

Abstract Title (166/170 char): First-in-Human Phase 1 Study of DR-01, a Non-Fucosylated Anti-CD94 Antibody in Patients with Relapsed/Refractory Cytotoxic Lymphomas: Dose Escalation and Optimization

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Abstract Category (1-3; see list): Ongoing Trials, Molecular Targeted Therapies

Abstract Keywords (1-3; see list): Molecular Targeted Therapies

COI info needed:

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Consultant or advisory role: Kyowa Kirin, Innate-Pharma, Mundipharma, Regeneron, Sanofi, Secura Bio, Galderma
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KD: Stock ownership: AbbVie, Inc, BMS, Nektar
Consultant or advisory role: Dren Bio

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RS: Employment or leadership position: Dren Bio

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Consultant or advisory role: Auxilius Pharma, Abcuro Inc., Corvus, Daiichi Sankyo, Dren Bio, Farallon Capital Management, L.L.C., Kyowa Hakko Kirin, March Bio, Neovii Pharmaceuticals AG, ONO Pharmaceuticals, Pfizer, Secura Bio, SymBio, Treeline Bio and Takeda Pharmaceuticals
Honoraria: ; Auxilius Pharma, Abcuro Inc., Corvus, CTI BioPharma Corp, Daiichi Sankyo, Dren Bio, Kyowa Hakko Kirin, March Bio, ONO Pharmaceuticals, Pfizer, Secura Bio, SymBio and Takeda Pharmaceuticals

ICML (CTL), 3000 char max (incl spaces): current = 2949

Introduction: DR-01 is a non-fucosylated human IgG antibody targeting CD94, expressed exclusively on terminal effector CD8⁺T cells, $\gamma\delta$ T cells, and NK cells. It depletes CD94-expressing malignant cells through antibody-dependent cellular cytotoxicity, including fratricide. Patients with relapsed/refractory (RR) cytotoxic T cell lymphomas (CTLs) have no established effective treatment options, with survival of only weeks to months.

Methods: This Phase 1/2 open-label study (NCT05475925) evaluated DR-01 in adult patients with CD94-driven RR CTLs after ≥ 1 prior lines of therapy. Dose escalation (0.3-10 mg/kg) was followed by expansion at 1 or 6 mg/kg with induction regimens of C1D1/D15 or C1D1/D8/D15.

Results: As of February 2025, 52 patients with CTL (33 males, 19 females) were enrolled, including 28 patients at 1 mg/kg and 12 patients at 6 mg/kg. The median age was 53 years (range 19–82) with a median of 3.5 prior lines of therapy (range 1–14). Disease was resistant/intolerant to the most recent therapy in 50% of cases (n=26), refractory to all prior lines in 31% (n=16), and 23% of patients (n=12) had previous autologous or allogeneic hematopoietic stem cell transplant (HSCT). No dose-limiting toxicities were observed. Infusion-related reactions were the predominant treatment-related adverse events (TRAEs), occurring in 37% of cases (n=19; including 2 Grade 3 events), primarily during initial administration and managed effectively with standard mitigation measures. Two possibly related serious adverse events were reported: Grade 2 pyrexia (n=1) and Grade 2 cytokine release syndrome (n=1), both resolving without sequelae. No treatment-related deaths occurred. Among 33 disease-evaluable patients in the combined 1 and 6 mg/kg optimization cohorts, the overall response rate (ORR) was 46% (15/33), with 10 complete responses (CR) and 5 partial responses (PR). In the 1 mg/kg cohort (n=21), the ORR was 52% (8 CR, 3 PR), while the 6-mg/kg cohort (n=12) demonstrated an ORR of 33% (2 CR, 2 PR). The 1 mg/kg dose with C1D1/D8/D15 regimen was selected for further development based on superior ORR and absence of an exposure-response relationship. Time to response in 11 responders at 1 mg/kg was 0.8–2.8 months, and median duration of response (DoR) was not reached; the maximum DoR was 16 months in one patient (PC $\gamma\delta$ TCL) with ongoing CR who previously relapsed post allogeneic HSCT. Three of 10 patients achieving CR on DR-01 proceeded to allogeneic HSCT; all continue in CR at up to 12 months since last DR-01 dose. Among responders in the 1 mg/kg dose-expansion cohort, disease progression occurred in only 3 of 11 cases. 30 of 31 evaluable CTL baseline tumor biopsies expressed CD94 in at least 1% of immune cells, with post-treatment samples showing depletion of CD94⁺ cells compared to baseline.

Conclusions: DR-01 demonstrates promising safety and efficacy, supporting its development as a potential treatment option for CTL.