hypersensitivity/infection-related reactions.**

### Study Terminology

- **The distribution of PFS, OS, and DoR will be estimated for each treatment arm using Kaplan-Meier methodology and compared between treatment arms using stratified log-rank tests.**

### Statistical Analysis

- **For PFS, OS, and DoR, a stratified Cox proportional hazard model will be used to estimate the HR for all-cause mortality and the corresponding 95% confidence interval.**

## Assessments

- **Radiographic imaging will be evaluated at screening, every 9 weeks for the first 54 weeks, and then every 12 weeks thereafter.**

- **Progression-free survival is defined as the time from the date of randomization until the date of radiologic disease progression, as assessed by IRC, or until death due to any cause, whichever occurs first.**

- **Overall survival is defined as the time from the date of randomization until the date of documented death from any cause.**

- **Objective response rate is defined as the proportion of subjects with a best overall response (BOR) of complete response (CR) or partial response (PR) on IRC per RECIST v1.1.**

- **The IRC is defined as the time at the date of the first response of CR or PR (whichever is first) recorded, as assessed by IRC, to the date of radiologic progression or death, whichever is earlier.**

- **The distribution of PFS, OS, and DoR will be estimated for each treatment arm using a Kaplan-Meier methodology and compared between treatment arms using stratified log-rank tests.**

## Acknowledgments

No conflicts of interest to disclose.

- **AA, JP:** Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Celgene, Incyte, Lilly, Merck Sharp & Dohme, Merck KGaA, EC:

- **KS:** Astellas, Merck, Bristol-Myers Squibb, Lilly, Gritstone, Taiho, Genentech/Roche, Daichii Sankyo – honoraria as a consultant.

- **FL:** Astellas – employment.

- **RX:** Bristol-Myers Squibb, Celgene, Lilly, Merck, Roche, Servier, Nordic Bioscience, Hospira, Medac, Novartis, Roche Pharma AG, Vifor – honoraria for speaking engagements.

## References