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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Odronextamab Demonstrates Durable Complete Responses in Patients with Diffuse Large B-Cell Lymphoma (DLBCL) Progressing after CAR-T Therapy: Outcomes from the ELM-1 Study

Jennifer L. Crombie[1], *Matthew Matasar*[2], *Max S. Topp, MD*[3], *John N. Allan, MD*[2], *Jeffrey A. Barnes*[4], *Jon E. Arnason, MD*[5], *Jean-Marie Michot*[6], *Neta Goldschmidt*[7], *Susan M. O'Brien*[8], *Uri Abadi, MD*[9,10], *Irit Avivi Mazza, MD*[11], *Jessica Cai*[12], *Dina M. Flink*[12], *Min Zhu*[12], *Jurriaan Brouwer-Visser*[12], *Hesham Mohamed*[12], *Aafia Chaudhry*[12], *Srikanth Ambati*[12], *Steve M Ansell*[13]

[1] Dana Farber Cancer Institute, Boston, MA
[2] Rutgers Cancer Institute of New Jersey, New Brunswick, NJ
[3] Universitätsklinikum Würzburg, Würzburg, Germany
[4] Massachusetts General Hospital Cancer Center, Boston, MA
[5] Beth Israel Deaconess Medical Center, Boston, MA
[6] Gustave Roussy Cancer Campus, Villejuif, France
[7] Hadassah Medical Center and Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel
[8] Chao Family Comprehensive Cancer Center, University of California, Irvine, Orange, CA
[9] Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[10] Hematology Institute, Meir Medical Center, Kfar Saba, Israel
[11] Ichilov University Hospital, Tel-Aviv, Israel
[12] Regeneron Pharmaceuticals, Inc., Tarrytown, NY
[13] Mayo Clinic, Rochester, MN

Background

Chimeric antigen receptor (CAR) T-cell therapies have recently been established as an important option for the management of relapsed/refractory (R/R) DLBCL. However, real-world studies suggest that approximately half of all patients (pts) receiving commercial CAR-T therapies will relapse within 6 months. These pts have a poor prognosis, with estimated overall survival (OS) of only 5 months, indicating a significant unmet need. Odronextamab is a novel, off-the-shelf, CD20×CD3 bispecific antibody that has demonstrated activity in both R/R follicular lymphoma and R/R DLBCL. We have previously reported encouraging results with odronextamab from the Phase 1 ELM-1 study (NCT02290951) in pts with R/R DLBCL post CAR-T therapy (Bannerji R, et al. *Lancet Haematol*. 2022). These results were consistent with the antitumor activity seen in pts with R/R DLBCL from the Phase 2 ELM-2 study (Kim WS, et al. ASH 2022). Here, we present an updated analysis of outcomes in a prespecified cohort of post CAR-T patients from ELM-1.

Methods

Intravenous odronextamab was administered weekly in 21-day cycles during Cycles (C) 1-4. Revisions to the step-up regimen were reported previously (Bannerji R, et al. *Lancet Haematol*. 2022). Odronextamab was administered with steroid prophylaxis and step-up doses of 0.7/4/20 mg during C1 to mitigate the risk of cytokine release syndrome (CRS), followed by 160 mg on Days (D) 1, 8, and 15 of C2-4. After C4, odronextamab maintenance treatment continued at 320 mg every 2 weeks until disease progression or unacceptable toxicity. Those pts who achieved a complete response (CR) that was durable for ≥9 months transitioned to dosing with 320 mg every 4 weeks. The primary endpoint was objective response rate (ORR), assessed by independent central review (ICR) according to the Lugano classification. Key secondary endpoints included duration of response (DoR), progression-free survival (PFS), and OS. Immune biomarker assessment was an exploratory endpoint.

Results

As of Dec 20, 2022, 46 pts were treated (safety-evaluable), with 44 pts evaluable for efficacy. For safety-evaluable pts, median age was 63 years (range 27-82), 67% male, 74% Ann Arbor stage III-IV, and 72% were refractory to CAR-T therapy administered in any prior line. 44 pts were evaluable for efficacy after 4.9 months median duration of follow-up. The ORR and CR rate by ICR were 48% (21/44) and 30% (13/44), respectively. Responses were durable, and both median DoR and median duration of

CR were not reached. The probability of maintaining a response for 12 months was 62% and the probability of maintaining a CR for 9 months was 86%.A responder analysis of the subgroup of pts who achieved a CR will be presented.
The CAR-T treated pts with DLBCL who were evaluable for biomarker analysis (n=10) had lower T-cell counts at baseline compared with CAR-T naive DLBCL pts (n=41 comparable pts who received odronextamab in ELM-2), yet the fold-change of T-cell expansion at C4D15 was greater in CAR-T treated pts versus CAR-T naive pts. T-cell dynamics, such as changes in activation, exhaustion, and memory subsets, will be presented.
Safety was generally consistent with that previously reported. Six (13%) pts permanently discontinued odronextamab due to a treatment-emergent AE (device-related infection, pneumonia, dysphagia, gait disturbance, leukemia, and encephalopathy [n=1 each]). The most common treatment-emergent AE was CRS (any grade, 52%). The highest grade of CRS reported was Grade 2, and low-grade CRS events occurred in 46% of pts with the 0.7/4/20 mg step-up regimen. No cases of ICANS were reported in pts with the 0.7/4/20 mg regimen. Grade ≥3 infections occurred in 10 (22%) pts, with no Grade 5 events. No cases of tumor flare were reported.

Conclusions

Odronextamab monotherapy demonstrates encouraging antitumor activity in heavily pretreated pts who have progressed after CAR-T therapy, with a generally manageable safety profile. Durable CRs were achieved in this difficult-to-treat setting. These data support the potential role of odronextamab in the treatment paradigm for R/R DLBCL. Further studies to evaluate the optimal sequencing and combinations of odronextamab with CAR-T therapy are warranted.

Disclosures Crombie: *ADC Therapeutics:* Consultancy; *Merck:* Research Funding; *Genetech/Roche:* Research Funding; *Dana-Farber Cancer Institute:* Current Employment; *Abbvie:* Research Funding; *Bayer:* Research Funding; *Kite Pharma:* Consultancy; *MorphoSys/Incyte:* Consultancy; *Karyopharm:* Consultancy; *Seagen:* Consultancy; *Genmab:* Consultancy. **Matasar:** *Seattle Genetics:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Takeda:* Consultancy, Honoraria; *Teva:* Consultancy; *Genentech, Inc.:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *F. Hoffmann-La Roche Ltd:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Pharmacyclics:* Honoraria, Research Funding; *Immunovaccine Technologies:* Research Funding; *Janssen:* Honoraria, Research Funding; *Juno:* Consultancy; *Regeneron:* Honoraria, Other: Stipends; *Kite:* Honoraria, Other: Stipends; *Immunovaccine Technologies:* Honoraria; *Epizyme:* Other: Stipends; *Celegene:* Honoraria, Other: Stipends; *BMS:* Honoraria, Other: Stipend; *Bayer:* Consultancy, Honoraria, Research Funding; *AstraZeneca:* Honoraria, Other: Stipend; *Merck:* Current equity holder in private company; *ADC Therapeutics:* Consultancy, Honoraria, Other: Stipend; *Seagen:* Honoraria, Other: stipends. **Topp:** *Takeda:* Research Funding; *GenMab:* Consultancy; *Regeneron Pharmaceuticals, Inc.:* Consultancy, Research Funding; *Janssen:* Consultancy, Other: Travel support; *AbbVie:* Consultancy; *Kite, a Gilead Company:* Consultancy, Other: Travel support, Research Funding; *Bristol Myers Squibb:* Consultancy, Research Funding; *Roche:* Consultancy, Research Funding; *AstraZeneca:* Consultancy, Research Funding. **Allan:** *TG Therapeutics, Inc:* Consultancy, Research Funding; *Pharmacyclics LLC:* Consultancy, Speakers Bureau; *Lava Therapeutics:* Consultancy; *Adaptive Biotechnologies:* Consultancy; *Lilly:* Consultancy; *ADC Therapeutics SA:* Consultancy; *Janssen:* Consultancy, Research Funding, Speakers Bureau; *AbbVie:* Consultancy, Honoraria, Speakers Bureau; *AstraZeneca:* Consultancy, Honoraria; *BeiGene:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Epizyme:* Consultancy; *Genentech, Inc.:* Consultancy, Research Funding. **Arnason:** *Bristol Myers Squibb:* Speakers Bureau. **Michot:** *AstraZeneca:* Honoraria, Other: Non-financial support; *Bristol Myers Squibb:* Honoraria, Other: Non-financial support; *Celgene:* Honoraria, Other: Non-financial support; *Janssen:* Honoraria, Other: Non-financial support; *Gilead Sciences:* Other: Non-financial support; *Novartis:* Other: Non-financial support; *Roche:* Other: Non-financial support. **O'Brien:** *Astrazeneca:* Consultancy; *Beigene:* Consultancy, Research Funding; *Lilly:* Consultancy, Research Funding; *Janssen:* Consultancy; *Johnson & Johnson:* Consultancy; *Pfizer:* Consultancy, Research Funding; *Pharmacyclics:* Consultancy, Research Funding; *Regeneron:* Research Funding; *Abbvie:* Consultancy. **Avivi Mazza:** *AbbVie:* Honoraria. **Cai:** *Regeneron:* Current Employment, Current holder of *stock options* in a privately-held company. **Flink:** *Regeneron:* Current Employment, Current equity holder in publicly-traded company. **Zhu:** *Regeneron:* Current Employment, Current equity holder in publicly-traded company. **Brouwer-Visser:** *Regeneron:* Current Employment, Current equity holder in publicly-traded company. **Mohamed:** *Regeneron:* Current Employment, Current equity holder in publicly-traded company, Patents & Royalties. **Chaudhry:** *Regeneron:* Current Employment, Current holder of *stock options* in a privately-held company. **Ambati:** *Regeneron:* Current Employment, Current holder of *stock options* in a privately-held company. **Ansell:** *ADC Therapeutics:* Research Funding; *Pfizer:* Research Funding; *AstraZeneca:* Research Funding; *Affimed:* Research Funding; *Takeda:* Research Funding; *SeaGen:* Research Funding; *BMS:* Research Funding; *Regeneron Pharmaceuticals, Inc.:* Research Funding.

OffLabel Disclosure: Odronextamab, a CD20xCD3 bispecific antibody, for the treatment of patients with relapsed/refractory diffuse large B-cell lymphoma

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