The immunogenic nature of melanoma has been useful for the development of adoptive transfer of ex-vivo expanded tumor infiltrating lymphocytes (TIL). This adoptive cell transfer therapy has overall response rates of around 50%. B cells are frequently found in melanoma metastases, and display signs of antigen experience. Recently, B-cell tumor infiltration has been associated with improved clinical responses to immune checkpoint inhibitors. When CD40L is used to stimulate melanoma infiltrating B cells on the first day of ex-vivo TIL expansion, it was found that the expansion success rate from the frozen tumor digests was 69% compared to 23% with the standard protocol. Also, TILs expanded to higher numbers and had an increase in CD4+ T cells with an effector memory-like phenotype and a stem-like phenotype.

COMERCIAL OPPORTUNITY

- Iovance Biotherapeutics currently has TIL products in pivotal trials for both metastatic melanoma (post anti-PD1) and in cervical cancer (post chemo or post chemo and post anti-PD1), and Phase 2 trials in NSCLC and HNSCC.
- The metastatic melanoma market can be estimated at about 7,000 deaths in the US each year and about 62,000 deaths world-wide. Patients have few therapeutic choices after failure on checkpoint inhibitors and BRAF/MEK inhibitors.
- The TIL market is attractive as evidenced by the number of companies pursuing TIL therapy including Iovance, Instil Bio, Adaptimmune Therapeutics, Achilles Therapeutics, Intima Bioscience, and Turnstone Biologics.
- The solid tumor market is large with about 90% of all cancers being solid tumors, and it is thought that TIL therapies may do better with solid tumors than CAR-T therapies.

TECHNOLOGY

Melanoma infiltrating B cells were stimulated with human recombinant CD40L on the first day of ex-vivo TIL expansion to induce the expression of co-stimulatory ligands by B cells. Thirteen samples were expanded from melanoma tumor single cell suspensions in high dose IL-2 alone (standard protocol) or in high dose IL-2 plus CD40L. After up to 4 weeks of expansion, the TIL phenotype was analyzed by flow cytometry. The expansion success rate from the frozen tumor digests was 69% in the CD40L treatment condition compared to 23% with the standard protocol. Also TILs cultured in the presence of CD40L expanded to higher numbers than with the standard protocol (P=0.02). Most of the samples had a significant increase in the percentage of CD4+ T cells (P=0.03) but not to the detriment of CD8+ T cells. Treatment with CD40L increased the percentage of effector memory-like T cells (P=0.03) and of CD39- CD69- T cells (P<0.05) that were recently associated with response to TIL therapy.

PUBLICATION/PATENT

- Provisional patent application filed in March 2021 for Drs. Abate Daga and Pilon Thomas

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LICENSING OPPORTUNITY

CD40 Agonist improves ex-vivo TIL expansion for immunotherapy