



## The 65th ASH Annual Meeting Abstracts

## ORAL ABSTRACTS

**623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL****Clinical Outcomes of Patients with Relapsed/Refractory Follicular Lymphoma Treated with Tisagenlecleucel: Phase 2 Elara 3-Year Follow-up**

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

<sup>1</sup> Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA

<sup>2</sup> The University of Texas MD Anderson Cancer Center, Houston, TX

<sup>3</sup> BostonGene, Corp., Waltham, MA

<sup>4</sup> Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia

<sup>5</sup> Hospital Universitario 12 de Octubre, CIBER-ONC CB16/12/00369, CNIO, Madrid, Spain

<sup>6</sup> Oslo University Hospital, Oslo, Norway

<sup>7</sup> Royal Brisbane Hospital, Herston, QLD, Australia

<sup>8</sup> Division of Hematology/Oncology, University of Michigan, Ann Arbor, MI

<sup>9</sup> Department of Hematology and HCT, City of Hope National Medical Center, Duarte, CA

<sup>10</sup> Department of Malignant Hematology, Moffitt Cancer Center, Tampa, FL

<sup>11</sup> Clinical Hematology, Hospices Civils de Lyon and Claude Bernard Lyon 1 University, Lyon, France

<sup>12</sup> Department of Hematology, Oncology, and Cardiovascular Medicine, Kyushu University Hospital, Fukuoka, Japan

<sup>13</sup> Department of Hematology, Tohoku University Graduate School of Medicine, Sendai, Japan

<sup>14</sup> Cancer Center Amsterdam, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands

<sup>15</sup> Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA

<sup>16</sup> David and Etta Jonas Center for Cellular Therapy, University of Chicago, Chicago, IL

<sup>17</sup> Royal Prince Alfred Hospital, Sydney, AUS

<sup>18</sup> Department of Hematology, University Hospital Virgen del Rocío-IBIS. Universidad de Sevilla., Sevilla, Spain

<sup>19</sup> Oregon Health and Science University, Portland, OR

<sup>20</sup> Department I of Internal Medicine, Medical Faculty and University Hospital Cologne, University of Cologne, Cologne, Germany

<sup>21</sup> Department of Hematology and Stem Cell Transplantation, West German Cancer Center (WTZ), University Hospital Essen, University of Duisburg-Essen, Essen, Germany

<sup>22</sup> Unit of Lymphoid Malignancies, Department of Onco-Haematology, IRCCS San Raffaele Scientific Institute, Milano, Italy

<sup>23</sup> Department of Hematology, Hokkaido University, Sapporo, Japan

<sup>24</sup> King's College London, London, GBR

<sup>25</sup> University of Kansas Medical Center, Westwood, KS

<sup>26</sup> Internal Medicine I, Ordensklinikum Linz Barmherzige Schwestern-Elisabethinen, Linz, Austria

<sup>27</sup> Universitair Ziekenhuis Gent, Gent, Belgium

<sup>28</sup> Department of Internal Medicine III, University Hospital of Ulm, Ulm, Germany

<sup>29</sup> Universitaria di Bologna, Istituto Di Ematologia, Bologna, ITA

<sup>30</sup> Institute of Hematology "Seràgnoli" University of Bologna, Bologna, Italy

<sup>31</sup> Hospitals NHS Foundation Trust, Cambridge University, Cambridge, United Kingdom

<sup>32</sup> Novartis Pharma AG, Basel, CHE

<sup>33</sup> Novartis Pharmaceuticals, East Hanover, NJ

<sup>34</sup> Novartis Pharmaceuticals Corporation, East Hanover, NJ

<sup>35</sup> Novartis Pharma AG, Basel, Switzerland

<sup>36</sup> Service d'hémo-oncologie, Hôpital Saint-Louis, Paris, France

<sup>37</sup> Department of Medicine, Medical Clinic III, Ludwig-Maximilians-University Hospital, Munich, Germany

**Background:** Tisagenlecleucel is approved in the United States and Europe for adults with relapsed/refractory follicular lymphoma (r/r FL) after  $\geq 2$  lines of prior therapy. The primary analysis of the Phase II ELARA trial (median follow-up: 17 months) reported high response rates and a favorable safety profile in heavily pretreated patients with r/r FL. Here we report longer-term efficacy, safety, pharmacokinetic, and exploratory biomarker analyses after a median follow-up of more than 3 years.

**Methods:** Eligible patients with r/r FL (grades 1-3A) previously treated with  $\geq 2$  lines of systemic therapy (including an anti-CD20 monoclonal antibody [mAb] and alkylating agent) received a single tisagenlecleucel infusion ( $0.6 \times 10^8$  CAR+ viable T cells). Bridging therapy was permitted. Baseline clinical characteristics and circulating blood naive T cells were correlated with clinical response. Cellular kinetics were assessed using quantitative polymerase chain reaction.

**Results:** As of March 29, 2023, 97 patients were infused and had a median follow-up of 41 months (range, 34.2-49.7). At baseline, 68% of patients were double refractory to anti-CD20 mAb and alkylating agent, 65% had bulky disease ( $> 7$  cm or 3 lesions  $> 3$  cm), and 63% had progression of disease within 2 years of frontline systemic therapy (POD24). Comorbidities included cardiac disorders (9%), diabetes (9%), and renal insufficiency (5%). Among 94 patients evaluable for efficacy, best overall response (BOR) of complete response (CR) rate by independent review committee assessment was 68% (95% CI, 57.7%-77.3%) and overall response rate (CR + partial response) 86% (95% CI, 77.5%-92.4%). Median progression-free survival (PFS) was 37 months; 36-month PFS was 53% in all patients and 69% in patients with a BOR of CR. In the POD24 subgroup, 36-month PFS was 50% (n=61) compared with 59% for patients without POD24 (n=33) (Figure). CAR transgene persistence was observed for up to 1290 days. Patients without POD24 had higher median in vivo CAR expansion and longer persistence than patients with POD24. Median duration of response (DOR) was not reached; 64% of responding patients had ongoing response at the time of the 36-month analysis. Among patients with a BOR of CR, 73% had an ongoing response at the time of the 36-month analysis. High baseline levels of circulating CD8+ naive T cells ( $> 2.14\%$  of total T cells) were associated with prolonged PFS and DOR. Median overall survival (OS) and median time to next treatment were not reached. The OS rate at 36 months was 82%, and probability of starting a new treatment at 36 months was 35%. In the POD24 subgroup, 36-month OS rate was 83% compared with 81% in patients without POD24 (Figure). No new safety signals were reported. The most common grade  $\geq 3$  adverse events (AEs) were neutropenia (43%) and anemia (19%). The most common serious AEs were cytokine release syndrome (20% [Lee grading]), pneumonia (11%), and febrile neutropenia (8%). To date 18 patients have died during the study (progressive disease, n=8; AE, n=9; euthanasia, n=1).

**Conclusions:** Patients with r/r FL maintained a high rate of durable responses more than 3 years after tisagenlecleucel infusion, including patients in high-risk subgroups such as POD24. Tisagenlecleucel's safety profile remains favorable with no new safety signals during extended follow-up. Correlative analyses suggest higher baseline levels of CD8+ naive T cells ( $> 2.14\%$ ) are associated with improved long-term clinical outcomes.

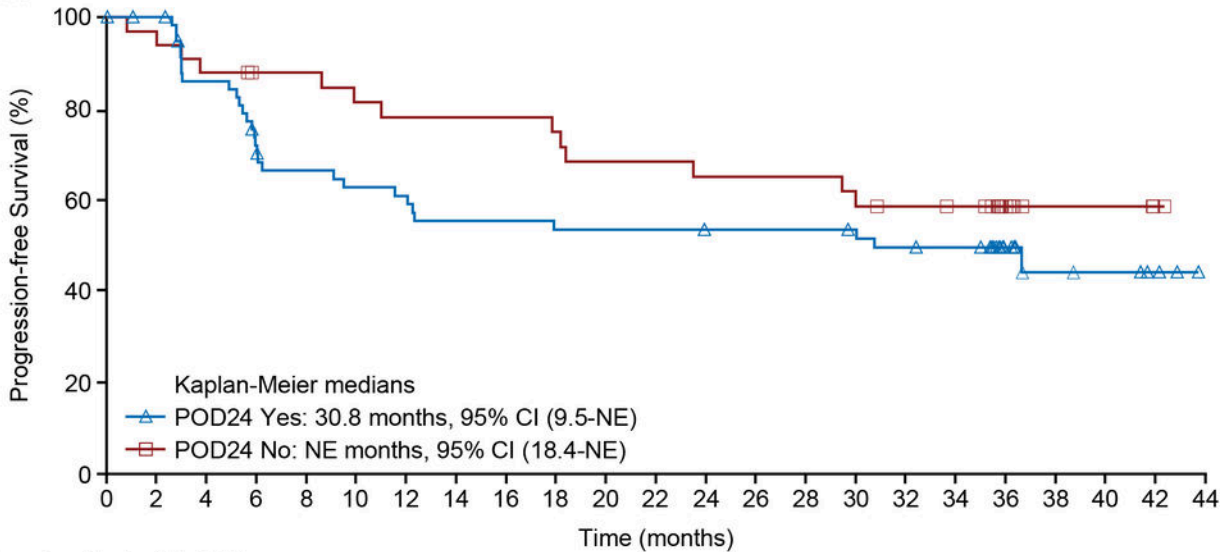
**Disclosures Schuster:** Janssen: Consultancy; Legend Biotech: Consultancy; Loxo: Consultancy; Acerta: Consultancy; Bi-Gene: Consultancy; Celgene: Consultancy, Research Funding; Nanovector: Consultancy; Pharmacyclis: Consultancy; Merck: Research Funding; DTRM: Research Funding; Juno Therapeutics: Research Funding; Abbvie: Research Funding; Adaptive Biotechnologies: Research Funding; TG Therapeutics: Research Funding; Genentech/Roche: Consultancy, Research Funding; Incyte: Consultancy, Research Funding; MustangBio: Consultancy; Morphosys: Consultancy; Nordic: Consultancy; Regeneron: Consultancy; Novartis: Consultancy, Research Funding. **Fowler:** Celgene: Membership on an entity's Board of Directors or advisory committees, Research Funding; Novartis: Membership on an entity's Board of Directors or advisory committees, Research Funding; TG Therapeutics: Membership on an entity's Board of Directors or advisory committees, Research Funding; Roche: Research Funding; BostonGene, Corp.: Current Employment, Current equity holder in private company, Current holder of stock options in a privately-held company. **Dickinson:** F. Hoffmann-La Roche Ltd: Other: travel, accommodation, expenses; F. Hoffmann-La Roche Ltd, Amgen, MSD, Janssen, Bristol-Myers Squibb, Novartis, Gilead Sciences, Abbvie: Honoraria; Novartis, F. Hoffmann-La Roche Ltd, Takeda, Celgene, MSD, Abbvie, Lilly: Research Funding; Novartis, F. Hoffmann-La Roche Ltd, Bristol-Myers Squibb, Gilead Sciences, Janssen, Abbvie, Genmab: Consultancy. **Kolstad:** Nordic Nanovector: Research Funding; Nordic Nanovector: Consultancy. **Butler:** Janssen, Novartis: Honoraria; Gilead Sciences, Janssen, Novartis: Consultancy; Gilead Sciences, Novartis, Janssen, Roche, Takeda: Speakers Bureau. **Ghosh:** Bristol-Myers Squibb, Kite, Takeda, Fate, Atara, Incyte, Miltenyi: Research Funding. **Popplewell:** La Roche: Honoraria; Hoffmann: Honoraria; Seattle Genetics: Consultancy, Honoraria; Novartis: Consultancy; Pfizer: Honoraria. **Chavez:** Epizyme: Speakers Bureau; Genmab: Honoraria; Kite/Gilead: Membership on an entity's Board of Directors or advisory committees; Karyopharm: Membership on an entity's Board of Directors or advisory committees; Beigene: Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; BMS: Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; Cellectar: Membership on an entity's Board of Directors or advisory committees; Adaptive: Research Funding; ADC Therapeutics: Membership on an entity's Board of Directors or advisory committees, Research Funding; Astra Zeneca: Research Funding; Lilly: Honoraria; Merck: Research Funding; Morphosys: Speakers Bureau; Novartis: Membership on an entity's Board of Directors or advisory com-

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**Figure. (A) Progression-free survival by POD24, (B) Overall survival by POD24.**  
NE, not evaluable; POD24, progression of disease within 2 years of frontline systemic therapy.

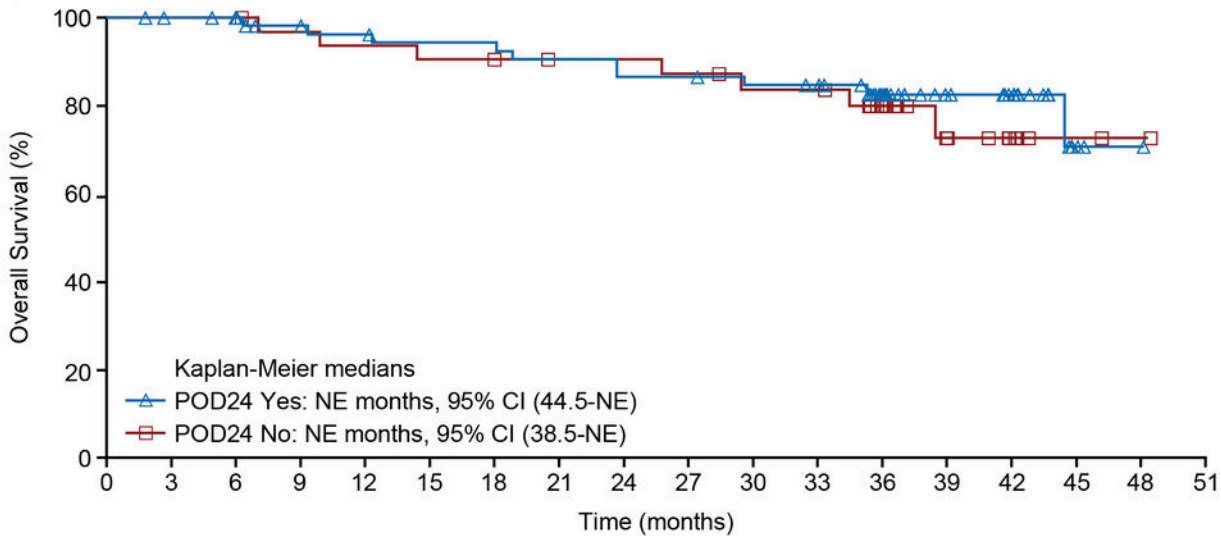
**Panel A**



Number of patients still at risk

POD24 Yes	61	59	49	40	36	34	33	30	30	29	29	29	28	28	28	27	25	24	14	7	6	3	0
POD24 No	33	32	29	27	27	25	24	24	24	23	21	21	20	20	20	18	17	16	8	3	3	1	0

**Panel B**



Number of patients still at risk

POD24 Yes	61	59	58	53	51	49	49	47	45	45	43	42	30	19	15	3	1	0
POD24 No	33	33	33	31	30	29	29	27	27	26	24	24	17	9	5	2	1	0

**Figure 1**

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