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Outcomes of Patients with Large B-Cell Lymphomas and Progressive Disease Following CD19-Specific CAR T-cell Therapy

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Background

CD19-specific CAR T-cell therapy (CART) is effective in patients with relapsed/refractory (R/R) large B-cell lymphomas.

- Durable complete response (CR) rates of ~ 40%

Patients generally do not experience prolonged disease control if they are unable to achieve a CR.

Little data exists on outcomes of patients if they progress following CD19-specific CART.

Methods

We identified patients at our institution who met the following criteria:

1) Developed progressive disease (PD) after CD19-specific CART

2) Did not receive any protocol-specified anti-lymphoma therapy after CART infusion

3) Treated for one of the following histologies:

- Diffuse large B-cell lymphoma (DLBCL)
- Transformed follicular lymphoma (tFL)
- Primary mediastinal B-cell lymphoma (PMBCL)
- High-grade B-cell lymphoma (HGBCL)

Methods

Primary Analysis: Overall Survival (OS) after PD

Secondary Analyses: OS based on the following characteristics

1) Timing of PD

- **Initial PD** – progression on initial disease response assessment
- **Delayed PD** – progression on subsequent disease response assessment

2) Use of bridging therapy – any anti-lymphoma therapy given between T-cell collection and CART

3) Ability to receive subsequent therapy after PD

Methods

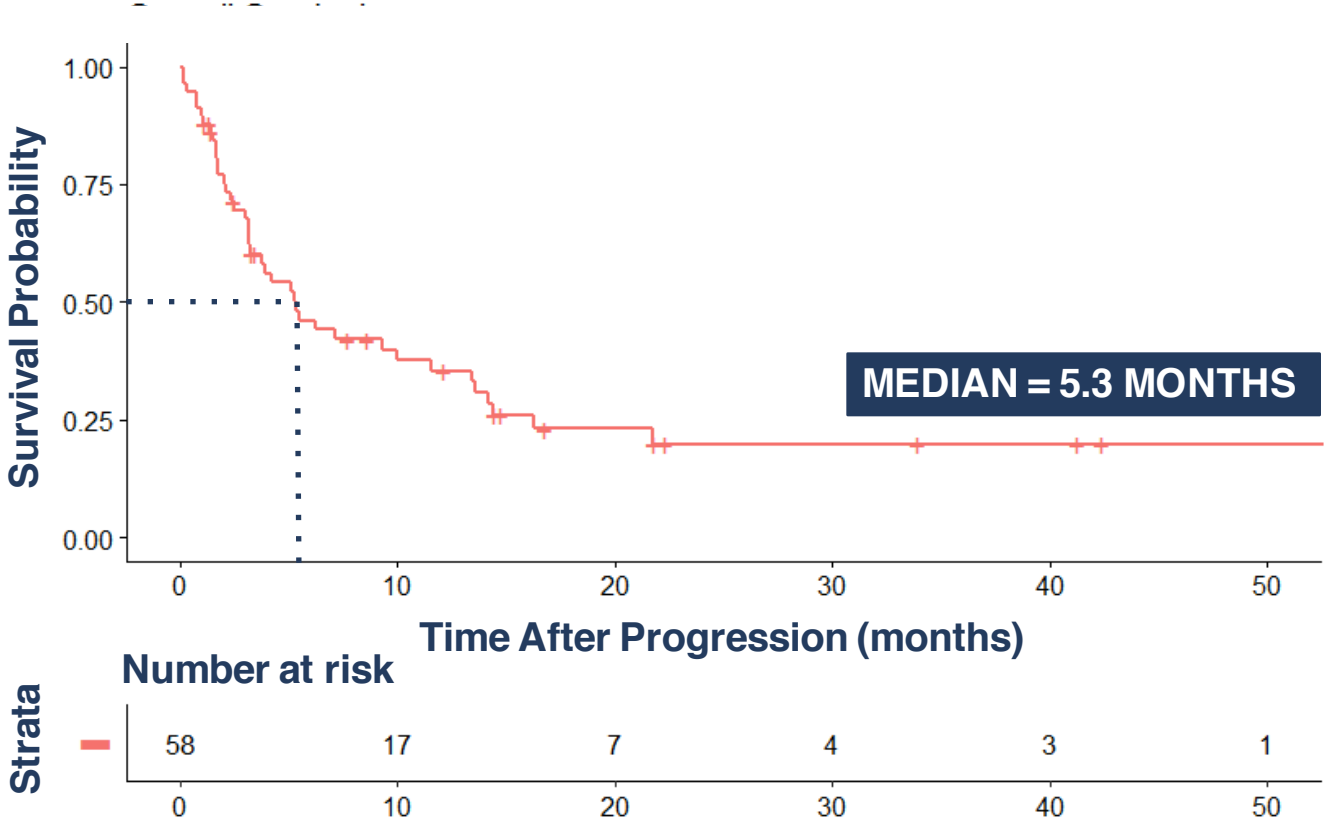
NOT INCLUDED IN THIS ANALYSIS:

CART product and construct
CART dose
Lymphodepleting chemotherapy regimen
Inflammatory markers
Cytokine release syndrome
Neurotoxicity
Potential mechanism(s) of escape and progression

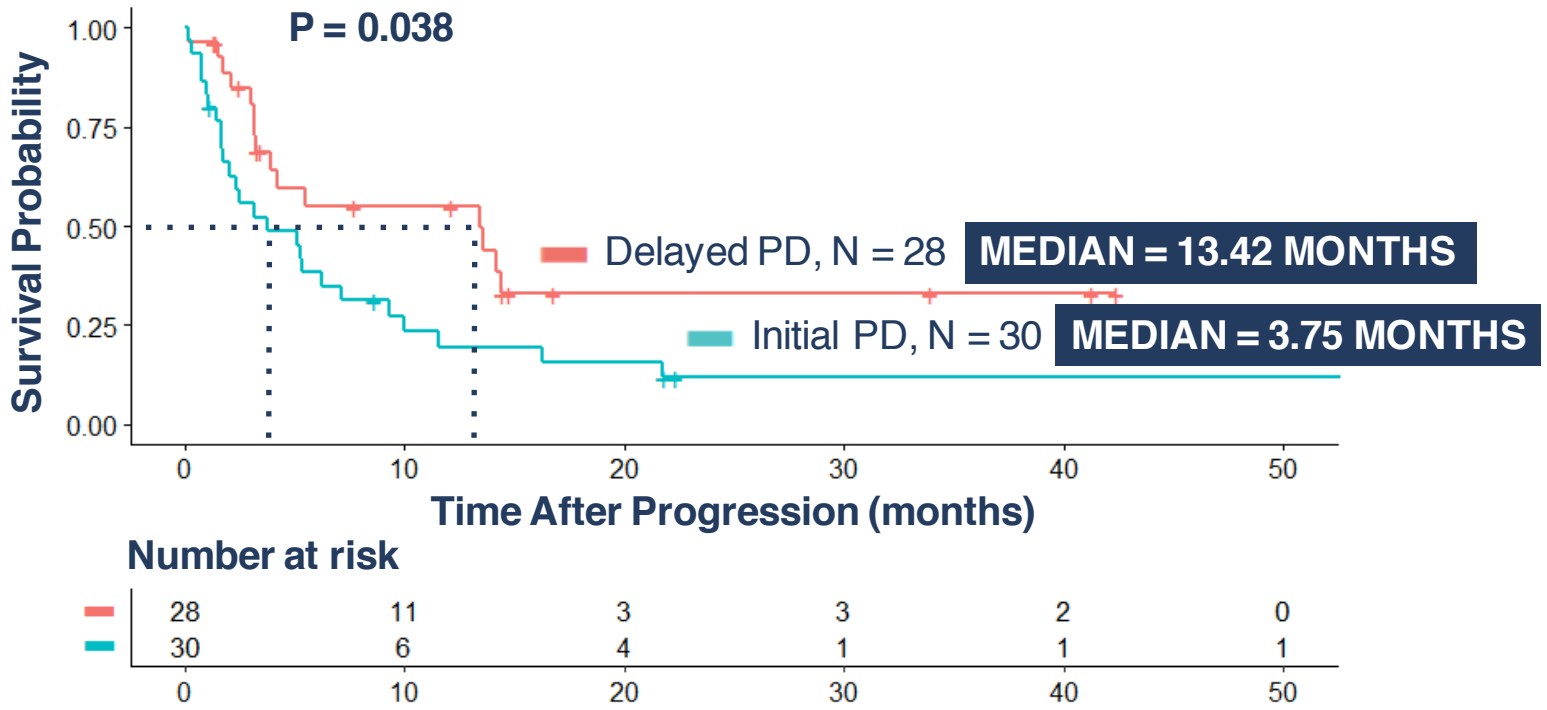
Results: Patient Characteristics

CHARACTERISTICS	TOTAL (N = 58)	INITIAL PD (N = 30)	DELAYED PD (N = 28)	P value
Median Age	60 (26 - 75)	58 (29 - 70)	60.5 (26 - 75)	0.251
Histology				0.536
DLBCL	34 (58.6%)	19 (63.3%)	15 (53.6%)	
HGBCL	12 (20.7%)	4 (13.3%)	8 (28.6%)	
PMBCL	3 (5.2%)	2 (6.7%)	1 (3.6%)	
tFL	9 (15.5%)	5 (16.7%)	4 (14.3%)	
IPI				0.358
0-1	12 (20.7%)	4 (13.3%)	8 (28.6%)	
2-3	37 (63.8%)	21 (70.0%)	16 (57.1%)	
4-5	9 (15.5%)	5 (16.7%)	4 (14.3%)	
Median LDH (pre-CART)	210 (111 - 2339)	250 (117 - 2339)	189 (111 - 691)	**0.026**

Poor OS after progressive disease



Initial PD is associated with inferior survival

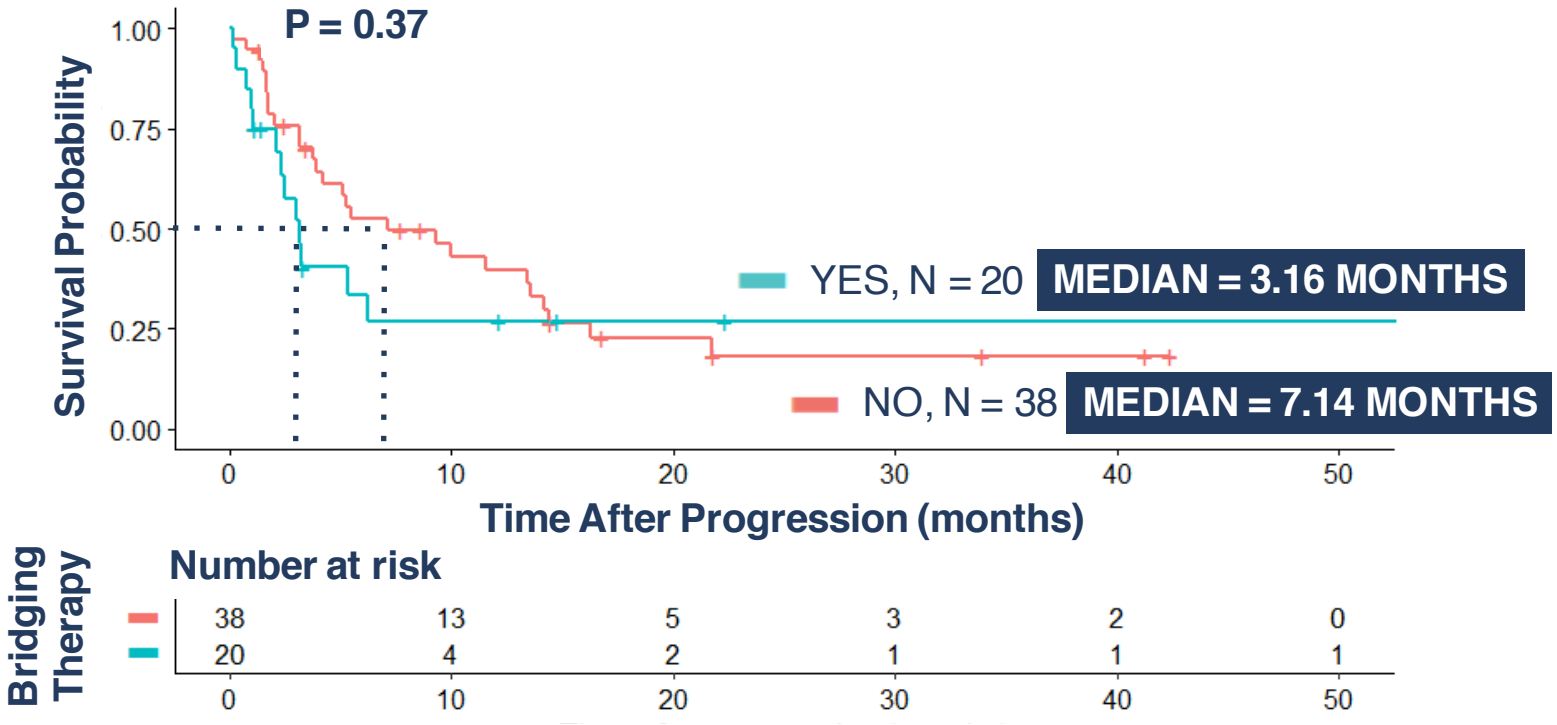


Results: Bridging Therapy

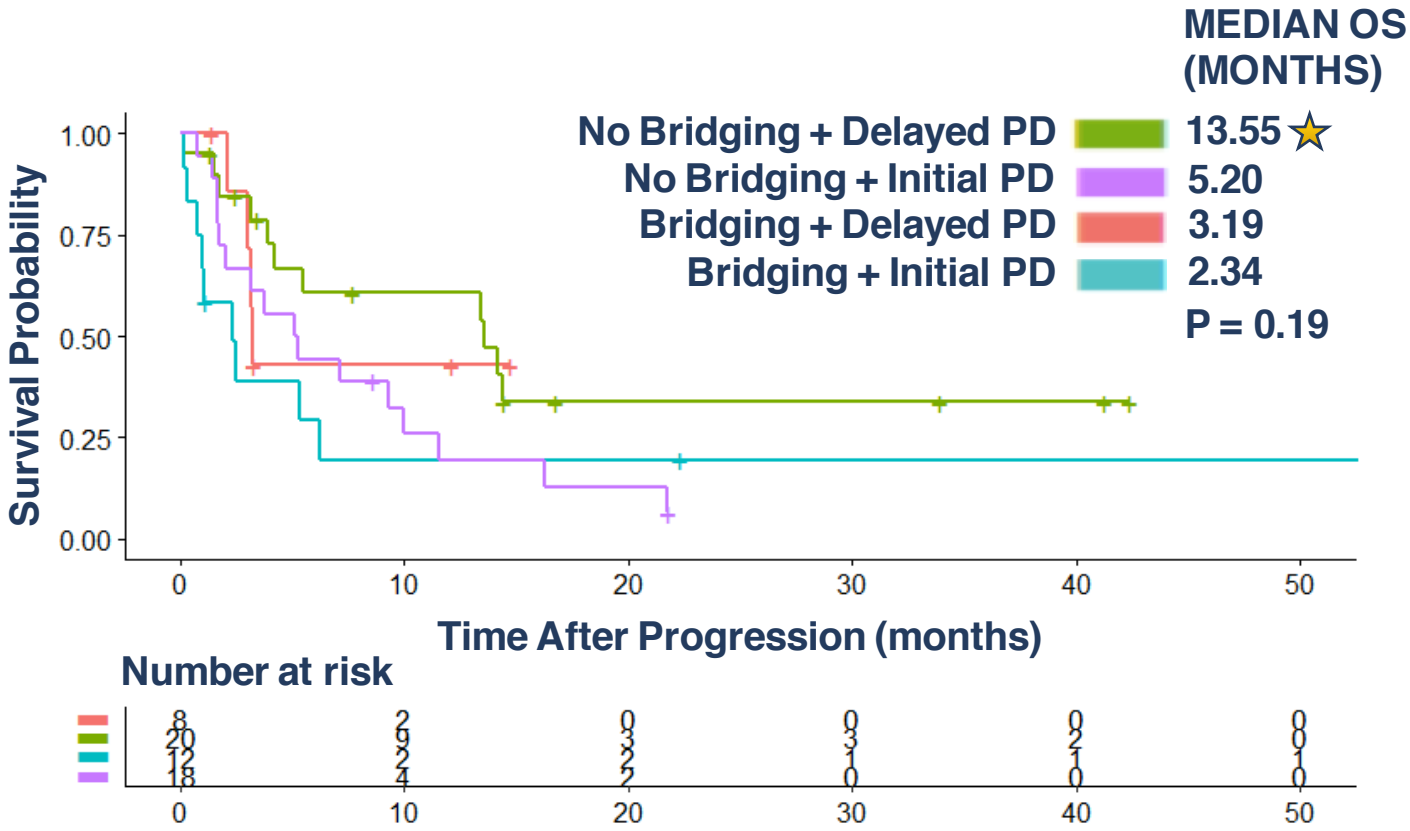
	TOTAL N = 20 (34.5%)	INITIAL PD N = 12 (40.0%)	DELAYED PD N = 8 (28.6%)
Chemotherapy +/- steroids	9 (45.0%)	4 (33.3%)	5 (62.5%)
Intrathecal chemotherapy	1 (5.0%)	0 (0.0%)	1 (12.5%)
Novel/targeted agent +/- steroids	5 (25.0%)	4 (33.3%)	1 (12.5%)
Steroids	5 (25.0%)	4 (33.3%)	1 (12.5%)

BRIDGING THERAPY:
Any anti-lymphoma therapy given between T-cell collection and CART

Impact of bridging therapy on survival



Impact of bridging therapy and type of progression on survival



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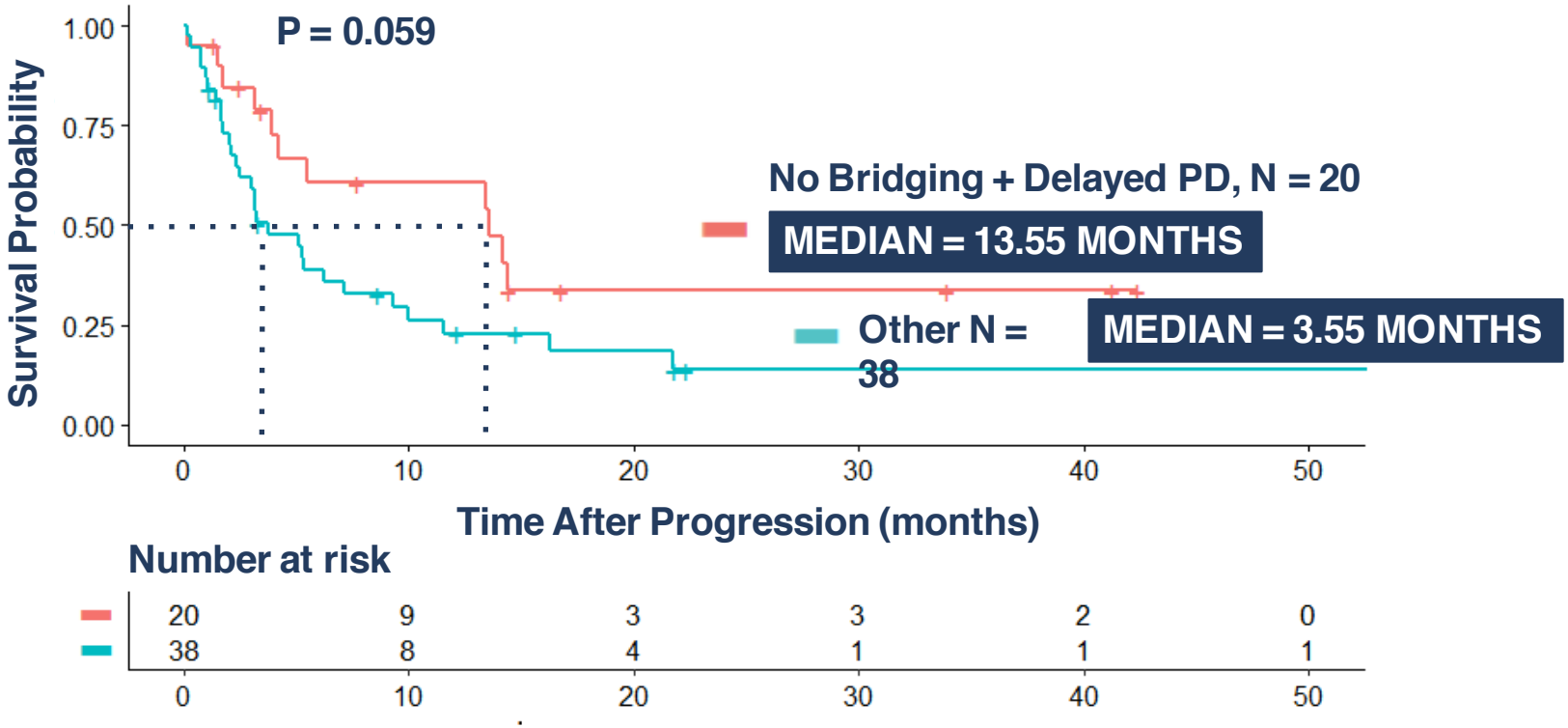

Next treatment after progression

INITIAL SUBSEQUENT THERAPY	TOTAL (N = 44)
CAR T-CELL	14
NOVEL THERAPY	13
CHEMOTHERAPY +/- R	7
ANTI-PD1 INHIBITOR	4
RADIOTHERAPY	4
INTRATHECAL	1
ALLOGENEIC HSCT	1

44 (76%) patients received ≥ 1 subsequent therapies after PD.

Patients receiving ≥ 1 subsequent therapies after PD had a lower risk of death, compared to those who did not.

- HR 0.48, 95% CI 0.234-0.99, P = 0.0476

6 (10%) patients enrolled onto a clinical trial as next line therapy.

5 (9%) patients eventually received an allogeneic HSCT, 2 of whom are still alive.

Conclusions

Patients with PD following CD19-specific CART have poor outcomes.

Patients with initial PD had inferior overall survival.

More effective strategies are needed to improve CR rates and prevent PD.

Planning for the potential of PD following CART should figure into the treatment algorithm for R/R disease.

These data set the stage for novel combinations in the future (eg bridging therapy, maintenance therapy).

These data should inform clinical trial design.

Acknowledgments

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