**Background:** CMB305 is an active immunotherapy regimen designed to generate and expand anti-NY-ESO-1 T and B cells. It consists of priming with a dendritic cell-targeting lentiviral vector encoding NY-ESO-1, and a boost with NY-ESO-1 recombinant protein plus TLR-4 agonist. This first-in-human study of CMB305 examined safety, immune response (IR), and efficacy in pts with NY-ESO-1 positive (+) solid tumors. At ASCO2017, median overall survival (OS) for soft tissue sarcoma (STS) was not reached (12 mos OS rate 83%).

**Methods:** Adults with previously treated NY-ESO-1+ solid tumors were enrolled in a 3 + 3 dose-escalation with an expansion phase Ib study. The CMB305 regimen included 4 intraderal injections of the prime, alternating with 3 intramuscular boost injections over 3 months, then bimonthly boost injections up to 1 yr. An updated STS survival analysis was performed.

**Results:** As of 06 April 2018, 25 pts with STS (15 synovial (SS), 8 myxoid/round cell liposarcoma (MRCL), 2 other) were evaluable for safety; 24 pts were evaluable for IR and efficacy. All pts received prior therapy for advanced disease, 67% > 2 prior chemo regimens. No dose limiting toxicities were observed. The most treatment related adverse events were Grade 1 or 2; one Grade 3 (prostatic pain); no grade 4 or 5 events. Best tumor response was stable disease in 8/15 (53%) SS pts and 6/8 (75%) MRCL pts with evidence of tumor growth arrest. The median progression free survival (PFS) was 3.9 mos (2.1, 7.5) for STS and 3.7 mos (2.1, 7.8) for SS. Median OS was 23.7 mos (15.5, NR) for STS and 29.2 mos (12.2, NR) for SS. Presence of anti-NY-ESO-1 antibodies (Ab) at baseline (25.0% pts) was associated with longer survival. Anti-NY-ESO-1 specific T cells and Ab developed in 46% and 67% STS pts, respectively. Pts with baseline and induced anti-NY-ESO-1 IR (T-cells and/or antibodies) had a trend to improved clinical outcomes. T cell receptor sequencing indicated increased clonality and antigen spreading was observed.

**Conclusions:** CMB305 is well tolerated, broadly immunogenic, and impacts patient survival favorably when compared with approved agents for recurrent STS. These results support a randomized phase 3 trial evaluating CMB305 in the maintenance setting after 1st line therapy in SS patients.

**Clinical trial identification:** NCT02387125.

**Legal entity responsible for the study:** Immune Design Corp.


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**1607PD Immune response, safety, and overall survival of NY-ESO-1+ soft tissue sarcoma patients treated with CMB305 therapy**

S.P. Chawla1, S. Polack2, M. Block1, M. Druta4, K. Do1, J.C. Morris3, J.W. Kim5, C. Bohac6, H. Lu7, S. Grjegi10, R.L. Jones7, P. Hvu2, N. Somaiah12

1Medical Oncology, Sarcoma Oncology Center, Santa Monica, CA, USA, 2Medical Oncology, Fred Hutchinson Cancer Research Center, Seattle, WA, USA, 3Department of Oncology, Mayo Clinic, Rochester, NY, USA, 4Medical Oncology, Moffit Cancer Center, Tampa, FL, USA, 5Medical Oncology, Dana Farber Cancer Institute, Boston, MA, USA, 6Medical Oncology, University of Cincinnati, Cincinnati, OH, USA, 7Medical Oncology, Yale University, New Haven, CT, USA, 8Internal Medicine, St. Martin Hospital, Koblenz, Germany, 9Science, Immune Design, Seattle, WA, USA, 10Immunology, Mount Sinai, New York, NY, USA, 11Medical Oncology, Royal Marsden Hospital NHS Foundation Trust, London, WA, UK, 12Medical Oncology, MD Anderson Cancer Center, Houston, TX, USA

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