Rapid Ramp-up of Bi-specific Antibodies in Relapsed or Refractory Large B-cell Lymphoma

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BACKGROUND

- The CD3/CD20 bi-specific antibodies (BsAb) epcoritamab and glofitamab are approved by the US FDA for treatment of relapsed or refractory (R/R) large B-cell lymphoma (LBCL).
- Dosing of epcoritamab and glofitamab typically involves weekly ramp-up to reach full dose at the 3rd dose.
- For patients with R/R LBCL with aggressive presentation, it is appealing to ramp up BsAb faster to reach the full dose.
- We conducted a retrospective study to explore the feasibility of rapid ramp-up of epcoritamab and glofitamab in patients with R/R LBCL.

METHODS

- Patients with R/R LBCL who received epcoritamab or glofitamab with a rapid ramp-up schedule (e.g., aiming to ramp up every 2-4 days instead of the standard 7 days) in routine practice were included.
- Baseline characteristics, BsAb treatment details, adverse events (including cytokine release syndrome [CRS] and immune effector cell-associated neurotoxicity syndrome [ICANS]), and treatment responses were analyzed using descriptive statistics.
- Survival outcomes were analyzed using Kaplan-Meier method.

RESULTS

Table 1. Baseline characteristics (n=38)

Variable	n (%)
Age at BsAb start	
Median (range)	67 (31-84)
≥65	23 (61%)
Sex	
Female	18 (47%)
Male	20 (53%)
Pathology at initial diagnosis	
Diffuse large B-cell lymphoma (DLBCL)	21 (55%)
DLBCL transformed from indolent B-cell lymphoma	9 (24%)
High grade B-cell lymphoma with *MYC* and *BCL2*/*BCL6* rearrangements	8 (21%)
Progression after frontline therapy	
Primary refractory	16 (42%)
Early relapse (<12 months)	13 (34%)
Late relapse (>12 months)	9 (24%)
Lines of therapy prior to BsAb	
Median (range)	3 (2-9)
Prior CAR T-cell therapy	
Yes	24 (63%)
No	14 (37%)
Refractory to last line of therapy prior to BsAb	
Yes	21 (60%)
No	14 (40%)
Missing	3
ECOG performance status at BsAb start	
0-1	23 (64%)
≥2	13 (36%)
Missing	2
Ann Arbor stage at BsAb start	
I-II	7 (19%)
III-IV	30 (81%)
Missing	1
Number of extranodal sites at BsAb start	
0	11 (30%)
1	15 (40%)
>1	11 (30%)
Missing	1
LDH elevation at BsAb start	
Yes	29 (76%)
No	9 (24%)
Bulky disease at BsAb start	
≥10 cm	6 (17%)
≥5cm, <10 cm	13 (37%)
<5 cm	16 (46%)
Missing	3
CNS involvement prior to BsAb	
Yes	6 (16%)
No	32 (84%)

Figure 1. Summary of BsAb ramp-up schedules in all cases (n=38)

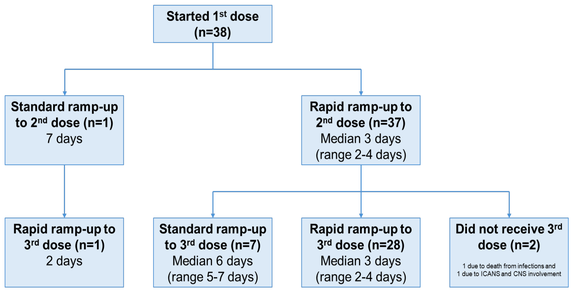
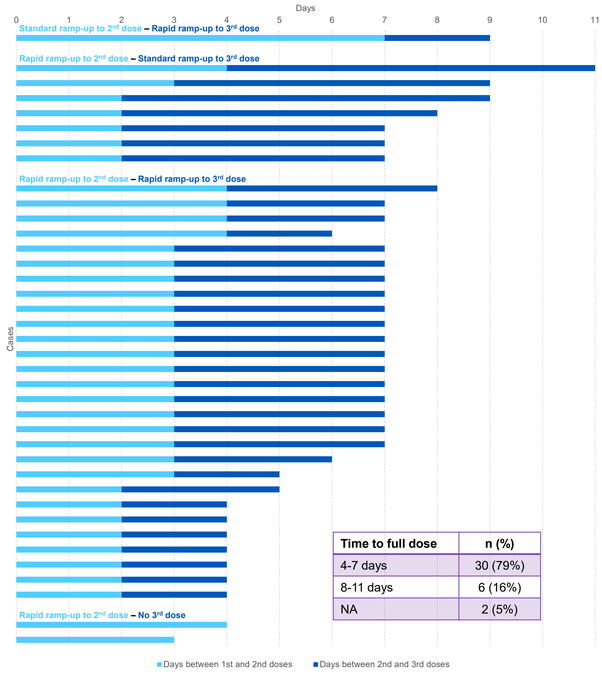


Figure 2. Detailed BsAb ramp-up schedule in each individual case (n=38)



Time to full dose	n (%)
4-7 days	30 (79%)
8-11 days	6 (16%)
NA	2 (5%)

RESULTS (CONT')

Table 2. Rates of CRS and ICANS during rapid ramp-up of BsAb

	1st dose (n=38)		2nd dose (n=38)		3rd dose (n=36)		Entire ramp-up from 1st to 3rd dose (n=38)	
	n (%)	Duration in days, median (range)	n (%)	Duration in days, median (range)	n (%)	Duration in days, median (range)	n (%)	Duration in days, median (range)
CRS	4 (10.5%)	2 (2-3)	6 (15.8%)	2 (2-2)	11 (30.6%)	2 (2-3)	16 (42.1%)	2 (2-6)
Grade 1-2	4 (10.5%)	2 (2-3)	6 (15.8%)	2 (2-2)	10 (27.8%)	2 (2-3)	15 (39.5%)	2 (2-6)
Grade 3	0		0		1 (2.8%)	2	1 (2.6%)	2
ICANS	0		1 (2.6%)	3	4 (11.1%)	2.5 (2-4)	5 (13.2%)	3 (2-4)
Grade 1-2	0		0		2 (5.6%)	3 (2-4)	2 (5.3%)	3 (2-4)
Grade 3	0		1 (2.6%)	3	2 (5.6%)	2.5 (2-3)	3 (7.9%)*	3 (2-3)

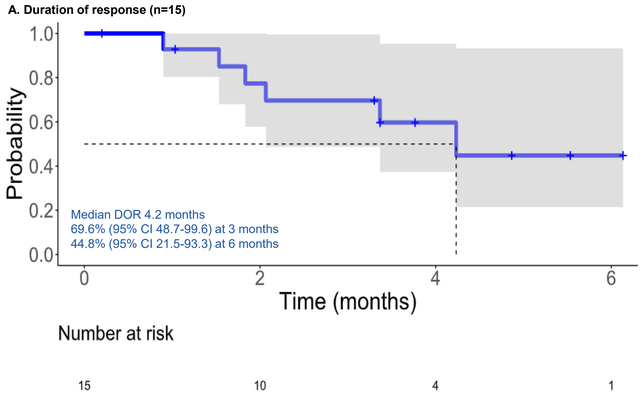
*Among the three patients with grade 3 ICANS reported, two had alternative explanations of neurological symptoms: one patient had seizure and was found to have new CNS involvement by lymphoma, and the other was in septic shock with altered mental status.

Table 3. Response to BsAb

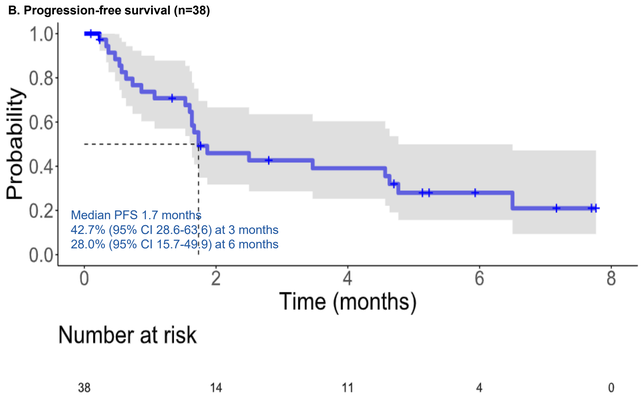
Response	n (%)
Overall response	15 (48.4%)
Complete response	6 (19.4%)
Partial response	9 (29.0%)
Stable disease	1 (3.2%)
Progressive disease	15 (48.4%)
Not evaluable	7

Figure 3. Survival outcomes after BsAb

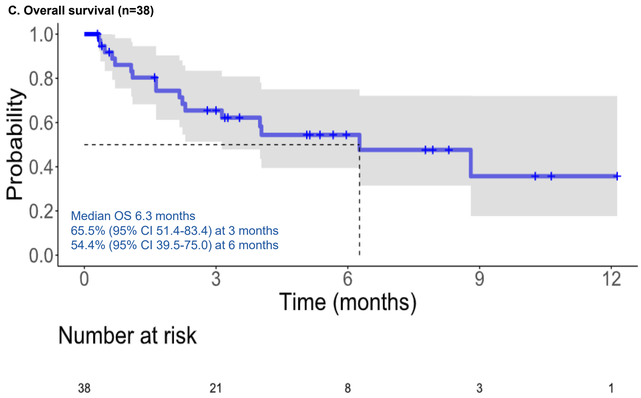
A. Duration of response (n=15)



B. Progression-free survival (n=38)



C. Overall survival (n=38)



CONCLUSIONS

- BsAb rapid ramp-up appears feasible in patients with R/R LBCL, with similar CRS and ICANS rates and treatment responses compared to other real-world datasets.
- Larger studies, ideally prospective, are needed to further investigate the feasibility, safety, and efficacy of rapid ramp-up dosing of BsAb in patients with R/R LBCL.

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