



## The 65th ASH Annual Meeting Abstracts

## ORAL ABSTRACTS

**623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL****TRANSCEND FL: Phase 2 Study Primary Analysis of Lisocabtagene Maraleucel as Second-Line Therapy in Patients with High-Risk Relapsed or Refractory Follicular Lymphoma**

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Background: Results with CD19-directed CAR T cell therapy in patients (pts) with second-line (2L) R/R follicular lymphoma (FL) and high-risk features, such as progression of disease within 24 months (POD24) from diagnosis or double refractory to

anti-CD20 antibody plus alkylator, have not been previously reported. TRANSCEND FL (NCT04245839), a global, phase 2, open-label, single-arm, multicohort, pivotal study, assessed efficacy and safety of the anti-CD19 CAR T cell therapy lisocabtagene maraleucel (liso-cel) in pts with second line or later (2L+) R/R indolent NHL. Some data from the primary analysis were previously reported, including safety in 2L+ R/R FL, and focused on efficacy in third line or later R/R FL (Morschhauser F, et al. *Hematol Oncol* 2023;41[S2]:877–880). Here, we report primary analysis results in the cohort of pts with 2L high-risk R/R FL.

Methods: Eligible pts in the 2L R/R FL cohort had biopsy-confirmed FL before enrollment and must have had POD24 with treatment  $\leq$  6 months from original FL diagnosis and/or must have had high tumor burden as defined by modified Groupe d'Etude des Lymphomes Folliculaires (mGELF) criteria. All pts received 1 prior combination systemic therapy with an anti-CD20 antibody and alkylator. Eligible pts received liso-cel ( $100 \times 10^6$  CAR<sup>+</sup> T cells) after lymphodepleting chemotherapy (LDC). Bridging therapy was allowed with reconfirmation of PET-positive disease before LDC. The primary endpoint was ORR per independent review committee (IRC) by PET/CT using Lugano 2014 criteria. Secondary endpoints included CR rate, duration of response (DOR), PFS, OS, safety, and cellular kinetics. Pharmacodynamic endpoints were exploratory.

Results: At data cutoff (January 27, 2023), 23 of 25 leukapheresed pts received liso-cel and were evaluable for safety and efficacy per IRC; 1 received nonconforming product and 1 reached CR after bridging therapy and no longer met eligibility criteria. Median (range) age was 53 y (34–69), 74% had stage III/IV disease, and 35% were high-risk per FL International Prognostic Index (FLIPI). Sixty-five percent of pts had POD24 from initiation of first-line combination chemoimmunotherapy (52% had POD24 from diagnosis), 70% met mGELF criteria (mGELF only, 48%; mGELF and POD24 from diagnosis, 22%), and 48% were double refractory to anti-CD20 antibody plus alkylator. Median (range) on-study follow-up was 18.1 months (1.0–26.8). In efficacy-evaluable pts, the ORR and CR rate were both 95.7% (95% CI, 78.1–99.9; 1-sided  $P < 0.0001$ ; Table).

With a median follow-up of 16.8 months and 17.8 months, respectively, median DOR and PFS were not reached; 12-month DOR and PFS were 89.8% and 91.3%, respectively. The most common grade (gr)  $\geq$  3 treatment-emergent AEs (TEAE) were cytopenias; neutropenia was most frequent (52%). Cytokine release syndrome (CRS) occurred in 12 (52%) pts (no gr  $\geq$  3). Median (range) time to onset and resolution of CRS was 6 days (2–9) and 3 days (2–7), respectively. Neurological events (NE) occurred in 4 (17%) pts, with 1 (4%) gr 3 and no gr 4–5 (Table). Median (range) time to onset and resolution of NEs was 8.5 days (6–11) and 2.5 days (1–4), respectively. Three (13%) pts received tocilizumab/steroids for CRS/NEs. Prolonged cytopenia (gr  $\geq$  3 laboratory values at Day 29) occurred in 3 (13%) pts; all recovered to gr  $\leq$  2 by Day 90. No gr  $\geq$  3 infections were reported. One TEAE death occurred in the context of IRC-assessed disease progression due to gr 5 macrophage activation syndrome (MAS). Liso-cel showed rapid expansion with median (range) time to maximum transgene levels of 10 days (7–11). Persistence of liso-cel transgene was detected up to Month 12 in 5 of 18 (28%) pts. B-cell aplasia ( $< 3\%$  CD19<sup>+</sup> B cells in peripheral blood lymphocytes) after liso-cel infusion was rapid and maintained in  $\geq 95\%$  of pts through Month 2.

Conclusions: This is the first report of outcomes in 2L high-risk R/R FL with CD19-directed CART cell therapy. In this population, liso-cel achieved very high CR rates (22 of 23 pts); deep and durable remissions, with follow-up ongoing; and a favorable safety profile with low rates of severe (gr  $\geq$  3) CRS, NEs, and prolonged cytopenia, and no severe infections. These data support liso-cel as a potential new treatment option in pts with 2L R/R FL at high-risk for treatment failure.

**Disclosures Morschhauser:** Janssen: Honoraria; Gilead: Consultancy, Other: Advisory Board; BMS: Consultancy, Other: Advisory Board; AbbVie: Consultancy, Other: Advisory Board; Celgene: Other: Advisory Board; Novartis: Consultancy, Other: Advisory Board; Incyte: Other: Advisory Board; Epizyme: Other: Advisory Board; Genmab: Consultancy, Other: Advisory Board; Roche: Consultancy, Honoraria, Other: Advisory Board. **Dahiya:** Adaptive Biotechnologies: Consultancy; Bristol Myers Squibb: Consultancy; Incyte: Consultancy; Kite, a Gilead Company: Consultancy, Research Funding. **Palomba:** Rheos: Honoraria; Seres Therapeutics: Honoraria, Patents & Royalties; Smart Immune: Honoraria; Thymofox: Honoraria; Ceramedix: Honoraria; BMS: Honoraria; Juno: Honoraria, Patents & Royalties; Cellectar: Honoraria; Novartis: Honoraria; MustangBio: Honoraria; Pluto Immunotherapeutics: Honoraria; Kite: Honoraria; Garuda Therapeutics: Honoraria; Synthekine: Honoraria. **Martin Garcia-Sancho:** Kyowa Kirin: Consultancy, Honoraria; Clinigen: Consultancy; Eusa Pharma: Consultancy, Honoraria; Novartis: Consultancy, Honoraria; Gilead / Kite: Consultancy, Honoraria; Incyte: Consultancy, Honoraria; Lilly: Consultancy, Honoraria; Takeda: Consultancy, Honoraria; ADC Therapeutics America: Consultancy, Honoraria; Miltenyi: Consultancy, Honoraria; Ideogen: Consultancy, Honoraria; AbbVie: Consultancy, Honoraria; F. Hoffmann-La Roche Ltd, BMS / Celgene, Kyowa Kirin, Novartis, Gilead / Kite, Incyte, Lilly, ADC Therapeutics America, Miltenyi, Ideogen, Abbvie, Sobi: Consultancy; F. Hoffmann-La Roche Ltd, BMS/Celgene, Janssen, Gilead/Kite, Takeda, Eusa Pharma, Abbvie: Honoraria; Roche: Consultancy, Honoraria; Bristol Myers Squibb: Consultancy, Honoraria. **Reguera:** BMS: Speakers Bureau; KITE: Speakers Bureau; AMGEN: Speakers Bureau; Janssen: Consultancy, Speakers Bureau. **Kuruville:** Abbvie, BMS, Gilead, Merck, Roche, Seattle Genetics: Consultancy; Abbvie, Amgen, Astra Zeneca, BMS, Genmab, Gilead, Incyte, Janssen, Merck, Novartis, Pfizer, Roche, Seattle Genetics: Honoraria; Roche, Astra Zeneca, Merck: Research Funding; Karyopharm: Other: DSMB. **Jaeger:** Innovative Medicines Initiative 2 Joint Undertaking: Research Funding; BMS, Novartis, Gilead, Miltenyi, Janssen and Roche: Honoraria. **Cartron:** MabQi: Consultancy; MedxCell: Consultancy; Janssen: Honoraria; Novartis: Honoraria; Gilead: Honoraria; Emercell: Consultancy; BMS: Consultancy, Honoraria; AbbVie: Consultancy, Honoraria; Jansen, Gilead, Novartis, F. Hoffmann-La Roche Ltd, BMS, Abbvie: Honoraria; MedxCell, Ownards Therapeutics, MabQi, Emercell, F. Hoffmann-La Roche Ltd, BMS, Abbvie: Consultancy; MabQi, Ownards Therapeutics, Abbvie, Roche, Bristol Myers Squibb: Membership on an entity's Board of Directors or advisory committees; Ownards Therapeutics: Consultancy; Roche: Consultancy, Honoraria. **Izutsu:** Nihon Kayaku: Honoraria; Meiji Seika: Honoraria; Eli Lilly: Honoraria; Symbio Pharmaceuticals: Honoraria; Janssen: Honoraria; Regeneron: Research Funding; Loxo Oncology: Research Funding; Beigene: Research Funding; Daiichi Sankyo: Honoraria, Research Funding; Yakult: Research

Funding; *Novartis*: Honoraria, Research Funding; *Bristol Myers Squibb*: Honoraria, Research Funding; *Incyte*: Research Funding; *Astellas Amgen*: Research Funding; *Nippon Shinyaku*: Consultancy; *Mitsubishi Tanabe Pharma*: Consultancy; *Zenyaku Kogyo*: Consultancy; *Kyowa Kirin*: Honoraria, Research Funding; *Chugai Pharma*: Honoraria, Research Funding; *Pfizer*: Honoraria, Research Funding; *MSD*: Honoraria, Research Funding; *Genmab*: Consultancy, Honoraria, Research Funding; *AstraZeneca*: Consultancy, Honoraria, Research Funding; *Ono Pharmaceuticals*: Consultancy, Honoraria; *Takeda*: Consultancy, Honoraria; *Eisai*: Consultancy, Honoraria, Research Funding; *Otsuka*: Consultancy, Research Funding; *Abbvie*: Consultancy, Honoraria, Research Funding. **Dreyling**: *Astra Zeneca, Beigene, Gilead/Kite, Janssen, Lilly, Novartis, Roche*: Honoraria; *Abbvie, Bayer, BMS/Celgene, Gilead/Kite, Janssen, Roche*: Research Funding; *Abbvie, Astra Zeneca, Beigene, BMS/Celgene, Gilead/Kite, Janssen, Lilly/Loxo, Novartis, Roche*: Other: Scientific advisory boards. **Ghesquieres**: *Gilead, Roche, BMS, Abbvie*: Honoraria; 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**Table. Summary of efficacy and safety**

	<b>Patients with 2L FL (n = 23)</b>
<b>Efficacy</b>	
<b>ORR, n (%)</b> 95% CI; 1-sided <i>P</i> value	22 (95.7) 78.1–99.9; < 0.0001
<b>CR rate, n (%)</b> 95% CI; 1-sided <i>P</i> value	22 (95.7) 78.1–99.9; < 0.0001
<b>PR, n (%)</b>	0
<b>Stable disease, n (%)</b>	0
<b>PD, n (%)</b>	1 (4.3)
<b>DOR, median (95% CI)</b> Probability of continued response at 12 months, % (SE)	NR (19.3–NR) 89.8 (6.866)
<b>PFS, median (95% CI)</b> PFS rate at 12 months, % (SE)	NR (20.2–NR) 91.3 (5.875)
	<b>Patients with 2L FL (n = 23)</b>
<b>Safety</b>	
<b>AEs of special interest, n (%)</b>	
Any-grade CRS <sup>a</sup>	12 (52.2)
Grade 1	7 (30.4)
Grade 2	5 (21.7)
Grade 3	0
Grade 4 or 5	0
Any-grade NEs <sup>b</sup>	4 (17.4)
Grade 1	3 (13.0)
Grade 2	0
Grade 3	1 (4.3)
Grade 4 or 5	0
Prolonged cytopenia <sup>c</sup>	3 (13.0)
Grade ≥ 3 infection	0
MAS	1 (4.3)
Hypogammaglobulinemia	1 (4.3)

<sup>a</sup>CRS was graded based on Lee 2014 criteria; <sup>b</sup>NEs were defined as investigator-identified neurological AEs related to liso-cel and were graded per the NCI CTCAE, version 5.0; <sup>c</sup>Defined as grade ≥ 3 laboratory abnormalities of neutropenia, anemia, or thrombocytopenia on Day 29. NR, not reached; SE, standard error.

**Figure 1**

<https://doi.org/10.1182/blood-2023-179474>