ELSEVIER

Blood 142 (2023) 105–108

The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Lisocabtagene Maraleucel as Second-Line Therapy for R/R Large B-Cell Lymphoma in Patients Not Intended for Hematopoietic Stem Cell Transplant: Final Analysis of the Phase 2 PILOT Study

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Background: For the 30%-40% of patients with large B-cell lymphoma (LBCL) who are not cured after first-line therapy, traditional second-line therapy has been high-dose chemotherapy (HDCT) and hematopoietic stem cell transplantation (HSCT). Recent studies have challenged this paradigm, showing a PFS/OS benefit to CAR T cell therapy over HDCT/HSCT in patients with high-risk, transplant-intended disease at first relapse. Given the lack of effective therapeutic options, outcomes have been historically poor for patients not intended to receive HDCT/HSCT. Lisocabtagene maraleucel (liso-cel) is an autologous, CD19-directed, 4-1BB CAR T cell product administered at equal target doses of $CD8^+$ and $CD4^+$ CAR^+ T cells. The open-label phase 2 PILOT study (NCT03483103) evaluated the efficacy and safety of liso-cel in patients with R/R LBCL not intended for HSCT after 1 prior line of therapy. In the primary analysis, the primary endpoint was met with an ORR of 80%. Here, we report the final analysis results from PILOT after a median follow-up of 18.2 mo (range, 1.2-32.8).
Methods: Adults with R/R LBCL were eligible if they had received 1 prior line of therapy with an anthracycline and CD20-targeted agent, were not intended for HSCT, and met ≥ 1 transplant not-intended criterion by investigator (age ≥ 70 years, ECOG PS of 2, diffusing capacity of the lung for carbon monoxide ≤ 60%, LVEF < 50%, CrCl < 60 mL/min, or alanine aminotransferase/aspartate transaminase > 2 × upper limit of normal). Patients received lymphodepleting chemotherapy (intravenous fludarabine 30 mg/m² and intravenous cyclophosphamide 300 mg/m² daily for 3 days) followed by liso-cel infusion 2-7 days later. The primary endpoint was ORR by independent review committee (IRC) per Lugano 2014 criteria; secondary endpoints included safety; CR rate, duration of response (DOR), and PFS by IRC; and OS.
Results: A total of 61 patients were included in the liso-cel-treated analysis set. Median age was 74 years (range, 53–84 years; ≥ 75 years, 46%), 39% were female, 26% had ECOG PS of 2, 25% had CrCl < 60 mL/min, 54% had diffuse LBCL not otherwise specified, 30% had high-grade lymphoma with diffuse LBCL histology (HGBCL), 33% had double-/triple-hit disease, and 54%

had refractory disease. ORR was 80.3% (95% CI, 68.2-89.4),with 54.1% (95% CI, 40.8-66.9) achieving CR (Table). Responses were durable, with a median DOR of 23.3 mo (95% CI, 6.2-not reached [NR]) after a median follow-up of 23.1 mo (95% CI, 22.9-23.3); median DOR for those with CR was NR (95% CI, 21.65-NR) versus 2.1 mos (95% CI, 1.4-3.3) for those with PR. Median PFS was 9.0 mo (95% CI, 4.2-NR) and median OS was NR (95% CI, 16.3-NR).

Twenty-four patients died, mostly because of disease progression (n = 20). During the treatment-emergent (TE) period (≤ 90 days after liso-cel administration), 96.7% of patients had TEAEs (grade ≥ 3, 78.7%), 37.7% had cytokine release syndrome (CRS; grade 3, 1.6%; no grade 4-5), 31.1% had neurological events (NE; grade 3, 4.9%; no grade 4-5), 8.2% had hypogammaglobulinemia, and 6.6% had grade ≥ 3 infections. A total of 57 patients were included in the post-TE period (starting from 91 days after liso-cel administration, initiation of subsequent anticancer therapy, or liso-cel retreatment before Day 91, whichever came first). Of those patients, 50.9% experienced AEs (grade ≥ 3, 17.5%; Table). The most common grade ≥ 3 AEs in the post-TE period were anemia (5.3%) and thrombocytopenia (5.3%). In the post-TE period, 1 (1.8%) patient had hypogammaglobulinemia, and 1 (1.8%) had grade ≥ 3 infections (bacteremia and sepsis). Overall, 2 (3.5%) patients had second primary malignancies (squamous cell carcinoma of skin and malignant external ear neoplasm [n = 1] and myelodysplastic syndrome [n = 1]).

Cellular kinetics and B-cell aplasia data will be presented.

Conclusions: After a median of 18.2 mo of follow-up, the final analysis of the PILOT study demonstrated a high CR rate and durable CRs with liso-cel treatment in patients with R/R LBCL for whom HSCT was not intended. Despite the high incidence of HGBCL, primary refractory disease, advanced age, and comorbidities in this population, the safety profile was consistent with previous reports, with no new or increased safety signals. These results continue to support liso-cel as second-line therapy for this underserved population of patients with R/R LBCL.

Disclosures Sehgal: *PeerView Live:* Speakers Bureau; *Bristol Myers Squibb:* Research Funding; *Chimagen:* Research Funding; *Cytoagents:* Research Funding; *Kite/Gilead:* Research Funding; *OncLive:* Speakers Bureau. **Riedell:** *Fate Therapeutics:* Research Funding; *CRISPR Therapeutics:* Research Funding; *Calibr:* Research Funding; *CVS Caremark:* Consultancy; *Xencor:* Research Funding; *Tessa Therapeutics:* Research Funding; *MorphoSys:* Research Funding; *Nkarta:* Research Funding; *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Abbvie:* Consultancy; *Genmab:* Membership on an entity's Board of Directors or advisory committees; *ADC Therapeutics:* Membership on an entity's Board of Directors or advisory committees; *Pharmacyclics:* Consultancy; *BeiGene:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Janssen:* Consultancy; *Kite/Gilead:* Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Nurix Therapeutics:* Membership on an entity's Board of Directors or advisory committees; *Intellia Therapeutics:* Membership on an entity's Board of Directors or advisory committees; *Nektar Therapeutics:* Membership on an entity's Board of Directors or advisory committees; *Sana Biotechnology:* Consultancy; *Roche:* Research Funding. **Ghosh:** *AstraZenca, Janssen, Pharmacyclics, Kite pharma, BMS, Epizyme:* Speakers Bureau; *Roche NHL soultions panel:* Speakers Bureau; *TG Therapeutics, Genentech/Roche, Bristol Myers Squibb, Gilead, Morphosys, AbbVie, Pharmacyclics:* Research Funding; *Seagen, TG Therapeutics, AstraZeneca, Phamacyclics, Janssen, Bristol Myers Squibb, Gilead Sciences, Kite Pharma, Beigene, Incyte, Lava Therapeutics, Incyte, Roche/Genentech, Novartis, Loxo Oncology, AnbbVie, Genmab, Adaptive Biotech, ADC Therapeutics:* Consultancy. **Hamadani:** *BeiGene:* Speakers Bureau; *Genentech:* Honoraria; *Incyte:* Consultancy; *Kite, a Gilead Company:* Consultancy, Speakers Bureau; *Genmab:* Consultancy; *Takeda:* Research Funding; *Spectrum Pharmaceuticals:* Research Funding; *Novartis:* Consultancy; *AstraZeneca:* Speakers Bureau; *ADC therapeutics:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Abbvie:* Consultancy; *Omeros:* Consultancy; *CRISPR:* Consultancy; *Genmab:* Consultancy; *Bristol Myers Squibb:* Consultancy; *Caribou:* Consultancy; *Gamida Cell:* Consultancy; *Kadmon:* Consultancy; *Legend Biotech:* Consultancy; *MorphoSys:* Consultancy; *SeaGen:* Consultancy; *Astra Zeneca:* Speakers Bureau; *BeiGene:* Speakers Bureau; *Sanofi Genzyme:* Speakers Bureau; *Astellas:* Research Funding; *Myeloid Therapeutics:* Honoraria. **Hildebrandt:** *Kite, Incyte, Pfizer, Falk Foundation, Jazz Pharmaceuticals, Astellas Pharm, Takeda:* Other: travel accommodations ; *Pfizer, Kite, Incyte, Jazz Pharmaceuticals, Morphosys. Alexion Pharmaceuticals, Karyopharm Therapeutics, Seattle Genetics:* Consultancy; *Sangamo Bioscience, Axim Biotechnologies, Juno Therapeutics, Kite, Novartis, Insys Therapeutics, Abbvie, GW Pharmaceuticals, Cardinal Health, Immunomedica, Endocyte, Clovis Oncology, Cellectis, Aetna, CVS Health, Celgene, Bluebird Bio, Bristol Myers Squib:* Current holder of *stock options* in a privately-held company; *Takeda, Jazz Pharmaceuticals, Pharmacyclics, Incyte, AstraZeneca:* Research Funding. **Godwin:** *BMS:* Research Funding. **Reagan:** *Seagen:* Research Funding; *Caribou biosciences:* Consultancy; *Genentech:* Research Funding; *Kite, a Gilead Company:* Consultancy, Other: speaker. **Wagner-Johnston:** *ADC Therapeutics:* Research Funding; *Merck:* Research Funding; *Beigene:* Consultancy, Research Funding; *Astex:* Research Funding; *Genentech:* Research Funding. **Essell:** *Kite:* Speakers Bureau; *BMS:* Speakers Bureau. **Nath:** *Actinium:* Consultancy; *ADC Therapeutics:* Consultancy; *Allovir:* Consultancy; *Incyte:* Consultancy. **Champion:** *Abbvie:* Speakers Bureau. **Fanning:** *Abbvie:* Consultancy; *Genmab:* Consultancy; *Genetech:* Consultancy. **Gupta:** *Corvus:* Consultancy, Honoraria; *Atara:* Consultancy, Honoraria. **Chow:** *Bristol Myers Squibb:* Current Employment, Current equity holder in publicly-traded company. **Yuan:** *Bristol Myers Squibb:* Current Employment, Current equity holder in publicly-traded company. **Yang:** *NanoString Technologies, Inc:* Current equity holder in publicly-traded company, Ended employment in the past 24 months; *Bristol Myers Squibb:* Current Employment, Current equity holder in publicly-traded company. **Ogasawara:** *Bristol Myers Squibb:* Current Employment, Current equity holder in publicly-traded company. **Thorpe:** *Bristol Myers Squibb:* Current Employment, Current equity holder in publicly-traded company. **Gordon:** *Ono Pharmaceuticals:* Consultancy; *Bris-*

tol Meyers Squibb: Honoraria, Membership on an entity's Board of Directors or advisory committees; *Kite Pharmaceuticals:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Other: data and safety monitoring board ; *nanoparticles:* Patents & Royalties: nanoparticles for cancer therapy (HDL NP As Inducers of Ferroptosis in Cancer, PCT/US2020/051549; *Nanostructures:* Patents & Royalties: Nanostructures for Treating Cancer and Other Conditions, PCT/US2013/027431); *Zylem Biosciences:* Other: co-founder.

Table. Summary of efficacy (liso-cel–treated efficacy analysis set) and safety (liso-cel–treated analysis set) outcomes

Efficacy outcomes	Liso-cel–treated efficacy analysis set (N = 61)
ORR (CR + PR), n (%) [95% CI][a]	49 (80.3) [68.2–89.4]
CR rate, n (%) [95% CI][a]	33 (54.1) [40.8–66.9]
BOR, n (%)	
CR	33 (54.1)
PR	16 (26.2)
SD	3 (4.9)
PD	8 (13.1)
NE	1 (1.6)
DOR	
Continued response at 12 mo, % (95% CI)[b]	54.9 (39.6–67.9)
Continued response at 18 mo, % (95% CI)[b]	52.6 (37.4–65.8)
Median follow-up, mo (95% CI)[c]	23.1 (22.9–23.3)
PFS	
18-mo PFS rate, % (95% CI)[b]	42.9 (29.9–55.2)
Median follow-up, mo (95% CI)[c]	24.0 (23.8–24.15)
OS	
18-mo OS rate, % (95% CI)[b]	59.0 (45.2–70.4)
Median follow-up, mo (95% CI)[c]	24.25 (23.95–24.8)
Summary of AEs[d]	**Post-TE period[e] (n = 57)**
Any AE, n (%)	29 (50.9)
Grade 3–4	9 (15.8)
Grade 5	1 (1.8)
Any serious AE	5 (8.8)
Most common (> 3%) grade ≥ 3 AEs, n (%)	
Anemia	3 (5.3)
Thrombocytopenia	3 (5.3)
Lymphopenia	2 (3.5)

[a]Two-sided 95% exact Clopper-Pearson CIs; [b]Kaplan-Meier method used to obtain 2-sided 95% CIs; [c]Reverse Kaplan-Meier method used to obtain median follow-up and its 95% CIs; [d]AEs were graded using NCI CTCAE, version 4.03; [e]Post-TE period started from 91 days after liso-cel administration, initiation of subsequent anticancer therapy, or liso-cel retreatment that started before Day 91, whichever came first.
BOR, best overall response; NE, not evaluable; SD, stable disease.

Figure 1

https://doi.org/10.1182/blood-2023-180952