A Phase 1 Study of ALX148: CD47 Blockade in Combination with Anti-Cancer Antibodies to Bridge Innate and Adaptive Immune Responses for Advanced Malignancy *(#P335)*

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Disclosures

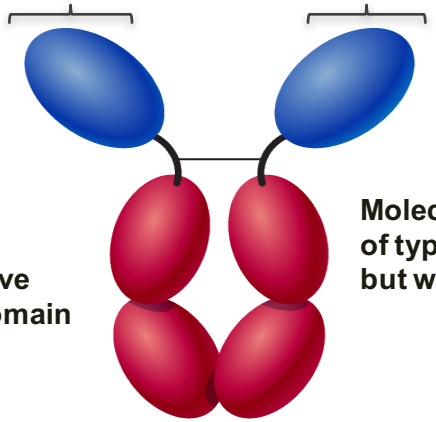
- ALX Oncology
- Amgen
- Arqule
- Ascentage
- Apexian
- Asana Biosciences
- Formation Biologics
- Beigene
- Constellation Pharma
- CytomX
- Daiichi Sankyo
- Forty Seven, Inc
- InhibRx
- Incyte
- Macrogenics
- Loxo
- Livzon Mabpharm
- Merck
- Northern Biologics
- Pfizer
- Regeneron
- Symphogen
- TaiRx

ALX148: A Unique High Affinity SIRPα Fusion Protein

- CD47, a marker of self, is upregulated by tumors to evade the immune system
- CD47-SIRPα signaling represents a myeloid checkpoint mechanism in cancer
- CD47 engages SIRPα and signals the macrophage to ignore the cell on which it is expressed

ALX148 is a Myeloid Checkpoint Inhibitor

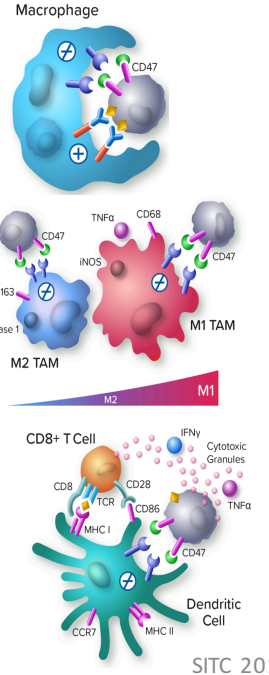
High Affinity CD47 Binding Domains of SIRPα



Inactive Fc Domain

Molecular weight half of typical antibody but with antibody-like PK

1. ALX148 blocks CD47 and enhances macrophage phagocytosis
2. ALX148 increases the ratio of inflammatory M1 tumor associated macrophages (TAMs) to suppressive M2 TAMs
3. ALX148 activates dendritic cells and enhances cross-priming of T cells



SIRPα ALX148 Fc Receptor Tumor Antigen Anticancer Antibody Cancer Cell

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

AT148001 Phase 1 Study Design and Combination Demography

Data Cutoff 12Oct2018

Part 1 ALX148 Single Agent – enrollment complete

- **Primary**: Safety DLT; **Secondary**: Response, PK/PD

Cohort	Dose mg/kg	Schedule
1	0.3	QW
2	1.0	QW
3	3.0	QW
4	10.0	QW
5	30.0	QOW

No MTD reached

Part 2 ALX148 Combinations – enrollment ongoing

- ALX148 (10 mg/kg IV QW), pembrolizumab (200 mg IV Q3W), trastuzumab (8 mg/kg IV followed by 6 mg/kg Q3W)
- **Primary**: Safety DLT; **Secondary**: Response, PK/PD

Dose Escalation	Advanced solid tumors (each combo)
Dose Expansion	NSCLC (pembrolizumab); *progressed on prior CPI/TPS<50%*
	HNSCC (pembrolizumab); *progressed on prior platinum*
	Gastric/GEJ (trastuzumab); *progressed on prior fluoropyrimidine*

		+Pembrolizumab n=39*	*+Trastuzumab n=18*
Median Age, yr (range)		59 (32-79)	57 (45-71)
Sex, n	F	20	7
	M	17	11
ECOG PS, n	0	11	7
	1	26	11
Primary Tumor		*+Pembrolizumab n=39*	*+Trastuzumab n=18*
Lung		24	-
HNSCC		9	-
Gastric/GEJ		-	11
Breast		-	2
Colorectal		2	-
Esophageal		-	2
Ovarian		2	1
Pancreatic		-	1
Peritoneal		1	-
Appendiceal		1	-
Urothelial		-	1

*Partial demography for 2 pembrolizumab patients in database.

ALX148 Generally Well Tolerated in Combination with Standard Regimens of Pembrolizumab and Trastuzumab

Data Cutoff 12Oct2018

Treatment Related Adverse Events in ≥ 2 Patients

ALX148 + Pembrolizumab (N=39)	
Adverse Event	**Total n(%)**
ALT increased	4 (10)
AST increased	3 (8)
Anaemia	2 (5)
Fatigue	2 (5)
Infusion reaction	2 (5)
Myalgia	2 (5)
Pruritus	2 (5)
Alkaline phosphatase incr	2 (5)
Rash	2 (5)

ALX148+Trastuzumab (N=18)	
Adverse Event	**Total n(%)**
Fatigue	3 (16)

Treatment Related Adverse Events ≥ Grade 3 in any Patient

Adverse Event	ALX148+Pembrolizumab (N=39)		
	Grade		
	3	4	Total
AIHA/pancytopenia	-	1*	1
ALT increased	1	-	1
Anaemia	1#	-	1
Febrile neutropenia	1#	-	1
Platelet count decr	-	1#	1
Hyponatremia	1	-	1
Lymphocyte count decr	1	-	1

Adverse Event	ALX148+Trastuzumab (N=18)		
	Grade		
	3	4	Total
Thrombocytopenia	1	-	1
Neutrophil count decr	1^	-	1
WBC count decr	1^	-	1

#^ All reported as one event in patient

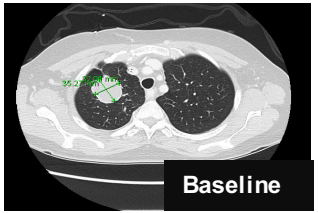
*Dose Limiting Toxicity

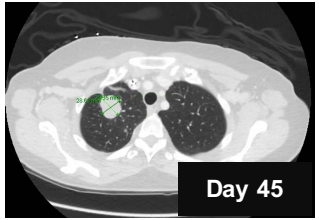
ALX148 Exposure/Patient Disposition

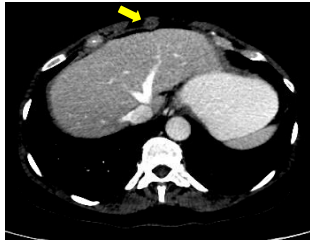
	ALX148 + Pembrolizumab (N=39)	ALX148 + Trastuzumab (N=18)
Dose interruptions due to TRAEs, n	4	2
Dose reductions, n	2	-
Discontinuation due to TRAE, n	1	-
Discontinuation due to PD, n	13	8
Global Deterioration of Health Status, n	1	-
Ongoing Treatment, n	24	10

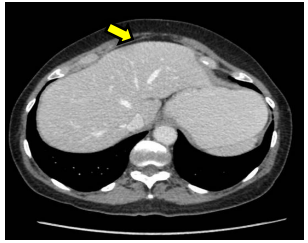
Preliminary Anti-Cancer Activity Seen Across all ALX148 Combinations and Tumor Histologies in Expansion Cohorts

Data Cutoff 25Oct2018





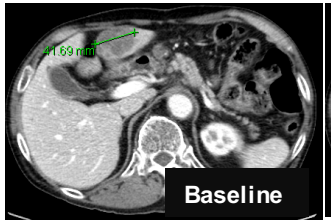


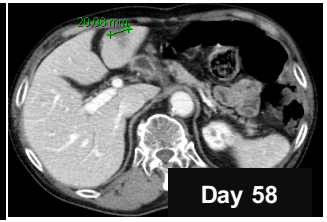


64 yo pt with NSCLC-adenocarcinoma (TPS 10%,CMET/TP53)

ALX148 + pembrolizumab

- 6 prior therapies; nivolumab refractory; CMET inhibitor refractory
- Day 45 partial response (↓48%), disappearance of chest wall lesion;
- Day 100 confirmed PR (↓51%)
- The patient continues on treatment





71 yo pt with Her2+ gastric cancer-adenocarcinoma

ALX148 + trastuzumab

- Prior therapy: cisplatin/5FU; oxaliplatin/capecitabine/trastuzumab; paclitaxel/ramucirumab
- Day 58 partial response ↓52%;
- The patient continues on treatment

Response Summary

- **NSCLC ALX148 + pembrolizumab:** 16 evaluable patients (progressed on prior CPI and/or TPS<50%) as of data cutoff. Patients experienced a best response of **1PR** (↓51%), **5SD** (one SD >24 weeks) with 5 patients continuing on trial.
- **HNSCC ALX148 + pembrolizumab:** 6 evaluable patients (progressed on prior platinum therapy) as of data cutoff. Patients experienced a best response of **1PR** (↓47%), **2SD** with 3 patients continuing on trial.
- **Her2+ Gastric/GEJ ALX148 + trastuzumab:** 5 evaluable patients (progressed on prior fluoropyrimidine-containing regimen) as of data cutoff. Patients experienced a best response of **1PR** (↓52%), **1SD** (↓48% + new CNS lesion) with both continuing on trial.

70% evaluable continuing patients had only one response assessment at point of data cutoff.

AT148001: Conclusions

Intended for combination, ALX148 is designed to avoid the dose-limiting toxicities associated with other CD47-targeted approaches in the clinic, while maximizing the efficacy of antibody-based therapies

- No MTD was reached with ALX148 in combination. The maximum administered dose of ALX148 is 10 mg/kg QW in combination with standard regimens of pembrolizumab and trastuzumab.
- ALX148 contains an inactive Fc region that eliminates dose-dependent hematologic toxicity.
- ALX148 has antibody-like PK and maintains complete CD47 target occupancy over the dosing interval at ≥ 3 mg/kg QW. (*#P340*)
- ALX148 demonstrates preliminary anti-cancer response in combination with pembrolizumab and trastuzumab in patients resistant and refractory to prior checkpoint inhibitors or trastuzumab.

Enrollment into combination expansion cohorts is ongoing (NCT03013218)

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