GB261, AN FC-FUNCTION ENABLED AND CD3 AFFINITY DE-TUNED CD20/CD3 BISPECIFIC ANTIBODY, DEMONSTRATED A HIGHLY ADVANTAGEOUS SAFETY/EFFICACY BALANCE IN AN ONGOING FIRST-IN-HUMAN STUDY IN PATIENTS WITH RELAPSED/REFRACTORY NON-HODGKIN LYMPHOMA (R/R B-NHL)

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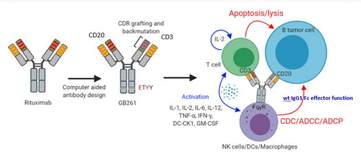
INTRODUCTION

GB261 is a novel and highly differentiated CD20/CD3 bispecific T cell engager antibody computationally designed to maintain Fc effector function, i.e., antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement-dependent cytotoxicity (CDC) to broaden the mechanisms of action (MOA) for tumor cell killing. Furthermore, the "imbalanced" design of GB261 integrates de-tuned CD3 binding to reduce CRS incidence and improve safety features of the Fc effector function. Extensive pre-clinical studies have shown that GB261 has a highly advantageous safety/efficacy balance.[1]



METHODS

GB261-001 Study *(NCT04923048)*
A Phase I/II, Single Arm, Multicenter Study

Key Enrollment Criteria

A. ECOG: 0-1
B. Disease:
  a) CD20+ B-NHL
  b) no available standard of care treatments
  (R/R>=1 prior line for dose-escalation; R/R>=2 prior lines for dose-expansion)
C. Adequate organ function
  a) Platelet count ≥ 75 × 10^9/L; neutrophil count ≥ 1.0 × 10^9/L; Hemoglobin≥8g/dL
  b) AST and ALT ≤ 3 × ULN, total bilirubin ≤ 1.5 × ULN
  c) Calculated creatinine clearance(Cockcroft-Gault) ≥50 mL/min

Treatment Schedule

- 1 cycle=3 weeks
- QW for first 2 cycles
- Q3W from cycle 3
- till progression or intolerable toxicity

Tumor Assessment

- 2 cycles (6 weeks), then
- 1st year: every 4 cycles (12 weeks)
- 2nd year: every 8 cycles (24 weeks)

Primary Objectives

- Phase I: safety/tolerability/DLT/MTD
- Phase II: recommended dose(s)/regimen, efficacy

RESULTS

As of June 17, 2023, 47 r/r B-NHL patients (DLBCL:76.6%; FL:23.4%) were enrolled at flat or step-up doses of GB261 ranging from 1mg to 300 mg. Median age was 60.0 years (range: 28-81), 55.3% of patients were male. Median prior lines of therapy were 3 (range: 1-10). 78.7% of patients were refractory to any anti-CD20 therapy, 70.2% refractory to their last systemic therapy. Median time since last prior therapy to first study treatment was 1.9 months.

Table 1. Baseline Characteristics

	R/R DLBCL (N=36)	R/R FL (N=11)	All patients (N=47)
Age, year			
median(range)	63.0 (36-81)	57.0 (28-72)	60.0 (28-81)
Sex			
female	15 (41.67%)	6 (54.55%)	21 (44.68%)
male	21 (58.33%)	5 (45.45%)	26 (55.32%)
Race			
White	6 (16.67%)	2 (18.18%)	8 (17.02%)
Asian	30 (83.33%)	9 (81.82%)	39 (82.98%)
ECOG performance status			
0	21 (58.33%)	10 (90.91%)	31 (65.96%)
1	15 (41.67%)	1 (9.09%)	16 (34.04%)
Ann Arbor stage			
I	0	0	0
II	2 (5.56%)	0	2 (4.26%)
III	7 (19.44%)	3 (27.27%)	10 (21.28%)
IV	27 (75.00%)	8 (72.73%)	35 (74.47%)
Extranodal disease, No, (%)	29 (80.56%)	8 (72.73%)	37 (78.72%)
Prior therapy, No. (%)			
Anti-CD20 Ab	35 (97.22%)	11 (100.00%)	46 (97.87%)
Anthracycline	36 (100.00%)	10 (90.91%)	46 (97.87%)
CART	3 (8.33%)	1 (9.09%)	4 (8.51%)
ASCT	3 (8.33%)	1 (9.09%)	4 (8.51%)
Prior lines of therapy, No.			
Median	3.0	2.0	3.0
Range	1-6	1-10	1-10
≥3	19 (52.78%)	5 (45.45%)	24 (51.06%)
Treatment-refractory to:			
anti-CD20 primary refractory, No. (%)	23 (63.89%)	8 (72.73%)	31 (65.96%)
last line of systemic therapy, No. (%)	27 (75.00%)	6 (54.55%)	33 (70.21%)
last anti-CD20 therapy, No. (%)	31 (86.11%)	9 (81.82%)	40 (85.11%)
any prior therapy, No. (%)	32 (88.89%)	9 (81.82%)	41 (87.23%)
any prior anti-CD20 therapy, No. (%)	28 (77.78%)	9 (81.82%)	37 (78.72%)

Efficacy

In efficacy evaluable patients (n=22) from 3mg to 100mg, with at least 75% dose exposure before the first radiographic assessment, the median duration of study follow-up was 4.5 months (95%CI: 4.0, 7.4). The overall response rate (ORR) was 73% (16/22), and complete response rate (CRR) was 45.5% (10/22). ORR and CRR were 100% and 100% in 3mg, 56% and 22% in 10mg, 67% and 33% in 30mg. At 100mg dose, there were 5 evaluable patients, with ORR 100% (5/5), CRR 80% (4/5) and PR (20%, 1/5; mosunetuzumab-refractory rrDLBCL patient). Median time to response (TTR) was 1.3 months (95%CI: 1.2, 1.5), the same as median time to CR. Median duration of response (DOR) was not reached.

Table 2. Efficacy Summary

	3mg(N=2)	10mg(N=9)	30mg(N=6)	100mg(N=5)	All(N=22)
ORR	100.0%(2/2)	55.6%(5/9)	66.7%(4/6)	100.0%(5/5)	72.7%(16/22)
CR	100.0%(2/2)	22.2%(2/9)	33.3%(2/6)	80.0%(4/5)	45.5%(10/22)
PR	0%	33.3%(3/9)	33.3%(2/6)	20.0%(1/5)	27.3%(6/22)

Figure 1. Maximum Change From Baseline of Target Lesion After GB261 Therapy

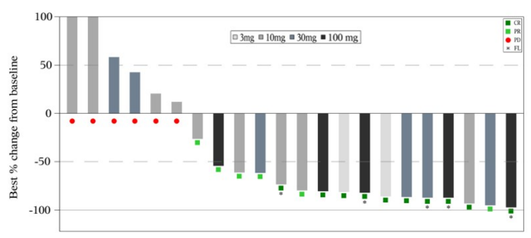
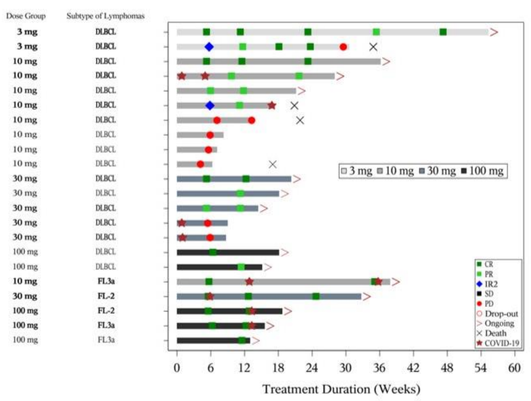


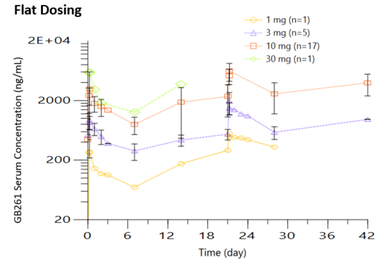
Figure 2. Time on Treatment and Duration of Response



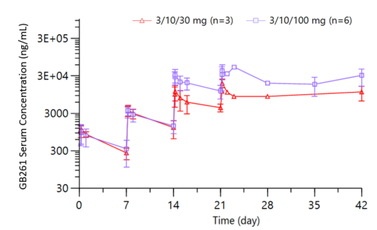
Pharmacokinetics (PK)

- GB261 generally exhibits linear PK in the dose range studied (1mg-100mg).
- Effective half-life appeared to be 2-3 weeks. Potential dosing frequency of every 3-4 weeks

Flat Dosing



SUD Dosing



Safety

In safety evaluable patients (n=47), the median duration of study follow-up was 4.1 months (95%CI: 2.9, 5.3). The most common TEAEs were COVID-19 infection (40.4%; grade 1 or 2: 27.6%; grade >=3: 12.8%) and neutropenia (31.9%; grade 1or 2: 14.9%; grade >=3: 17.0%).

- **CRS of GB261 was mild and transient**
  — Low incidence: 12.8%(14.3% in 100mg) all grade 1 or 2; no grade 3; no anti-IL6 used; no dose interruption
  — For flat-dosing: median onset date: day 2, median duration: 5.8hrs
  — For step-up dosing: day 16 (1 day after the target dose firstly given for step-up-dosing) , median duration: 16.7hrs
- **ICANS was not reported.**

Table 3. Safety Profile

	1mg	3mg	10mg	30mg	100mg	300mg	Total
N	N=1	N=5	N=18	N=7	N=14	N=2	N=47
Any adverse event	1 (100.0%)	5 (100.0%)	18 (100.0%)	7 (100.0%)	12 (85.7%)	2 (100.0%)	45 (95.7%)
Any drug-related event	0	4 (80.0%)	18 (100.0%)	7 (100.0%)	10 (71.4%)	1 (50.0%)	40 (85.1%)
Any AE leading to interruption	0	1 (20.0%)	12 (66.7%)	3 (42.9%)	3 (21.4%)	0	19 (40.4%)
Any COVID-19 leading to interruption	0	1 (20.0%)	5 (27.8%)	2 (28.6%)	2 (14.3%)	0	10 (21.3%)
Any drug-related AE leading to interruption	0	0	5 (27.8%)	0	1 (7.1%)	0	6 (12.8%)
Any AE leading to dose reduction	0	0	0	0	0	0	0
Any COVID-19 leading to dose reduction	0	0	0	0	0	0	0
Any drug-related AE leading to dose reduction	0	0	0	0	0	0	0
Any AE leading to dose discontinuation	0	0	2 (11.1%)	0	0	0	2 (4.3%)
Any COVID-19 leading to dose discontinuation	0	0	2 (11.1%)	0	0	0	2 (4.3%)
Any drug-related AE leading to dose discontinuation	0	0	0	0	0	0	0
Any grade >=3 AE	0	3 (60.0%)	13 (72.2%)	1 (14.3%)	4 (28.6%)	0	21 (44.7%)
Any COVID-19-related grade >=3 AE	0	1 (20.0%)	2 (11.1%)	0	1 (7.1%)	0	4 (8.5%)
Any drug-related grade >=3 AE	0	1 (20.0%)	8 (44.4%)	1 (14.3%)	2 (14.3%)	0	12 (25.5%)
Any SAE	0	4 (80.0%)	10 (55.6%)	1 (14.3%)	4 (28.6%)	0	19 (40.4%)
Any COVID-19-related SAE	0	1 (20.0%)	4 (22.2%)	0	0	0	5 (10.6%)
Any drug-related SAE	0	1 (20.0%)	3 (16.7%)	0	2 (14.3%)	0	6 (12.8%)
Any grade 5 AE	0	0	2 (11.1%)	0	0	0	2 (4.3%)
Any COVID-19-related grade 5 AE	0	0	2 (11.1%)	0	0	0	2 (4.3%)
Any drug-related grade 5 AE	0	0	0	0	0	0	0

Table 4. Adverse Events

	1mg (N=1)		3mg (N=5)		10mg (N=18)		30mg (N=7)		100mg (N=14)		300mg (N=2)		Total (N=47)	
	All	≥G3	All	≥G3	All	≥G3	All	≥G3	All	≥G3	All	≥G3	All	≥G3
CRS	***0***	***0***	***1 (20.0%)***	***0***	***2 (11.1%)***	***0***	***1 (14.3%)***	***0***	***2 (14.3%)***	***0***	***0***	***0***	***6 (12.8%)***	***0***
COVID19 infection	***0***	***0***	***1 (20.0%)***	***1 (20.0%)***	***10 (55.6%)***	***4 (22.2%)***	***3 (42.9%)***	***0***	***5 (35.7%)***	***1 (7.1%)***	***0***	***0***	***19 (40.4%)***	***6 (12.8%)***
Neutropenia	0	0	1 (20.0%)	1 (20.0%)	7 (38.9%)	4 (22.2%)	2 (28.6%)	1 (14.3%)	5 (35.7%)	2 (14.3%)	0	0	15 (31.9%)	8 (17.0%)
Leukopenia	0	0	1 (20.0%)	0	7 (38.9%)	2 (11.1%)	2 (28.6%)	0	3 (21.4%)	0	0	0	13 (27.7%)	2 (4.3%)
Anemia	0	0	2 (40.0%)	0	6 (33.3%)	0	3 (42.9%)	0	2 (14.3%)	0	0	0	13 (27.7%)	0
Thrombocytopenia	0	0	0	0	4 (22.2%)	1 (5.6%)	1 (14.3%)	0	1 (7.1%)	0	0	0	6 (12.8%)	1 (2.1%)
Pyrexia	0	0	1 (20.0%)	0	4 (22.2%)	0	0	0	2 (14.3%)	0	0	0	7 (14.9%)	0
Constipation	0	0	1 (20.0%)	0	1 (5.6%)	0	1 (14.3%)	0	3 (21.4%)	0	0	0	6 (12.8%)	0
Vomiting	0	0	0	0	4 (22.2%)	0	0	0	0	0	0	0	4 (8.5%)	0
Diarrhea	0	0	0	0	2 (11.1%)	0	0	0	1 (7.1%)	0	0	0	3 (6.4%)	0
Hypotension	0	0	2 (40.0%)	0	4 (22.2%)	0	2 (28.6%)	0	2 (14.3%)	0	0	0	10 (21.3%)	0
Rash	0	0	0	0	1 (5.6%)	0	1 (14.3%)	0	2 (14.3%)	0	1 (50.0%)	0	5 (10.6%)	0
Hepatic function abnormal	0	0	1 (20.0%)	0	4 (22.2%)	2 (11.1%)	1 (14.3%)	0	0	0	0	0	6 (12.8%)	2 (4.3%)

CONCLUSIONS

- GB261, a novel and highly differentiated CD20/CD3 bispecific antibody, is the first clinical stage Fc+ CD20/CD3 T cell engager.
- In heavily pretreated B-NHL patients, GB261 showed a highly advantageous safety/efficacy balance, consistent with the MOA.
- The safety profile is excellent especially for the CRS which is very mild, transient and less frequent.
- The response after GB261 treatment was early, deep and durable.
- Clinical benefit seen in other CD20/CD3 bispecific antibody failed patient provides clinical support to the unique and differentiated MOA of GB261.

CONTACT INFORMATION

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