THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

A phase I investigator-initiated trial of evorpacept (ALX148), lenalidomide and rituximab for patients with relapsed or refractory B-cell non-Hodgkin lymphoma

Paolo Strati, Lei Feng, Dai Chihara, Jason Westin, Sairah Ahmed, Luis Fayad, Jared Henderson, Jeffrey Davidson, Elizabeth McChesney, Loretta J Nastoupil, Sattva S Neelapu, Christopher R Flowers

Department of Lymphoma and Myeloma, Biostatistics
The University of Texas MD Anderson Cancer Center
Houston, Texas, USA

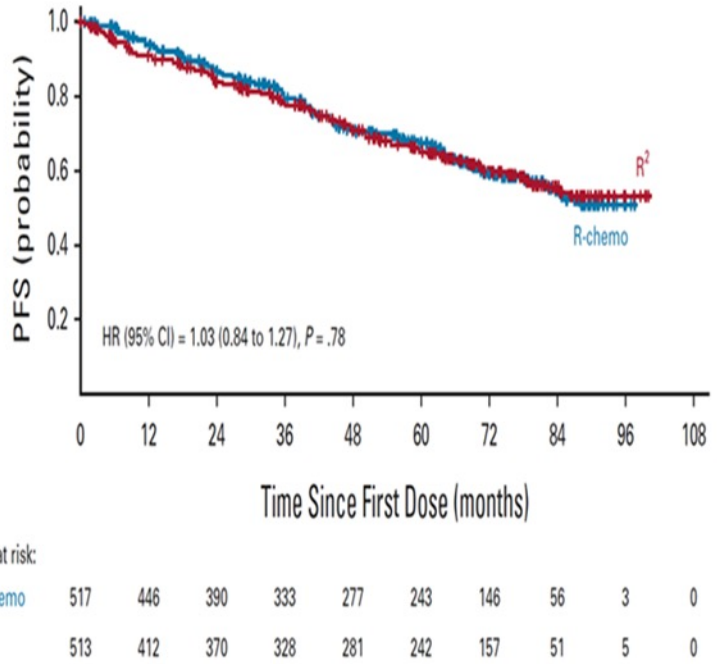
AACR Abstract #10285

Disclosures

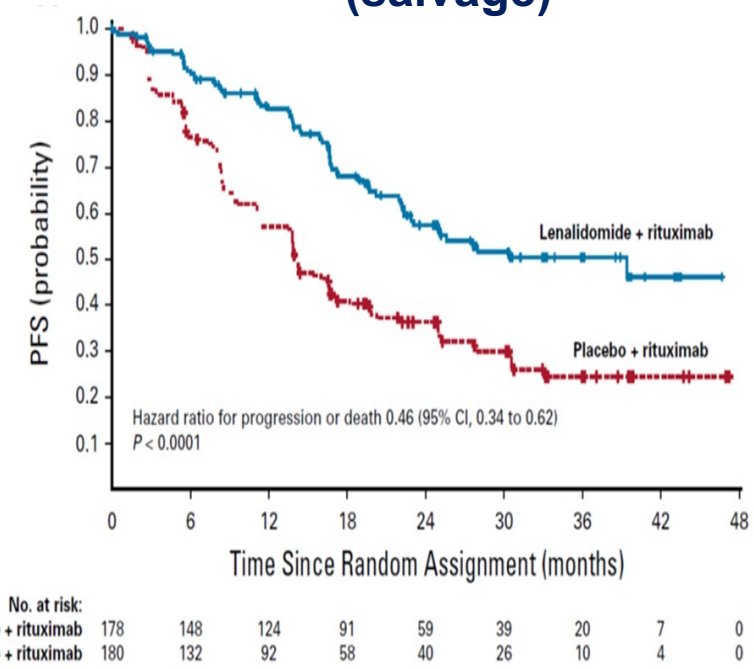
- **Research support**: Sobi, Astrazeneca Acerta, ALX Oncology, ADC Therapeutics, Kite-Gilead
- **Advisory Board/Consultancy**: Kite Gilead, Hutchinson Medipharma, ADC Therapeutics, TG Therapeutics, Incyte Morphosys, Astrazeneca Acerta, Sobi, Roche Genentech, Abbvie-Genmab
- **Active grants**: Leukemia Lymphoma Society, Kite-Gilead, Sabin Family

Lenalidomide and rituximab (R^2) is active in patients with follicular lymphoma (FL)

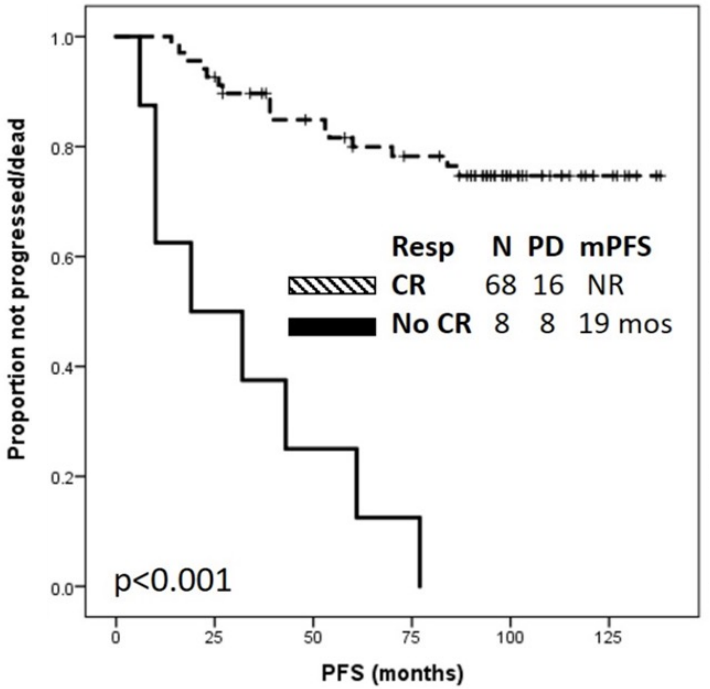
RELEVANCE trial (frontline)



AUGMENT trial (salvage)



Phase II trial at MDACC



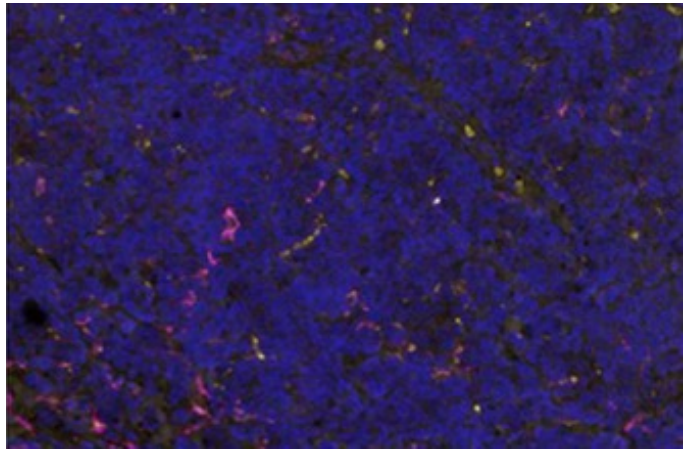
Only CR associated with PFS

CR rate for R^2 in relapsed FL only 34%

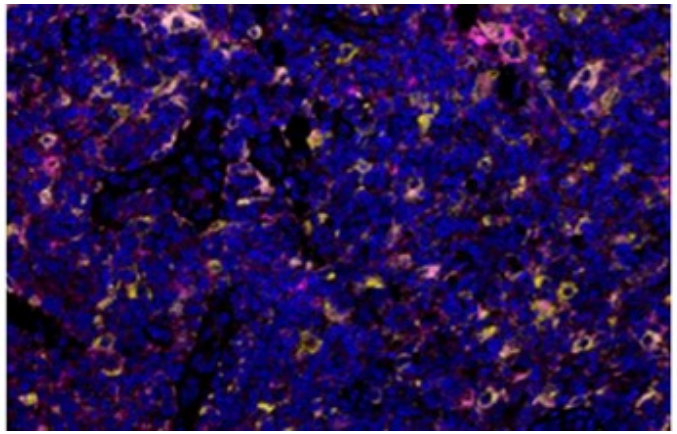
Morschhauser F et al, JCO 2022
Leonard JP et al, JCO 2019
Strati P et al, Blood 2021

SIRPα-positive macrophages increase at time of progression after R^2 in patients with FL

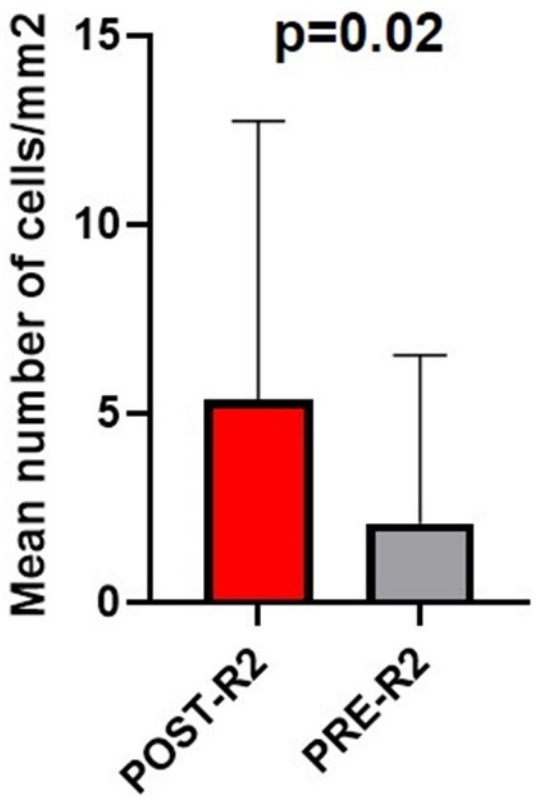
CSF1-R+ SIRPα+ M before R^2



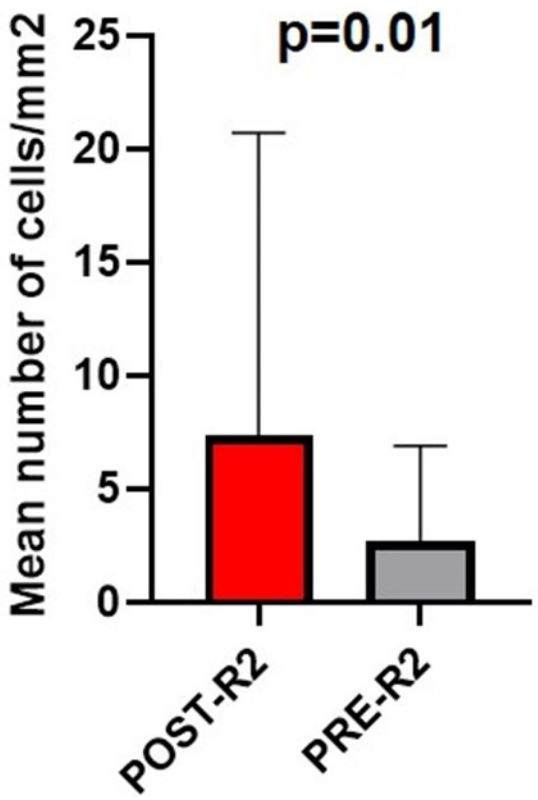
CSF1-R+ SIRPα+ M after R^2



CSF1-R+ SIRPα+ M

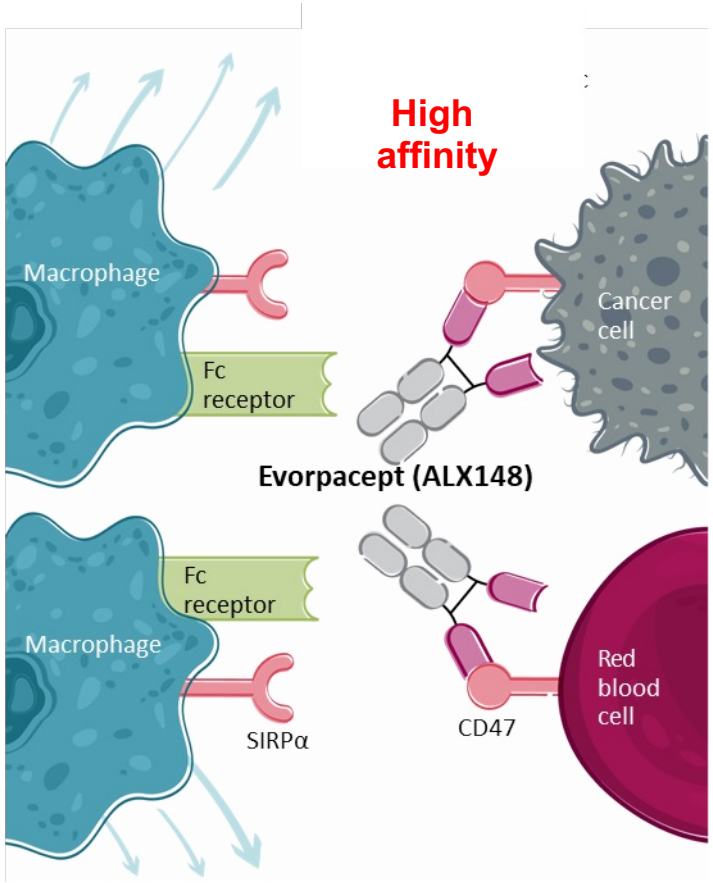


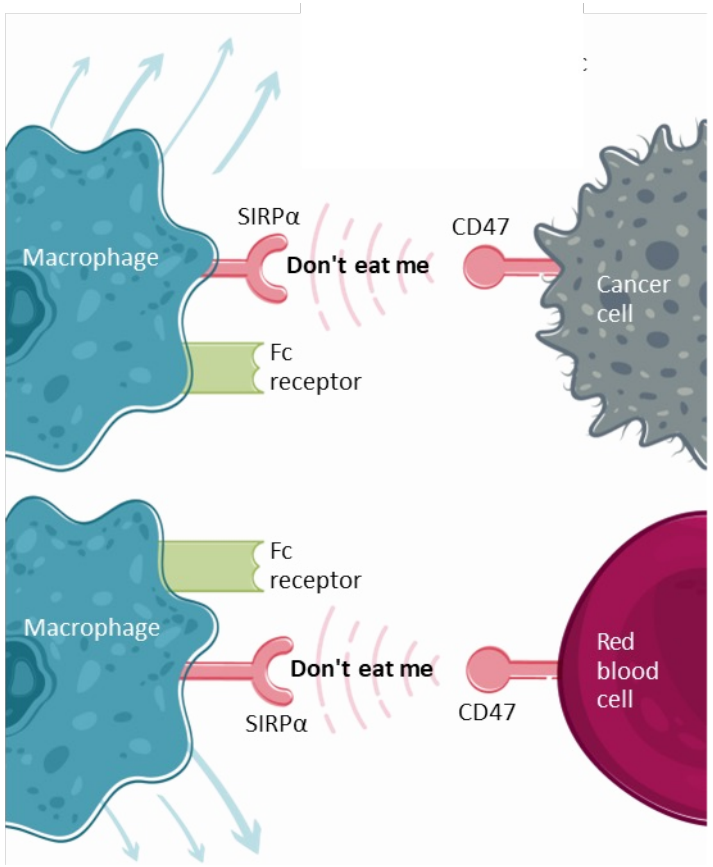
CD163+ SIRPα+ M

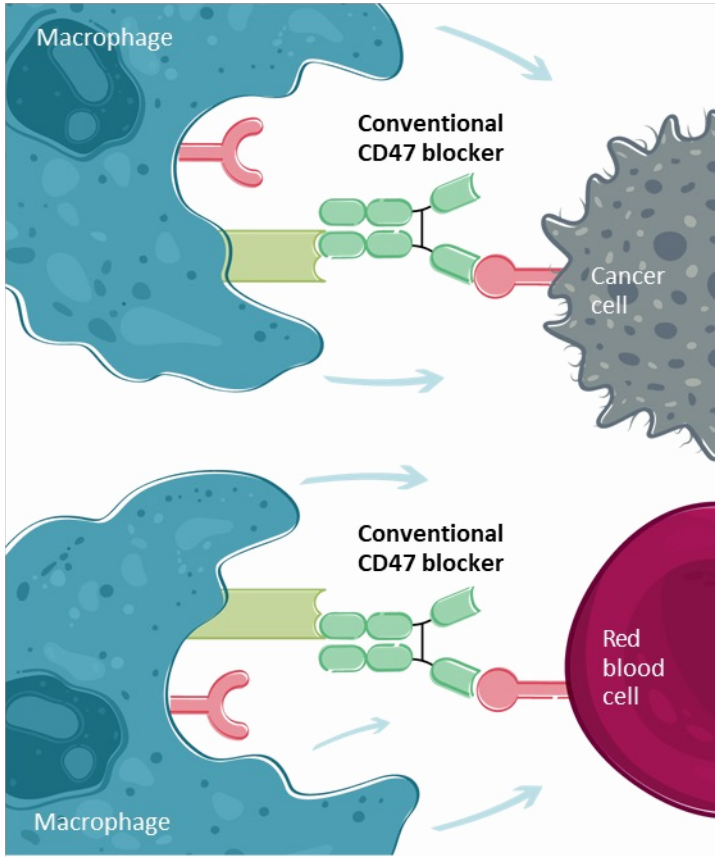


Marques-Piubelli M et al, Blood Adv 2022

Evorpacept (ALX148) abrogates the ‘do-not-eat-me signal’ for SIRPα+ macrophages without targeting red blood cells

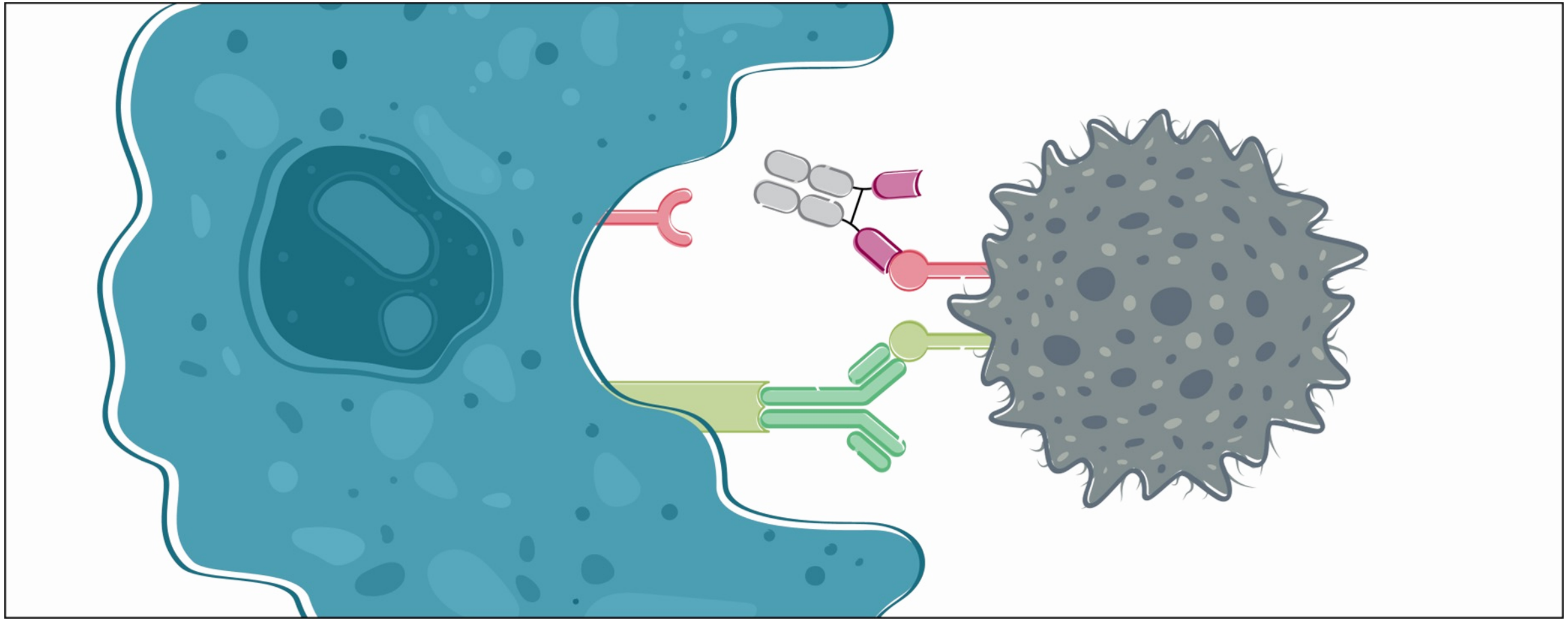






Courtesy of ALX Oncology

Evorpacept increases antibody-dependent cellular phagocytosis in combination with rituximab



Courtesy of ALX Oncology

The combination of evorpacept and rituximab is well tolerated and active in patients with relapsed B-NHL

ALX148 + Rituximab (N=33)

Treatment 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 (3.0)**
Myalgia	**2 (6.1)**	—
Pruritus	**2 (6.1)**	—

Data Cutoff: October 1, 2020

	10 mg/kg QW		15 mg/kg QW	
Population	N	ORR	N	ORR
All	**22**	**40.9%**	**10**	**70.0%**
Aggressive	15	33.3%	6	50.0%
Indolent	7	57.1%	4	100.0%

Indolent B-NHL
10 mg/kg QW: 3 CR, 1 PR
15 mg/kg QW: 3 CR, 1 PR

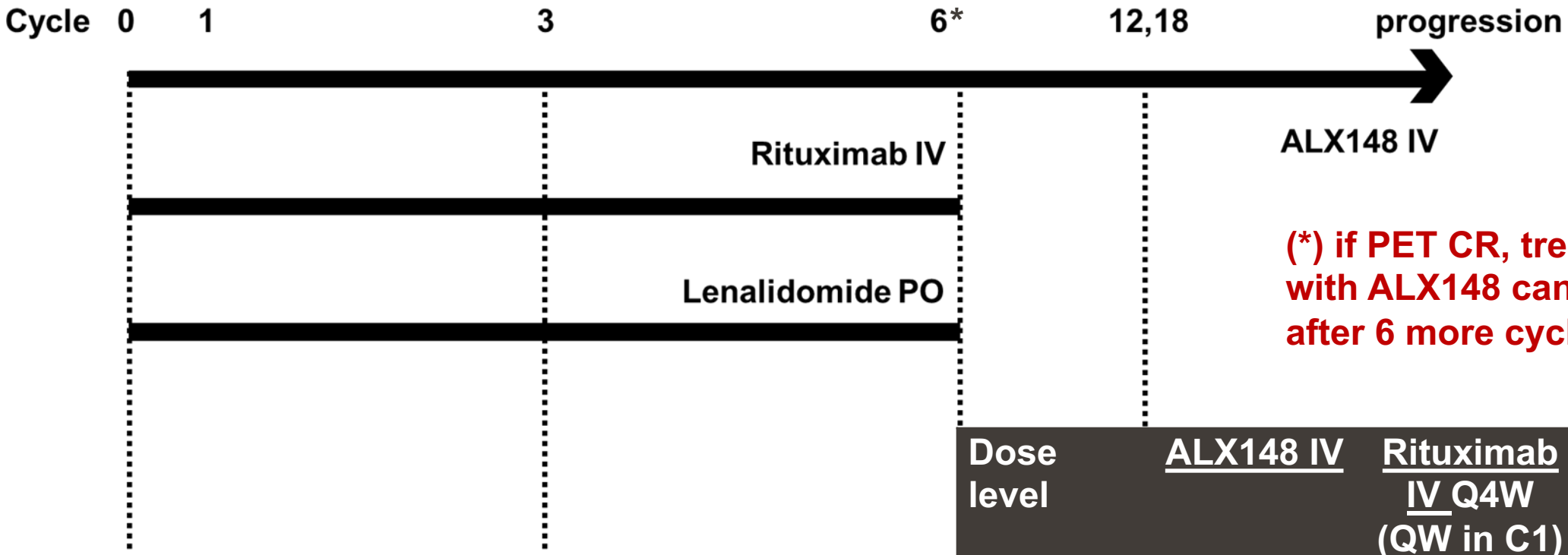
Lakhani N et al, ASCO 2018
Kim TM et al, ASH 2019

Hypothesis and Methods

We hypothesize that evorpacept and R^2 will be synergize, and be safe and effective for the treatment of pts with relapsed refractory B-NHL

- Phase 1 single arm study (NCT05025800) conducted between 11/2021 and 09/2023 (data cutoff 12/2023).
- Adult pts with relapsed refractory B-NHL
- ≥2 prior lines of systemic therapy (1 in case of indolent B-NHL); patients previously treated with lenalidomide excluded.
- Evorpacept administered IV every 28 days x 12 cycles, at two dose levels: 30 mg/Kg on D1 and D15, or 60 mg/Kg on D1. Standard R^2.
- Dose limiting toxicity evaluated by CTCAE v5 during cycle 1, with a target DLT rate of 0.3 (Bayesian Optimal Interval design).
- Response was assessed by Lugano 2014 criteria.

Treatment schema



(*) if PET CR, treatment with ALX148 can be stopped after 6 more cycles

Dose level	ALX148 IV	Rituximab IV Q4W (QW in C1)	Lenalidomide PO DAILY (D1-21)
Cohort -1	15 mg/Kg QW	375 mg/m^2	20 mg
Cohort 1	30 mg/Kg Q2W	375 mg/m^2	20 mg
Cohort 2	60 mg/Kg Q4W	375 mg/m^2	20 mg

Baseline characteristics

Patients (N=20)	Number (%); Median [Range]
Age	61 [27-85]
Caucasian	13 (65)
Male	10 (50)
Hemoglobin (g/dL)	12.8 [9.2-15.2]
β2-microglobulin (mg/L)	2.3 [0.8-6.2]
LDH (U/L)	222 [129-338]
Follicular lymphoma	**15 (75)**
Marginal zone lymphoma	**3 (15)**
Mantle cell lymphoma	1 (5)
Richter Syndrome	1 (5)
Grade 3A	3/15 (20)
Bone marrow, involved	4 (20)
B-symptoms, present	3 (15)
Ann Arbor Stage III-IV	18 (90)
Involved nodal areas (n)	3 [1-5]
Largest lymph node (cm)	2.9 [1.5-5.6]
Extra-nodal disease, present	11 (55)
SUV_{max}	15.8 [3.9-53.7]

Patients (N=20)	Number (%); Median [Range]
FLIPI score, low	3/18 (17)
Intermediate	6/18 (33)
high	9/18 (50)
FLIPI-2 score, low	4/18 (22)
Intermediate	10/18 (56)
high	4/18 (22)
PRIMA PI, low	13 (72)
Intermediate	4 (22)
high	1 (6)
Previous systemic therapies (n)	1 [1-3]
Previous anti-CD20 antibody	**20 (100)**
Previous chemotherapy	**13 (72)**
Previous POD24	**16 (80)**

Dose adherence

Patients (N=20)	Number (%); Median [Range]
Cycles (n)	12 [1-12]
Cycle delay	**8 (40)**
Lenalidomide dose reduction	6 (30)
Lenalidomide delay	12 (60)
Lenalidomide discontinuation	**1 (5)**
Evorpacept dose reduction	0 (0)
Evorpacept delay	7 (38)
Evorpacept discontinuation	**1 (5)**
Rituximab omission	0 (0)

Protocol modified to allow treatment with G1 LFT elevation
Delays mainly driven by R^2-related complications

1 case of biopsy proven lenalidomide associated myocarditis

Treatment-emergent adverse events

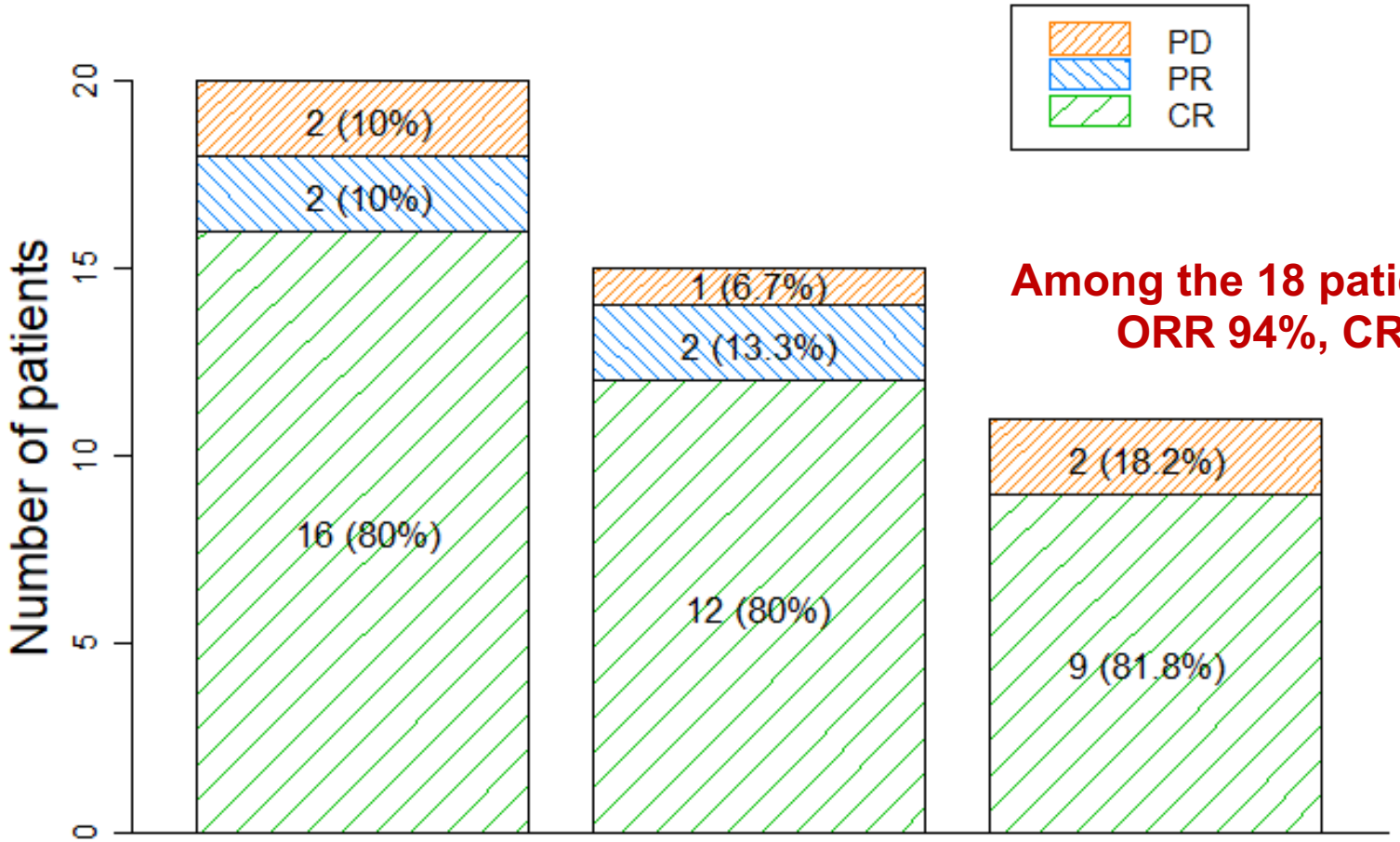
Patients (N=20)	Grade 1-2	Grade 3-4
Neutropenia	6 (30)	**11 (55)**
Infections	5 (23)	**6 (30)**
ALT increased	**12 (60)**	**3 (15)**
Skin rash	8 (40)	2 (10)
Anemia	**12 (60)**	2 (10)
AST increase	**12 (60)**	2 (10)
ALP increased	4 (20)	1 (5)
Infusion-related reaction	6 (30)	1 (5)
Myocarditis	0 (0)	1 (5)

3 patients received DL1; 17 patients DL2

No DLT observed

Patients (N=20)	Grade 1-2	Grade 3-4
Fatigue	**13 (65)**	0 (0)
Thrombocytopenia	**10 (50)**	0 (0)
Creatinine increase	**10 (50)**	0 (0)
Musculo-skeletal pain	9 (45)	0 (0)
Constipation	7 (35)	0 (0)
Nausea	5 (25)	0 (0)
COVID infection	5 (25)	0 (0)
Hyponatremia	4 (20)	0 (0)
Diarrhea	4 (20)	0 (0)
Dizziness	4 (20)	0 (0)
Bilirubin increase	4 (20)	0 (0)
Peripheral neuropathy	3 (15)	0 (0)
Headache	3 (15)	0 (0)
Hypercalcemia	3 (15)	0 (0)
Xerostomia	2 (10)	0 (0)
Mucositis	2 (10)	0 (0)

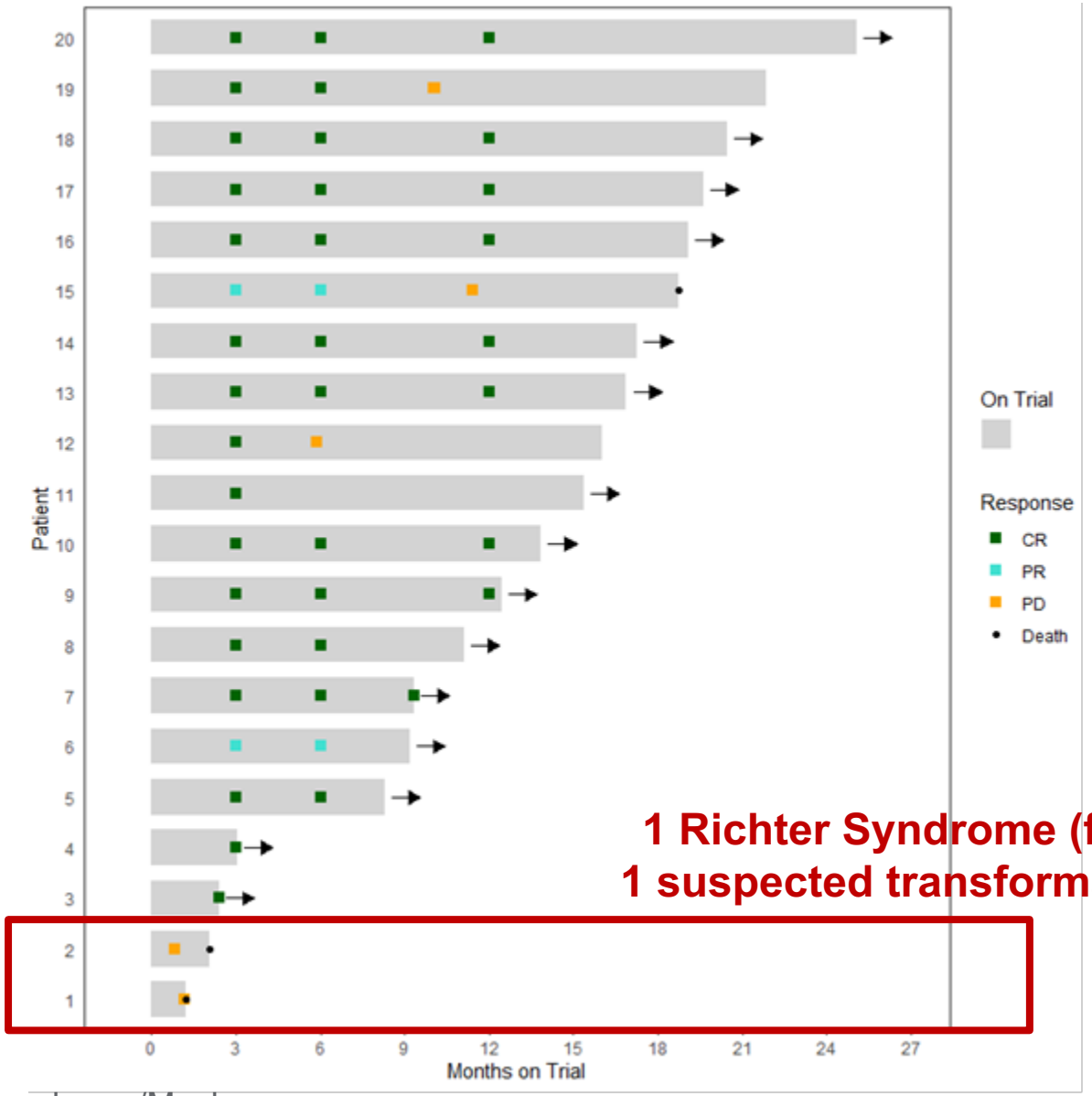
Efficacy results: Response rates



Among the 18 patients with iNHL
ORR 94%, CR rate 83%

Evaluable patients	**20**	**15**	**11**
	(3 cycles)	**(6 cycles)**	**(12 cycles)**

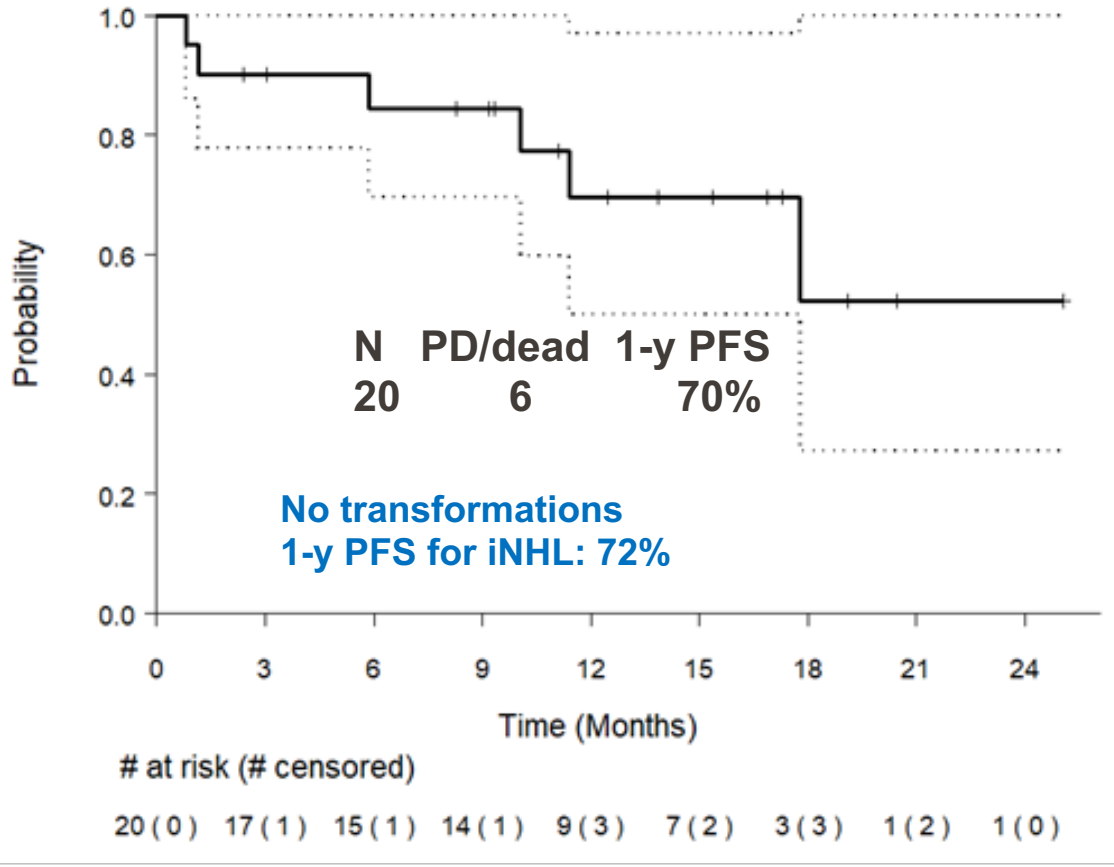
Efficacy results: duration of response



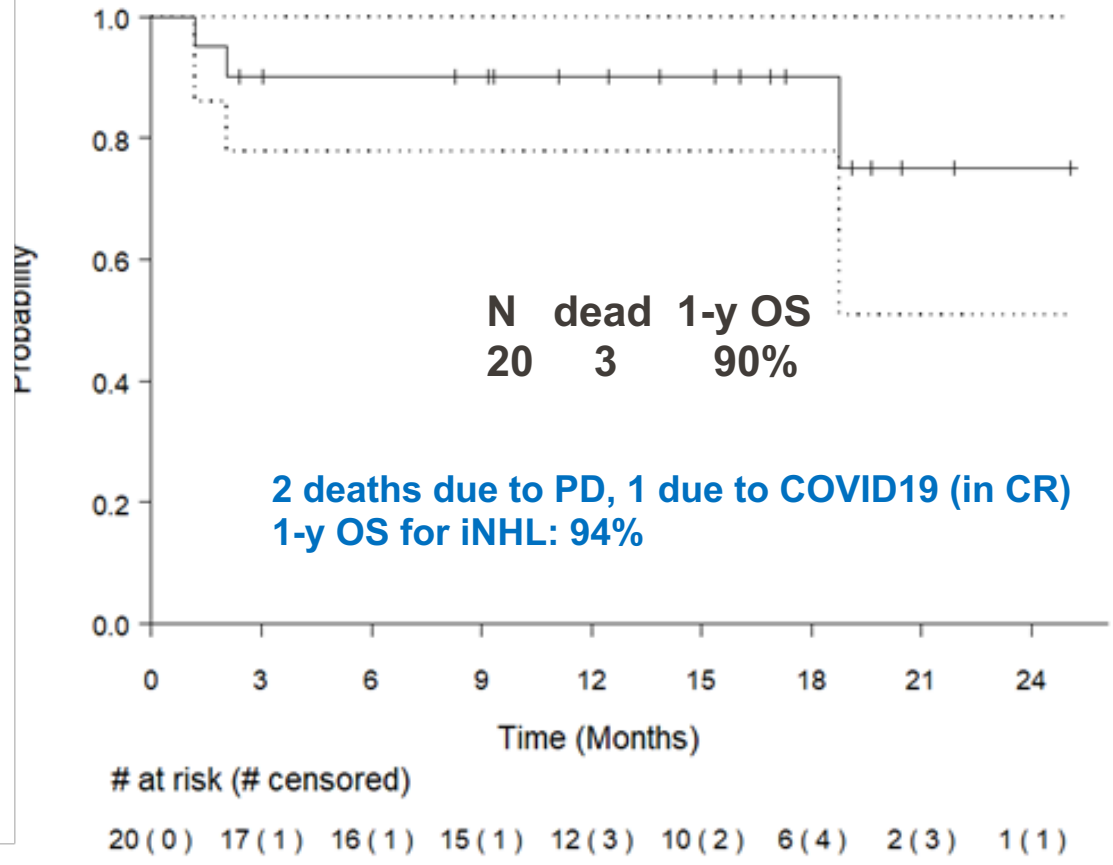
1 Richter Syndrome (from CLL)
1 suspected transformation of FL

Efficacy results: Progression-free and overall survival

Progression-free survival



Overall survival



… : 95% confidence interval

Median follow-up 16 months (95% CI, 12-20 months)

Conclusions and future directions

- The addition of evorpacept (ALX-148) to R^2 is a **well tolerated** salvage regimen for patients with relapsed B-NHL
- The combination results in **high CR rates** in patients with relapsed refractory iNHL (historical 30%)
- **Bulk RNA-sequencing** of pre-treatment and on-treatment (cycle 1) tissue biopsies is ongoing
- Phase 2 study at the **RP2D (60 mg/Kg IV Q4W)** for only 6 cycles is ongoing in patients with **previously untreated iNHL (N=24)**

Acknowledgments

Indolent Lymphoma
Loretta J Nastoupil
Christopher R Flowers
Sattva S Neelapu
Dai Chihara

Study coordinators
Jeffrey Davidson
Elizabeth McChesney

Lymphoma Department
Jason Westin
Sairah Ahmed
Luis E Fayad

Laboratory
Jared Henderson

Andrew Sabin Family Award

Biostatistics
Lei Fang

All patients and families
ALX Oncology

Questions: pstrati@mdanderson.org