blood®

AMERICAN SOCIETY OF HEMATOLOGY®

Reprinted from:

2020 ASH Annual Meeting Abstracts
Blood 2020

Selected abstract

Abstract 118

Safety and Preliminary Efficacy in Patients with Relapsed/Refractory Mantle Cell Lymphoma Receiving Lisocabtagene Maraleucel in Transcend NHL 001

Maria Lia Palomba et al.

ASH Abstracts
2020

62nd ASH Annual Meeting and Exposition
December 5-8, 2020

Abstract 118

Safety and Preliminary Efficacy in Patients with Relapsed/Refractory Mantle Cell Lymphoma Receiving Lisocabtagene Maraleucel in Transcend NHL 001

Maria Lia Palomba, MD[1], *Leo I. Gordon, MD*[2], *Tanya Siddiqi, MD*[3]*, *Jeremy S. Abramson, MD*[4]*, *Manali Kamdar, MD*[5]*, *Matthew A. Lunning, DO, FACP*[6], *David G. Maloney, MD, PhD*[7], *Charalambos Andreadis, MD, MSCE*[8]*, *Jon E. Arnason, MD*[9], *Nilanjan Ghosh, MD, PhD*[10], *Amitkumar Mehta, MD*[11], *Scott R. Solomon, MD*[12], *Thalia Farazi, MD, PhD*[13]*, *Jacob Garcia, MD*[13]*, *Christine Dehner, BSc*[13]*, *Ken Ogasawara, PhD, MPH*[14]*, *Jie Gao, PhD*[14]* *and Michael Wang, MD*[15]

[1]Memorial Sloan Kettering Cancer Center, New York, NY
[2]Northwestern University, Feinberg School of Medicine, Robert H. Lurie Comprehensive Cancer Center, Chicago, IL
[3]City of Hope National Medical Center, Duarte, CA
[4]Massachusetts General Hospital Cancer Center, Boston, MA
[5]University of Colorado Cancer Center, Aurora, CO
[6]University of Nebraska Medical Center, Omaha, NE
[7]Fred Hutchinson Cancer Research Center, Seattle, WA
[8]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, CA
[9]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA
[10]Levine Cancer Institute, Atrium Health, Charlotte, NC
[11]University of Alabama at Birmingham, Birmingham, AL
[12]Immunotherapy Program, Northside Hospital Cancer Institute, Atlanta, GA
[13]Juno Therapeutics, a Bristol-Myers Squibb Company, Seattle, WA
[14]Bristol-Myers Squibb Company, Princeton, NJ
[15]Department of Lymphoma and Myeloma, U.T. M.D. Anderson Cancer Center, Houston, TX

*signifies non-member of ASH

Background: Mantle cell lymphoma (MCL) is an aggressive subtype of B-cell non-Hodgkin lymphoma (NHL). Most patients with MCL relapse after first-line immunochemotherapy, with poor responses to salvage therapy. Chimeric antigen receptor (CAR) T cell therapy has shown clinical efficacy in patients with relapsed/refractory (R/R) NHL. We report the results of the dose-finding and dose-expansion parts of the ongoing phase 1 TRANSCEND NHL 001 study (NCT02631044) in patients with R/R MCL (MCL cohort) who received lisocabtagene maraleucel (liso-cel), an investigational, CD19-directed, defined composition, 4-1BB CAR T cell product administered at equal target doses of $CD8^+$ and $CD4^+$ CAR^+ T cells.

Methods: Eligible patients had confirmed MCL (cyclin D1 expression, t[11;14]) with R/R disease after ≥1 prior line of therapy. After lymphodepleting chemotherapy, patients received liso-cel infusion at 1 of 2 dose levels (DLs): DL1 (50×10^6 CAR^+ T cells) or DL2 (100×10^6 CAR^+ T cells). Bridging therapy was allowed between leukapheresis and initiation of lymphodepleting chemotherapy. Primary endpoints were safety and objective response rate (ORR). Secondary endpoints included complete response (CR) rate, duration of response, progression-free survival, overall survival, and pharmacokinetics (PK).

Results: At data cutoff, 41 patients had undergone leukapheresis and 32 had received liso-cel (DL1, n = 6; DL2, n = 26). Among the 32 patients who received liso-cel, the median (range) age was 67 (36–80) years and 27 patients (84%) were male. Twelve patients (37.5%) had blastoid morphology, 23 (72%) had documented Ki67 ≥30%, 7 (22%) had a *TP53* mutation, and 11 (34%) had a complex karyotype. Patients had a median (range) sum of the product of perpendicular diameters before lymphodepleting chemotherapy of 28.7 (0–209.6) cm^2 and median lactate dehydrogenase of 251.5 (117–811) U/L. Patients had received a median (range) of 3 (1–7) prior systemic therapies, and most (72%) were refractory to their last prior therapy. Of 28 patients (87.5%) who had received a prior Bruton tyrosine kinase inhibitor, 11 (34%) were refractory to the therapy. Seventeen patients (53%) received bridging therapy.

Eighteen patients (56%) had serious treatment-emergent adverse events (TEAEs), and 27 (84%) had grade ≥3 TEAEs, primarily neutropenia (41%), anemia (34%), and thrombocytopenia (31%). Grade ≥3 thrombocytopenia was more frequent at DL2 (n = 9/26 [35%]) than at DL1 (n = 1/6 [17%]). Prolonged grade ≥3 cytopenias (present at study Day 29) occurred in 11 patients (34%). Sixteen patients (50%; DL1, n = 2/6 [33%]; DL2, n = 14/26 [54%]) had cytokine release syndrome (CRS), including 1 grade 4 event at DL2. There were no grade 3 or 5 CRS events. Median (range) time to CRS onset and resolution was 6 (2–10) days and 4 (2–9) days, respectively. Nine patients (28%) had neurological events (NEs), all at DL2, including 3 grade 3 NEs. No grade 4 or 5 NEs were reported. Median (range) time to NE onset and resolution was 8 (2–25) days and 3 (1–51) days, respectively. Ten patients (31%) received tocilizumab and/or corticosteroids for treatment of CRS and/or NEs. Grade 5 TEAEs occurred in 2 patients (at DL2): one patient with high tumor burden had tumor lysis syndrome and 1 patient had cryptococcal meningoencephalitis. DL2 was selected for dose expansion.

Of 32 patients, 27 responded to liso-cel (ORR, 84%: DL1, n = 4/6 [67%]; DL2, n = 23/26 [88%]), and 19 (59%) achieved a CR (DL1, n = 2/6 [33%]; DL2, n = 17/26 [65%]). Among the 12 patients with blastoid morphology, 9 patients had a response (ORR, 75%), including 7 (58%) who achieved a CR. Overall, the median (range) time to first CR was 1 (1–6) month. At data cutoff, 20 (74%) of 27 responders were censored with an ongoing response or had completed the study. Median (range) follow-up duration was 10.9 (1.2–24.8) months for DL1 and 3.1 (0.4–23.0) months for DL2. Preliminary PK analysis indicated that median maximum expansion was higher among patients at DL2 than at DL1.

Conclusions: In this phase 1 study of patients with R/R MCL, treatment with liso-cel was associated with a low incidence of grade ≥3 CRS and NEs, late onset of CRS/NEs, and promising clinical activity. Dose confirmation is ongoing at DL2 in the MCL cohort.

Disclosures:

Palomba: *Pharmacyclics:* Honoraria; *Juno:* Honoraria; *Celgene:* Honoraria; *Merck:* Honoraria; *Novartis:* Honoraria; *Regeneron:* Research Funding; *Juno:* Research Funding; *Genentech:* Research Funding. **Gordon:** *Zylem Biosciences:* Patents & Royalties: Patents, No Royalties. **Siddiqi:** *Juno:* Membership on an entity's Board of Directors or advisory committees; *Kite:* Membership on an entity's Board of Directors or advisory committees; *Celgene:* Membership on an entity's Board of Directors or advisory committees; *BeiGene:* Other: DMC member; *Juno Therapeutics, Pharmacyclics LLC, an AbbVie Company, AstraZeneca, Celgene, Kite Pharma, and BeiGene:* Consultancy; *Pharmacyclics LLC, an AbbVie Company, Seattle Genetics, Janssen, and AstraZeneca:* Speakers Bureau; *Pharmacyclics LLC, an AbbVie Company, Juno Therapeutics, KITE Pharma, AstraZeneca, TG Therapeutics, Celgene, Oncternal, and BeiGene:* Research Funding; *AstraZeneca:* Other: Travel/accommodations/expenses; *Astrazenca:* Membership on an entity's Board of Directors or advisory committees; *PCYC:* Membership on an entity's Board of Directors or advisory committees. **Abramson:** *Celgene:* Honoraria, Other: Scientific Advisory Board; *Juno Therapeutics:* Other: Scientific Advisory Board; *AbbVie:* Other: Scientific Advisory Board; *EMD Serono:* Other: Scientific Advisory Board; *Genentech/Roche:* Other: Scientific Advisory Board; *Janssen:* Other: Scientific Advisory Board; *Karyopharm:* Other: Scientific Advisory Board; **Gilead:** Other: Scientific Advisory Board; *Verastem:* Other: Scientific Advisory Board; *Bayer:* Other: Scientific Advisory Board; *Merck:* Other; KIte Pharma: Other; *Novartis:* Other; *Amgen:* Other; *Seattle Genetics:* Other; *Allogene:* Other; *Morphosys:* Other; *C4 Therapeutics:* Other; *BeiGene:* Other; *AstraZeneca:* Honoraria; *Incyte:* Honoraria. **Kamdar:** *Seattle Genetics:* Speakers Bureau; *Karyopharm:* Consultancy; *BMS:* Consultancy; *Abbvie:* Consultancy; *AstraZeneca:* Consultancy; *Pharmacyclics:* Consultancy. **Lunning:** *Acrotech:* Consultancy; *ADC Therapeutics:* Consultancy; *Bristol Meyers Squibb:* Consultancy, Honoraria, Research Funding; *Curis:* Research Funding; *Gilead:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria; *Karyopharm:* Consultancy, Honoraria; *Kite:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *TG Therapeutics:* Research Funding; *Verastem:* Consultancy, Honoraria; *AstraZeneca:* Consultancy, Honoraria; *Legend:* Consultancy; *Beigene:* Consultancy, Honoraria; *Aeratech:* Consultancy, Honoraria. **Maloney:** *Kite, a Gilead Company:* Consultancy, Honoraria, Research Funding; *MorphoSys:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *Pharmacyclics:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *Gilead Sciences:* Consultancy, Honoraria; *A2 Biotherapeutics:* Consultancy, Current equity holder in publicly-traded company, Honoraria; *Juno Therapeutics:* Consultancy, Honoraria, Patents & Royalties: Patents are pending, but not issued, licensed, no royalties, no licensees., Research Funding; *Bioline Rx:* Consultancy, Honoraria; *Genentech:* Consultancy, Honoraria; *Celgene:* Consultancy, Honoraria, Research Funding. **Andreadis:** *Genentech:* Other: Spouse Employee (salary and stock); *Novartis:* Research Funding; *Celgene/Juno:* Research Funding; *Amgen:* Research Funding; *Merck:* Research Funding; *Gilead/Kite:* Other: Advisor; *Jazz Pharmaceuticals:* Other: Advisor; *Astellas:* Other: Advisor; *Seattle Genetics:* Other: Advisor; *Karyopharm:* Other: Advisor; *Incyte:* Other. **Arnason:** *Regeneron:* Consultancy; *Juno:* Consultancy. **Ghosh:** *Forty Seven Inc:* Consultancy, Other: Research Bureau, Research Funding; *Genmab:* Consultancy, Speakers Bureau; *AbbVie:* Speakers Bureau; *Karyopharm:* Consultancy; *Juno/Celgene/Bristol-Myers Squibb:* Consultancy, Research Funding; *Kite/Gilead:* Consultancy, Speakers Bureau; *AstraZeneca:* Speakers Bureau; *Roche/Genentech:* Research Funding; *SGN:* Consultancy, Research Funding, Speakers Bureau; *TG Therapeutics:* Consultancy, Research Funding; *Celgene/Bristol-Myers Squibb:* Speakers Bureau; *Janssen:* Consultancy, Research Funding, Speakers Bureau; *Pharmacyclics LLC, an AbbVie Company:* Consultancy, Research Funding, Speakers Bureau. **Mehta:** *Innate Pharmaceuticals:* Research Funding; *Kite/Gilead:* Research Funding; *Merck:* Research Funding; *Gelgene/BMS:* Research Funding; *Oncotartis:* Research Funding; *TG Therapeutics:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Seattle Genetics:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Juno Parmaceuticals/BMS:* Research Funding; *fortyseven Inc/Gilead:* Research Funding; *Takeda:* Research Funding; *Roche-Genentech:* Research Funding; *Incyte:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Affimed:* Research Funding. **Farazi:** *Juno Therapeutics, a Bristol-Myers Squibb Company:* Current Employment; *Bristol-Myers Squibb:* Current equity holder in publicly-traded company. **Garcia:** *Juno Therapeutics, a Bristol-Myers Squibb Company:* Current Employment; *Bristol-Myers Squibb Company:* Current equity holder in publicly-traded company. **Dehner:** *Juno Therapeutics, a Bristol-Myers Squibb Company:* Current Employment; *Bristol-Myers Squibb:* Current equity holder in publicly-traded company. **Ogasawara:** *Bristol-Myers Squibb:* Current Employment; *Bristol-Myers Squibb:* Current equity holder in publicly-traded company. **Gao:** *Bristol-Myers Squibb:* Current equity holder in publicly-traded company; *Bristol-Myers Squibb:* Current Employment. ***Wang:*** *Juno:* Consultancy, Research Funding; *Acerta Pharma:* Research Funding; *Loxo Oncology:* Consultancy, Research Funding; *AstraZeneca:* Consultancy, Honoraria, Other: Travel, accommodation, expenses, Research Funding; *InnoCare:* Consultancy; *Kite Pharma:* Consultancy, Other: Travel, accommodation, expenses, Research Funding; *Pharmacyclics:* Consultancy, Honoraria, Other: Travel, accommodation, expenses, Research Funding; *Janssen:* Consultancy, Honoraria, Other: Travel, accommodation, expenses, Research Funding; *MoreHealth:* Consultancy; *Lu Daopei Medical Group:* Honoraria; *Beijing Medical Award Foundation:* Honoraria; *OncLive:* Honoraria; *Molecular Templates:* Research Funding; *Verastem:* Research Funding; *Dava Oncology:* Honoraria; *Guidepoint Global:* Consultancy; *Pulse Biosciences:* Consultancy; *Celgene:* Consultancy, Other: Travel, accommodation, expenses, Research Funding; *Oncternal:* Consultancy, Research Funding; *Nobel Insights:* Consultancy; *OMI:* Honoraria, Other: Travel, accommodation, expenses; *Targeted Oncology:* Honoraria; *BioInvent:* Research Funding; *VelosBio:* Research Funding.

Springer Healthcare Ibérica S.L.
Rosario Pino, 14 - 4ª Planta. 28020 Madrid. Spain
Tel.: +34 91 555 40 62. Fax: +34 91 555 76 89
E-mail: Miguel.Quesada@springer.com
www.springerhealthcare.com
www.springernature.com

Part of the Springer Nature group