CRS occurred in all pts (53% CRS °1, 29% °2 and 18% °3) with a median onset on day 2 (range days 0–7) and a median duration of 4 days (range 1–21). Tocilizumab was administered at least once in all pts. Ten pts (59%) experienced Immune Effector Cell associated Neurotoxicity Syndrome (ICANS, 30% °1, 10% °2, 30% °3, 20% °4 and 10% °5) with a median onset between day 7 and 8 and a median duration of 8 days (range 3–49). Cytopenia was significant following CAR T-cell treatment: all but one pts had neutropenia <500/µl for more than seven days.

Response assessment four weeks after CAR T-cell transfusion was available for 15 pts.

Objective response rate (ORR) at this early follow-up was 67%, with complete remission (CR) in four (27%) and partial remission (PR) in six pts (40%). Interestingly, ORR was higher in the four pts not receiving bridging chemotherapy between leukapheresis and CAR T-cell therapy than in pts in which bridging was applied (100% vs. 55%). Responders had significantly higher LDH levels at apheresis, start of lymphodepletion and CAR T-cell transfusion than non-responders.

Conclusions Since January 2019, the CAR T cell program has been successfully initiated at the LMU Munich, and 17 r/r DLBCL pts have been treated at our center to date. CAR T cells induced responses in heavily pretreated pts with response rates within the expected range. Toxicity was significant but manageable in most pts. Involvement of a multidisciplinary ImmunoTaskforce was a key element for adequate patient care. Preliminary data supports the hypothesis that low tumor dynamics are associated with favorable outcomes of CD19 CAR T cell therapy.

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P07.02 HIGH-AFFINITY TCRS SPECIFIC FOR CANCER TESTIS ANTIGENS AS A THERAPY FOR MULTIPLE MYELOMA AND SOLID TUMORS

MAJ de Rooij*, DM van der Steen, D Remst, A Wouters, M van der Meent, RS Hagedoorn, MGD Kester, PA van Veelen, FJH Falkenburg, MHM Heemskerk. *LUMC, Leiden, Netherlands*

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Background Cancer Testis Antigens (CTAs) are highly expressed in multiple different tumor types, but silent in normal tissue, except the testis. This tumor-restricted expression pattern makes them an ideal target for adoptive T-cell therapy. However, the responsiveness in clinical setting may be hampered because high-affinity T cells against self-antigens presented in the context of self-HLA are deleted in the thymus by negative selection. In this study, we aim to identify high-affinity T cell receptors (TCRs) specific for CTAs from the allogeneic-HLA repertoire.

Materials and Methods In this study, HLA class I binding peptides derived from different CTA genes were identified by HLA-peptide elution experiments and subsequent mass spectrometric analysis. From the identified peptides HLA tetramers were generated to isolate peptide specific $CD8^+$ T cells from healthy allogeneic donors. Efficacy and safety of the TCRs was determined by various different stimulation assays. The most potent TCRs were sequenced, analyzed and transduced into peripheral $CD8^+$ and $CD4^+$ T cells to confirm CTA specific cytokine production and cytotoxicity.

Results MAGE and CTAG peptides were eluted from multiple myelomas, EBV-transformed lymphoblastic cells, acute myeloid leukemia and ovarium carcinomas. We selected TCRs recognizing 3 different MAGE-A1 peptides in the context of HLA-A*02:01, HLA-A*03:01 and HLA-B*07:02. Furthermore, we selected TCRs specific for MAGE-A3 in the context of HLA-B*35:01 and HLA-A*01:01; TCRs specific for MAGE-A9 in the context of HLA-A*01:01 and TCRs specific for CTAG1 in the context of HLA-A*02:01. The selected T-cell clones demonstrated efficient recognition of MAGE-A1, MAGE-A3 or CTAG1 positive multiple myeloma and solid tumor cell lines without detectable cross-reactivity.

Conclusions We identified multiple different TCRs from the allogeneic-HLA repertoire specific for CTA genes. These TCRs demonstrate efficient recognition and killing of CTA positive multiple myeloma and solid tumor cell lines and did not show any cross-reactivity. The peptides recognized by the TCRs are presented in different HLA alleles. Since, 71% of the world population contains one of these HLA-alleles, a large percentage suffering from a MAGE or CTAG positive tumor could potentially be treated with the identified TCRs by TCR-gene therapy.

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P08 Combination Therapy

P08.01 LOW-DOSE CHECKPOINT INHIBITORS WITH HYPERTHERMIA AND IL-2 ARE SAFE AND EFFECTIVE IN STAGE IV CANCER WITH UNFAVORABLE IMMUNOLOGICAL PROFILE (MSI^{LOW}, PD-L1 UNDER 1%, TMB^{LOW}) – A SINGLE-INSTITUTION EXPERIENCE FROM 2015 TO 2020

[1]R Kleef*, [1]R Nagy, [1]V Bacher, [2]T Bakacs, [1]T Lausch, [3]D McKee, [4]R Moss, [5]H Bojar, [6]N Thoennissen. *[1]Ralf Kleef Immunology and Integrative Oncology, Vienna, Austria; [2]PRET Therapeutics Ltd., Budapest, Hungary; [3]Integrative Cancer Therapies, London, UK; [4]Moss Reports, Blue Hill, ME, USA; [5]NextGen Oncology Group, Duesseldorf, Germany; [6]Oncology at Lenbachplatz, Munich, Germany*

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Background Close to 10 million cancer deaths occurred worldwide in 2017 primarily due to stage IV disease, the management of which is still palliative by intent. Differently from melanoma and non-small cell lung cancer, where the use of ground-breaking immune checkpoint inhibitors (ICI) results in a relatively high efficacy, the response rate in many other stage IV tumors, such as gastrointestinal cancers, breast cancers, sarcomas, and part of genitourinary cancers remains low. In addition, administration of this type of cancer immunotherapy is known for its potentially severe and even fatal side effects due to their severe immune-related adverse events (irAEs).

Materials and Methods Here, we report a retrospective analysis of 129 patients with stage IV cancer who exhausted conventional treatments, who were treated by an low-dose ipilimumab (0.3 mg/kg) plus nivolumab (0.5 mg/kg) blockade in