UNIVERSAL EXPANSION OF CBL-B-INHIBITED TUMOR INFILTRATING LYMPHOCYTES, DETIL-0255, FROM WOMEN WITH OVARIAN CANCER: PROCESS VALIDATION

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Background Despite objective responses to immune checkpoint blockade in patients with ovarian cancer (OC), therapies providing durable clinical benefit are lacking. An increased density of OC tumor infiltrating lymphocytes (TIL), specifically memory T cells with enhanced CD28 signaling, are associated with improved survival and immunotherapy response. Adoptive cell therapy (ACT) utilizing ex vivo expanded TIL has demonstrated durable complete responses in several epithelial malignancies, but has shown limited clinical benefit in OC. This is due in part to extended manufacturing times and use of TIL products with a differentiated and exhausted phenotype. Casitas B lineage lymphoma-B (CBL-B) is an E3 ubiquitin ligase that limits T cell activation in the absence of CD28 co-stimulation following T cell receptor engagement. Ex vivo inhibition of CBL-B with the small molecule inhibitor NX-0255 increases the expansion of stem-like TIL with improved survival and immunotherapy response. In contrast to prior OC TIL products, OC DeTIL-0255 were primarily effector memory (CD4: 59.7±30.6%; CD8: 55.6±29.8%) and central memory cells (CD4: 21.0±23.7%; CD8: 12.4±16.9%) displaying limited T cell exhaustion (CD4: PD-1 26.2±22.8%, LAG-3 15.1±13.5%, CD57 4.4±4.3%, CD8: PD-1 17.7±19.6%, LAG-3 4.5±28.4%, CD57 2.9±2.5%).

Conclusions OC DeTIL-0255 demonstrate a favorable phenotype amenable for ACT. A Phase 1 clinical study of DeTIL-0255 in women with recurrent/platinum resistant OC is ongoing (NCT05107739).

REFERENCES

Ethics Approval All studies were performed in full accordance with the guidelines for good clinical practice and the Declaration of Helsinki and approved by the cited institutional protocol review committee and IRB.

Consent Written informed consent was obtained from the patient for use of patient specimens for research and subsequent publication.