ASPEN-06: Final analysis of the randomized phase 2 part of the ASPEN-06 study: A phase 2/3 study of Evorpacept (ALX148) , a CD47 myeloid checkpoint inhibitor, in patients with HER2-overexpressing gastric/gastroesophageal cancer (GC)

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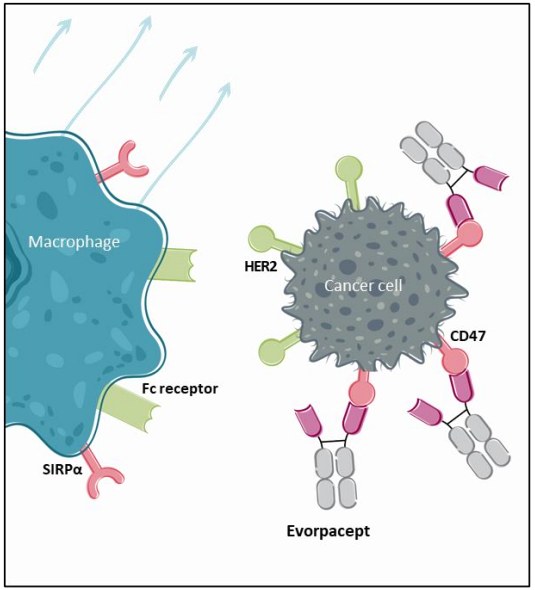
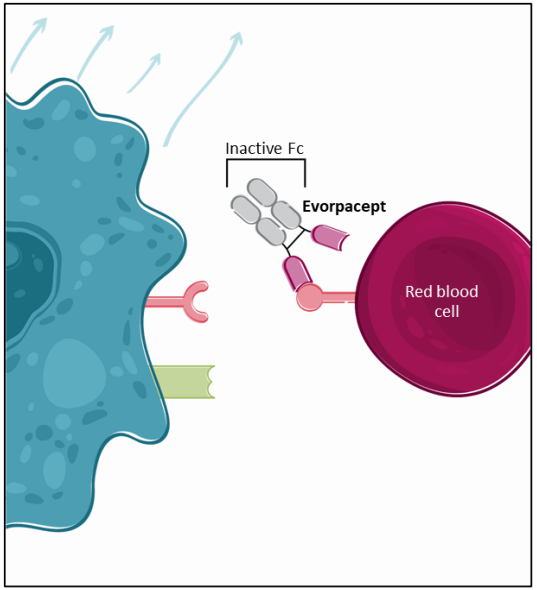
ALX ONCOLOGY

Evorpacept increases antibody dependent cellular phagocytosis (ADCP) in combination with trastuzumab without Fc-driven toxicity

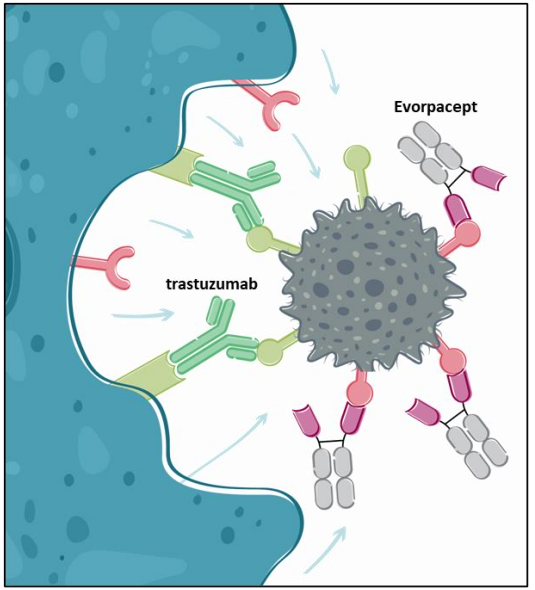
Evorpacept, with an inactive Fc, binds and blocks CD47-SIRPα interaction



Inactive Fc spares normal cells, minimizing toxicity…



…maximizing the antibody dependent cellular phagocytosis of targeted antibodies



Evorpacept is a differentiated CD47 blocker that works in combination to spare healthy cells and deliver cancer cells for macrophage destruction

ASPEN-06 is a global, randomized Phase 2/3 study which evaluated evorpacept plus TRP in 2nd and 3rd line GC/ GEJ patients

Phase 2 portion

Key eligibility criteria:

- HER2+ GC or GEJ that has progressed on or after prior HER2-directed therapy
- 2L or 3L
- Prior trastuzumab deruxtecan (T-DXd) and/or checkpoint inhibitors allowed
- Prior CD47-agent, anti-SIRPα, or ramucirumab excluded

ITT patients N=127

Includes subpopulation of fresh HER2+ biopsy patients N=48

1:1

Evorpacept
T + R + P

vs.

Control:
T + R + P

Primary objectives in both ITT and fresh biopsy populations:

- Improvement in ORR* vs assumed historical control of 30% (Wilke et al, Lancet October 2014)
- Improvement in ORR* over internal control (Difference ≥ 10%)

Secondary endpoints

- DOR, PFS, OS

All patients enrolled received a prior HER2-targeted therapy (eg, trastuzumab) and were enrolled with either a HER2+ fresh or archival biopsy

Dosing: Evorpacept 30 mg/kg IV Q2W, trastuzumab 6 mg/kg › 4 mg/kg Q2W, ramucirumab 8 mg/kg Q2W, paclitaxel 80 mg/m^2 on day 1, 8, 15 of 28-day cycle

GC- gastric cancer, GEJ- gastroesophageal junction, TRP- trastuzumab, ramucirumab, paclitaxel

Minimization factors: Primary tumor place (i.e., Gastric vs GEJ); Time of biopsy (i.e., fresh vs archival); Region (Asia vs other); Treatment line (i.e., 2nd vs 3rd line); HER2 status (3+ vs 2+/ISH+); Prior T-DXd

*Based on investigator assessment

ASPEN-06: Patient Demographics

Study population:

		Evo + T + R + P N=63	T + R + P N=64
Median age, years (range)		64 (34-81)	63 (31-86)
Sex, n%	Male	55 (87.3%)	48 (75.0%)
	Female	8 (12.7%)	16 (25.0%)
Race, n%	Asian	31 (49.2%)	31 (48.4%)
	White	19 (30.2%)	19 (29.7%)
	Other	1 (1.6%)	0 (0%)
	Unknown	12 (19.0%)	13 (20.3%)
ECOG PS, n%	0	30 (47.6%)	27 (42.2%)
	1	33 (52.4%)	37 (57.8%)
Cancer Type, n%	Gastric	48 (76.2%)	44 (68.8%)
	GEJ	15 (23.8%)	20 (31.3%)
Treatment Line, n%	2nd line	49 (77.8%)	44 (68.8%)
	3rd line	14 (22.2%)	20 (31.3%)
HER2 status, n%	**IHC 3+**	52 (82.5%)	53 (82.8%)
	IHC2+/ISH+	11 (17.5%)	11 (17.2%)
Fresh, n%	**Yes**	22 (34.9%)	26 (40.6%)
ctDNA HER2+	**Yes**	43 (68.3%)	43 (67.2%)
Prior T-DXd, n%	Yes	8 (12.7%)	10 (15.6%)
Prior anti-PD1, n%	Yes	11 (17.5%)	16 (25.0%)
Asia Region, n%	Yes	31 (49.2%)	30 (46.9%)

- Patients with a fresh HER2+ biopsy underwent a biopsy at a median of 1.1 months before dosing (vs. 14.1 months for patients with an archival biopsy)
- As an exploratory endpoint, ctDNA extracted from plasma samples collected on Cycle 1 Day 1 prior to dosing was assessed for HER2 amplification utilizing Guardant360 comprehensive genome profiling (Guardant Health®)*

*HER2 plasma gene amplification reportable range ≥2.18 copies

Data Cutoff as of 02 Dec 2024

ALX ONCOLOGY

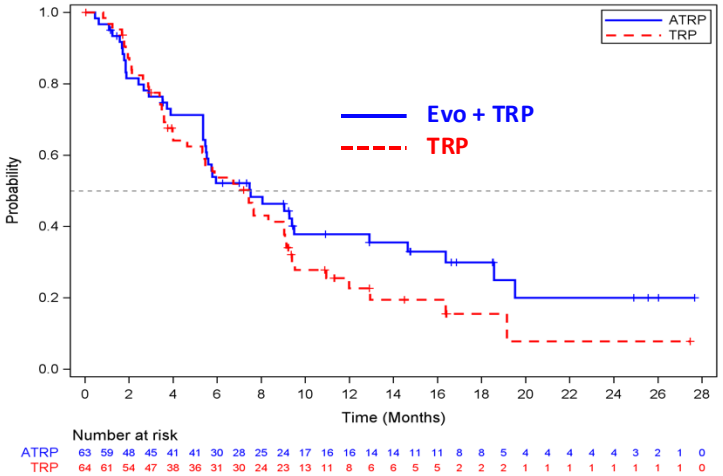
ASPEN-06: ORR, DOR in the ITT population

	Evo +T+R+P	T+R+P
N evaluable	63	64
Confirmed ORR, n (%) [95% CI]	**26 (41.3%) [29.0%; 54.4%]**	**17 (26.6%) [16.3%; 39.1%]**
CR (Complete Response)	1 (1.6%)	1 (1.6%)
PR (Partial Response)	25 (39.7%)	16 (25.0%)
SD (Stable Disease)	21 (33.3%)	35 (54.7%)
PD (Progressive Disease)	9 (14.3%)	7 (10.9%)
NE (Not Evaluable)	2 (3.2%)	1 (1.6%)
No Post baseline assessment	5 (7.9%)	4 (6.3%)
Median DOR (months) [95% CI]	**15.7 [7.7; NR]**	**9.1 [5.3; NR]**
Number of events	12 (46.2%)	9 (52.9%)

NR: not reached
Data Cutoff as of 02 Dec 2024

ASPEN-06: ORR, DOR and PFS in the ITT population

	Evo + T + R + P	T + R + P
N evaluable	63	64
Confirmed ORR, n (%) [95% CI]	**26 (41.3%) [29.0%; 54.4%]**	**17 (26.6%) [16.3%; 39.1%]**
CR (Complete Response)	1 (1.6%)	1 (1.6%)
PR (Partial Response)	25 (39.7%)	16 (25.0%)
SD (Stable Disease)	21 (33.3%)	35 (54.7%)
PD (Progressive Disease)	9 (14.3%)	7 (10.9%)
NE (Not Evaluable)	2 (3.2%)	1 (1.6%)
No Post baseline assessment	5 (7.9%)	4 (6.3%)
Median DOR (months) [95% CI]	**15.7 [7.7; NR]**	**9.1 [5.3; NR]**
Number of events	12 (46.2%)	9 (52.9%)



Number of patients with events	Number of patients censored	mPFS [95% CI]
40 (63.5%)	23 (36.5%)	7.5 [5.5-12.9]
47 (73.4%)	17 (26.6%)	7.4 [4.6-9.0]

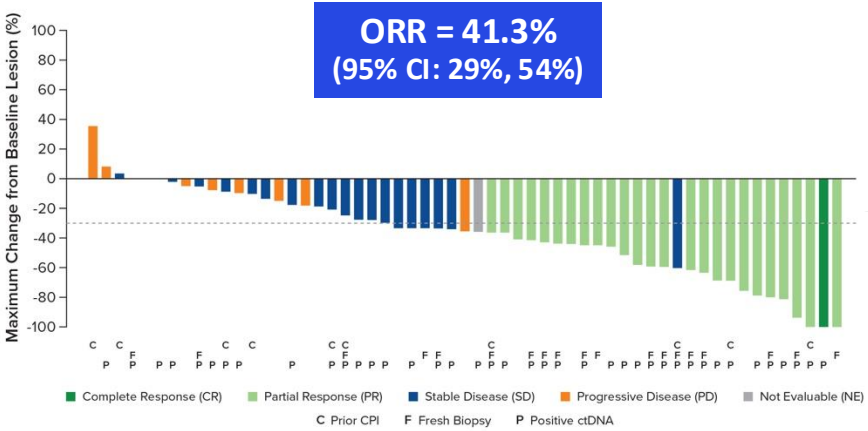
PFS Hazard Ratio: 0.77 [0.49; 1.20]

NR: not reached
Data Cutoff as of 02 Dec 2024

Waterfall Plots: Tumor Size Reduction by Treatment Arm (ITT)

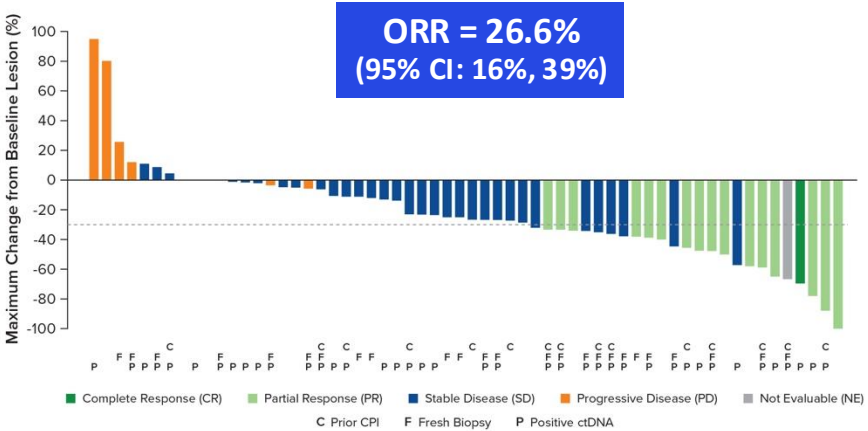
Evo + T + R + P

ORR = 41.3%
(95% CI: 29%, 54%)



T + R + P

ORR = 26.6%
(95% CI: 16%, 39%)



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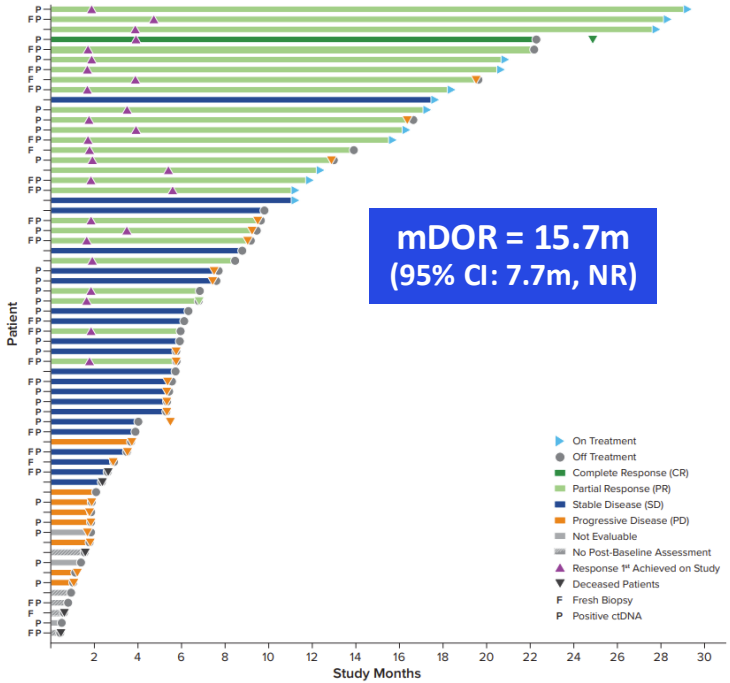
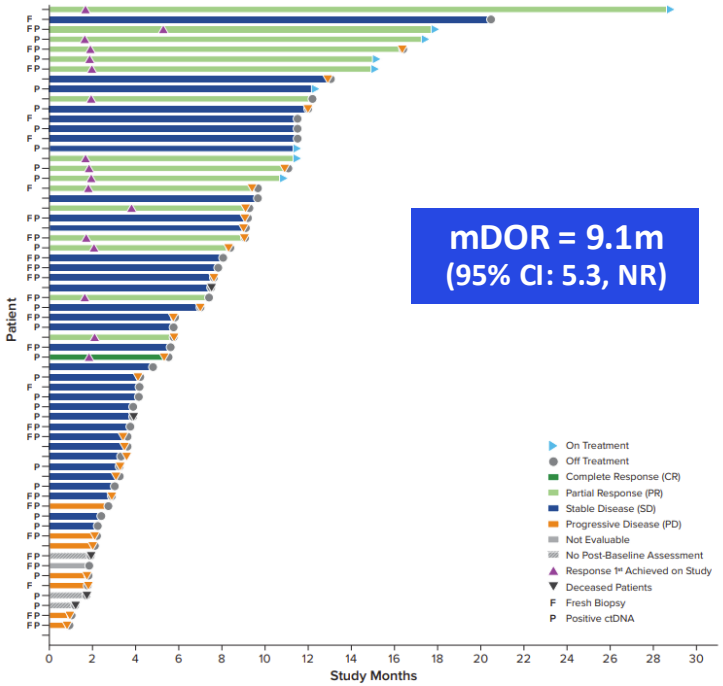
ALX ONCOLOGY

Swimmer Plots: Duration of Response by Treatment Arm (ITT)

Evo + T + R + P



T + R + P



ASCO GI 2025

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ALX ONCOLOGY

ASPEN-06: Anti-Tumor Response (ORR and DOR) in confirmed HER2+ patients via fresh biopsy or ctDNA

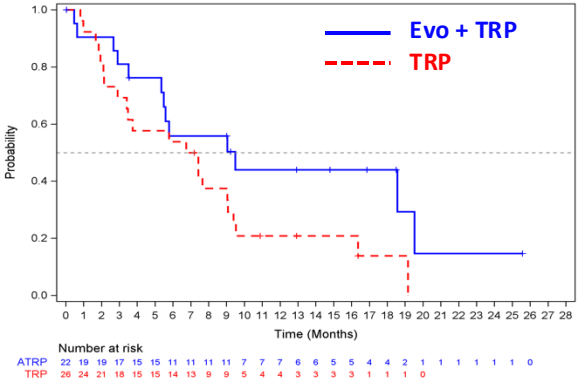
	HER2+ confirmed with Fresh Biopsy		HER2+ confirmed with Fresh Biopsy OR ctDNA+	
	Evo + T + R + P	T + R + P	Evo + T + R + P	T + R + P
N evaluable	22	26	47	49
Confirmed ORR, n (%) [95% CI]	**13 (59.1%) [36.4%; 79.3%]**	**6 (23.1%) [9.0%; 43.6%]**	**23 (48.9%) [34.1%; 63.9%]**	**12 (24.5%) [13.3%; 38.9%]**
CR (Complete Response)	0	0	1 (2.1%)	1 (2.0%)
PR (Partial Response)	13 (59.1%)	6 (23.1%)	22 (46.8%)	11 (22.4%)
SD (Stable Disease)	6 (27.3%)	13 (50.0%)	15 (31.9%)	27 (55.1%)
PD (Progressive Disease)	0	5 (19.2%)	4 (8.5%)	6 (12.2%)
NE (Not Evaluable)	0	1 (3.8%)	2 (4.3%)	1 (2.0%)
No Post baseline assessment	3 (13.6%)	1 (3.8%)	3 (6.4%)	3 (6.1%)
Median DOR (months) [95% CI]	**15.7 [4.0; NR]**	**14.5 [7.4; NR]**	**15.7 [7.7; NR]**	**9.1 [3.5; NR]**
Number of events	6 (46.2%)	3 (50.0%)	11 (47.8%)	7 (58.3%)

NR: not reached
Data Cutoff as of 02 Dec 2024

ASPEN-06: PFS by Treatment Arm in confirmed HER2+ patients via fresh biopsy or ctDNA

Progression-free survival (PFS) based on investigator assessment

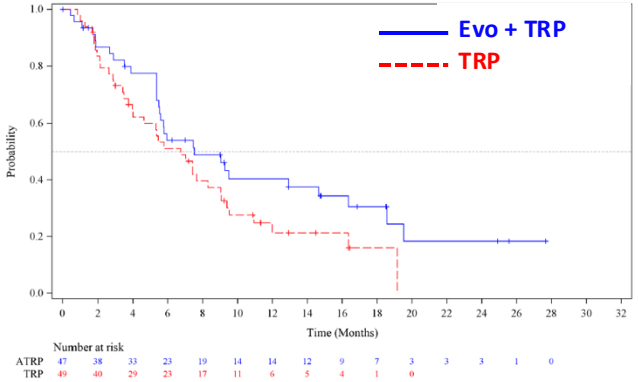
HER2+ fresh biopsy (n=48)



Number of patients with events	Number of patients censored	mPFS [95% CI]
13 (59.1%)	9 (40.9%)	9.5 [5.4-19.5]
22 (84.6%)	4 (15.4%)	7.1 [2.9-9.1]

Hazard Ratio: 0.62 [0.28; 1.36]

HER2+ (fresh biopsy OR ctDNA+) (n=96)



Number of patients with events	Number of patients censored	mPFS [95% CI]
30 (63.8%)	17 (36.2%)	7.5 [5.5-14.7]
37 (75.5%)	12 (24.5%)	6.7 (4.0-9.0)

Hazard Ratio: 0.64 [0.39; 1.07]

Data Cutoff as of 02 Dec 2024

ALX ONCOLOGY

ASPEN-06: Safety

Summary of treatment-emergent adverse events grades 3-5
(with frequency >5% on either arm)

Grade	Evo + T + R + P N=63			T + R + P N=63		
	3	4	5	3	4	5
Neutrophil count decreased	12 (19.0%)	7 (11.1%)	-	12 (19.0%)	4 (6.3%)	-
Anemia	14 (22.2%)	-	-	11 (17.5%)	-	-
Neutropenia	11 (17.5%)	4 (6.3%)	-	7 (11.1%)	2 (3.2%)	-
White blood cell count decreased	7 (11.1%)	-	-	6 (9.5%)	-	-
Hypertension	6 (9.5%)			4 (6.3%)		
Sepsis	2 (3.2%)	-	2 (3.2%)	2 (3.2%)	-	1 (1.6%)
Asthenia	2 (3.2%)	-	-	4 (6.3%)	-	-
Febrile neutropenia	1 (1.6%)	-	-	3 (4.8%)	2 (3.2%)	-

- The incidence of adverse events due to any cause was comparable by arm
- There were 11 Grade 5 treatment emergent adverse events, 2 of which were deemed to be treatment related: esophageal perforation (ETRP) and pneumopathy (TRP)

All G5 TEAEs: ETRP (N=4): Sepsis N=2, Esophageal perforation N=1, Respiratory failure N=1; TRP (N=7) : Sepsis N=1, Pneumonia/pneumopathy/respiratory infection N=1 each, Sudden death N=1, death from unknown cause N=1, esophageal hemorrhage N=1

Evorpacept's safety profile was consistent with its prior experience in over 700 patients treated to date

Data Cutoff as of 02 Dec 2024

Conclusions

- **In the ITT population, the addition of evorpacept to TRP demonstrated an ORR of 41.3% and DOR of 15.7 months compared to the TRP control ORR of 26.6% and DOR of 9.1 months**
- **Patients with confirmed HER2+ expression via either fresh biopsy or ctDNA received the greatest benefit in ORR, DOR, and PFS, indicating that HER2+ expression is a key biomarker and validating evorpacept's MOA**
  - In 48 patients with HER2+ fresh biopsies, the addition of evorpacept to TRP resulted in a 59.1% ORR vs. 23.1% in control, with a PFS HR of 0.62
  - In 96 patients with HER2+ fresh biopsies or ctDNA+, the addition of evorpacept to TRP resulted in a 48.9% ORR vs. 24.5% in control, with a PFS HR of 0.64
- **The safety data confirm that evorpacept can be safely combined with TRP and is consistent with evorpacept's favorable safety profile as seen in other studies**
- **As data compares favorably both with the control arm and approved therapies, evorpacept + TRP warrants further evaluation in 2L and 3L patients with gastric/ GEJ cancer**

Acknowledgments
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