HIGH-DOSE TIL PRODUCT WITH IMPROVED PHENOTYPE AND FUNCTIONALITY

Christina Friese, Christina Heeke, Nikolaj Kirketerp-Møller*, Sandra Færch, Maria Juul Nielsen, Amalie Hey, Ulrik Cordes. *Cbio, Søborg, Denmark*

Background Adoptive cell transfer (ACT) with autologous tumor-infiltrating lymphocytes (TILs) has proven to be one of the most successful immune therapies with overall response rates of around 50% in patients with metastatic melanoma including complete responses in up to 20% of the patients. Current protocols combine a first expansion of TILs from tumor fragments or tumor digest with high-dose IL-2, followed by further expansion with a rapid-expansion-protocol (REP) using allogeneic feeder cells, α CD3 and IL-2. Following this protocol, TIL production takes 4–7 weeks, and many patients deteriorate before they can receive therapy. With success rates of TIL expansion ranging from 70–90%, a TIL product cannot be generated for every patient. Furthermore, clinical response to TIL therapy is lower in other solid tumors such as ovarian cancer, likely due to a lower number of expanded TILs and lower frequencies of tumor reactive CD8 + T cells. Therefore, there is a clinical need for improvement of current TIL expansion protocols to make this therapy available to more cancer patients.

Methods In this project, TILs from tumor fragments of patients with various solid tumors have been cultured under two different conditions using novel culture vessels. TIL yield, viability, composition, phenotype, reactivity and expansion time were compared to TILs expanded following the standard protocol.

Results Using the two novel culture conditions, success rates of expansion across all tumor types increased from 70% to >95%. Additionally, significantly higher frequency and total numbers of viable CD8+ T cells per fragment were obtained compared to standard expansion with IL-2 alone. The majority of these CD8+ T cells exhibit an effector memory phenotype with elevated levels of exhaustion markers. A third of CD8+ T cells can be activated unspecifically and express any combination of the cytotoxicity markers IFN γ , TNF α or CD107a. Overall, the initial expansion time could be reduced from 2–5 weeks to 10–14 days and the rapid expansion time from 2 weeks to 8–12 days. Thus, the total culture time was shortened from 4–7 weeks to 18–26 days. As the REP TILs still comprise a majority of CD8+ T cells (~75%), the clinical dose would contain a total number of 3–10 billion functional CD8+ T cells.

Conclusions With this study, we show that by improving the initial culture conditions, we can shorten expansion time while simultaneously improving the characteristics of the TIL product with a high dose of functional CD8+ T cells with potential anti-tumor activity.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.175>