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CD20 × CD3 bispecific antibodies for lymphoma therapy: latest updates from ASCO 2023 annual meeting

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Abstract

Multiple bispecific antibodies (bsAbs) have been approved for cancer immunotherapy. Several CD20 × CD3 bsAbs have demonstrated significant anti-B-cell non-Hodgkin lymphoma (NHL) activity by engaging T cells to target $CD20^+$ NHL cells in clinical trials. Mosunetuzumab, epcoritamab and glofitamab have been approved recently for B-cell NHL therapy. In this study, we summarized several latest reports on CD20 × CD3 bsAbs for the therapy of B-cell NHL from the ASCO 2023 annual meeting (ASCO2023).

Keywords Non-Hodgkin's lymphoma, Bispecific antibody, CD20, CD3, EPCORE NHL-1

To the editor

Several CD20 × CD3 bispecific antibodies (bsAbs) have demonstrated significant anti-B-cell non-Hodgkin lymphoma (NHL) activity by engaging T cells to target $CD20^+$ NHL cells in clinical trials. Mosunetuzumab (Mosun), epcoritamab (Epcor) and glofitamab (Glofit) have been approved recently for refractory/relapsed (R/R) B-cell NHL therapy. We summarized several latest reports on CD20 × CD3 bsAbs from the ASCO 2023 annual meeting.

Properties of CD20 × CD3 bsAbs

Glofit is a full-length IgG1 bsAb with a 2:1 molecular configuration of anti-CD20 and anti-CD3 (Table 1). The Fc of Glofit has a PG LALA mutation, resulting in the loss of the Fc-FcγRs interaction while retaining its binding ability to FcRn [1]. This particular structure possesses a longer half-life of 10 days when compared to earlier generation of bsAbs. Glofit is currently being investigated as a single agent and in combination regimens [2–4].

Mosun is a fully humanized IgG1 bsAb (Table 1). Mosun was administered as a fixed-duration regimen with step-up dosing to minimize cytokine release syndrome (CRS). The intravenous (IV) formulation has been approved, while subcutaneous (SC) Mosun is still in trials [5]. Mosun has been evaluated in clinical trials as a monotherapy or in combination regimens for the treatment of B-cell NHL [6–8].

Epcor is another IgG1 bsAb. It was designed to bind to a unique epitope on CD20 antigen, allowing co-binding of other anti-CD20 agents (Table 1) [5]. Compared with IV administration, SC Epcor (also known as GEN3013) demonstrated comparable bioavailability and B-cell depletion in cynomolgus monkeys [9].

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Table 1 Properties of CD20 × CD3 bispecific antibodies

Agent	Glofitamab	Mosunetuzumab	Epcoritamab
Length	Full-length IgG1	Fully humanized Full-length IgG1	Full-length IgG1
Configuration	Anti-CD20: anti-CD3 = 2:1	Anti-CD20: anti-CD3 = 1:1	Anti-CD20: anti-CD3 = 1:1
Fc mutation	PG LALA	N297	L234F, L235E, and D265A
Administration	IV	SC/IV	SC
Dosing	Step-wise	Step-wise	Step-wise
Depleting of B cells prior to bsAb	Yes	No	No
Combined with CD20 mAbs	Yes	No	Yes
References	[1, 4]	[5, 6]	[5, 9]

bsAb, bispecific antibody; Epcor, epcoritamab; Glofit, glofitamab; IV, intravenous; Mosun, Mosunetuzumab; SC, subcutaneous

Efficacies of CD20 × CD3 bsAbs as a single agent

In a phase II clinical trial for patients (pts) with R/R large B cell lymphoma (LBCL), obinutuzumab was administered prior to Glofit monotherapy to first reduce the tumor load [2, 4]. Glofit was given at a step-up dosing regimen. In the latest update, the complete response (CR) and overall response rates (ORR) were 38% and 59%, respectively, with a median follow-up (mFU) of 20.1 months (m) (Table 2). Notably, prior CAR T cell therapy did not adversely affect ORR. The median duration of CR was 24.1 m [95% CI: 19.8–not reached (NR)]. Among pts who received doses lower than recommended but ≥ 10 mg, the CR duration was extended to 30.1 m. The 18-m overall survival (OS) rate was 41%. CRS was the most frequently reported adverse event (AE). Glofit was recently approved for R/R LBCL.

In the EPCORE NHL-1 trial for R/R LBCL, single-agent Epcor was administered with a step-wise dosing regimen [10]. The CR and ORR were 39.5% and 63.1%, respectively (Table 2). Median OS was 18.5 m. CRS

Table 2 2023 ASCO updates from clinical trials of CD20 × CD3 bispecific antibodies for lymphoma therapy

Regimen	Epcor	Glofit	Epcor + R-CHOP	Glofit + Pola-R-CHP	Epcor + R^2
Lymphoma	R/R LBCL	R/R LBCL	1L high-risk DLBCL	1L DLBCL	R/R FL
Pts	157	154	47	24	109
mFU	20 m	20.1 m	11.5 m	5.1 m	8.8 m
	(range: 0.3+–28.2)	(range: 0–32)	(range: 0.8–15.5)	(range: 3–8)	(range: 1.2–18.5)
ORR	63.1%	59%	100%	100%	97%
CR/CMR	CR: 39.5%	CR: 38%	CMR: 76%	CMR: 76.5%	CMR: 86%
mDoCR	20.8 m	24.1 m (95% CI 19.8–NR)	NR	NR	NR
PFS	87.2% at 1 year in pts with a CR	80% at 1 year in pts with a CR at EOT	NR	NR	NR
OS	mOS:18.5 m (95% CI 11.7–NR)	41% (18-m) (95% CI 32.1–49.3)	NR	NR	NR
CRS	51%	64%	60%	13%	48%
G1–2	48%	60%	57%	13%	46%
G ≥ 3	3%	4%	2%	0	2%
NAE/ICANS	ICANS: 6%	NA	ICANS: 2%	NAE: 46%	ICANS: 2%
G1–2	6%		2%	42%	2%
G ≥ 3	1%		0	4%	0%
Clinical trial number	NCT03625037	NCT03075696	NCT04663347	NCT03467373	NCT04663347
References	[10]	[4]	[11]	[3]	[12]

CMR, complete metabolic response; CR, complete response; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; EOT: end of treatment; Epcor, epcoritamab; FL, follicular lymphoma; G: grade; Glofit, glofitamab; ICANS, immune effector cell-associated neurotoxicity syndrome; m, months; mDoCR, median duration of CR; mFU, median follow-up; mOS: median OS; Mosun, Mosunetuzumab; NA: not available; NAE, neurological adverse events; NR, not reached; ORR, overall response rate; OS, overall survival; PFS: progression-free survival; Pola, polatuzumab vedotin; Pts, patients; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R/R, relapsed/refractory; 1L, 1 line

occurred in 51% of pts, and immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in 6% of pts. Epcor was recently approved for R/R LBCL.

Efficacies of CD20 × CD3 bsAbs in combination regimens

In the EPCORE NHL-2 trial, Epcor was combined with R-CHOP in adults with untreated high-risk DLBCL [11]. In the latest report, 47 pts had received Epcor 48 mg + R-CHOP with a mFU of 11.5 m (Table 2). All pts achieved a response (100%), and 76% achieved a complete metabolic response (CMR). The CMR occurred in 82% double/triple-hit pts. CRS occurred in 60% of pts, and 1 pt experienced ICANS.

In the EPCORE NHL-2 trial, SC Epcor was combined with R + lenalidomide in treating R/R follicular lymphoma (FL) [12]. One hundred and nine pts were treated with a mFU of 8.8 m. The CMR and ORR were 86% and 97%, respectively ($n = 101$) (Table 2). CRS occurred in 48% of pts, while 2 pts developed ICANS.

Glofit was employed in combination with polatuzumab vedotin (Pola) plus R-CHP for untreated DLBCL pts, with Pola-R-CHP given on Day 1 of each cycle (C) and Glofit administered in C2–C6 at a step-up dosing [3]. The CMR and ORR occurred in 76.5% and 100% of the 24 enrolled pts after a mFU of 5.1 m (Table 2). CRS and neurological AEs occurred in 13% and 46% pts, respectively.

In addition to the above trials, several clinical trials on CD20 × CD3 bsAbs in combination regimens are enrolling now. These include SC Mosun + IV Pola in pts with R/R NHL [8], SC Mosun with lenalidomide augmentation in pts with untreated FL and marginal zone lymphoma [7], and SC Epcor + R-CHOP in pts with newly diagnosed DLBCL [13].

In summary, Mosun, Epcor and Glofit have been approved recently for R/R B-cell NHL therapy. SC administration of Epcor offers convenience. CD20 × CD3 bsAbs in combination regimens are in clinical trials.

Abbreviations

AE	Adverse events
ASCO	American Society of Clinical Oncology
bsAb	Bispecific antibody
CMR	Complete metabolic response
CR	Complete response
CRS	Cytokine release syndrome
DLBCL	Diffuse large B-cell lymphoma
Epcor	Epcoritamab
FL	Follicular lymphoma
Glofit	Glofitamab
ICANS	Immune effector cell-associated neurotoxicity syndrome
IV	Intravenous
m	Months
mDoCR	Median duration of CR
mFU	Median follow-up
Mosun	Mosunetuzumab
NHL	Non-Hodgkin lymphoma
NR	Not reached
ORR	Overall response rate
OS	Overall survival
Pola	Polatuzumab vedotin
pts	Patients
R-CHOP	Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone
R/R	Relapsed/refractory
SC	Subcutaneous
1L	1 Line

Author contributions

YPS designed the study. XYL and JJZ drafted the manuscript and prepared the tables. All authors participated in the process of drafting and revising the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The material supporting the conclusion of this study has been included within the article.

Declarations

Ethics approval and consent to participate

This is not applicable for this summary.

Consent for publication

This is not applicable for this summary.

Competing interests

The authors have no relevant competing interests.

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