(PF1030) UPDATED CLINICAL DATA FROM THE PHASE 1/2 STUDY OF DIBOTATUG (DR-01), A NON-FUCOSYLATED ANTI-CD94 ANTIBODY, IN PATIENTS WITH RELAPSED/REFRACTORY CYTOTOXIC T/NK CELL LYMPHOMAS

Topic: 20. Other aggressive lymphomas

Swaminathan Iyer*[1], Christina Poh[2], Jasmine Zain[3], Christiane Querfeld[2], John C. Reneau[4], Jonathan Brammer[4], Costas K. Yannakou[5, 6], Mengyang Di[7], Cinzia Pellegrini[8], Pier Luigi Zinzani[8], Oleg Akilov[9], Youn H. Kim[10], Michael Khodadoust[10], Enrica Marchi[11], Yok Lam Kwong[12], Ji Hyun Lee[13], Youngil Koh[14], Hyeon-Seok Eom[15], Wonseog Kim[16], Jake Shortt[17], Alejandro Gru[18], Alissa Keegan[19], Wan-Jen Hong[19], Ruoshi Shi[19], Jennifer Richardson[19], Nenad Tomasevic[19], H. Miles Prince[5], Steven Horwitz[3]

[1]MD Anderson Cancer Center, Houston, United States of America;[2]City of Hope, Duarte, United States of America;[3]Memorial Sloan Kettering Cancer Center, New York, United States of America;[4]The Ohio State University Comprehensive Cancer Center, Columbus, United States of America;[5]Epworth HealthCare, Melbourne, Australia;[6]University of Melbourne, Melbourne, Australia;[7]Fred Hutchinson Cancer Center, Seattle, United States of America;[8]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy;[9]University of Pittsburgh Medical Center, Pittsburgh, United States of America;[10]Stanford Cancer Center, Stanford, United States of America;[11]University of Virginia Comprehensive Cancer Center, Charlottesville, United States of America;[12]University of Hong Kong, Hong Kong, Hong Kong;[13]Dong-A University, Busan, South Korea;[14]Seoul National University Hospital, Seoul, South Korea;[15]National Cancer Center, Seoul, South Korea;[16]Samsung Medical Center, Seoul, South Korea;[17]Monash University, Victoria, Australia;[18]Columbia University Irving Medical Center, New York, United States of America;[19]Dren Bio, San Carlos, United States of America;

Background

Dibotatug (DR-01) is a non-fucosylated human IgG antibody targeting CD94, which is selectively expressed on NK cells, γδ T cells, and terminal effector $CD8^+$T cells. Cytotoxic T/NK cell lymphomas (CTLs) are a group of lymphoma histologies that are characterized by CD94-expressing cytotoxic cells and presence of cytotoxic markers, such as granzyme B, TIA1 or perforin. Dibotatug leads to depletion of $CD94^+$ malignant cells by antibody-dependent cellular cytotoxicity and represents a potential new targeted therapy for patients with relapsed/refractory (R/R) CTL who have no effective therapies.

Aims

Assess safety, pharmacodynamics, and efficacy of dibotatug in R/R CTL patients.

Methods

This Phase 1/2 open-label study (NCT05475925) enrolled R/R CTL patients who failed ≥1 prior line of therapy. All patients provided informed consent. Patients received intravenous dibotatug (0.3–10 mg/kg) in one of three induction regimens followed by monthly dosing during dose escalation, followed by dose optimization at 1 or 6 mg/kg and dose expansion at 1 mg/kg with induction regimen of C1D1/D8/D15. Efficacy was assessed using Lugano criteria (Cheson 2014), Olsen criteria (Olsen 2021) for cutaneous histologies or modified TPLL criteria (Staber 2019) for hepatosplenic or leukemic disease. The study also assessed correlations between baseline CD94 expression and responses and $CD94^+$ cell depletion after dibotatug treatment.

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Results

As of October 2025, 81 patients with CTL were enrolled. Forty-five (56%) were male, median age was 53 (18–82 years) and ECOG performance status was approximately evenly distributed between 0 and 1. The most common histologies enrolled (>5%) were extranodal NK/T-cell lymphoma (ENKTL) (n=19, 23%), primary cutaneous γδ T-cell lymphoma (PCγδTCL) (n=16, 20%), cytotoxic peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) (n=12, 15%), monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) (n=8, 10%), subcutaneous panniculitis-like T-cell lymphoma (SPTCL) (n=7, 9%), primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma (PCAETCL) (n=7, 9%), and hepatosplenic T-cell lymphoma (HSTCL) (n=6, 7%). Median lines of prior therapy were 3 (range 1–14) and 16% (n=13) were post autologous/allogeneic stem cell transplant. Disease was resistant or intolerant to the most recent therapy in 48% (n=39) of patients. Infusion-related reactions were the predominant treatment-related AEs, occurring in 27 (33%) patients primarily during initial administration, and were managed effectively with standard mitigation measures.
In the 47 response-evaluable patients at the selected dose (1 mg/kg), the ORR was 53% (14 CR, 11 PR) with responses across histologic subtypes. Highest ORRs were observed in the following histologies; SPTCL (n=5) with ORR 80% (3 CR, 1 PR), PCγδTCL (n=8) with ORR 75% (1 CR, 5 PR), HSTCL (n=4) with ORR 75% (2 CR, 1 PR), MEITL (n=3) with ORR 67% (1 CR, 1 PR), and ENKTL (n=14) with ORR 50% (5 CR, 2 PR). The longest duration of response is ongoing at 22 months in a patient with PCγδTCL. Biomarker analyses showed near universal expression (95%) of CD94 across histologies and responses were not correlated with CD94 expression level. By C2D1, dibotatug treatment had markedly depleted $CD94^{+}$ cells in patient samples.

Summary/Conclusion

Dibotatug continues to demonstrate promising safety and efficacy with responses across CTL histologies, supporting development as a targeted therapy in patients with R/R CTL.

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