Supplementary Information

First-in-Human Trial of Engineered NK Cells in Lung Cancer Refractory to Immune Checkpoint Inhibitors

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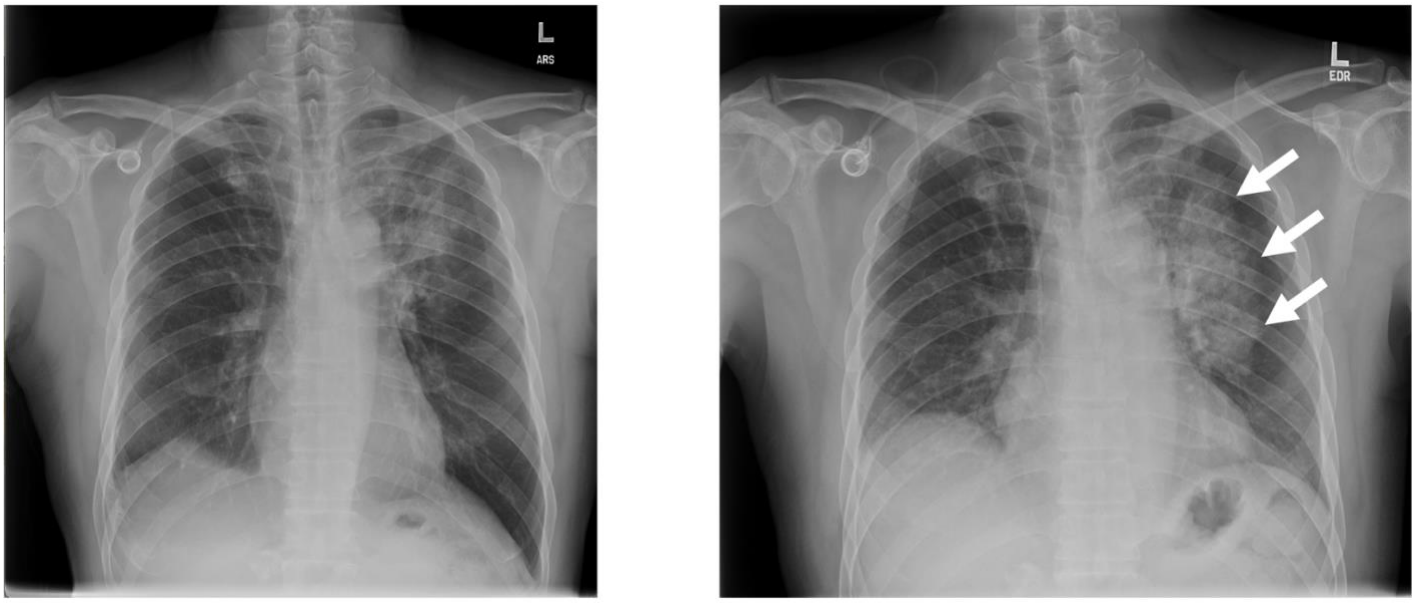
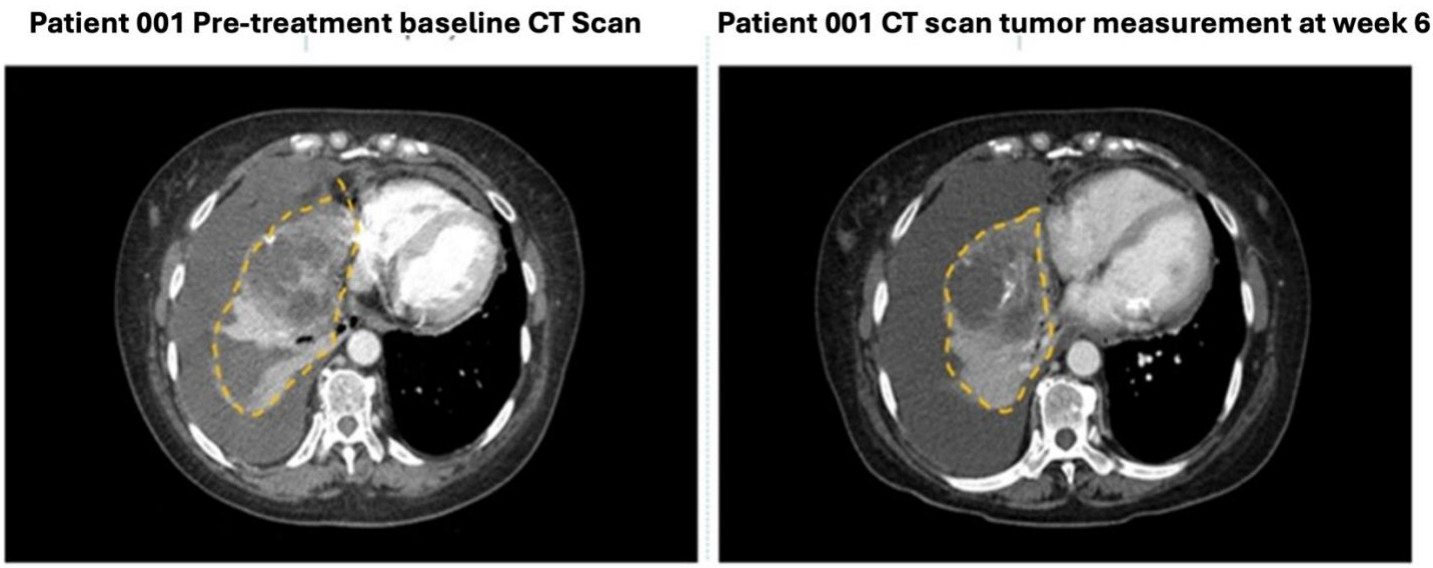
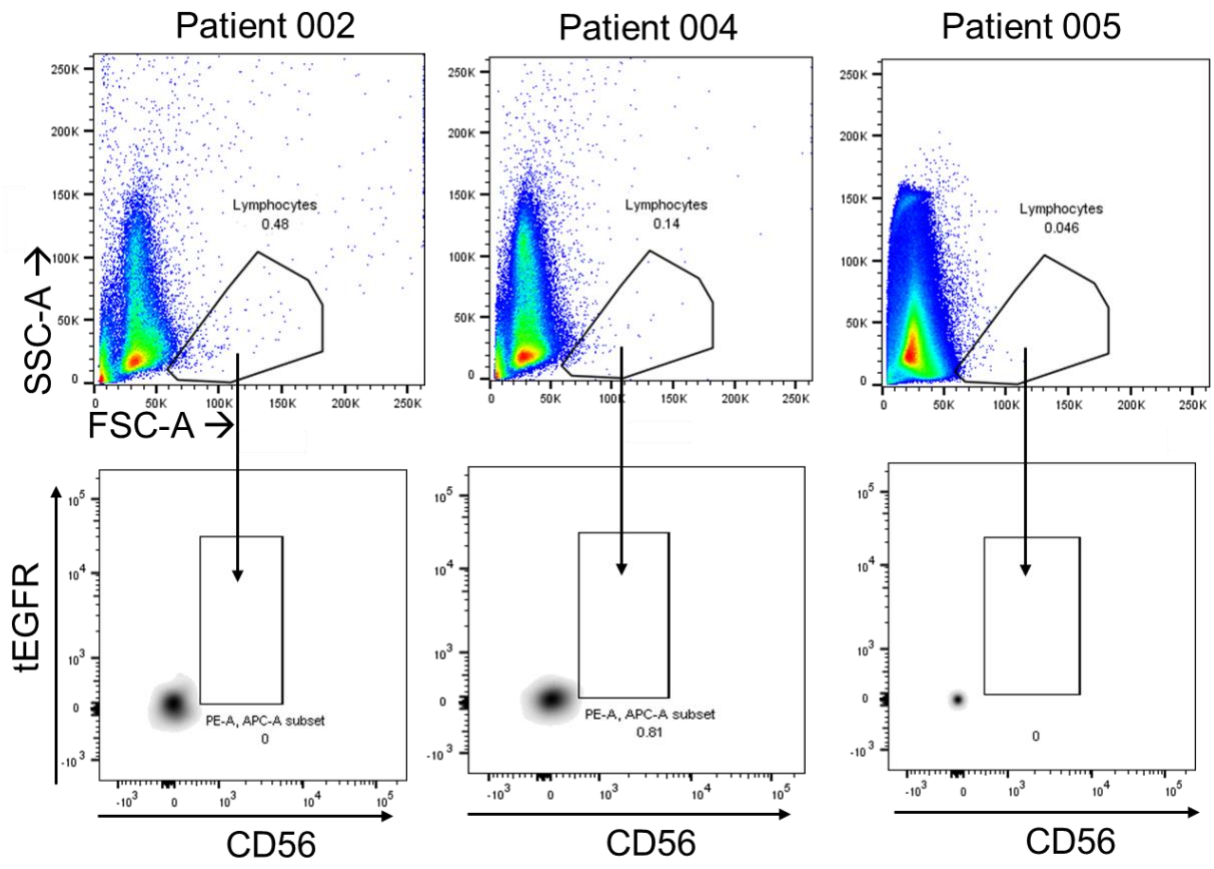
Conflict of interest statement: Drs. Yu and Caligiuri are co-founders and shareholders of CytoImmune Therapeutics; both serve as consultants to CytoImmune Therapeutics, a financial sponsor of this study. Drs. Yu and Caligiuri have a patent filed through City of Hope for sIL15_TRACK NK cells (US20220249564A1). All other authors have no conflict of interest.



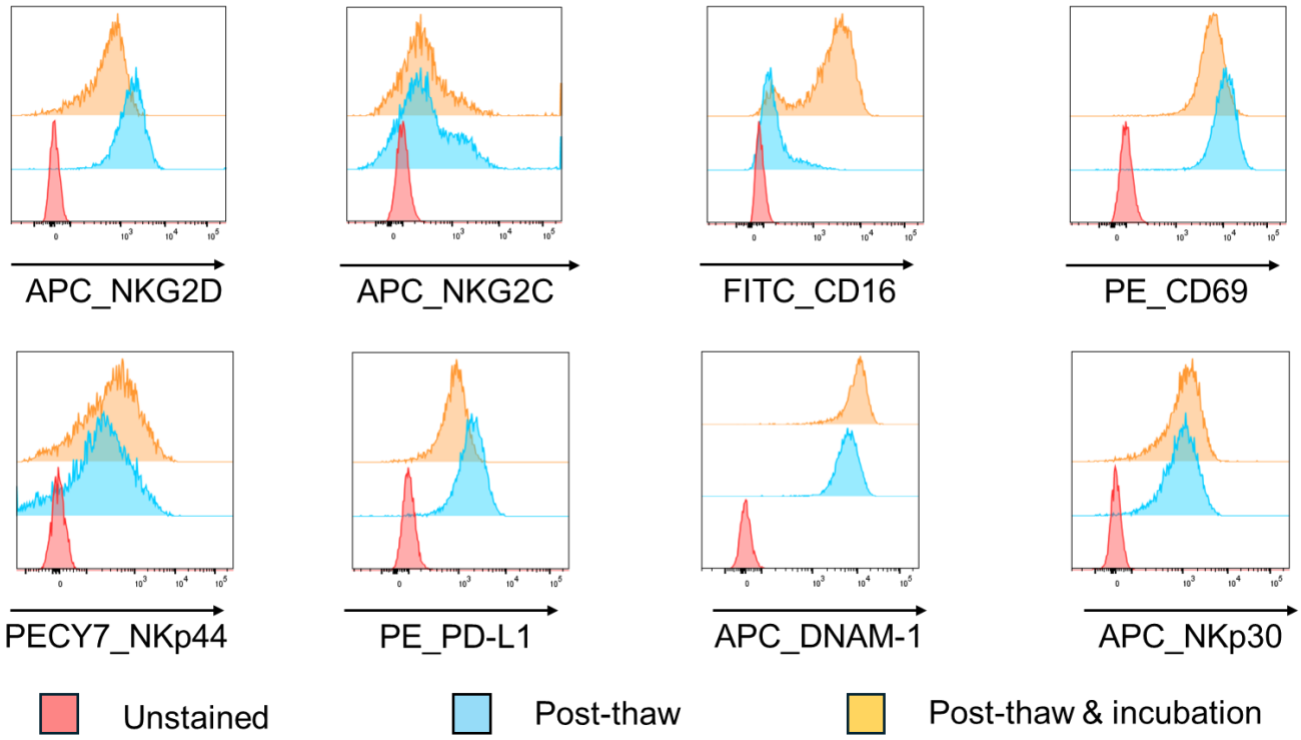
Supplementary Figure 1. The chest X-Ray on the left shows a baseline film of patient 005 before starting cycle 2 of sIL15_TRACK NK cell infusions at a dose of 4.0 x 10^6 transduced cells/kg. The patient became acutely short of breath following the third weekly infusion of cycle 2 and a chest X-Ray was again obtained demonstrating a new infiltrate (white arrows) that subsequently improved spontaneously within seven days without the onset of fever or additional intervention.



Supplementary Figure 2. The CT scan on the left shows a baseline tumor measurement of patient 001 immediately prior to starting cycle 1 of sIL15_TRACK NK cell infusions at a dose of 1.5 x 10^6 transduced cells/kg. The yellow dashed line indicates the size of the target lesion. The CT scan on the right shows an approximately 12% reduction in tumor volume when measured 6 weeks after the start of cycle 1 and 2 weeks after completion of cycle 1. Patient 001 died unexpectedly of a cardiac event with a diagnosis of COVID while on cycle 2 of sIL15_TRACK NK cells without evidence of progression.



Supplementary Figure 3. Three patient lung biopsies were collected between 1 and 7 days following the 4th infusion of sIL15_TRACK NK cells and digested to single cell suspension using collagenase I and DNase I. Cells were stained with antibodies against CD56 and EGFR and assessed by flow cytometry to identify CD56+tEGFR+ sIL15_TRACK NK cells within the lymphocyte gate. Very few (< 0.5%) lymphocytes were collected in biopsies from each of the three patients shown here, yielding no CD56+tEGFR+ sIL15_TRACK NK cells.



Supplementary Figure 4. Phenotype of cryopreserved sIL15_TRACK NK cells immediately post-thaw and two days after thaw and after 48 hours of in vitro incubation at 37ºC with low dose IL-2.