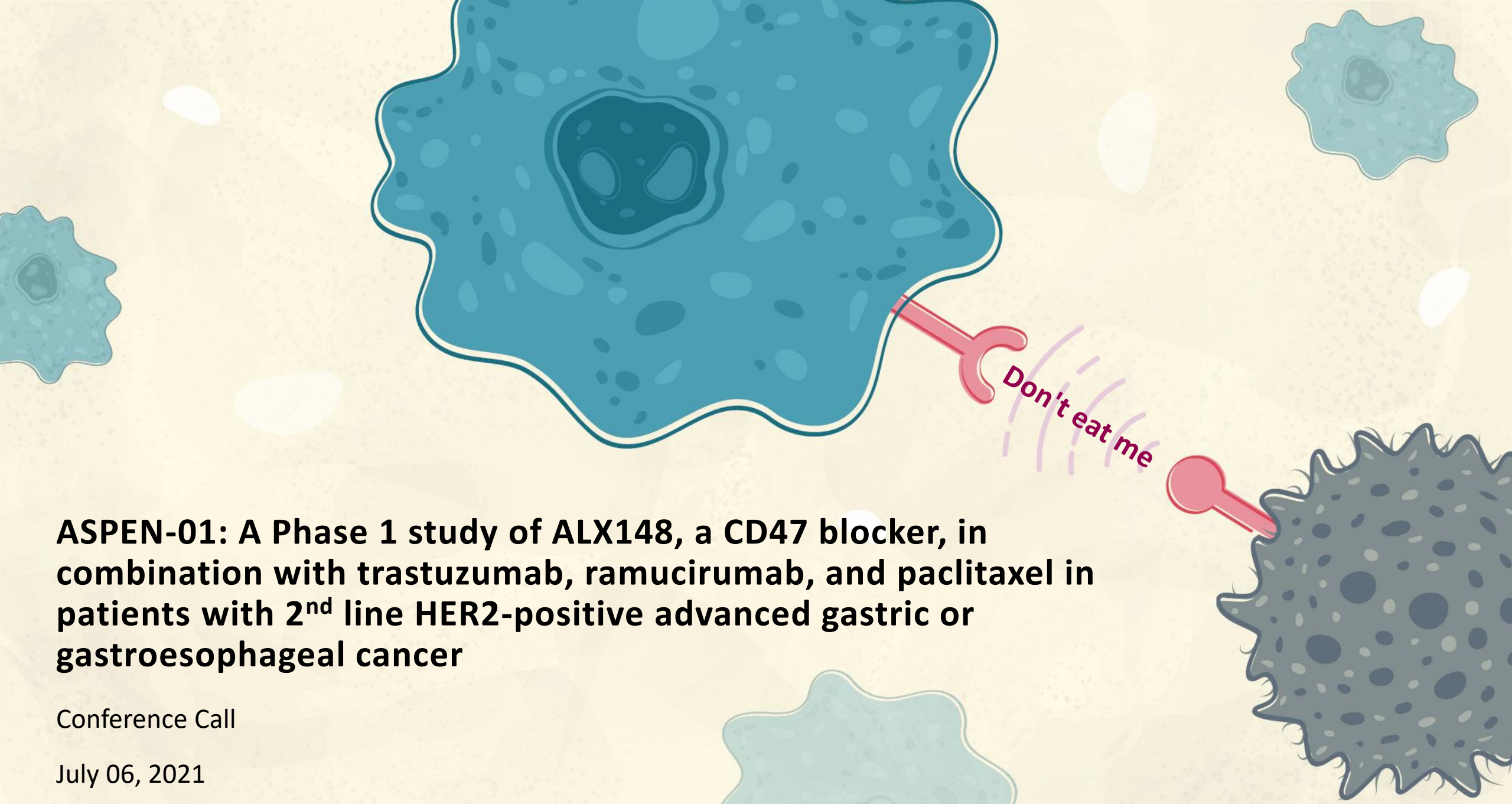


# ASPEN-01: A Phase 1 study of ALX148, a CD47 blocker, in combination with trastuzumab, ramucirumab, and paclitaxel in patients with 2nd line HER2-positive advanced gastric or gastroesophageal cancer

Conference Call

July 06, 2021

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ALX ONCOLOGY

# OVERVIEW

ALX Oncology (Nasdaq: ALXO) is a clinical-stage immuno-oncology company focused on helping patients fight cancer by developing therapies that block the CD47 checkpoint pathway and bridge the innate and adaptive immune system

**Lead product candidate ALX148 initiating multiple Phase 2 trials**

CD47 blocker

- Designed for use in combination
- Tolerability profile enables higher dosing
- Higher dosing may enable greater efficacy

Clinical proof-of-principle in both hematologic and solid tumors

Initial focus on solid tumors, MDS, and AML

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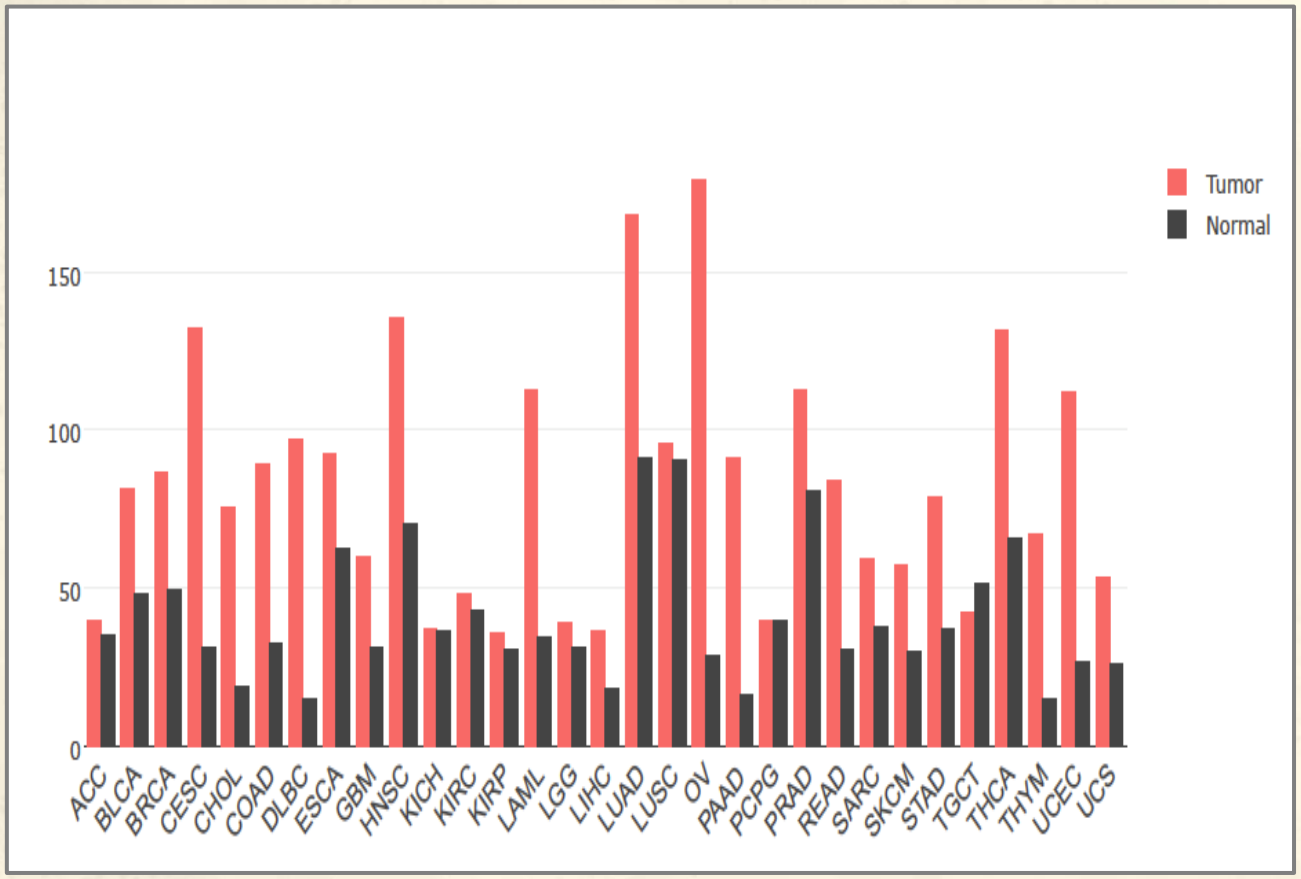
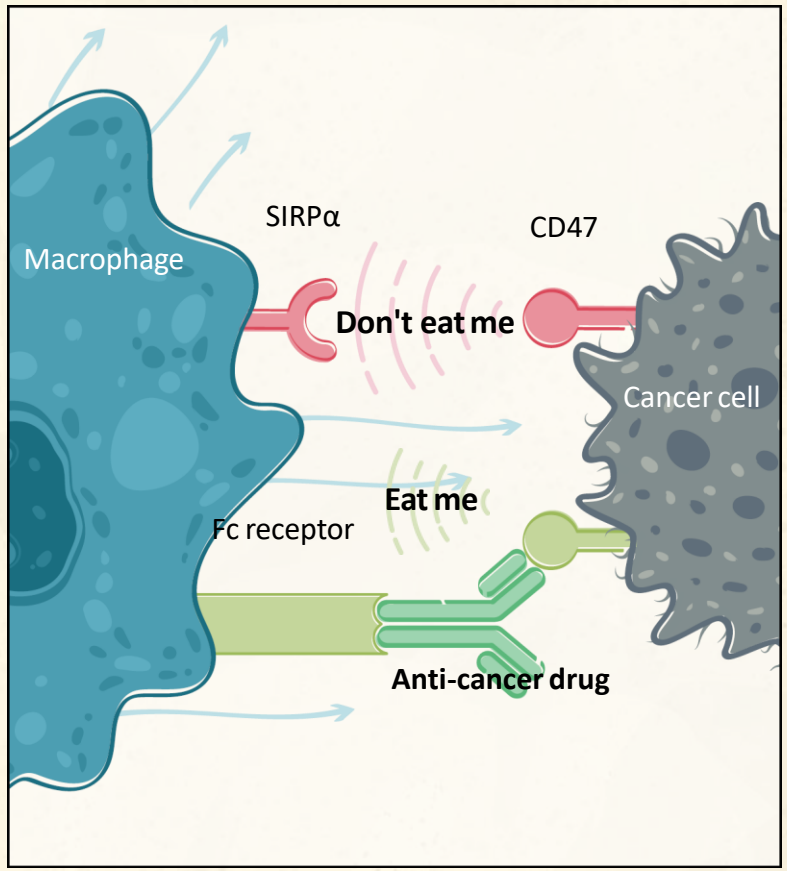
# CD47: TUMOR ASSOCIATED ANTIGEN (TAA)- MYELOID CHECKPOINT DUALITY

**TAA-Expression levels on cancer and normal cells**




**Checkpoint Mechanism: "do not eat me"**

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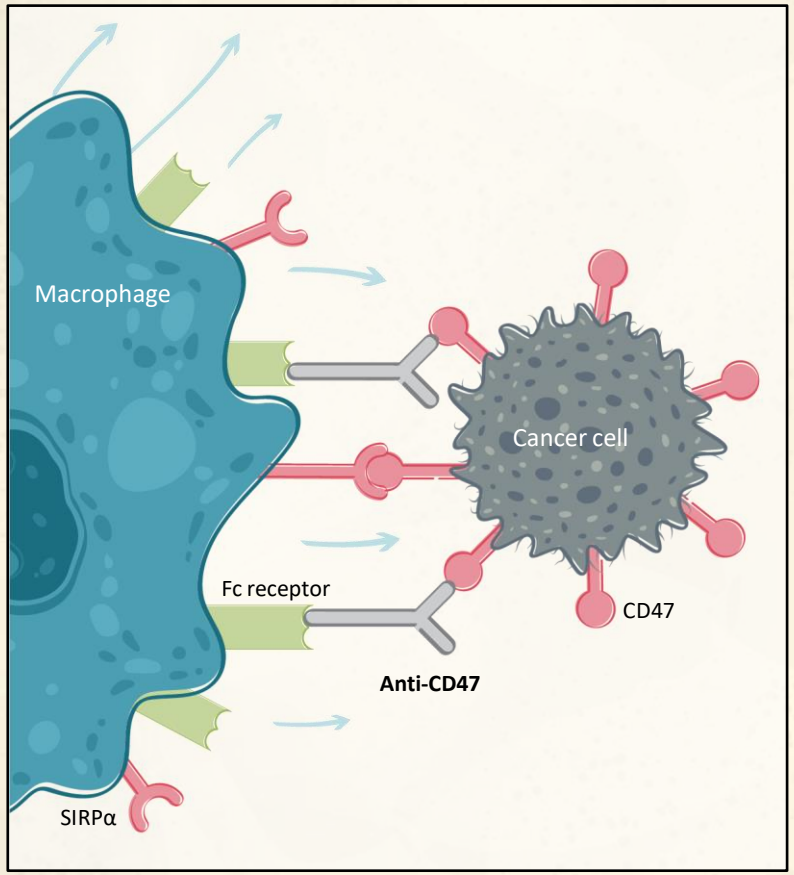
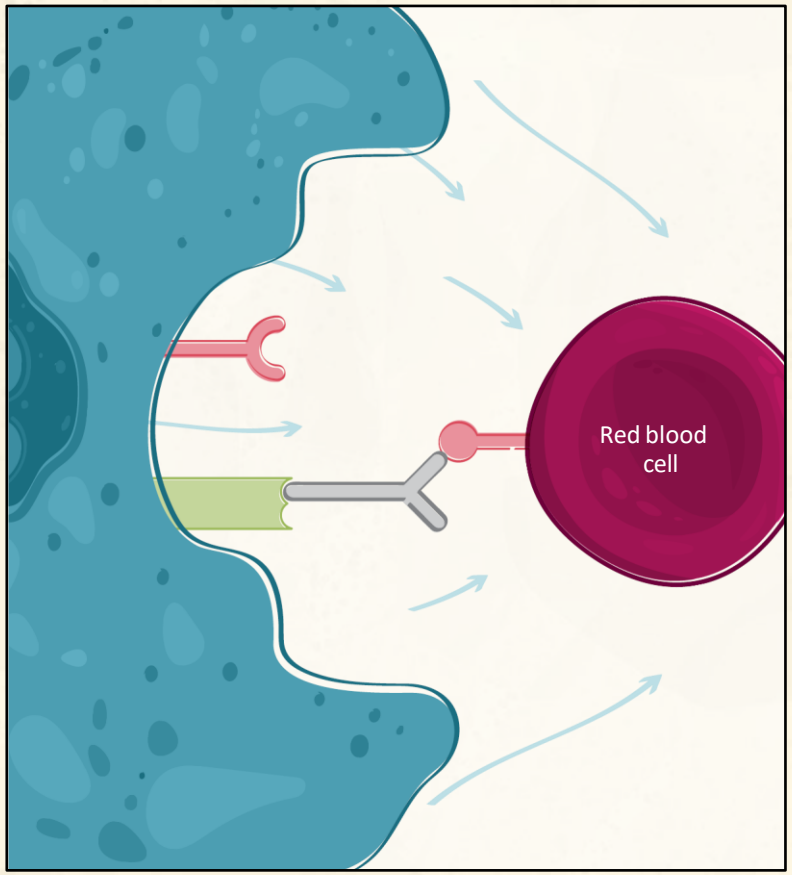
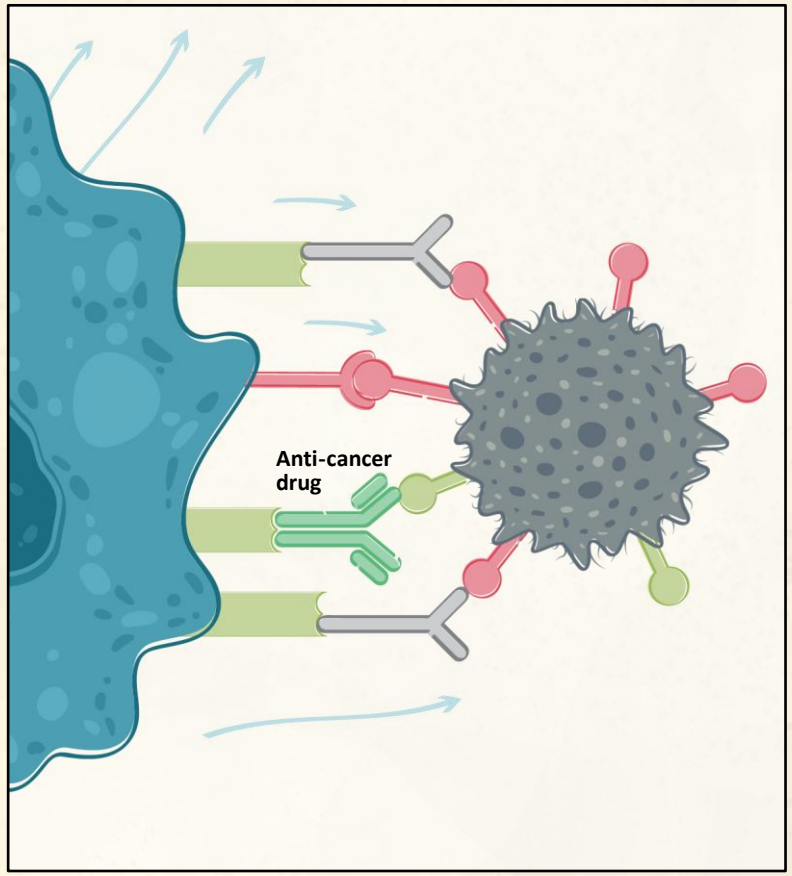
# TARGETING CD47 AS TUMOR ASSOCIATED ANTIGEN

But also targets normal cells




Anti CD47 with active Fc directly targets cancer cells

Dose limitations prevent full blockade of CD47 and active Fc competes with combo drug

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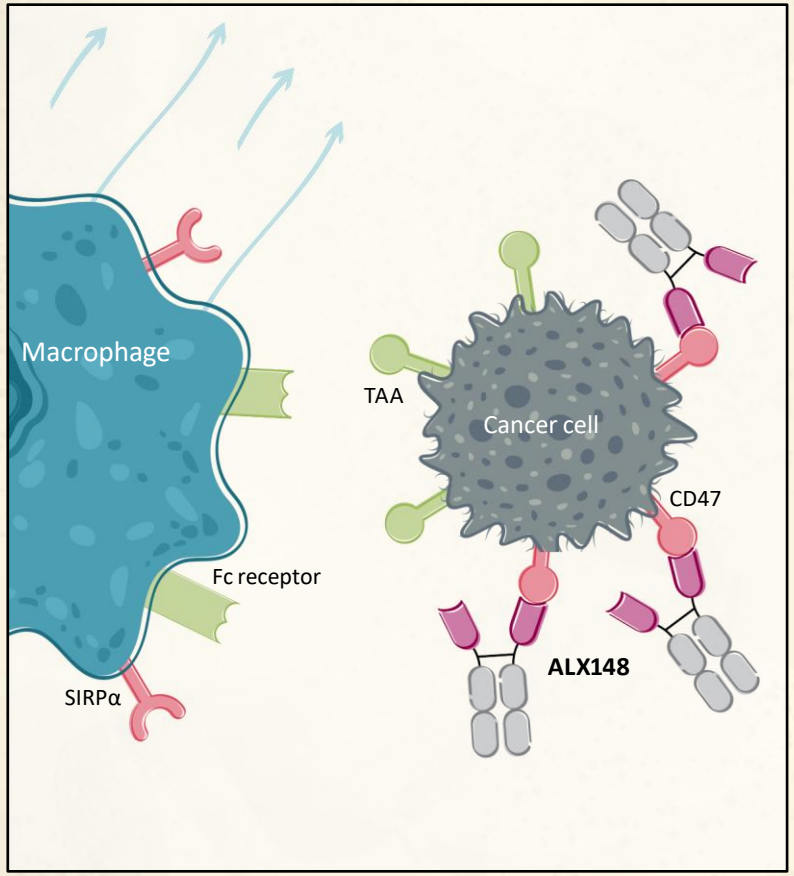
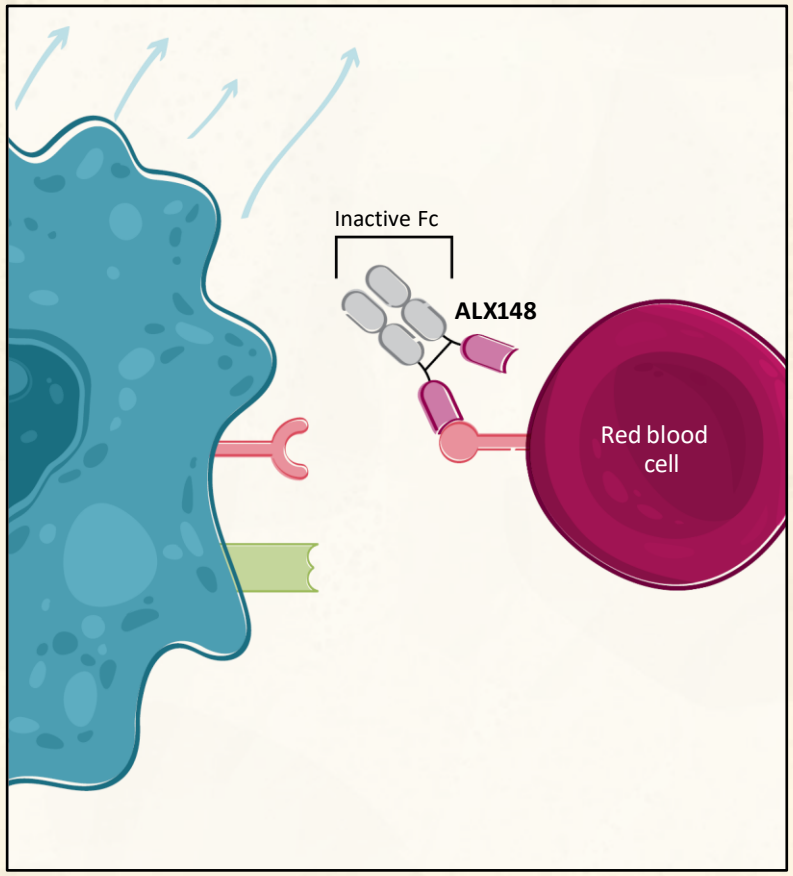
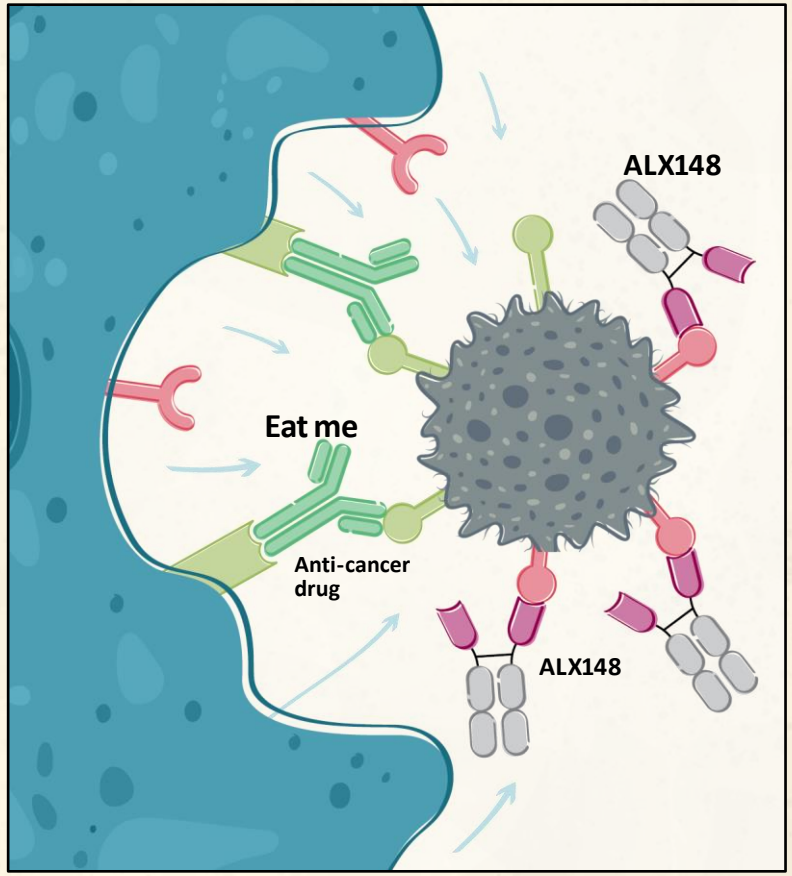
# TARGETING CD47 AS CHECKPOINT: ALX ONCOLOGY'S APPROACH

It spares normal cells




Anti CD47 with inactive Fc binds and block CD47-SIRPα interaction

High dose allows full blockade of CD47 and maximizes activity of combo drug

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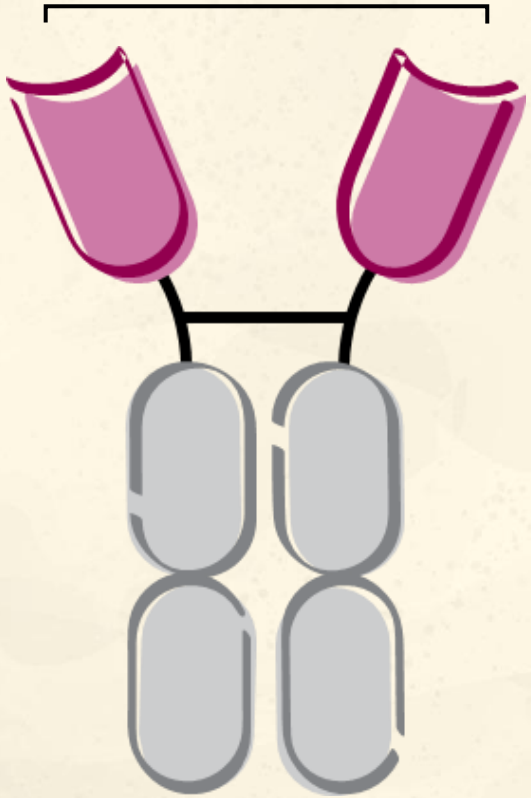
# ALX148 POTENTLY AND SELECTIVELY BINDS CD47 TO BLOCK SIRPα INTERACTION

High affinity CD47 binding domains of SIRPα



Inactive Fc domain

**Optimized, picomolar binding affinity**

**Fc domain mutated to eliminate Fcγ receptor binding and minimize associated toxicity**

- **Fc domain enables antibody-like PK.**
- **Molecular weight half the size of typical antibody.**

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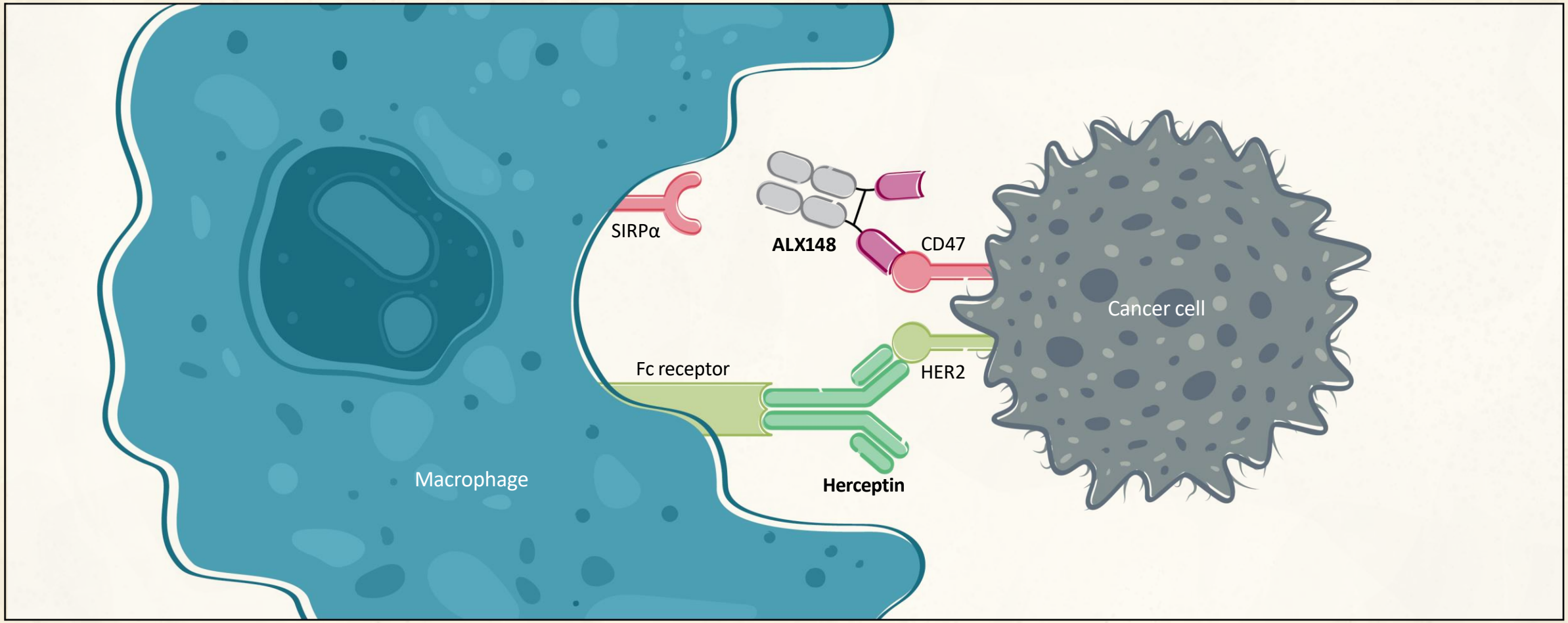
# GASTRIC CANCER (GC) TRIAL: ALX148 + HERCEPTIN MECHANISM OF ACTION




**ALX148 increases antibody dependent cellular phagocytosis in combination with Herceptin**

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# ASPEN-01: A PHASE 1 STUDY OF ALX148, A CD47 BLOCKER, IN COMBINATION WITH TRASTUZUMAB, RAMUCIRUMAB, AND PACLITAXEL IN PATIENTS WITH 2ND LINE HER2-POSITIVE ADVANCED GASTRIC OR GASTROESOPHAGEAL CANCER

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*HCC and KWL contributed equally to this abstract; **LQMC currently at University of Texas at Austin, TX.

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# METHODS
# STUDY DESIGN

**Part 1 (single agent):** Patients were administered escalating doses of intravenous ALX148 (0.3 to 10 mg/kg QW; or 30 mg/kg Q2W)[3].

**Part 2 (combination):** A subgroup of patients with HER2 positive Gastric/GEJ cancer were administered ALX148 10 or 15 mg/kg QW in combination with trastuzumab (8 mg/kg IV→6 mg/kg Q3W) with or without ramucirumab (8 mg/kg Days 1, 15 Q4W) and paclitaxel (80 mg/m2 Days 1, 8, 15 Q4W).

- Adequate organ function and hemoglobin ≥9 g/dL.
- No prior treatment with an anti-CD47 or anti-SIRPα agent.
- HER2-positive-status for study eligibility as locally assessed by sites using an FDA approved test for gastric cancer.

**Primary:** Safety DLT

**Secondary:** Response, PK/PD

Here we report tolerability data from fully enrolled GC patient cohorts receiving ALX148 + trastuzumab + ramucirumab + paclitaxel as well as updated clinical activity of all GC cohorts as of May 03, 2021.

**ASPEN-01 – Gastric/Gastroesophageal (GC) Combination Cohorts**

**Dose Expansion ALX148**
10 mg/kg QW (n=20)

**≥2L HER2-Positive GC**
**ALX148 + Trastuzumab**

*progressed on prior fluoropyrimidine*
*(progression on trastuzumab and platinum allowed)*

**Dose Escalation ALX148**
10 mg/kg QW (n=3)
15 mg/kg QW (n=15)

**≥2L HER2-Positive GC**
**ALX148 + Trastuzumab + Ramucirumab + Paclitaxel**
*progressed on prior trastuzumab and fluoropyrimidine, or platinum*

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# RESULTS
# PATIENT BASELINE CHARACTERISTICS

**Table 1.** Baseline Characteristics

| | | ALX148 + Trastuzumab + Ramucirumab + Paclitaxel ≥2L GC (N=18) | ALX148 + Trastuzumab ≥2L GC (N=20) |
|---|---|---|---|
| **Median Age, Years (range)** | | 63 (36-83) | 58 (45-79) |
| **Sex, n** | **M** | 13 | 15 |
| | **F** | 5 | 5 |
| **Race, n** | **Asian** | 15 | 13 |
| | **White** | 3 | 6 |
| | **Other** | – | 1 |
| **ECOG PS, n** | **0** | 8 | 7 |
| | **1** | 10 | 13 |
| **Progressed Upon Prior Anti-HER2 Therapy, n ( %)** | | 17 (94) | 19 (95) |
| **Progressed Upon ≥2 Prior Anti-HER2 Therapy n (%)** | | 1 (6) | 9 (45) |
| **Progressed Upon Prior CPI Therapy, n (%)** | | 2 (11) | 9 (45) |
| **Visceral Distant Metastasis, n (%)** | | 17 (94) | 17 (85) |

- **38 patients have been enrolled into Part 2 GC combination cohorts.**

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# ADVERSE EVENT PROFILE IN PATIENTS WITH GC BY DOSE LEVEL

**Table 2.** Treatment Related Adverse Events

**ALX148 + Trastuzumab + Ramucirumab + Paclitaxel (N=18)**

| | Total n (%) | |
|---|---|---|
| **Adverse Event** | ALX148 10 mg/kg | ALX148 15 mg/kg |
| Diarrhea | – | 3 (16.7) |
| Rash | – | 3 (16.7) |
| Urticaria | – | 3 (16.7) |
| Pruritus | – | 2 (11.1) |
| Fatigue | 1 (5.6) | 1 (5.6) |
| Lymphocyte Count Decreased | – | 1 (5.6) |
| Abdominal Pain | – | 1 (5.6) |
| Anemia | – | 1 (5.6) |
| Back Pain | – | 1 (5.6) |
| Dermatitis Acneiform | – | 1 (5.6) |
| Stomatitis | – | 1 (5.6) |
| Vision Blurred | – | 1 (5.6) |

- **There were no dose limiting toxicities, on study deaths, or ALX148-related SAEs.**

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# ADVERSE EVENT PROFILE IN PATIENTS WITH GC BY DOSE LEVEL

**Table 3.** ≥ Grade 3 Adverse Events

**ALX148 + Trastuzumab + Ramucirumab + Paclitaxel (N=18)**

| Adverse Event | Total n(%) All Causality | | | | Total n(%) Related | | | |
|---|---|---|---|---|---|---|---|---|
| Grade | 3 | | 4 | | 3 | | 4 | |
| ALX148 Dose QW | 10 mg/kg | 15 mg/kg | 10 mg/kg | 15 mg/kg | 10 mg/kg | 15 mg/kg | 10 mg/kg | 15 mg/kg |
| Neutrophil Count Decreased | 1 (5.6) | 4 (22.2) | 1 (5.6) | 1 (5.6) | – | – | – | – |
| Hypertension | 2 (11.1) | 4 (22.2) | – | – | – | – | – | – |
| Anemia | – | 3 (16.7) | – | – | – | – | – | – |
| Fatigue | – | 2 (11.1) | – | – | – | – | – | – |
| Hypophosphatemia | – | 1 (5.6) | – | – | – | – | – | – |
| Lymphocyte Count Decreased | – | 1 (5.6) | – | – | – | 1 (5.6) | – | – |
| Platelet Count Decreased | – | 1 (5.6) | – | – | – | – | – | – |
| Urinary Tract Infection | – | 1 (5.6) | – | – | – | – | – | – |
| Aspartate Aminotransferase Increased | – | 1 (5.6) | – | – | – | – | – | – |
| Asthenia | – | 1 (5.6) | – | – | – | – | – | – |
| Diverticulitis | – | 1 (5.6) | – | – | – | – | – | – |
| Dysphagia | – | 1 (5.6) | – | – | – | – | – | – |
| Non-Cardiac Chest Pain | – | 1 (5.6) | – | – | – | – | – | – |

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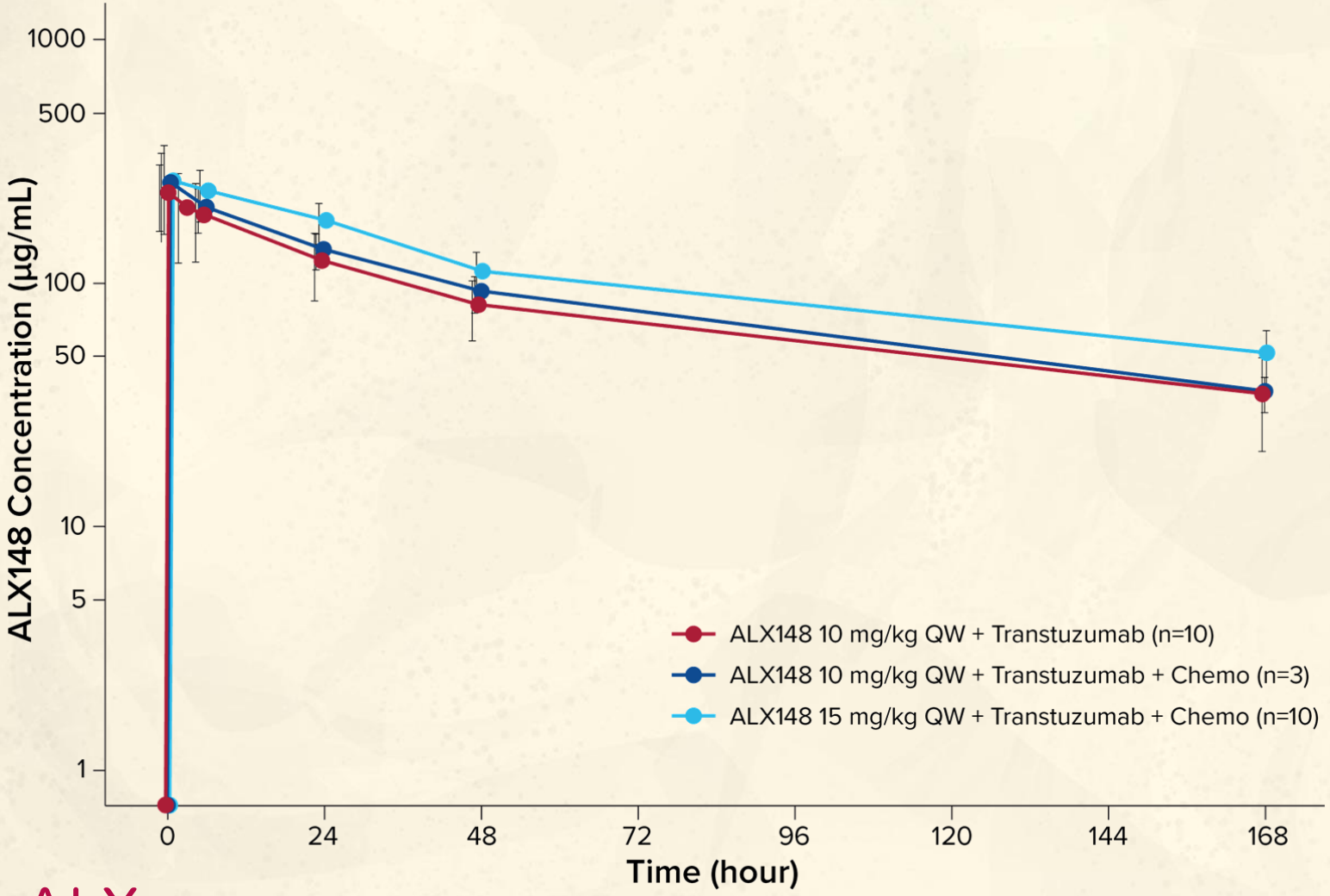
# ALX148 CONCENTRATION-TIME PROFILES BY DOSE LEVEL AND COMBINATION PARTNER




**ALX148 PK following combination therapies with trastuzumab is comparable with and without chemotherapy (ramucirumab + paclitaxel).**

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# RESPONSE

## ALX148 Combination Expansion Cohorts – Confirmed Objective Responses in Evaluable Patients

- **HER2 positive GC Expansion**
  - ALX148 (15 mg/kg QW) + trastuzumab + ramucirumab + paclitaxel, ≥2L GC: N=15 [1 CR*, 10 PR, 2 SD, 2 PD].
  - ALX148 (10 mg/kg QW) + trastuzumab + ramucirumab + paclitaxel, ≥2L GC: N=3 [2 PR, 1 SD].
  - ALX148 (10 mg/kg QW) + trastuzumab, ≥2L GC: N=19 [4 PR (1 unconfirmed), 5 SD, 10 PD].

* Objective response confirmed after data cut off date.

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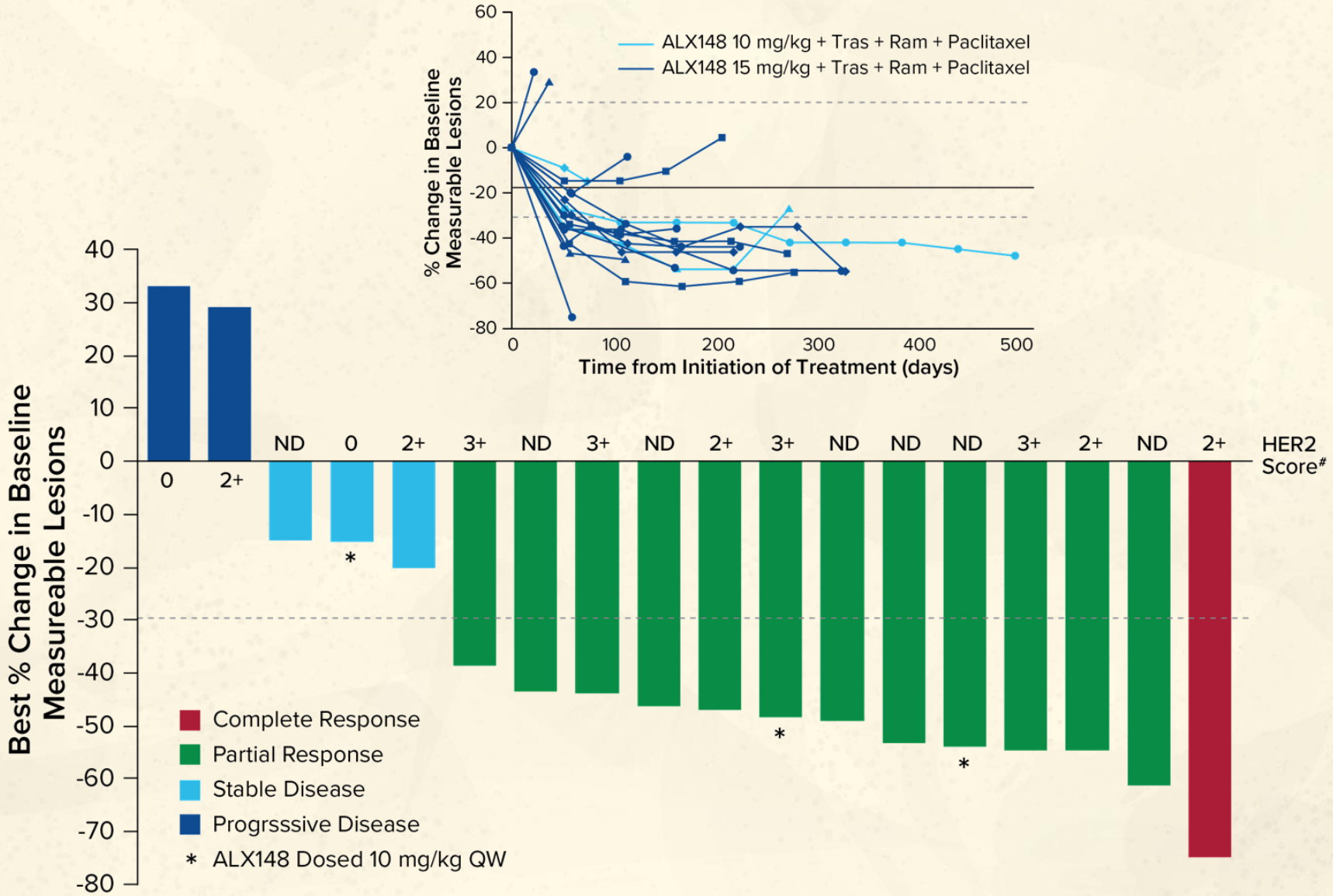
# CLINICAL ACTIVITY OF ALX148 + TRASTUZUMAB + RAMUCIRUMAB + PACLITAXEL IN PATIENTS WITH GC

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# CLINICAL ACTIVITY OF ALX148 COMBINATIONS IN RESPONSE EVALUABLE PATIENTS WITH ≥2L HER2 POSITIVE GC CANCER

| Population | N (EVAL) | ORR (%) [95% CI] | DOR (m) [95% CI] | PFS (m) [95% CI] | PFS rate at 6 m | OS (m) [95% CI] | 0S rate at 12 m | Follow up (m) [95% CI] |
|---|---|---|---|---|---|---|---|---|
| ≥2L Gastric (ALX-10 mg/kg or 15 mg/kg + tras/ram/pac) | 18 | 72.2 [ 49.1% ; 87.5%] | NR | 9.1 [3.8 ; NR] | 74.5% | NR | 75.8% | 10.5 [4.8 ; 12.5] |
| Gastric (ALX-10 mg/kg + TRP) | 3 | 66.7 [20.8% ; 93.9%] | NR | NR | 100% | NR | 66.7% | 14.3 [12.0;NR] |
| Gastric (ALX-15 mg/kg + TRP) | 15 | 73.3 [48.1% ; 89.1%] | NR | NR | 68.3% | NR | 80.8% | 9.4 [4.2 ; 12.5] |
| ≥2L Gastric tras/ram/paclitaxel Rha et al ASCO 2021[3] | 50 | 52 | 5.1 | 7.4 | - | 13.6 | - | 22.9 |
| 3L Gastric Enhertu DESTINY 01[1] | 126 | 41 | 11.3 | 5.6 | 43% | 12.5 | 52% | - |
| ≥2L Gastric ramucirumab/paclitaxel RAINBOW-ASIA Region3[2] | 109 | 34 | - | 5.5 | - | 12.1 | - | 7.9 |
| ≥2L Gastric (ALX-10 mg/kg + tras) | 19 | 21.1 [8.5% ; 43.3%] | 8.7 [5.6; NR] | 2.2 [1.9 ; 5.5] | 16.7% | 8.1 [3.4 ; 12.6] | 38.2% | 27.0 [NR] |
| ≥3L Gastric Irinotecan or Paclitaxel DESTINY 01ControlArm[1] | 62 | 11.3 | 3.9 | 3.5 | 21% | 8.4 | 29% | - |

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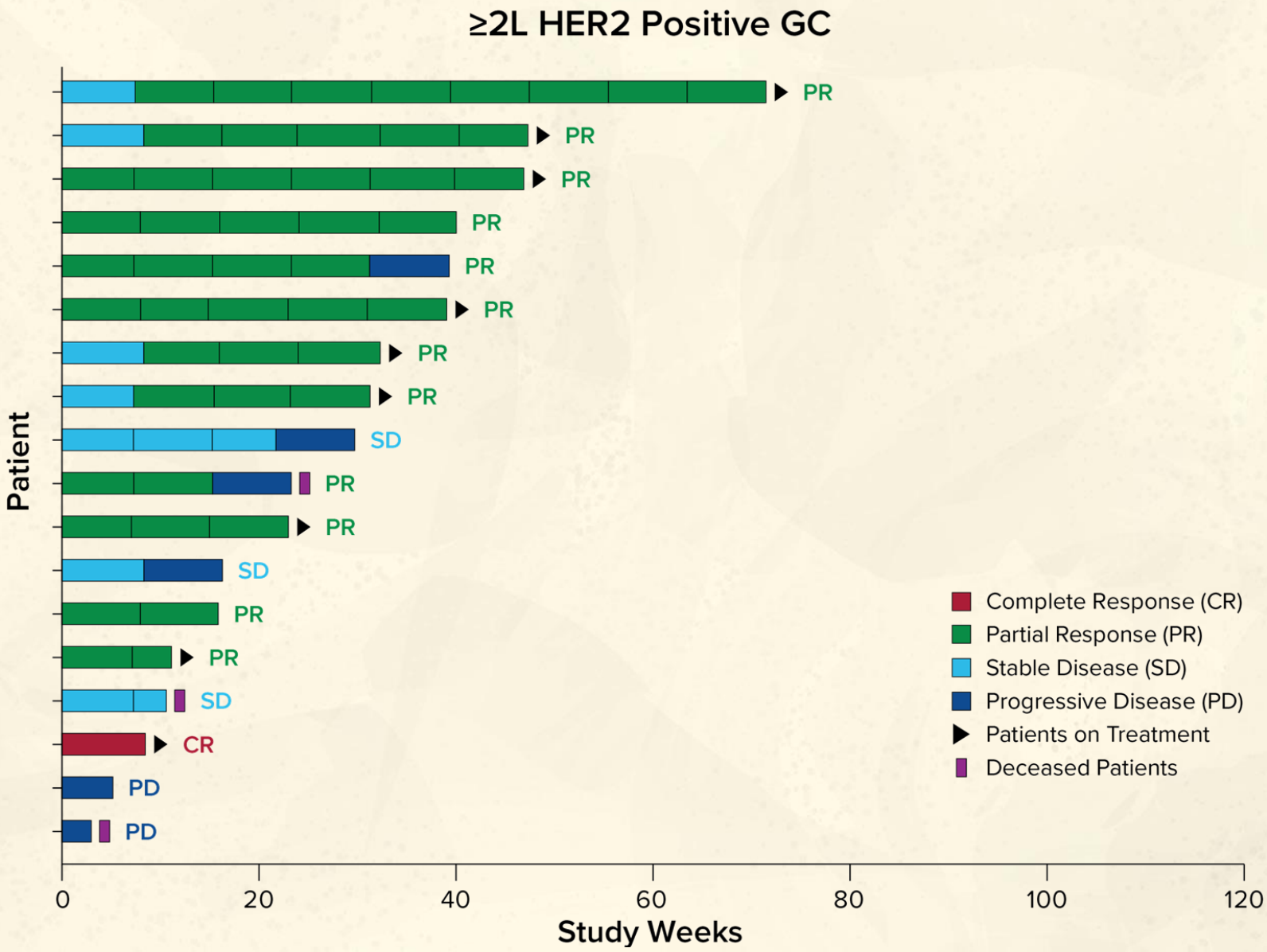
[1]Enhertu product insert, and Shitara et al, NEJM June 18, 2020; [2]Wilke et al, Lancet October 2014; [3] Rha et al #4063 ASCO 2021

# BEST OVERALL AND DURATION OF RESPONSE IN PATIENTS WHILE RECEIVING ALX148 + TRASTUZUMAB + RAMUCIRUMAB + PACLITAXEL (N=18)

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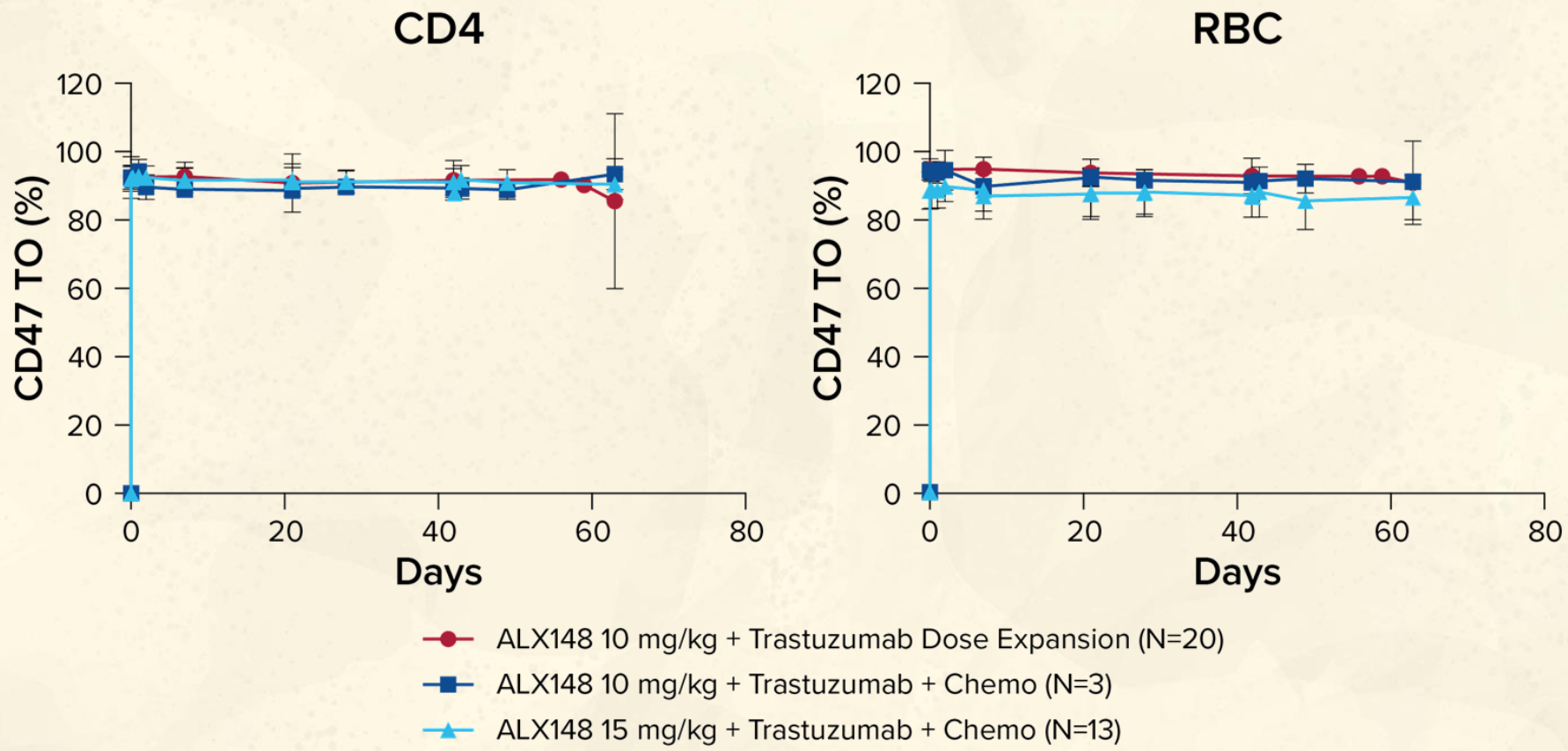
# CD47 TARGET OCCUPANCY FROM CHEMOTHERAPY COMBINATION COHORTS




**Near complete CD47 target occupancy is maintained throughout ALX148 dosing interval over Cycles 1-3 when combined with chemotherapy-containing regimens. (For a subset of patients, target occupancy was measured up to or beyond 300 days with similar results being observed.)**

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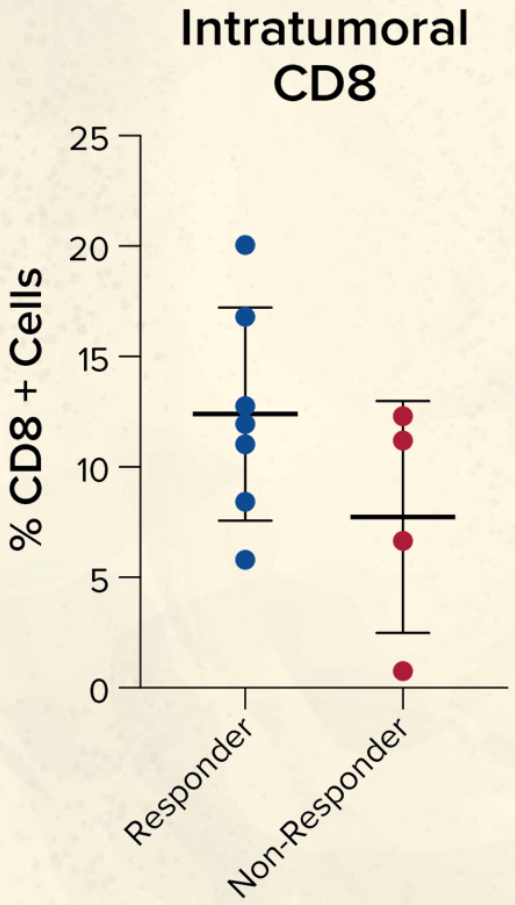
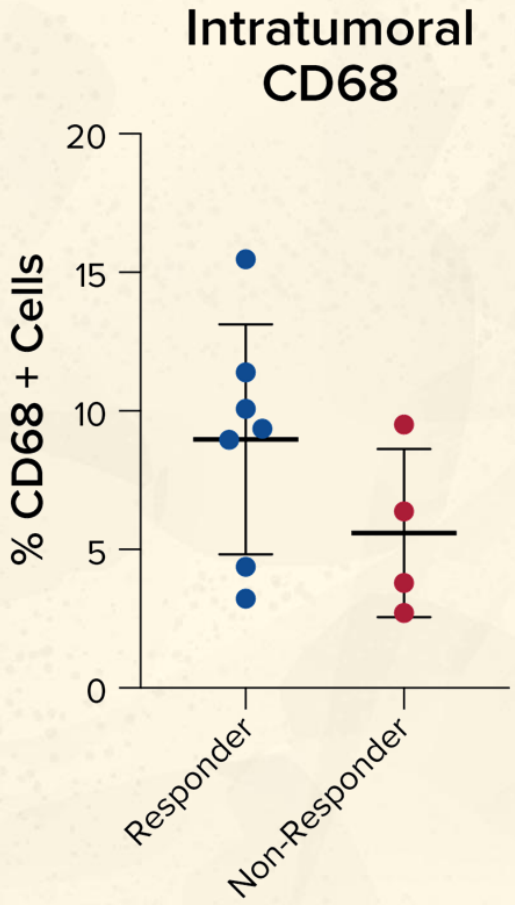
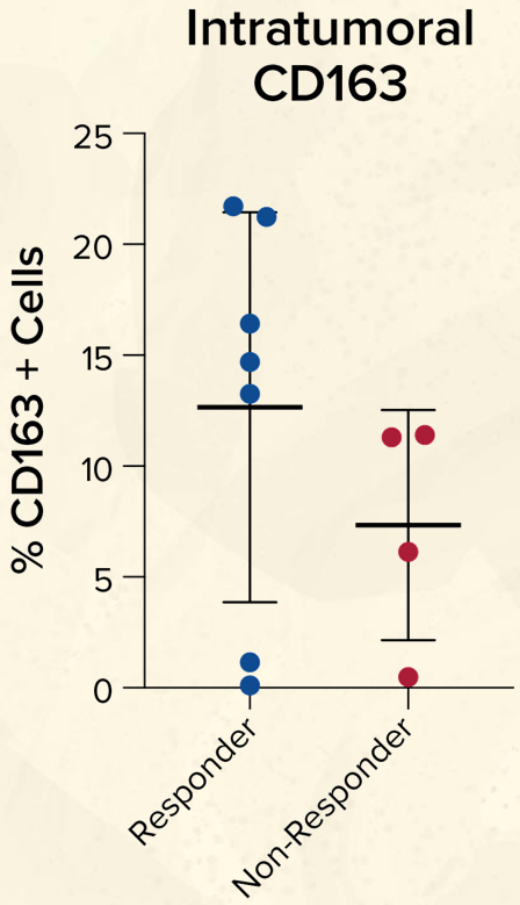
# BASELINE TUMOR INFILTRATING IMMUNE CELLS IN RESPONDERS AND NON-RESPONDERS RECEIVING ALX148 (10 OR 15 MG/KG) + TRP




- **Responder**: CR+PR (N=7)
- **Non-Responder**: SD+PD (N=4)
- Plots represent mean and standard deviation.

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# CONCLUSIONS

## Intended for combination, ALX148 exhibits favorable tolerability in combination with trastuzumab + ramucirumab + paclitaxel and demonstrates objective response in patients with GC

- Preliminary data suggest that ALX148 can be combined with trastuzumab, ramucirumab and paclitaxel with no maximum tolerated dose reached. The maximum administered dose of ALX148 in combination was 15 mg/kg QW.
- Preliminary PK/PD analysis demonstrates no impact of the combination partners upon ALX148 exposure levels with full CD47 receptor occupancy achieved and numeric increases demonstrated in % baseline tumor infiltrating immune cells in responding patients.
- ALX148 in combination with trastuzumab, ramucirumab and paclitaxel demonstrates an initial ORR of 72% and estimated OS at 12 months of 76% in patients with GCs that have progressed on or after a prior trastuzumab-containing regimen. This compares favorably with both RAINBOW[5] and DESTINY-01[6] randomized historical controls.
- Updated data from patients receiving ALX148 + trastuzumab after their tumors have progressed upon prior trastuzumab therapy suggests clinical activity beyond that expected from either trastuzumab or chemotherapy alone.

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# ACKNOWLEDGMENTS

**We would like to thank all of the participating patients and their families as well as site research staff.**

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Presented at the 2021 European Society of Medical Oncology World Congress in Gastrointestinal Cancer (ESMO-GI) Annual Meeting July 03, 2021 Abstract SO-31

[1] Weiskopf, K. *Eur J Cancer*. 2017 May;76:100-109

[2] Kauder, SE. et al. *PLoS ONE*. 2018 August;13(8): e0201832

[3] Lakhani, N. *Journal of Clinical Oncology* 2018 36:15_suppl, 3068-3068

[4] Chow et al. *Journal of Clinical Oncology* 2020 38:15_suppl, 3056-3056

[5] Wilke et al, *Lancet* October 2014

[6] Shitara et al, *NEJM* June 18, 2020 and Enhertu Package Insert

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