Abstract Submission

25. Gene therapy, cellular immunotherapy and vaccination - Clinical

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SAFETY AND EFFICACY FINDINGS OF AUTO1, A FAST-OFF RATE CD19 CAR, IN RELAPSED/REFRACTORY B-CELL NON-HODGKIN'S LYMPHOMA (B-NHL), AND CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) / SMALL LYMPHOCYTIC LYMPHOMA (SLL)

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Background: We have previously described AUTO1, a CD19 CAR with a fast off-rate CD19 binding domain, designed to reduce CAR T-cell immune toxicity and improve engraftment. Its clinical activity has been tested in r/r paediatric and adult B-ALL (Ghorashian S et al., Nat Med 2019; Roddie C et al., JCO 2021). This data confirms the intended function of the receptor, with low levels of CRS/ICANS and long-term engraftment of CAR T-cells observed in both patient groups.
Aims: We have initiated testing of AUTO1 in the setting of B-NHL and CLL/SLL (NCT02935257).
Methods: ***Manufacturing:*** CAR T-cell products were generated using a semi-automated closed process from non-mobilised patient leukapheresate.
Study design: Subjects ≥ 16y underwent lymphodepletion with fludarabine (30mg/m x3) and cyclophosphamide (60mg/kg x1) prior to AUTO1 infusion, with the exception of the DLBCL cohort who additionally received a single dose of pembrolizumab (200mg) on day -1 to potentiate CAR-T expansion. AUTO1 dose varies based on the indication. Split dosing of 230 $x10^6$ CD19 CAR T-cells at day 0 and day 9 is employed in the CLL cohort. A single dose of 200 $x10^6$ CD19 CAR T-cells is delivered to patients with B-NHL. Study endpoints include feasibility of manufacture, grade 3-5 toxicity and remission rates at 1 and 3 months.
Results: As of 8th February 2022, we enrolled 23 patients: 11 low grade NHL (LG-NHL:7 with FL and 3 with MCL), 7 DLBCL and 5 CLL. Apheresis was successful in all 23 patients and product manufacture was successful in 22 (pending in the last). 19 patients were infused: 10 with LG-NHL, 6 with DLBCL and 3 with CLL. 1 CLL patient was pending infusion at time of data cut-off and 2 patients died pre-infusion: 1 MCL patient, from COVID-19 and 1 CLL patient, from intracerebral haemorrhage. Patients treated with AUTO1 had a median age of 60 years (range 39-79), had received a median of 3 prior lines of treatment (range 2-8). Grade 1 CRS was reported in 6/19 and Grade 2 CRS in 3/19. No ICANS was observed in the B-NHL and CLL cohorts. CAR engraftment was observed in 13/13 patients evaluated by qPCR with ongoing persistence in 12/13 patients at last follow-up.
In the LG-NHL and DLBCL cohorts 10/10 and 4/5 evaluable patients respectively were in CMR by 18FDG PET-CT post-treatment. Responses were ongoing in 9/10 LG-NHL at 12 months and in 4/4 DLBCL at months 1, 3, 3 and 6. In the CLL cohort, 2/3 evaluable patients achieved MRD negative remission in the bone marrow with residual small volume lymph nodes by CT at 6 and 3 months of follow-up respectively. 1 CLL patient did not engraft and had SD at month 1.
Summary/Conclusion: AUTO1 has a tolerable safety profile in patients with r/r B-NHL and CLL despite high disease burden. Early data shows excellent complete remission rates and excellent CAR engraftment/expansion. Additional patients, updated data and longer follow up will be presented.

Keywords: CAR-T, Chronic lymphocytic leukemia, Non-Hodgkin's lymphoma