A CASE OF CD19-DIRECTED CAR-T CELL THERAPY IN A PATIENT WITH REFRACTORY ANTI-JO1-ANTISYNTHETASE-SYNDROME

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CD19-directed CAR-T cell therapy recently successfully entered the field of autoimmune diseases. Preceding case reports demonstrated promising results in patients with idiopathic inflammatory myositis.
We report the case of a 54-year-old female patient with refractory anti-Jo1-antisynthetase syndrome treated with a second generation CD19-directed CAR-T cell therapy (KYV-101, Kyverna Therapeutics).
Before CAR-T cell therapy, the patient had received extensive immunosuppressive and immunomodulatory treatments with inadequate response demonstrated by refractory worsening of myositis, arthritis, interstitial lung disease and skin involvement. Glucocorticoid treatment, required for disease control, was tapered to 17.5 mg prednisolone daily at the time of apheresis, decreased to 12.5 mg before CAR-T cell infusion and continued at that level following the CAR-T cell infusion. A single infusion of 1.1x10^8 anti-CD19 CAR-T cells was administered after lymphodepletion with fludarabine (30 mg/m2 on day -5, -4, -3) and cyclophosphamide (300 mg/m2 on day -5, -4, -3). The patient developed reoccurring cytokine release syndrome (CRS) grade I and II with fever and hypotension, which was successfully treated with sequential administration of tocilizumab, dexamethasone and anakinra. No neurotoxicity occurred. Hematotoxicity was observed including neutropenia grade CTCAE 3, requiring G-CSF treatment. CAR-T cell kinetics demonstrated rapid expansion with a maximum peak expansion of 36 cells/uL on day 8 in the peripheral blood. Throughout the clinical course post-infusion, the patient showed continuous improvement of muscle strength and arthritis, measured by MMT8, DAS28 and PGA-score. In the first month post-infusion systemic prednisolone treatment was tapered to 10 mg. A flare up of the skin symptoms one month after infusion was successfully treated with topical steroids. CAR T cells remained detectable within the peripheral blood until the month 3 by which a reappearance of B cells (33/µl) was observed. Arthritis and muscle strength further improved to the point that walking distance increased from several hundred meters to 6 kilometers by day 90 post-infusion.
We report a tolerable safety profile in a case of CD19-directed CAR-T cell therapy in treatment refractory anti-Jo1-synthetase syndrome. Short-term results indicate promising clinical improvements with an isolated flare of skin manifestations. To evaluate long-term efficacy and safety follow-up data is needed.