ALX148, a CD47 Blocker, in Combination with Rituximab in Patients with Relapsed/Refractory (R/R) Non-Hodgkin Lymphoma; ASPEN-01

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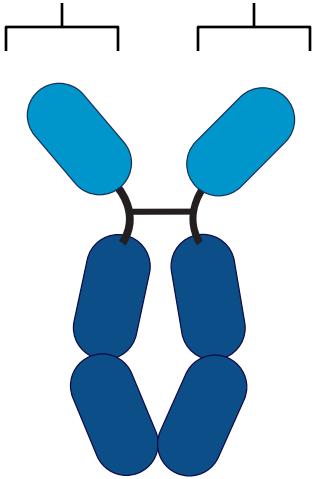
Disclosures

TMKim: AstraZeneca-KHIDI; AstraZeneca; Novartis; Takeda; Sanofi; Roche/Genentech; Voronoi and Boryung. **NLakhani:** Alexion; Alpine Immune; ALX Oncology; Apexian; Asana Biosciences; Ascentage Pharma; Beigene; Celgene; Cerulean; Constellation; Coordination Therapeutics; Cytomx; Formation Biologics; Forty Seven; Ikena Oncology; Incyte; Inhib Rx; Innovent Bio; Jounce; Livzon; Loxo; Macrogenics; Merck; Mersana; Northern Biologics; Odonate; Pfizer; Regeneron; Sapience; Shattuck Labs; Symphogen; TaiRx and Tesaro. **JGainor:** Ironwood; Agios; Amgen; Array; Blueprint Medicines; Bristol-Myers Squibb; Genentech; Jounce; Gilead; Lilly; Merck; Moderna; Oncorus; Regeneron; Takeda; Theravance; Adaptimmune; Ariad; AstraZeneca; Novartis and Tesaro. **MKamdar:** Roche. **PFanning:** ALX Oncology. **PSquifflet:** ALX Oncology and IDDI. **FJin:** ALX Oncology. **AForgie:** ALX Oncology. **HWan:** ALX Oncology and Tallac. **JPons:** ALX Oncology. **SRandolph:** ALX Oncology. **WSKim:** Roche; Pfizer; Johnson and Johnson; Celltrion; Kyowa Kirin; Dongs and Mundipharma.

ALX148 Potently and Selectively Binds CD47 to Block SIRPα Interaction

- CD47-SIRPα signaling is a myeloid checkpoint mechanism that signals the macrophage to ignore the cell on which CD47 is expressed.[1] Tumors upregulate CD47 to evade the immune response, and high expression of CD47 in NHL is reported to correlate with a worse OS, while CD47 blockade in addition to rituximab augments rituximab-mediated phagocytosis.[2,3]
- ALX148 is an engineered fusion protein comprised of a high affinity CD47 blocker linked to an inactive human immunoglobulin Fc region. It blocks the CD47-SIRPα interaction, thereby enhancing anti-tumor immunity.[3]

High Affinity CD47 Binding Domains of SIRPα



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.

ASPEN-01: A First-in-Human Phase 1 Study of ALX148

ASPEN-01 evaluates ALX148 administered as a single agent (Part 1) and in combination with established anticancer antibodies (Part 2) including in combination with rituximab in patients with relapsed or refractory B-cell non Hodgkin lymphoma (NHL).

- **Part 1 (single agent):** No MTD reached, maximum administered dose 30 mg/kg QOW.[4]
- **Part 2 (combination):** ALX148 (administered 10 mg/kg or 15 mg/kg QW) combined with standard regimens of rituximab (administered 375 mg/m^2 QW x 4 followed by once monthly x 8).[5]
  - **Primary Endpoint:** First cycle ALX148 dose limiting toxicity (DLT) in combination with rituximab.

		ALX148 10 mg/kg QW + rituximab (n=22)	ALX148 15 mg/kg QW + rituximab (n=11)
Primary Disease, n	**Follicular**	5	3
	Marginal Zone (MZL)	2	1
	Mantle Cell (MCL)	4	1
	DLBCL	11	6
Median Age, Years (range)		66 (32-80)	64 (53-78)
Sex, n	**M**	17	6
	F	5	5
Race, n	**Asian**	18	9
	White	4	2
ECOG, PS, n	**0**	7	2
	1	15	9
Median Prior Therapy, n (range)		3 (1-7)	3 (1 -5)

- As of October 1, 2020, ALX148 in combination with rituximab has been administered to 33 patients with advanced relapsed and refractory non-Hodgkin lymphoma.
- The majority of patients enrolled were male (70%), Asian (82%) and had an ECOG PS score of 1 (73%).

ASPEN-01: Preliminary Clinical Safety and Anti-Cancer Activity

Clinical Safety of ALX148 in Combination with Rituximab

- Twenty-eight (84.8%) patients experienced any adverse event. Nineteen (57.6%) patients experienced any TRAE.
- No ALX148 dose limiting toxicities were reported, the maximum administered dose was 15 mg/kg QW.

Clinical Activity of ALX148 in Combination with Rituximab in Response-Evaluable Patients

- ALX148 10 mg/kg + rituximab (N=22)
  - 4CR ([2] Follicular, [1] Marginal Zone, [1] MCL)
  - 5PR ([2] DLBCL, [1] Follicular, [2] Mantle Cell)
  - 6SD ([2] DLBCL, [2] Follicular, [1] Mantle Cell, [1] Marginal Zone)
- ALX148 15 mg/kg + rituximab (N=10)
  - 3CR ([2] Follicular, [1] Marginal Zone)
  - 4PR ([2] DLBCL, [1] MCL, [1] Follicular)

ALX148 + Rituximab (N=33)		
Related Adverse Event	**Total n (%)**	**≥Grade 3 n (%)**
Rash	8 (24.2)	—
Fatigue	4 (12.1)	—
Nausea	2 (6.1)	—
Neutrophil Count Decreased	2 (6.1)	2 (6.1)
Anemia	2 (6.1)	1 (3)
Myalgia	2 (6.1)	—
Pruritus	2 (6.1)	—

Data Cutoff 01Oct2020.

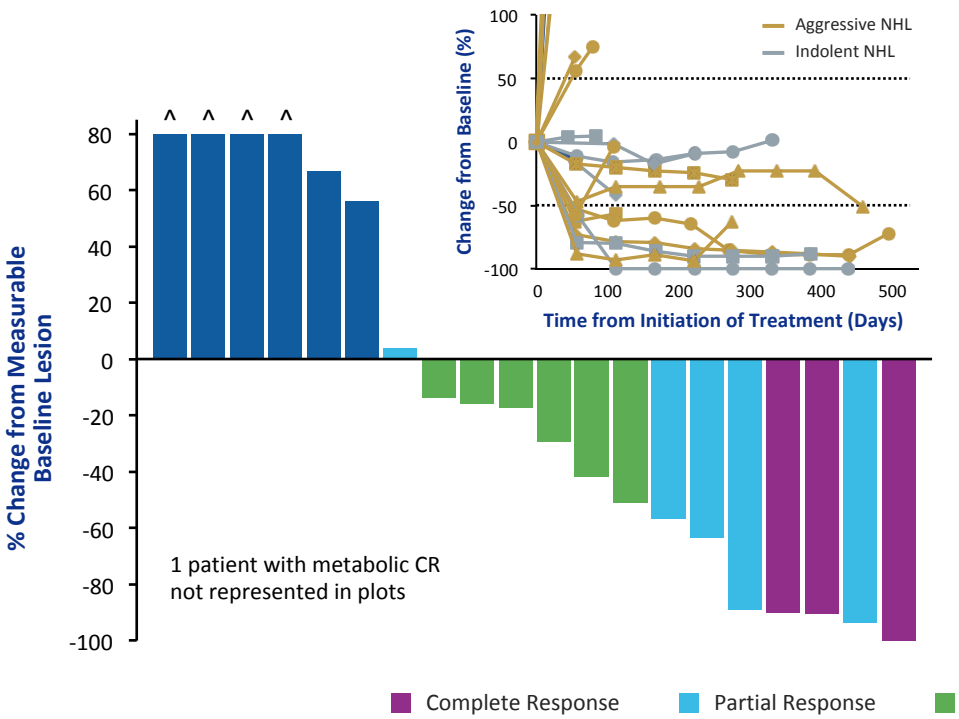
Clinical Activity of ALX148 + Rituximab in Response-Evaluable Patients

Population ALX148 Dose	N	ORR (95% CI)	DCR (95% CI)	Median DOR (95% CI)	Median TTR (range)	Median PFS (95% CI)	Median OS (95% CI)
NHL (10 mg/kg ALL)	**22**	**40.9% [20.7; 63.6]**	**59.1% [36.4; 79.3]**	**14.9 [1.81; 14.9]**	**1.88 [1.51 - 2.07]**	**7.43 [1.88; 13.2]**	**18.5 [7.34; NC]**
NHL (10 mg/kg aggressive)	15	33.3% [11.8; 61.6]	46.7% [21.3; 73.4]	5.56 [NC; NC]	1.88 [1.81 - 1.91]	2.53 [0.95; 7.43]	8.95 [2.50; NC]
NHL (10 mg/kg indolent)	7	57.1% [18.4; 90.1]	85.7% [42.1; 99.6]	NC	1.92 [1.51 - 2.07]	NC	NC
NHL (15 mg/kg ALL)	**10**	**70.0% [34.8; 93.3]**	**70.0% [34.8; 93.3]**	**NC**	**1.88 [1.71 - 5.43]**	**NC**	**NC**
NHL (15 mg/kg aggressive)	6	50.0% [11.8; 88.2]	50.0% [11.8; 88.2]	NC	1.88 [1.71 - 5.43]	NC	NC
NHL (15 mg/kg indolent)	4	100% [NC; NC]	100% [NC; NC]	NC	1.74 [1.71 - 1.88]	NC	NC

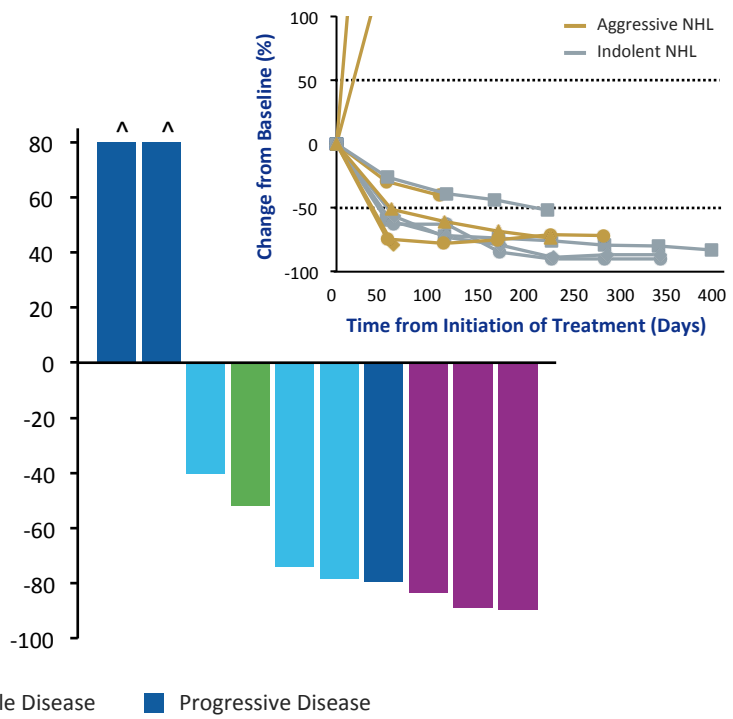
Aggressive: Relapse/refractory Diffuse Large B Cell Lymphoma and Mantle Cell Lymphoma; **Indolent**: Follicular Lymphoma and Marginal Zone Lymphoma; **ORR**: Objective response rate (complete + partial response rate); **DCR**: Disease control rate (CR+PR+SD≥24 weeks); **DOR**: Duration of response (months); **TTR**: Time to response (months); **PFS**: Progression free survival (months); **OS**: Overall survival (months); **CI**: Confidence interval; **NC**: Could not be calculated. Data Cutoff 01Oct2020.

Clinical Activity of ALX148 + Rituximab by Patient with NHL

ALX148 (10 mg/kg QW)* + Rituximab



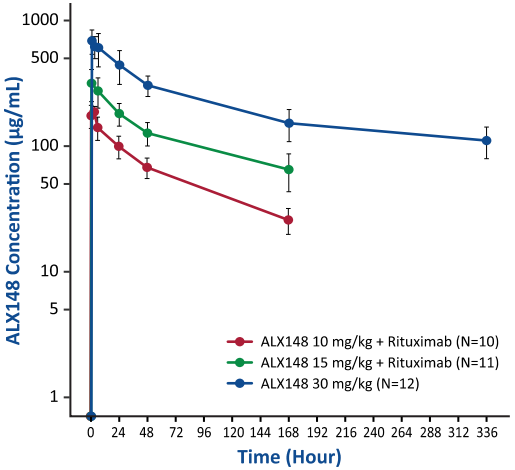
ALX148 (15 mg/kg QW) + Rituximab

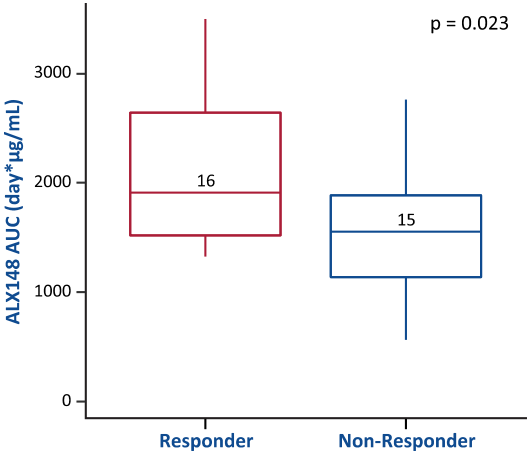


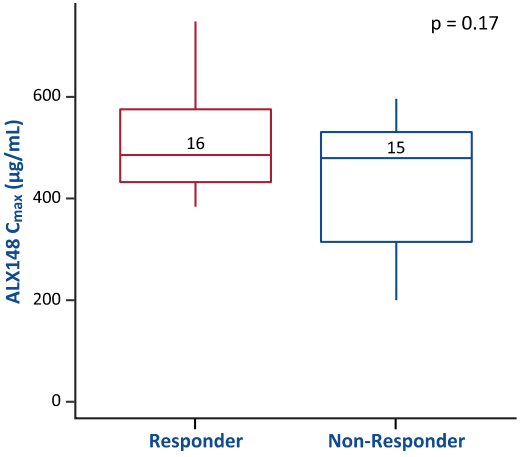
Complete Response | Partial Response | Stable Disease | Progressive Disease

Data Cutoff 01Oct2020; Response evaluable patients; Responses include metabolic response per Lugano Response Criteria.
^ more than 80% increase from baseline. * 1 patient with rapid fatal progressive disease not represented in plot

ALX148 Clinical Pharmacokinetics and Exposure-Response Analysis







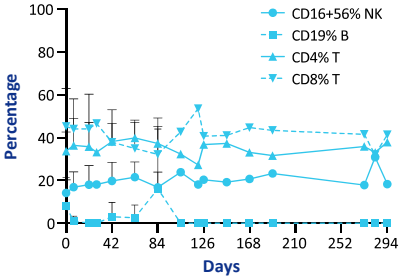
- ALX148 concentration-time profiles following first IV infusion at Cycle 1 Day 1 as single agent or in combination with rituximab.
- A significant improvement in patients with clinical response (PR,CR) with increased ALX148 exposure (AUC; p = 0.023) was observed across the exposure range evaluated (10 mg/kg QW - 15 mg/kg QW).

Data Cutoff 01Oct2020.

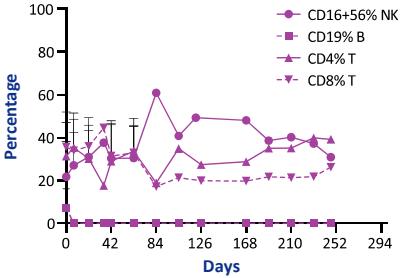
Biomarker Analyses of ALX148 + Rituximab

- In general, no changes in circulating T and NK cells were observed following ALX148 + Rituximab
- An expected, reduction in circulating B cells was seen
- Immunohistochemistry for CD8 (tumor infiltrating lymphocytes) and CD68 and CD163 (tumor associated macrophages and myeloid cells) was conducted on available baseline biopsies
- No correlation was observed for baseline intratumoral CD8 and CD68 expression and percent change from measurable baseline lesions
- A moderate correlation was seen for baseline intratumoral CD163 expression with poorer response (r= 0.4737; p=0.0405; Spearman nonparametric correlation)

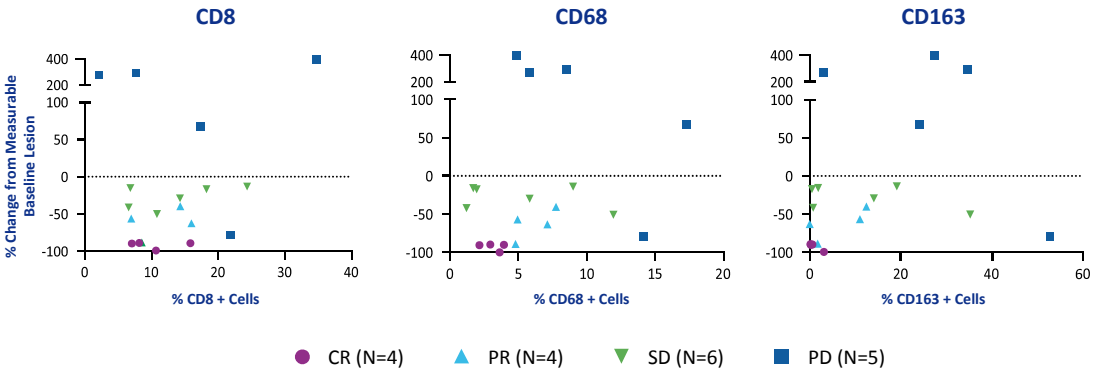
TBNK 10 mg/kg ALX148 + Rituximab (N=10)



TBNK 15 mg/kg ALX148 + Rituximab (N=11)



Baseline Intratumoral



Conclusions

ASPEN-01: ALX148 in combination with rituximab maximizes the innate and adaptive immune response to NHL while avoiding the dose-limiting hematologic toxicities associated with other CD47-targeted approaches in the clinic.

- ALX148 in combination with standard regimens of rituximab is well tolerated with a favorable hematologic safety profile and no maximum tolerated dose reached. The maximum administered dose is 15 mg/kg QW.
- ALX148 in combination with rituximab demonstrates linear PK at 10 mg/kg and 15 mg/kg QW with no impact upon circulating T or NK cells.
- ALX148 demonstrates encouraging anti-cancer activity with 70% ORR at 15 mg/kg QW and durable responses in combination with rituximab in patients with relapsed/refractory NHL (median of 3 prior therapies) that compare favorably to historic controls.
- Initial data suggests ALX148 is well tolerated and demonstrates significant improvement in clinical response with increased exposure across the exposure range evaluated.

We thank all of the participating patients and their families as well as the site research staff

- Presented at the American Society of Hematology (ASH) Annual Meeting.
- December 5-8, 2020. Abstract #3016; Contact email: info@alxoncology.com

[1] Weiskopf, K., Eur J Cancer. 2017 May;76:100; [2]Bouwstra, R. et al., Cancer Immuno Research 2019 Oct;7(10):1663; [3]Kauder, S.E. et al., PLoS ONE. 2018 August;13(8); [4]Lakhani N. et al, #P335, SITC 2018; [5]Kim et al., #EP1247, EHA 2020.