Safety and Efficacy of Third Generation CD20 Targeted CAR-T (MB-106) for Treatment of Relapsed/Refractory B-NHL and CLL

Mazyar Shadman, MD,MPH[1,2], Cecilia Yeung, MD[1], Mary Redman, PhD[1], Sang Lee, Ph.D.[1], Dong Lee, B.S.[1], Susan Ra, BS[1], Chaitra S. Ujjani, MD[1,2], Bruce J. Dezube, MD[3], Christina Poh, MD[1,2], Edus H. Warren, MD, PhD[1,2], Aude G. Chapuis, MD[1,2], Damian J. Green, MD[1,2], Andrew J. Cowan, MD[1,2], Ryan D. Cassaday, MD[1,2], Hans-Peter Kiem, MD PhD[1,2], Jordan Gauthier, MD[1,2], Cameron J. Turtle, MBBS, PhD[1,2], Ryan C. Lynch, MD[1,2], Stephen D. Smith, MD[1,2], Ajay K Gopal, MD[1,2], David G. Maloney, MD, PhD[1,2] and Brian G. Till, MD[1,2]

1.Fred Hutchinson Cancer Research Center, Seattle WA; 2.University of Washington, Seattle WA; 3.Mustang Bio, Worcester, MA

INTRODUCTION

- Chimeric antigen receptor (CAR) T cell therapy is now part of standard of care for relapsed/refractory B-NHLs
- Only 30-40% of DLBCL patients have durable remissions and there is limited follow-up for MCL and FL patients treated with CD19 CARs. Safety profile is a potential barrier for treating patients especially those with low-grade B-NHL histologies given the availability of alternative options
- CD20-targeted CAR-T is another adoptive immunotherapy option that could be potentially utilized instead of or in sequence with CD19 CAR-T
- We present interim results of our ongoing phase I/II clinical trial investigating safety and efficacy of a CD20 CAR-T for high-risk B-NHLs (NCT03277729)

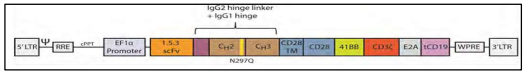
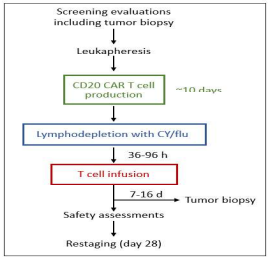


Figure 1: Lentiviral vector encoding bicistronic 3rd generation fully human CAR and truncated CD19 transduction marker

METHODS

Single institution phase I/II study

- Eligibility: previously treated B-NHLs CD20+ B-NHLs including but not limited to:
  - Large cell lymphoma after 2 lines of treatment (including anthracycline and an anti-CD20 antibody
  - FL and MCL after at least 1 prior line of treatment
  - CLL: Prior BTKi or Venetoclax failure (progression or intolerance)
  - Prior treatment with a CD19 CAR is allowed after recovery of normal B cells (≥ 20 B cells/μL)
- **Dose levels (DL) (cells/kg):** Dose level 0: 1 x 10^5 ; **Dose level 1: 3.3 x 10^5 ;** Dose level 2: 1 x 10^6 ; Dose level 3: 3.3 x 10^6 ; Dose level 4: 1 x 10^7
- Treatment is given in the outpatient setting (except for first pt treated on each dose level)



RESULTS

Table 1: Baseline information

N = 20	
Age, median (range)	**59 (43-81)**
Female sex, n(%)	**9 (45%)**
FL n(%)	**15 (75%)**
POD24	10/15 (67%)
History of transformation	3/15 (20%)
Prior lines of therapy median (range)	5 (1-12)
Prior PI3K inhibitor	6/15 (40%)
MCL n(%)	**2 (10%)**
Prior lines of therapy median (range)	6 (5-7)
Prior ASCT	2/2 (100%)
Prior BTK inhibitor	2/2 (100%)
CLL n(%)	**1 (5%)**
Complex karyotype	1/1 (100%)
Prior BTK inhibitor	1/1 (100%)
Prior Venetoclax	1/1 (100%)
DLBCL n(%)	**1 (5%)**
Transformed lymphoma	1/1 (100%)
Prior lines of therapy	5
WM n(%)	**1 (5%)**
Prior BTK inhibitor	1/1 (100%)
Prior lines of therapy	10

Table 2: Efficacy data

Histology	Best Response by Lugano PET criteria*	All dose levels	Dose level 0 (n=1)	Dose level 1 (n=2)	Dose level 2 (n=6)	Dose level 3 (n=9)	Dose level 4 (n=2)
			1 x 10^5 cells/kg	3.3 x 10^5 cells/kg	1 x 10^6 cells/kg	3.3 x 10^6 cells/kg	1 x 10^7 cells/kg
FL (n=15)	ORR, n(%)	14/15 (93%)	1	1	4	6	2
	CR, n(%)	11/15 (73%)	1	1	2	5	2
	PR,n (%)	3/15 (20%)	-	-	2	1	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	1/15 (7%)	-	1	-	-	-
MCL (n=2)	ORR, n(%)	2/2 (100%)	-	-	2	-	-
	CR,n(%)		-	-	-	-	-
	PR,n (%)	2/2 (100%)	-	-	2	-	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	-	-	-	-	-	-
CLL (n=1) *	ORR, n(%)	1/1 (100%)	-	-	-	1	-
	CR,n(%)	1/1 (100%)	-	-	-	1	-
	PR,n (%)	-	-	-	-	-	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	-	-	-	-	-	-
DLBCL (n=1)	ORR, n(%)	1/1 (100%)	-	-	-	1	-
	CR,n(%)	1/1 (100%)	-	-	-	1	-
	PR,n (%)	-	-	-	-	-	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	-	-	-	-	-	-
WM/LPL (n=1) *	ORR, n(%)	1/1 (100%)	-	-	-	1	-
	CR,n(%)	-	-	-	-	-	-
	PR,n (%)	1/1 (100%)	-	-	-	1	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	-	-	-	-	-	-
All patients (n=20)	ORR, n(%)	19/20 (95%)	1/1 (100%)	1/2 (50%)	6/6 (100%)	9/9 (100%)	2/2 (100%)
	CR, n(%)	13/20 (65%)	1/1 (100%)	1/2 (50%)	2/6 (33%)	7/9 (78%)	2/2 (100%)

Table 3: Adverse events of interest

	FL (n=15)					Other (MCL,CLL,DLBCL,LPL) (n=5)					All patients (n=20)				
	Grade n(%)					Grade n(%)					Grade n(%)				
	1	2	3	4	Any	1	2	3	4	Any	1	2	3	4	Any
CRS *	4 (27%)	1 (6%)	-	-	5 (33%)	1 (20%)	2 (40%)	-	-	3 (60%)	5 (25%)	3 (15%)	-	-	8 (40%)
ICANS *	-	-	-	-	-	1 (20%)	1 (20%)	-	-	2 (40%)	1 (5%)	1 (5%)	-	-	2 (10%)
Neutropenia	-	-	6 (40%)	8 (53%)	14 (93%)	-	-	1 (20%)	4 (80%)	5 (100%)	-	-	7 (35%)	12 (60%)	19 (95%)
Thrombocytopenia	-	3 (20%)	-	2 (13%)	5 (33%)	-	1 (20%)	-	1 (20%)	2 (40%)	-	4 (20%)	-	3 (15%)	7 (35%)
Anemia	-	3 (20%)	5 (33%)	1 (7%)	9 (60%)	-	1 (20%)	1 (20%)	-	2 (40%)	-	4 (20%)	6 (30%)	1 (5%)	11 (55%)
Febrile Neutropenia	1 (7%)	-	3 (20%)	-	4 (27%)	-	-	-	-	-	1 (5%)	-	3 (15%)	-	4 (20%)
Neuropathic pain	-	-	-	-	-	-	-	1 (20%)	-	1 (20%)	-	-	1 (5%)	-	1 (5%)

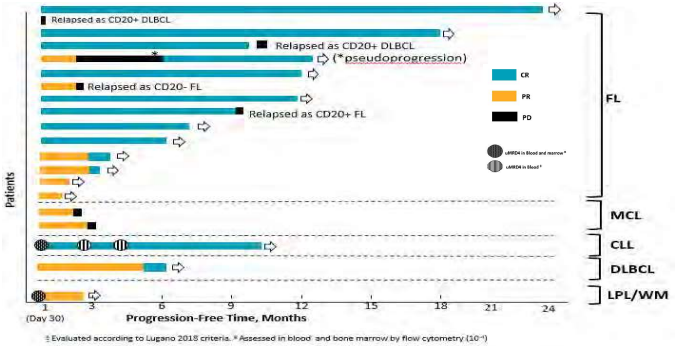


Figure 1: Swimmer plot

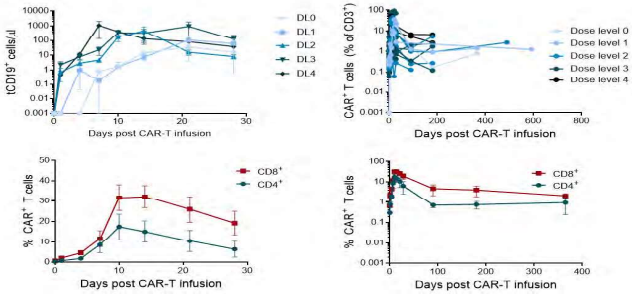


Figure 2: CAR-T expansion/persistence

HIGHLIGHTS

- Favorable safety profile for this outpatient CAR-T
  - No grade 3 or 4 CRS or ICANS
  - ICANS: Only 2 patients with grade 1-2 (10%)
  - No ICANS (any grade) in FL patients
- **High Efficacy**
  - High rate of durable responses in all B-NHLs
  - The only CLL patient in CR and uMRD
  - The only DLBCL patient in CR
  - The only WM patient with ongoing response
  - FL cohort:
    - ORR (93%),CR (73%)
- **CAR-T persistence in all dose levels**
  - Faster expansion with higher dose levels but comparable levels by day 28 between all dose levels

SUMMARY

- MB-106 is a 3rd generation CD20 targeting CAR-T with both 4-1BB and CD28 co-stimulatory domains
- In this single-institution study, we observed very favorable safety profile and high rate of complete and durable responses
- The current study is open to enrollment for all CD20+ B-NHLs and CLL including patients with prior treatment with CAR-T
- A multicenter study will be launched in 2022

Abstract #3872 #ASH21

@mshadman