Poster IBCL-271

Nathan Hale Fowler | nfowler@mdanderson.org

Clinical outcomes of patients with relapsed/refractory follicular lymphoma treated with tisagenlecleucel: phase 2 ELARA 3-year follow-up

Stephen J. Schuster,[1] Nathan Hale Fowler,[2,3] Michael Dickinson,[4] Joaquin Martinez-Lopez,[5] Arne Kolstad,[6] Jason Butler,[7] Monalisa Ghosh,[8] Leslie Popplewell,[9] Julio C. Chavez,[10] Emmanuel Bachy,[11] Koji Kato,[12] Hideo Harigae,[13] Marie José Kersten,[14] Charalambos Andreadis,[15] Peter A. Riedell,[16] P. Joy Ho,[17] José Antonio Pérez-Simón,[18] Andy I. Chen,[19] Loretta J. Nastoupil,[2] Bastian von Tresckow,[20,21] Andrés José María Ferreri,[22] Takanori Teshima,[23] Piers E.M. Patten,[24,25] Joseph P. McGuirk,[26] Andreas L. Petzer,[27] Fritz Offner,[28] Andreas Viardot,[29] Pier Luigi Zinzani,[30,31] Ram Malladi,[32] Aiesha Zia,[33] Rakesh Awasthi,[34] Ines Paule,[33] Davide Germano,[33] Roberto Ramos,[35] Pei Hsu,[33] Catherine Thieblemont,[36] Martin Dreyling[37]

[1]Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]BostonGene, Waltham, MA, USA; [4]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and the Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia; [5]Hospital 12 De Octubre, Complutense University, CNIO, Madrid, Spain; [6]Oslo University Hospital, Oslo, Norway; [7]Royal Brisbane Hospital, Herston, QLD, Australia; [8]Michigan Medicine, University of Michigan, Ann Arbor, MI, USA; [9]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [10]Department of Malignant Hematology, Moffitt Cancer Center, Tampa, FL, USA; [11]Hospices Civils de Lyon and Université Claude Bernard Lyon 1, Lyon, France; [12]Department of Hematology, Oncology, and Cardiovascular Medicine, Kyushu University Hospital, Fukuoka Prefecture, Japan; [13]Department of Hematology, Tohoku University Hospital, Sendai, Japan; [14]On behalf of HOVON/LLPC, Department of Hematology, Amsterdam UMC, Location University of Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands; [15]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA; [16]David and Etta Jonas Center for Cellular Therapy, University of Chicago, Chicago, IL, USA; [17]Institute of Haematology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia; [18]Department of Hematology, University Hospital Virgen del Rocío, Instituto de Biomedicina de Sevilla (IBIS) CSIC, Universidad de Sevilla, Seville, Spain; [19]Oregon Health and Science University, Portland, OR, USA; [20]Department I of Internal Medicine, Medical Faculty and University Hospital Cologne, University of Cologne, Cologne, Germany; [21]Department of Hematology and Stem Cell Transplantation, West German Cancer Center and German Cancer Consortium (DKTK partner site Essen), University Hospital Essen, University of Duisburg-Essen, Essen, Germany; [22]Lymphoma Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy; [23]Department of Hematology, Hokkaido University Hospital, Sapporo, Japan; [24]Comprehensive Cancer Centre, King's College London, London, United Kingdom; [25]Department of Haematology, King's College Hospital, London, United Kingdom; [26]University of Kansas Medical Center, Westwood, KS, USA; [27]Internal Medicine I, Ordensklinikum Linz Barmherzige Schwestern-Elisabethinen, Linz, Austria; [28]UZ Ghent, Ghent, Belgium; [29]Department of Internal Medicine III, University Hospital of Ulm, Ulm, Germany; [30]IRCCS Azienda Ospedaliero-Universitaria di Bologna Istituto di Ematologia "Seràgnoli", Bologna, Italy; [31]Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale, Università di Bologna, Bologna, Italy; [32]Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [33]Novartis Pharma AG, Basel, Switzerland; [34]Novartis Institutes for BioMedical Research, East Hanover, NJ, USA; [35]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [36]Hôpital Saint-Louis, Paris, France; [37]Medizinische Klinik III, LMU Klinikum, Munich, Germany

KEY FINDINGS & CONCLUSIONS

- Patients with R/R FL have a high rate of durable responses more than 3 years after tisagenlecleucel infusion
  - Median DOR, OS, and TTNT were not reached at a median follow-up of 41 months
- No new tisagenlecleucel-related safety signals were observed during extended follow-up
- Exploratory analyses suggest that higher baseline levels of CD8+ naive T cells (>2.14%) are associated with improved long-term clinical outcomes
- Patients with POD24 had reduced CAR-T cell expansion, which did not substantially affect 36-month PFS and OS

Scan to obtain:
- Poster

To download a copy of this poster, visit the web at: https://bit.ly/StephenJ271

Copies of this poster obtained through Quick Response (QR) code are for personal use only and may not be reproduced without permission of the authors

This study was sponsored by Novartis Pharmaceuticals Corporation.

Previously presented at the 65th American Society of Hematology (ASH) Annual Meeting and Exposition; December 9–12, 2023; San Diego, CA, USA and Virtual. Oral 601; the 2024 Tandem | Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR; February 21-24, 2024; San Antonio, TX, USA. Oral 43; and The European Hematology Association (EHA) Congress; June 13-16, 2024; Madrid, Spain. Poster P1455.

Poster presented at the 12th Annual Meeting of the Society of Hematologic Oncology (SOHO) 2024, Houston, Texas, USA, September 4-7, 2024.

INTRODUCTION

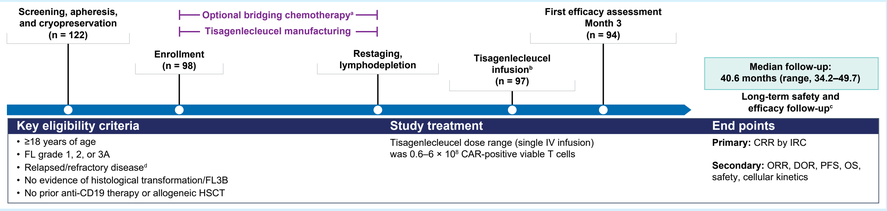
- Although regarded as an "indolent" disease, follicular lymphoma (FL) is considered incurable, with patients often experiencing multiple relapses over a usually lengthy disease course[1-3]
- Following treatment, remission durations generally become progressively shorter after each subsequent line of therapy[4]
- Patients with disease progression within 2 years of frontline systemic therapy (POD24) have a particularly poor prognosis with traditional therapies and may benefit from alternative treatment options[5-8]
- Tisagenlecleucel, a CD19-directed chimeric antigen receptor (CAR) T-cell therapy, is approved in the United States and Europe for adults with relapsed/refractory (R/R) FL after ≥2 lines of prior therapy

AIM

- The 2-year follow-up of the ELARA trial (median follow-up: 29 months) demonstrated high response rates and durable response[9]
  - Overall response rate (ORR): 86%
  - Complete response rate (CRR): 68%
  - 24-month progression-free survival (PFS): 57%
- Herein we report longer follow-up results, including duration of response, safety outcomes, and exploratory analyses, at a median follow-up of >3 years

ELARA STUDY DESIGN

- Bridging therapy was allowed and was followed by disease re-evaluation before tisagenlecleucel infusion



CAR, chimeric antigen receptor; CD, cluster of differentiation; CRR, complete response rate; DOR, duration of response; FL, follicular lymphoma; FL3B, FL grade 3B; HSCT, hematopoietic stem cell transplant; IRC, independent review committee; IV, intravenous; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.

[a]Disease was reassessed prior to infusion for all patients requiring bridging therapy; [b]Infusion was conducted on an in- or outpatient basis at investigator's discretion; [c]Every 3 months until Month 12, and every 6 months until end of the study; [d]Refractory to ≥2nd line of systemic therapy (including an anti-CD20 antibody and an alkylating agent) or relapsed within 6 months after ≥2nd line of therapy or after an autologous HSCT

RESULTS

Disease History and Baseline Patient Characteristics

- A total of 97 patients with a median age of 57 years were evaluable (**Table 1**)

Table 1. Baseline characteristics

	Infused set (N = 97)
Median age (range), years	57 (29-73)
ECOG PS ≥1 prior to infusion, n (%)	42 (43)
Stage at study entry III-IV, n (%)	83 (86)
Bone marrow involvement, n (%)	37 (38)
Bulky disease[a], n (%)	**62 (64)**
FLIPI high at study entry (≥3), n (%)	58 (60)
Median no. of prior therapies (range)	4 (2-13)
POD24 from first anti-CD20 mAb containing therapy, n (%)	**61 (63)**
Refractory disease to last line of therapy, n (%)	76 (78)
Refractory to ≥2 regimens, n (%)	69 (71)
Double refractory: anti-CD20 mAb + alkylating agent	**66 (68)**
Refractory to PI3K inhibitors	14 (14)
Prior autologous HSCT, n (%)	35 (36)
Comorbidities, n (%)	
Cardiac disorders	15 (16)
Diabetes	10 (10)
Renal insufficiency	8 (8)

CD20, cluster of differentiation 20; ECOG PS, Eastern Cooperative Oncology Group performance status; FLIPI, Follicular Lymphoma International Prognostic Index; HSCT, hematopoietic stem cell transplant; mAb, monoclonal antibody; PI3K, phosphatidylinositol 3-kinase; POD24, progression of disease within 2 years of frontline systemic therapy.
[a]Bulky disease defined as 1 lesion >7 cm or 3 lesions >3 cm.

Safety

- No new safety signals were reported
- The most common serious adverse events (AEs) were cytokine release syndrome (CRS, 20% [Lee grading]), pneumonia (11%), and febrile neutropenia (8%; **Table 2**)
- To date, 18 patients have died during the study (progressive disease, n=8; AE, n=9; euthanasia, n=1)
- AEs resulting in death included metastatic squamous cell carcinoma, encephalitis, pneumonia, bladder transitional cell carcinoma, acute myeloid leukemia, infection, CRS, gastrointestinal hemorrhage, and cardiac arrest

Table 2. Adverse events occurring anytime after tisagenlecleucel infusion

Preferred term	Infused set (N = 97) All grades n (%)	Infused set (N = 97) Grade ≥3 n (%)
Patients with at least one adverse event	96 (99)	79 (81)
Cytokine release syndrome	48 (50)	1 (1)
Neutropenia	**42 (43)**	**42 (43)**
Anemia	**26 (27)**	**18 (19)**
Diarrhea	25 (26)	3 (3)
Headache	23 (24)	1 (1)
White blood cell count decreased	22 (23)	17 (18)
Nausea	18 (19)	2 (2)
Pyrexia	18 (19)	2 (2)
Thrombocytopenia	18 (19)	11 (11)
Fatigue	17 (18)	3 (3)
Hypogammaglobulinemia	17 (18)	1 (1)
Neutrophil count decreased	17 (18)	17 (18)
Constipation	16 (17)	0

Efficacy

With a median follow-up of 41 months, median PFS was 37 months while median overall survival (OS) was not reached (Figure 1)

- 36-month PFS was 53% for all patients and 69% for patients with a CR
- 36-month OS was 82% for all patients

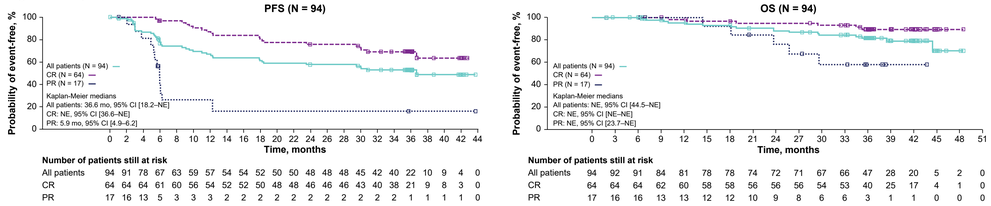
36-month PFS and OS rates were consistent for patients with or without POD24 (Figure 3)

- 36-month OS rate was 83% (95% CI, 69.1-90.5) in patients with POD24 and 80% (95% CI, 60.9-90.6) in patients without POD24

Median duration of response (DOR) and time to next treatment (TTNT) were not reached (Figure 2)

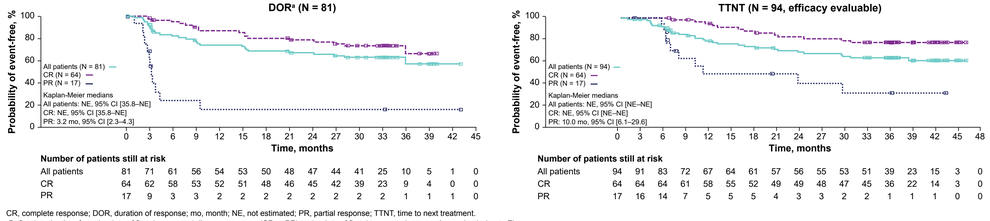
- 54% of responders had an ongoing response at data cutoff
- The probability of starting a new treatment at 36 months was 35%

Figure 1. Kaplan-Meier curve of PFS and OS



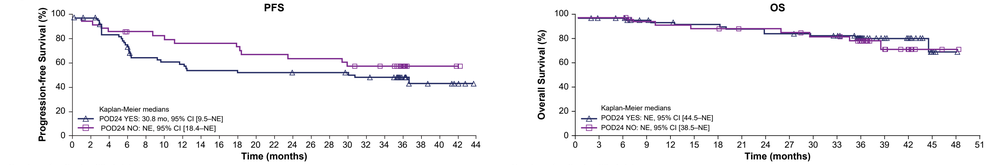
CR, complete response; mo, month; NE, not estimated; OS, overall survival; PFS, progression-free survival; PR, partial response.

Figure 2. Kaplan-Meier curve of DOR and TTNT



CR, complete response; DOR, duration of response; mo, month; NE, not estimated; PR, partial response; TTNT, time to next treatment.
[a]Defined as the time from the date of first documented disease response (CR or PR) to the date of first documented progression or death due to FL.

Figure 3. Kaplan-Meier curve of PFS and OS based on POD24 status



Schuster S, et al. Blood. 2023;142(suppl 1):601 [abstract]. doi.org/10.1182/blood-2023-180936. ©American Society of Hematology (2023). Reused with permission.

mo, month; NE, not estimated; OS, overall survival; PFS, progression-free survival; POD24, progression of disease within 2 years of frontline systemic therapy.

Exploratory Biomarker Analysis and Pharmacokinetics

- Higher baseline levels of peripheral CD8+ naïve T cells (>2.14%) were associated with prolonged PFS and DOR
- Patients without POD24 had higher mean CAR transgene expansion and longer persistence
  - Responses and durations were not different between the POD24 subgroups despite differences in expansion
  - CAR transgene persistence was observed up to 1290 days

References

1. Casulo C, Barr PM. *Blood*. 2019;133(14):1540-1547
2. Alcoceba M, et al. *Ann Lymphoma*. 2017;1:11
3. Prusila REI, et al. *Br J Haematol*. 2019;187(3):364-371
4. Link BK, et al. *Br J Haematol*. 2019;184(4):660-663
5. Lansigan F, et al. *Cancer Med*. 2019;8(1):165-173
6. Salles G, et al. *Lancet*. 2011;377(9759):42-51
7. Casulo C, et al. *Blood*. 2022;139(11):1684-1693
8. Casulo C, et al. *J Clin Oncol*. 2015;33(23):2516-2522
9. Dreyling M, et al. *Blood*. 2022;140(suppl 1):1459-1463.

Acknowledgments

The authors would also like to thank Jay Shah, Expert Scientific Writer, of Novartis Healthcare Pvt Ltd, Hyderabad, India, for the editorial support for this presentation.