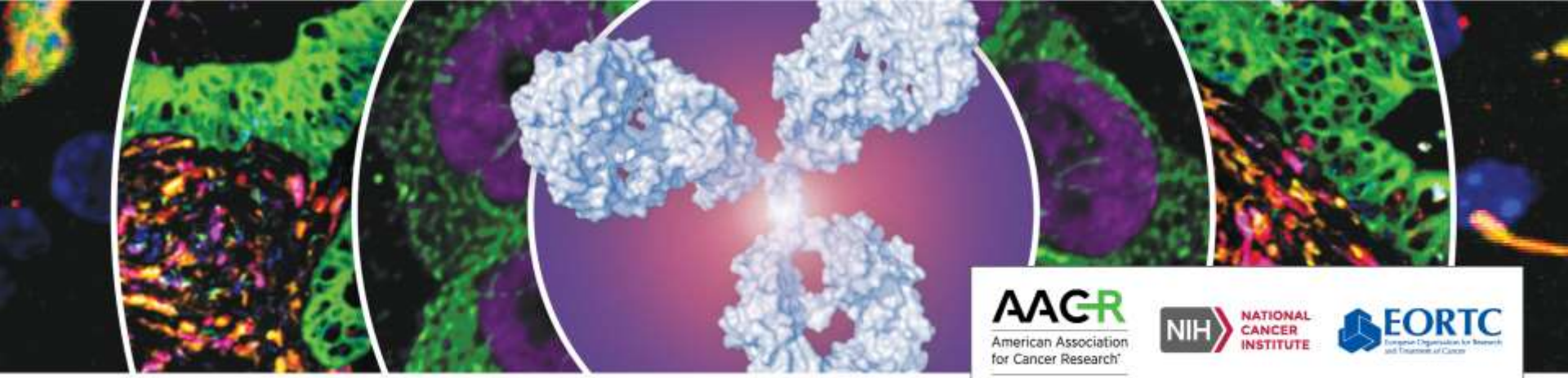

Updated Safety, Efficacy and Biomarker Analysis from the Phase I Monotherapy Study of Givastomig, a Novel Claudin 18.2/4-1BB Bispecific Antibody, in Claudin 18.2 Positive Advanced Gastroesophageal Carcinoma (GEC)

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AACR-NCI-EORTC MOLECULAR TARGETS AND CANCER THERAPEUTICS
October 22-26, 2025 | Hynes Convention Center | Boston, MA

Disclosure Information

Samuel J. Klempner

I have the following relevant financial relationships to disclose:

Employee of: Massachusetts General Hospital

Consultant for: Bristol-Myers Squibb, Merck, Astellas, Daiichi-Sankyo, Natera, Novartis, AstraZeneca, Mersana, Sanofi-Aventis, Amgen, Boehringer-Ingelheim, Taiho Oncology, Eisai, BeiGene, Elevation Oncology, EsoBiotec, and Gilead

Speaker's Bureau for: none

Grant/Research support: none

Stockholder in: Turning Point Therapeutics and Nuvalent

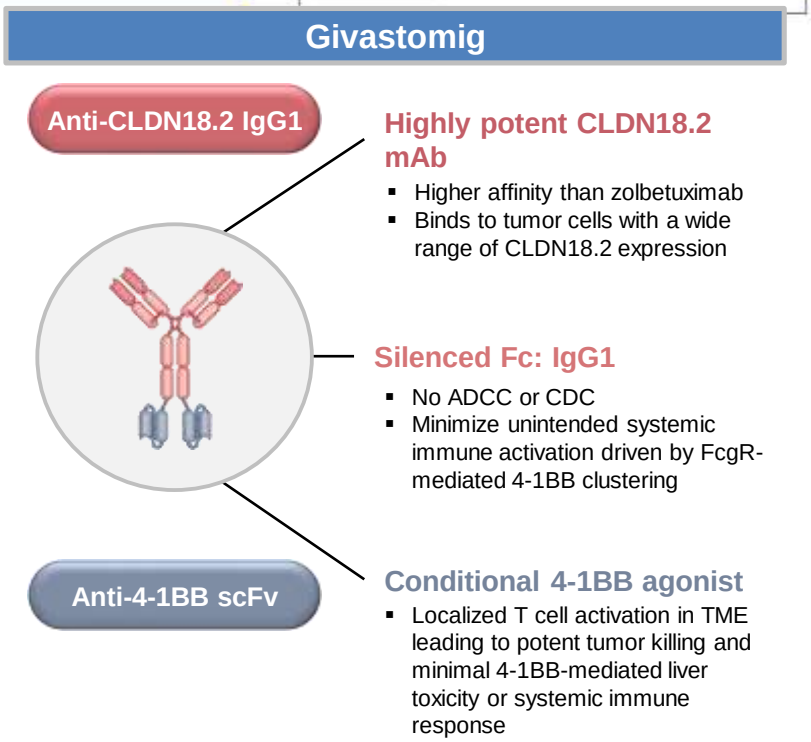
Honoraria from: none

- and -

My additional financial relationship disclosures are: currently participating as an investigator on the study being presented.

Background

- Givastomig, a CLDN18.2 x 4-1BB bispecific antibody, exerts anti-tumor activity through CLDN18.2-based, tumor-directed T-cell activation.[1]
- NCT04900818 is an open label, first-in-human, phase 1 study of givastomig monotherapy in patients with advanced solid tumors that was designed to evaluate the safety, efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) of givastomig.
- Initial data presentations from this study showed that givastomig was well tolerated, had activity in heavily pretreated CLDN18.2-positive gastric cancer patients, and exhibited dose-dependent pharmacokinetics and induction of soluble 4-1BB.[2]
- Here we report updated safety, efficacy and biomarker data with over 1 year of additional follow up from patients with CLDN18.2+ GEC treated with monotherapy givastomig at doses ≥ 5 mg/kg.

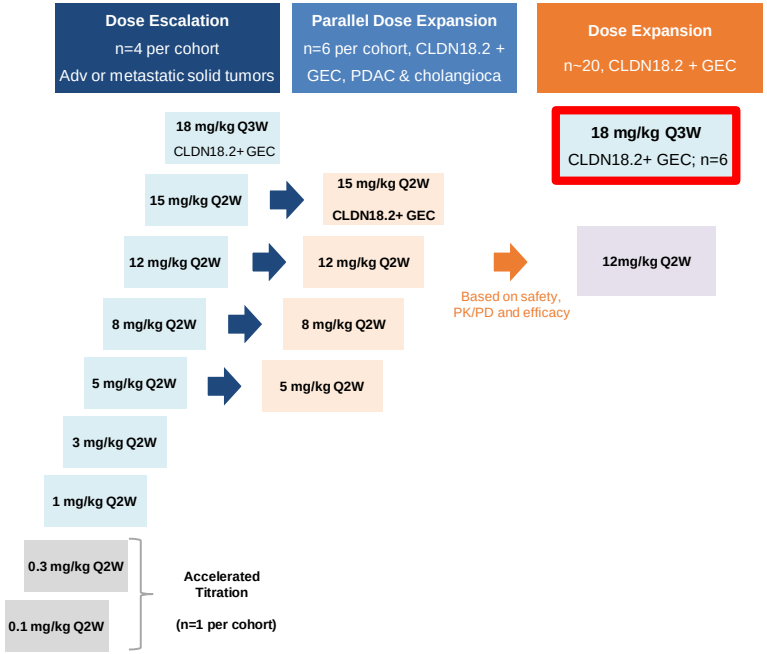


1. Shen JITC 2024
2. Ku CCR 2025

Phase 1 Study Design

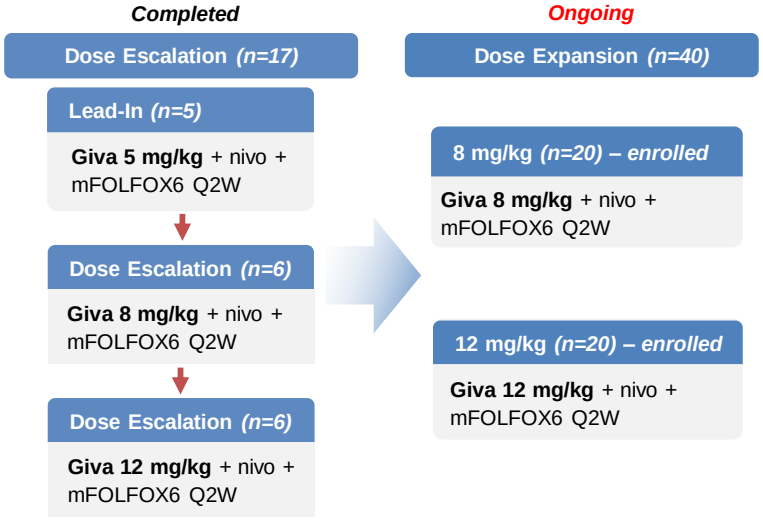
- Multi-center, dose-escalation and expansion phase Ib study
- Monotherapy: US and China. Combination: US only
- Escalation via BOIN design with at least four subjects per dose

Part 1 Givastomig Monotherapy



Part 2 Givastomig + Nivolumab + mFOLFOX

1L HER2(-) CLDN18.2+ unresectable or metastatic GC/GEJ/EAC



BOIN = Bayesian Optimal Interval Design **CLDN18.2-positive** = membrane intensity ≥1+ on ≥1% of tumor cells

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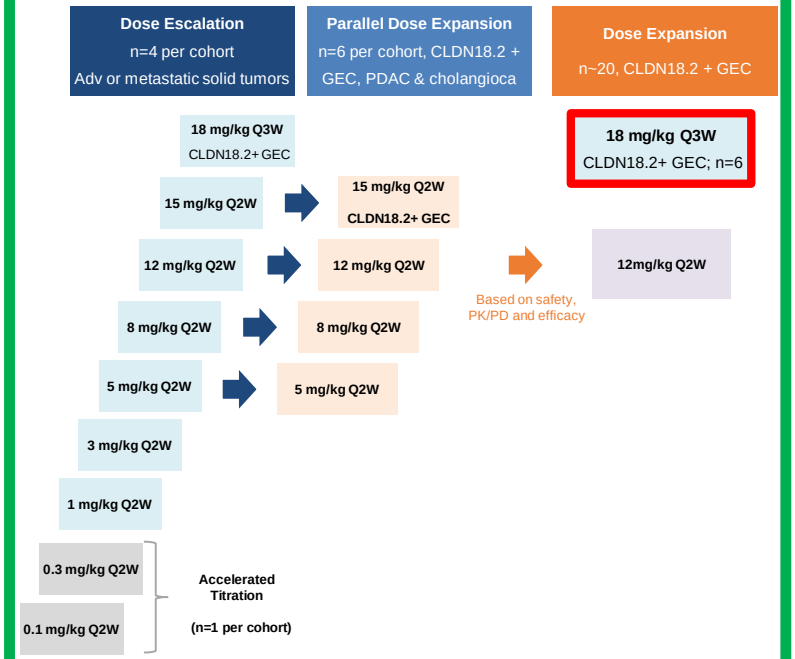
Part 1 Givastomig Monotherapy



Part 2 Givastomig + Nivolumab + mFOLFOX

1L HER2(-) CLDN18.2+ unresectable or metastatic GC/GEJ/EAC

Completed

Dose Escalation *(n=17)*

Lead-In *(n=5)*

Giva 5 mg/kg + nivo + mFOLFOX6 Q2W

Dose Escalation *(n=6)*

Giva 8 mg/kg + nivo + mFOLFOX6 Q2W

Dose Escalation *(n=6)*

Giva 12 mg/kg + nivo + mFOLFOX6 Q2W

Ongoing

Dose Expansion *(n=40)*

8 mg/kg *(n=20) – enrolled*

Giva 8 mg/kg + nivo + mFOLFOX6 Q2W

12 mg/kg *(n=20) – enrolled*

Giva 12 mg/kg + nivo + mFOLFOX6 Q2W

BOIN = Bayesian Optimal Interval Design **CLDN18.2-positive** = membrane intensity ≥1+ on ≥1% of tumor cells

Baseline Characteristics

- 45 patients with CLDN18.2+ GEC were enrolled into cohorts of escalating doses of givastomig 5*-15 mg/kg Q2W, and 18 mg/kg Q3W.
- Patients had received a median of 3 prior therapies, including 74% with prior programmed death-(ligand) 1 inhibitor.
- CLDN18.2 SP455 assay

		5 mg/kg (n=7)	8 mg/kg (n=5)	12 mg/kg (n=21)	15 mg/kg (n=6)	18 mg/kg (n=6)	Total (n=45)
Age	Median (range)	67 (38-82)	59 (36-75)	57 (32-76)	65 (55-70)	61 (42-77)	59 (32-82)
Gender	Female	29%	60%	48%	17%	50%	42%
	Male	71%	40%	52%	83%	50%	58%
Race	White	57%	20%	29%	33%	67%	38%
	Asian	43%	80%	62%	50%	33%	56%
	NR	0	0	9%	17%	0	6%
ECOG PS	0	43%	40%	19%	17%	50%	29%
	1	57%	60%	81%	83%	50%	71%
Tumor Location	Gastric	57%	80%	86%	83%	83%	80%
	GEJ	0	20%	4%	0	0	4%
	Esophageal	43%	0	10%	17%	17%	16%
CLDN18.2	≥ 75%	57%	0	71%	83%	83%	64%
	1-74%	43%	100%	29%	17%	17%	36%
PD-L1 CPS	≥ 1	29%	0	52%	33%	100%	47%
	<1	29%	40%	24%	33%	0	24%
	NA	42%	60%	24%	34%	0	29%
MSI	MSI-H	0	0	14%	0	17%	9%
	MSS	100%	100%	86%	100%	83%	91%

* 4-1BB induction was sustained at ≥5 mg/kg; Data cut-off: August 27, 2025

Safety

- No dose-limiting toxicities were observed up to 15mg/kg Q2W and 18 mg/kg Q3W. Maximum-tolerated-dose was not reached.
- Grade ≥3 TRAE occurred in 33% of patients. One patient experienced a grade 4 platelet count decreased*. Grade 3 TRAE occurring in more than one patient were anemia (9%), lymphocyte count decreased (9%), WBC decreased (7%), AST increased (4%), neutropenia (4%), and upper GI hemorrhage* (4%).
- TRAE leading to permanent withdrawal of givastomig occurred in 9% of patients. These events were grade 3 ALT increased (n=1, 5 mg/kg) grade 3 infusion related reaction (n=1, 5 mg/kg), grade 2 pulmonary embolism (n=1, 12 mg/kg) and grade 3 nausea (n=1, 18 mg/kg).
- There were no grade 5 treatment-related adverse events.

Data cut-off: August 27, 2025

* patient with grade 4 platelet count decreased also experienced grade 3 upper GU hemorrhage

Treatment Related Adverse Events

Common TRAE in ≥ 10% of subjects (n=45)

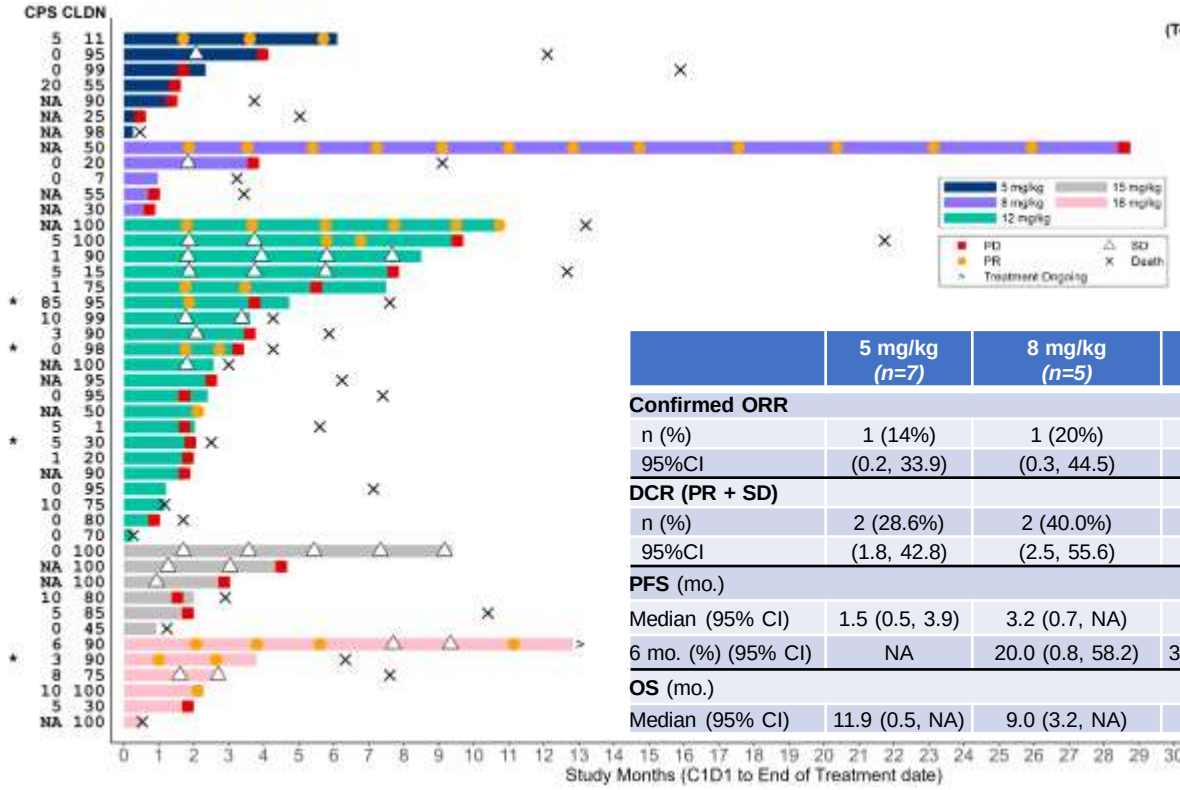
Preferred Term	Grade 1-2 n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grades n (%)
Anaemia	8 (18%)	4 (9%)	0 (0%)	12 (27%)
WBC decreased	7 (16%)	3 (7%)	0 (0%)	10 (22%)
Nausea	8 (18%)	1 (2%)	0 (0%)	9 (20%)
ALT increased	6 (13%)	1 (2%)	0 (0%)	7 (16%)
AST increased	5 (11%)	2 (4%)	0 (0%)	7 (16%)
Decreased appetite	6 (13%)	1 (2%)	0 (0%)	7 (16%)
Neutropenia	5 (11%)	2 (4%)	0 (0%)	7 (16%)
GGT increased	4 (9%)	1 (2%)	0 (0%)	5 (11%)
Vomiting	4 (9%)	1 (2%)	0 (0%)	5 (11%)

TRAE leading to discontinuation of givastomig

Preferred Term	Grade 1-2 n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grades n (%)
ALT increased	0%	0%	1 (2%)	1 (2%)
IRR	0%	0%	1 (2%)	1 (2%)
Nausea	0%	0%	1 (2%	1 (2%)
Pulmonary embolism	0%	1 (2%)	0%	1 (2%)

Data cut-off: August 27, 2025

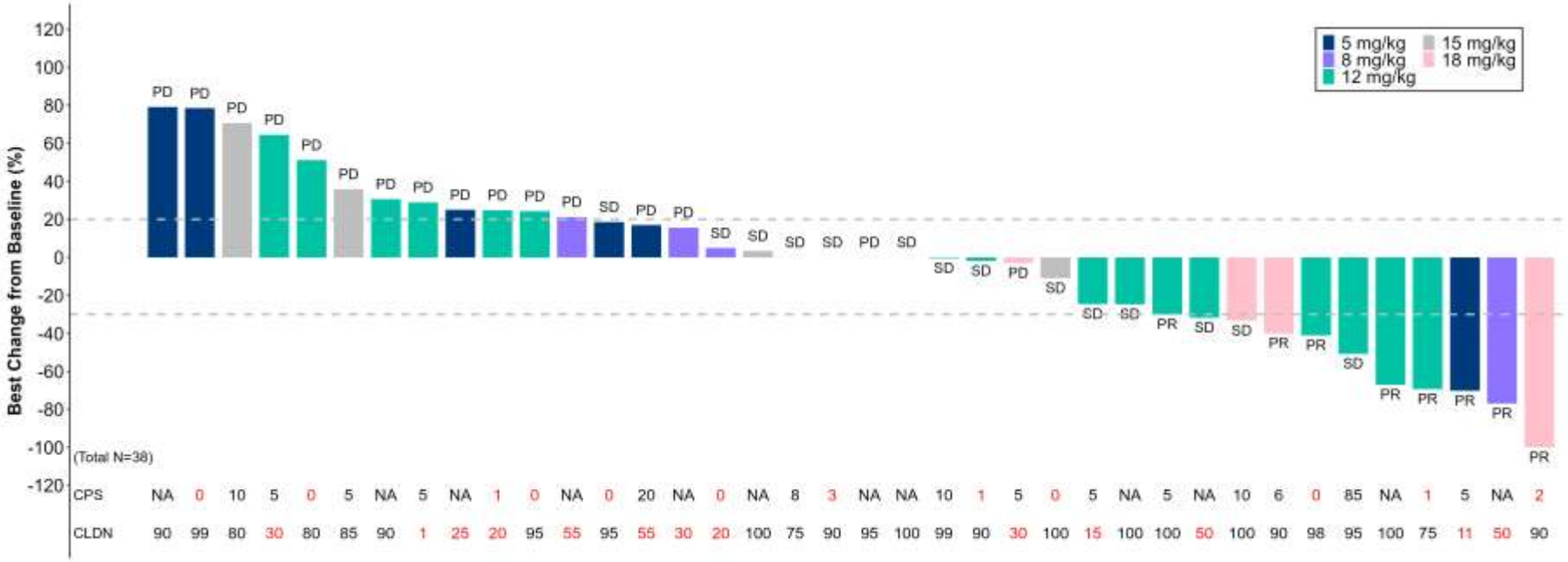
Swimmer Plot & Efficacy Summary



	5 mg/kg *(n=7)*	8 mg/kg *(n=5)*	12 mg/kg *(n=21)*	15 mg/kg *(n=6)*	18 mg/kg Q3W *(n=6)*	All *(n=45)*
Confirmed ORR						
n (%)	1 (14%)	1 (20%)	4 (19%)	0	2 (33%)	8 (18%)
95%CI	(0.2, 33.9)	(0.3, 44.5)	(2.7, 22.6)	(0.0, 45.9)	(2.1, 48.4)	(3.9, 16.8)
DCR (PR + SD)						
n (%)	2 (28.6%)	2 (40.0%)	11 (52.4%)	3 (50.0%)	4 (66.7%)	22 (48.9%)
95%CI	(1.8, 42.8)	(2.5, 55.6)	(13.9, 42.0)	(5.5, 57.2)	(9.9, 65.1)	(16.0, 34.6)
PFS (mo.)						
Median (95% CI)	1.5 (0.5, 3.9)	3.2 (0.7, NA)	3.2 (1.81, 7.0)	2.3 (1.2, NA)	6.2 (0.5, NA)	3.0 (1.7, 3.9)
6 mo. (%) (95% CI)	NA	20.0 (0.8, 58.2)	33.3 (14.9, 53.1)	16.7 (0.8, 51.7)	66.7 (19.5, 90.4)	30.0 (17.4, 43.8)
OS (mo.)						
Median (95% CI)	11.9 (0.5, NA)	9.0 (3.2, NA)	7.0 (4.2, 13.0)	10.25 (1.2, NA)	7.5 (0.5, NA)	7.5 (5.0, 12.5)

Data cut-off: August 27, 2025

Waterfall



Data cut-off: August 27, 2025

CLDN18.2 Expression vs. Clinical Efficacy

- No statistically significant differences in ORR, DCR, PFS, or OS between CLDN18.2-high and CLDN18.2-low groups, using a variety of cutoffs

CLDN18.2	N		ORR		DCR		mPFS (mo., 95% CI)		mOS (mo., 95% CI)		PFS Hazard Ratio (High vs. Low)	OS Hazard Ratio (High vs. Low)
	Low	High	Low	High	Low	High	Low	High	Low	High		
10% 2+/3+	4	41	25%	17%	50%	49%	5.4 (1.7-NA)	2.8 (1.7-3.9)	9.0 (3.2, NA)	7.5 (5.0-11.9)	1.5 (0.4-4.6)	0.9 0.3-2.9)
40% 2+/3+	15	30	20%	17%	40%	53%	1.9 (0.9-5.4)	3.0 (1.7-4.2)	9.0 (3.2-16.5)	7.5 (4.2-11.9)	1.1 (0.6-2.2)	1.2 (0.6-2.6)
75% 2+/3+	24	21	17%	19%	42%	57%	1.8 (1.2-3.7)	3.7 (1.7-6.2)	7.5 (3.2-16.5)	7.5 (4.2-13.0)	0.87 (0.5-1.7)	0.9 (0.4-1.8)

Data cut-off: August 27, 2025

CLDN18.2 Expression vs. Clinical Efficacy

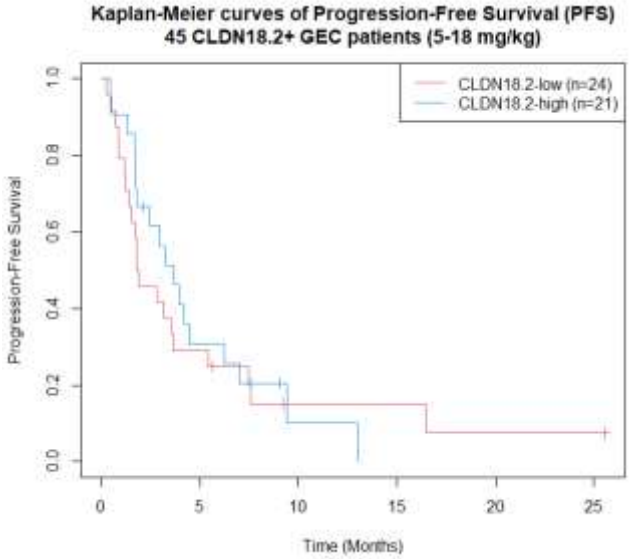
- No statistically significant differences in ORR, DCR, PFS, or OS between CLDN18.2-high and CLDN18.2-low groups, using a variety of cutoffs

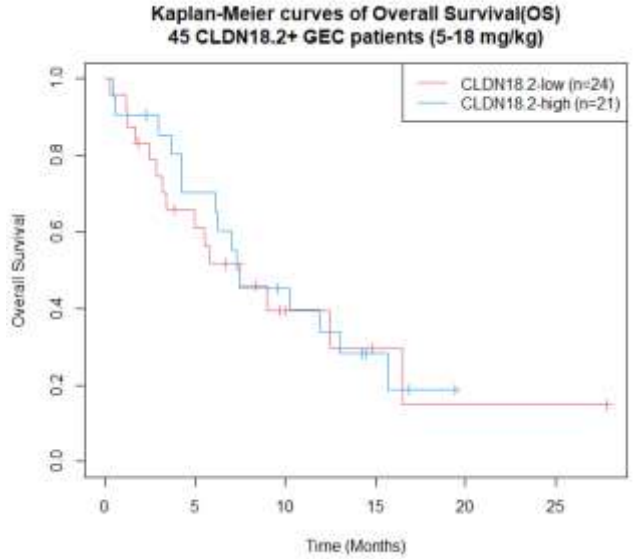
CLDN18.2 Expression Cutoff	CLDN18.2-Low (< Cutoff)					CLDN18.2-High (≥ Cutoff)					PFS Hazard Ratio (High vs. Low)	OS Hazard Ratio (High vs. Low)
	N	ORR	DCR	mPFS (months)	mOS (months)	N	ORR	DCR	mPFS (months)	mOS (months)		
10% 2+/3+	4	25%	50%	5.39 (1.71, NA)	9.0 (3.19, NA)	41	17%	49%	2.83 (1.71-3.91)	7.49 (4.96-11.9)	1.47 (0.43-4.63)	0.88 0.26-2.91)
40% 2+/3+	15	20%	40%	1.87 (0.85-5.42)	8.97 (3.19-16.5)	30	17%	53%	2.96 (1.71-4.21)	7.49 (4.21-11.9)	1.13 (0.56-2.24)	1.20 (0.55-2.64)
75% 2+/3+	24	17%	42%	1.84 (1.22-3.65)	7.49 (3.19-16.5)	21	19%	57%	3.68 (1.71-6.24)	7.49 (4.21-13.0)	0.87 (0.46-1.65)	0.88 (0.43-1.82)

Data cut-off: August 27, 2025

CLDN18.2 Expression vs. PFS and OS

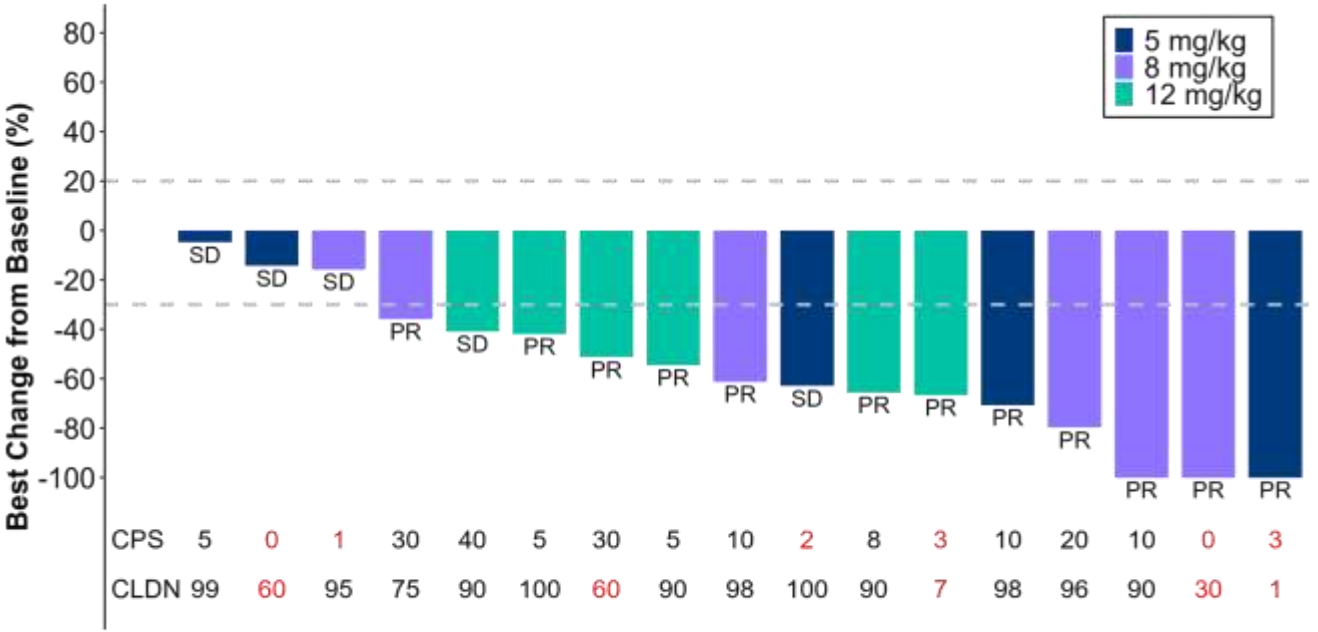
- No statistically significant differences in PFS or OS between CLDN18.2-high (defined as ≥ 75% of 2+/3+, n=21) and CLDN18.2-low (n=24)





Data cut-off: August 27, 2025

Givastomig 1L Combination Escalation



Data cut-off: May 15, 2025

Presented at ESMO GI 2025

Conclusions

- With over a year of additional follow up, givastomig continues to be well tolerated up to 15 mg/kg Q2W and 18 mg/kg Q3W and continues to show encouraging monotherapy activity in heavily pre-treated GEC patients with a wide range of CLDN18.2 expression (confirmed ORR 18%).
- There was no statistically significant difference in ORR, DCR, PFS, or OS between CLDN18.2-high and CLDN18.2-low groups, using a variety of cutoffs.
- Givastomig may have utility in patients with lower CLDN18.2 expression compared with other CLDN18.2 agents.
- The sustained tolerability and efficacy support the development of givastomig as an add on to 1L therapy in combination with nivolumab and mFOLFOX6 in advanced or metastatic gastric, gastroesophageal and esophageal adenocarcinomas (NCT04900818), as well as other CLDN+ GI malignancies.