Immunotherapy Using a 3rd Generation CD20 CAR T-Cell (MB-106) for B-NHL and CLL

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INTRODUCTION

- CAR-T therapy is effective for treatment of patients with relapsed/refractory B-NHL
- Only 30-40% of DLBCL patients have durable remissions with CD19 CARs and there is limited follow-up for MCL and FL patients treated with CD19 CARs.
- CD20-targeted CAR-T is another potential adoptive immunotherapy option that could be utilized instead of 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)

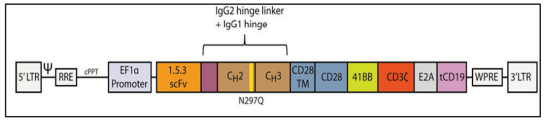

Figure 1: Lentiviral vector encoding bicistronic 3rd generation fully human CAR and truncated CD19 transduction marker

METHODS

Single institution phase I/II study

- Eligibility: CD20+ B-NHLs
  - 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)
  - Other previously treated B-NHLs
  - Prior treatment with a CD19 CAR is allowed after recovery of normal B cells (≥ 20 B cells/μL)
- **Lymphodepletion (LD):**
  - Cyclophosphamide and Fludarabine (Cy-Flu)
- **Dose levels (DL):**
  - Dose level 0: 1 x 10^5 cells/kg
  - **Dose level 1: 3.3 x 10^5 cells/kg**
  - Dose level 2: 1 x 10^6 cells/kg
  - Dose level 3: 3.3 x 10^6 cells/kg
  - Dose level 4: 1 x 10^7 cells/kg

RESULTS

Table 1: Baseline information

N = 15	
Age, median (range)	**59 (43-81)**
Female sex, n(%)	**9 (60%)**
FL n(%)	**11 (73%)**
POD24	8/11 (73%)
History of transformation	3/11 (27%)
Prior lines of therapy median (range)	4 (1-14)
Prior PI3K inhibitor	4/11 (36%)
MCL n(%)	**2 (13%)**
Prior lines of therapy median (range)	6 (5-7)
Prior ASCT	2/2 (100%)
Prior BTK inhibitor	2/2 (100%)
CLL n(%)	**1 (6.5%)**
Complex karyotype	1/1 (100%)
Prior BTK inhibitor	1/1 (100%)
Prior Venetoclax	1/1 (100%)
DLBCL n(%)	**1 (6.5%)**
Transformed lymphoma	1/1 (100%)
Prior lines of therapy	5

RESULTS

Table 2: Efficacy Data (N=15)

Histology	Best Response by Lugano PET criteria†	All dose levels	Dose level 0 (n=1)	Dose level 1 (n=2)	Dose level 2 (n=4)	Dose level 3 (n=6)	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=11)	ORR, n(%)	**10/11 (91%)**	1/1	1/2	2/4	4/6	2/2
	CR, n(%)	**9/11 (82%)**	1/1	1/2	1/4	4/6	2/2
	PR,n (%)	**1/11 (9%)**	-	-	1/4	-	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	**1/11 (9%)**	-	1/2	-	-	-
MCL (n=2)	ORR, n(%)	**2/2 (100%)**	-	-	2/4	-	-
	CR,n(%)		-	-	-	-	-
	PR,n (%)	**2/2 (100%)**	-	-	2/4	-	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	-	-	-	-	-	-
CLL (n=1)	ORR, n(%)	**1/1 (100%)**	-	-	-	1/6	-
	CR,n(%)	**1/1 (100%)**	-	-	-	1/6	-
	PR,n (%)		-	-	-	-	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	-	-	-	-	-	-
DLBCL (n=1)	ORR, n(%)	**1/1 (100%)**	-	-	-	1/6	-
	CR,n(%)		-	-	-	-	-
	PR,n (%)	**1/1 (100%)**	-	-	-	1/6	-
	SD,n (%)	-	-	-	-	-	-
	PD,n (%)	-	-	-	-	-	-
All patients (n=15)	ORR, n(%)	**14/15 (93%)**	1/1 (100%)	1/2 (50%)	4/4 (100%)	6/6 (100%)	2/2 (100%)
	CR, n(%)	**10/15 (67%)**	1/1 (100%)	1/2 (50%)	1/4 (25%)	5/6 (83%)	2/2 (100%)

†Cheson, et al. J Clin Oncol, 2014

Table 3: Adverse Events of interest

	FL (n=11)					Other Histologies (MCL,CLL,DLBCL) (n=4)					All patients (n=15)				
	Grade n(%)					Grade n(%)					Grade n(%)				
	1	2	3	4	Any	1	2	3	4	Any	1	2	3	4	Any
CRS [1]	**3 (27%)**	**1 (9%)**	-	-	**4 (36%)**	-	**2 (50%)**	-	-	**2 (50%)**	**3 (20%)**	**3 (20%)**	-	-	**6 (40%)**
ICANS [2]	-	-	-	-	-	-	**1 (25%)**	-	-	**1 (25%)**	-	**1 (6.5%)**	-	-	**1 (6.5%)**
Headache	3 (27%)	3 (27%)	1 (9%)	-	7 (64%)	1 (25%)	-	-	-	1 (25%)	4 (26%)	3 (20%)	1 (6.5%)	-	8 (53%)
Neuropathic pain	-	-	-	-	-	-	-	1 (25%)	-	1 (25%)	-	-	1 (6.5%)	-	1 (6.5%)
Febrile neutropenia	1 (9%)	-	2 (18%)	-	3 (27%)	-	-	-	-	-	1 (6.5%)	-	2 (13.5%)	-	3 (20%)
Fever	1 (9%)	1 (9%)	-	-	2 (18%)	-	2 (50%)	-	-	2 (50%)	1 (6.5%)	3 (19.5%)	-	-	4 (26%)
Neutropenia	-	-	4 (36%)	6 (54%)	10 (91%)	-	-	1 (25%)	3 (75%)	4 (100%)	-	-	5 (33%)	9 (60%)	14 (93%)
Thrombocytopenia	-	2 (18%)	-	1 (9%)	3 (27%)	-	2 (50%)	-	1 (25%)	3 (75%)	-	4 (26%)	-	2 (13%)	6 (40%)

1- Lee et al, Blood, 2014 ; 2- Lee, et al, BBMT, 2019

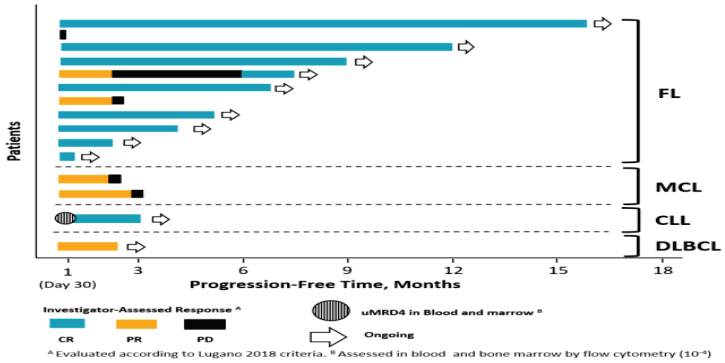

Figure 2: Swimmer Plot

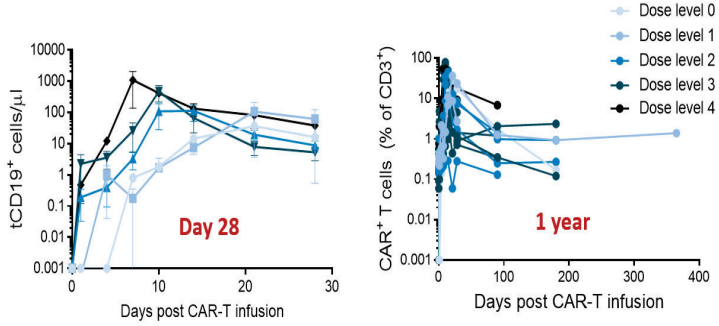

Figure 3: CAR-T Expansion/Persistence

HIGHLIGHTS

- **Favorable Safety profile**
  - CRS: only grade 1 (20%) and 2 (20%)
  - ICANS: only grade 2 (6.5%) – No ICANS in FL patients
- **High Efficacy**
  - High response rates in all B-NHLs – only CLL patient in CR and uMRD
  - FL cohort:
    - ORR (91%),CR (82%)
    - Dose levels 3 and 4: CR (100%)
    - Durable CRs – no relapse in CR patients – longest ~16 months (May 2021)
- **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 the near future