ABCL-406

Real-World Sequential Use of CD19-Directed Therapies for Relapsed or Refractory Diffuse Large B-Cell Lymphoma: Tafasitamab Preceding Chimeric Antigen Receptor T-Cell Therapy

Presented at the
12th Annual Meeting of the Society of Hematologic Oncology (SOHO 2024)
Houston, TX, USA • September 4-7, 2024

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Objective

- The purpose of this analysis was to report characteristics, treatment patterns, and outcomes from a prespecified subgroup, those who received CAR-T therapy following tafasitamab, among a larger real-world cohort of patients who received tafasitamab for R/R DLBCL identified in a previously reported study[5]

Conclusions

- **This small real-world analysis adds to the growing body of literature investigating treatment outcomes associated with sequential use of anti-CD19 therapies in patients with R/R DLBCL, demonstrating:**
  - **Detectable tumor CD19 expression immediately following tafasitamab treatment**
  - **Disease response to subsequent CD19-directed CAR-T therapy in patients previously treated with tafasitamab**
- **These findings remain to be validated by future studies with larger sample size**

Abbreviations

2L, second line; 3L, third line; 4L, fourth line; 5L, fifth line; CAR-T, chimeric antigen receptor T cell; DLBCL, diffuse large B-cell lymphoma; LOT, line of therapy; Q1, first quartile; Q3, third quartile; R/R, relapsed or refractory; rwCR, real-world complete response; rwORR, real-world overall response rate; rwPR, real-world partial response; RWS, real-world study; rwSD, real-world stable disease; tafa+len, tafasitamab plus lenalidomide.

Disclosures

Epperla: Research funding – *BeiGene, Lilly*; Speakers' bureau – *BeiGene, Genentech, Novartis*; Honoraria, consulting, advisory boards – *ADC Therapeutics*. **Nastoupil:** Honorarium – *AbbVie, ADC Therapeutics, Bristol Myers Squibb, Caribou Biosciences, Denovo Biopharma, Daichi Sankyo, Genentech, Genmab, Gilead Sciences/Kite Pharma, Incyte Corporation, Janssen, Merck, Novartis, Regeneron, Takeda*; Research support – *Bristol Myers Squibb, Caribou Biosciences, Daiichi Sankyo, Genentech, Genmab, Gilead Sciences/Kite Pharma, Janssen, Merck, Novartis, Takeda*. **Feinberg and Gentile:** Employment and stock ownership – *Cardinal Health*. **Pathak:** Employment – *Cardinal Health*. **Galvin, Amoloja, Saverno:** Employment and stock ownership – *Incyte Corporation*.

Acknowledgments

This study was sponsored by Incyte Corporation (Wilmington, DE, USA).

The authors would like to thank the patients and participating physicians for their contribution of real-world data. The authors would also like to acknowledge the contributions of Julie Wu (Incyte Corporation), Kristin Savill (formerly of Cardinal Health), Madison Brown (Cardinal Health), Lindsay McAllister (Cardinal Health), and Angelica Falkenstein (formerly of Cardinal Health) for contributions to the study design, conduct of the study, or data analysis. Additionally, project management support was provided by Kehinde Ogebule (Cardinal Health).

Medical writing assistance was provided by Emily Sun, PhD, of Envision Pharma Group (Fairfield, CT, USA) and funded by Incyte Corporation.

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Introduction

- Tafasitamab is a CD19-targeting immunotherapy indicated for use in combination with lenalidomide for R/R DLBCL in adults ineligible for autologous stem cell transplant[1]
- Use of sequential CD19-directed therapies, including CD19-directed CAR-T therapy, has raised concerns over potential CD19 antigen loss, either through temporary epitope masking secondary to antibody binding[2] or antigen escape via CD19 downregulation or genetic alterations[3]
  - Real-world data on optimal sequencing of CD19-directed therapies are limited[4]
- A recent US RWS investigated the treatment patterns and outcomes of patients with R/R DLBCL who received tafasitamab[5]
  - Here, we report results from a prespecified subgroup who received CAR-T therapy following tafasitamab treatment

Methods

Study Design and Data Source

- Retrospective, United States multisite, medical chart review
- Physicians from Cardinal Health's Oncology Provider Extended Network (OPEN) abstracted data for eligible patients (**Table 1**) into electronic case report forms between February 22, 2023, and March 29, 2023; additional follow-up data was gathered from participating physicians from December 18, 2023, to January 31, 2024
  - OPEN is a community of >7,000 oncologists/hematologists based in private practice and hospitals across the United States
- Lines of therapy were defined as follows:
  - The end of a LOT occurred when the patient discontinued treatment with a regimen
  - If a drug was added to a regimen, this was considered a new LOT
  - If a drug within a regimen was held or discontinued, this was not considered a new LOT
  - CAR-T therapy (with or without bridge therapy) was considered as a single LOT

Table 1. Patient Selection Criteria

Inclusion Criteria	• Initiation of tafasitamab (with or without concomitant lenalidomide) for R/R DLBCL on or after October 21, 2020 • Age ≥18 years at tafasitamab initiation • ≥4 months of follow-up since tafasitamab initiation (otherwise eligible patients who died during this 4-month interval were still eligible)
Exclusion Criteria	• Received tafasitamab as part of an interventional clinical trial

Statistical Analysis

- In this subgroup analysis, results of patients who received tafasitamab prior to CAR-T therapy were summarized using descriptive statistics

Results

Patient Characteristics and Treatment Patterns

- Of the 181 patients included in the overall RWS population, 9 patients received tafasitamab plus lenalidomide (tafa+len) as a line of therapy immediately preceding CAR-T therapy; **Table 2** summarizes the characteristics of these 9 patients
  - 7 patients received tafa+len in 2L followed by CAR-T therapy in 3L
  - 1 patient received tafa+len in 3L followed by CAR-T therapy in 4L
  - 1 patient received tafa+len in 4L followed by CAR-T therapy in 5L
- Among these 9 patients, median (Q1-Q3) follow-up time since tafasitamab initiation was 26.1 (18.0-28.0) months and median (Q1-Q3) follow-up time since CAR-T administration was 9.3 (1.9-16.7) months
  - All 9 patients were alive at the most recent follow-up

Outcomes From Treatment With Tafasitamab

- Of the 9 patients, the following real-world responses were observed with tafa+len treatment:
  - rwCR in 4 patients
  - rwPR in 4 patients
  - rwSD in 1 patient
  - rwORR was 88.9% (n=8/9)
- All 9 patients discontinued tafasitamab due to progression of disease confirmed on imaging
- Median (Q1-Q3) duration of tafasitamab therapy was 11.0 (8.1-14.1) months

CD19 Testing Following Tafasitamab Discontinuation

- 3 patients had CD19 testing following tafasitamab discontinuation and all test results were positive **(Table 3)**

CAR-T Therapy Treatment Utilization Patterns and Outcomes

- CAR-T therapy treatment and utilization patterns are summarized in **Table 4**
  - All patients received their CAR-T infusion in an inpatient setting

Table 2. Demographic and Clinical Characteristics of Patients Who Received Tafasitamab Preceding CAR-T Therapy for R/R DLBCL

Variable	Patients Receiving Tafasitamab Preceding CAR-T Therapy (N=9)
Sex at birth, male, n (%)	3 (33.3)
Age at tafasitamab initiation, median (Q1-Q3), years	63.3 (57.5-69.0)
Race, n (%)	
White	6 (66.7)
Asian	2 (22.2)
American Indian or Alaska Native	1 (11.1)
Ethnicity, n (%)	
Hispanic	1 (11.1)
Non-Hispanic/Non-Latino/Non-Latina	8 (88.9)
ECOG PS at tafasitamab initiation, n (%)	
0-1	7 (77.8)
≥2	2 (22.2)
Ann Arbor stage at tafasitamab initiation, n (%)	
III	1 (11.1)
IV	8 (88.9)
R-IPI score at tafasitamab initiation, n (%)	
1-2	2 (22.2)
3-5	7 (77.8)
Presence of double- or triple-hit B-cell lymphoma, n (%)	
Double-hit	2 (22.2)
Triple-hit	0
Negative	4 (44.4)
Unknown	3 (33.3)
Primary refractory disease, n (%)*	2 (22.2)
Tumor volume, n (%)	
Nonbulky (≤7500 mm)	4 (44.4)
Bulky (>7500 mm)	5 (55.6)

*Disease progression while receiving or ≤6 months after the completion of first-line therapy.
ECOG PS, Eastern Cooperative Oncology Group performance status; R-IPI, Revised International Prognostic Index.

Table 3. CD19 Testing Metrics

Variable	Patients Receiving Tafasitamab Preceding CAR-T Therapy (N=9)
CD19 test conducted following tafasitamab discontinuation, n (%)	3 (33.3)
Positive, n (%)*	3 (100)
Time to first CD19 test after tafasitamab discontinuation, median (Q1-Q3), days	7.0 (6.0-9.0)
Method of all CD19 tests conducted following tafasitamab discontinuation, n (%)†	
Immunohistochemistry	3 (100)
Flow cytometry	2 (66.7)

*Denominator = patients with ≥1 CD19 testing conducted following tafasitamab discontinuation. †Some patients had ≥1 CD19 tests conducted.

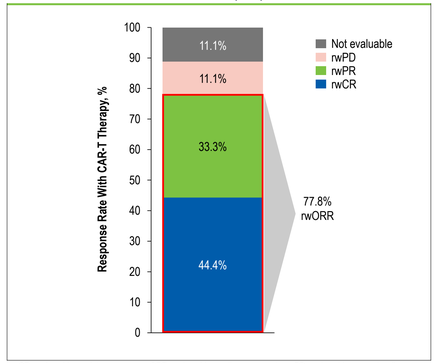
Table 4. Treatment and Utilization Patterns of CAR-T Therapy Following Tafasitamab for R/R DLBCL

Variable	Patients Receiving Tafasitamab Preceding CAR-T Therapy (N=9)
Distance patient had to travel to receive their CAR-T infusion, n (%)	
<30 miles	2 (22.2)
31-60 miles	5 (55.6)
61-120 miles	2 (22.2)
Bridge therapy received prior to CAR-T therapy, n (%)*	
Polatuzumab + BR	2 (22.2)
R-GemOx	2 (22.2)
Tafa+len	3 (33.3)
No bridge therapy	2 (22.2)
CAR-T received, n (%)	
Axicabtagene ciloleucel (axi-cel)	8 (88.9)
Tisagenlecleucel (tisa-cel)	1 (11.1)
Time between referral and CAR-T administration, median (Q1-Q3), months	3.5 (2.9-4.2)
Time from apheresis to CAR-T infusion, median (Q1-Q3), days†	34.0 (28.0-43.0)
Time from tafasitamab discontinuation (the latter of LOT or bridge therapy) to CAR-T initiation, median (Q1-Q3), months	3.2 (2.3-3.6)

*Bridge therapy was not defined in the eCRF, but left to physicians' discretion during data abstraction. †Among the 6 patients with apheresis dates available.
BR, bendamustine/rituximab; eCRF, electronic case report form; R-GemOx, gemcitabine/oxaliplatin/rituximab.

- Real-world best responses to CAR-T infusion following tafasitamab treatment are summarized in **Figure 1**
  - rwORR after CAR-T therapy was 77.8% (n=7/9)

Figure 1. Real-World Best Response to CAR-T Therapy Following Tafasitamab Treatment for R/R DLBCL (N=9)



rwCR, real-world complete response; rwORR, real-world overall response rate; rwPD, real-world progressive disease; rwPR, real-world partial response.

Study Limitations

- Data on tumor CD19 expression immediately following tafasitamab discontinuation were available for a minority of patients
- The sample size (N=9) in this study is small
- The study is limited by factors inherent in real-world studies such as missing/underreporting data, lost to follow-up, and lack of uniform assessment criteria for variables, such as disease response