until Day 19. Interferon gamma (IFN-γ) release in response to TIL co-culture with autologous tumour cultures was measured to a human IFN-γ ELISA kit. Data are presented as mean ±SEM.

Results Addition of checkpoint inhibitors at the initiation of HGSOC TIL culture in cohort 1 increased TIL expansion above untreated control in αPD-1 (1.20±0.04 fold, P<0.01, n=9) and αLAG-3 (1.31±0.08 fold, P<0.001, n=9) but not αTIM-3 treated cultures. However, intermittent dosing of HGSOC cultures in cohort 2 with either αPD-1, αTIM-3 or αLAG-3 antibodies did not increase TIL expansion above untreated cultures. In cohort 1, IFN-γ secretion was increased above untreated control in at least one treatment with a checkpoint inhibitor in 5/7 patients. However, there was no overall fold change in IFN-γ secretion in either αPD-1, αTIM-3 or αLAG-3 treated cultures.

Conclusions This data suggests that initial blockade of checkpoint proteins is effective in increasing the ex vivo expansion of TIL from HGSOC tumours, thus providing a method of improving the efficacy of TIL products in ovarian cancer patients.

Funding GO was funded through a CRUK Manchester Centre Clinical Fellowship. PJ was in receipt of a bursary from the Emma Gyles Bursary Fund. The project was funded by TESARO Inc.


Abstracts

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P06.11 IMMUNOTARGETING OF CD98HC FOR ELIMINATION OF RADIORESISTANT HEAD AND NECK SQAMOUS CELL CARCINOMA

1AS Köseer*, 1,2A Feldmann, 3,4A Linge, 1,3,4A Dubrovska, 1,2,4M Bachmann. 1National Center for Tumor Diseases (NCT), German Cancer Research Center (DKFZ), Faculty of Medicine and University Hospital Carl Gustav Carus, Technical Universität Dresden, and Helmholtz-Zentrum Dresden-Rossendorf (HZDR), Dresden, Germany; 2Helmholtz-Zentrum Dresden-Rossendorf (HZDR), Institute of Radiopharmaceutical Cancer Research, Dresden, Germany; 3OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technical Universität Dresden, Helmholtz-Zentrum Dresden-Rossendorf, Dresden, Germany; 4German Cancer Consortium (DKTK), partner site Dresden and German Cancer Research Center (DKFZ), Heidelberg, Germany

Background Most patients with head and neck squamous cell carcinomas (HNSCC) are diagnosed during a locally advanced stage and may show therapy resistance. Retrospectively, we showed that low CD98hc mRNA and protein levels are significantly associated with better locoregional tumor control in HNSCC patients. Inhibition of CD98hc expression decreased tumor radioresistance suggesting that CD98hc could be a target for HNSCC radiosensitization. One of the strategies for radiosensitization is targeted immunotherapy. However, Chimeric Antigen Receptor (CAR)-equipped T-cell therapy cannot be fully controlled. Therefore, we developed a switchable UniCAR system that is in phase I clinical trial (NCT04230265) [3]. UniCAR T cell activity and specificity are controlled by the presence of target modules (TM) with short half-lives. We aim to define the clinical value of treatment approaches by combining radio(chemo)therapy with CD98hc-targeted immunotherapy.

Materials and Methods We have used previously described radioresistant Cal33 HNSCC cells. These tumor cells were cocultured with UniCAR T cells in the presence or absence of a novel CD98 TM. Specific cell lysis in both in vitro 2D and 3D cultures and tumor cell targeting in the experimental mice was assessed.

Results Our data shows that CD98hc-directed UniCAR T cells can induce cell lysis of radioresistant HNSCC cells in vitro and in vivo models. The combination of the UniCAR system with radio(chemo)therapy can be potentially used for the improvement of the treatment efficacy in patients with metastatic radioresistant tumors. The most promising combination of therapeutic approaches will be further tested in xenograft tumor models to evaluate the best performing combination of immunotherapy and radio(chemo)therapy.

Conclusions Overall, it was shown that tumor cells with radioresistant properties can be eradicated via the UniCAR system by targeting CD98hc in an antigen-specific manner.

REFERENCES


Disclosure Information A.S. Köseer: None. C. Arndt: None. A. Feldmann: None. A. Linge: None. M. Krause: None. A. Dubrovska: None. M. Bachmann: E. Ownership Interest (stock, stock options, patent or other intellectual property); Significant; GEMoB.

P06.12 COMBINATION THERAPY OF CAR-NK-CELLS AND ANTIPD-1 ANTIBODY RESULTS IN HIGH EFFICACY AGAINST ADVANCED-STAGE Glioblastoma in a SYNGENEIC MOUSE MODEL AND INDUCES PROTECTIVE ANTI-TUMOR IMMUNITY IN VIVO

1,2,3J.W. Strasheimer, 1,2,3M. Stecker, 4,5J.A. Alekseeva, 2,5J. Macas, 6,2,3M. Demes, 1,2C. Milderbergen, 6,7T. Torn, 5,7P. Wild, 5,7S. Reiner, 5,7S. Riem, 5,7P. Jeppesen, 5,7J. Schmiede, 5,7M. Uhlig, 4,5S. Wess, 1,2,3M. Steinbach, 1,2,3M. Burger*. 1Dr. Senckenberg Institute of Neurooncology, Goethe University Hospital, Frankfurt, Germany; 2Frankfurt Cancer Institute (FCI), Frankfurt, Germany; 3German Cancer Consortium (DKTK), partner site Frankfurt/Mainz, and German Cancer Research Center (DKFZ), Heidelberg, Germany; 4Georg-Speyer-Haus, Institute for Tumor Biology and Experimental Therapy, Frankfurt, Germany; 5Institute of Neurology (Edinger Institute), Goethe University Hospital, Frankfurt, Germany; 6Dr. Senckenberg Institute of Pathology, Goethe University Hospital, Frankfurt, Germany; 7Department of Neurology, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany; 8Institute for Transfusion Medicine, German Red Cross Blood Donation Service North-East and Medical Faculty Carl Gustav Carus, TU Dresden, Dresden, Germany

Background Checkpoint inhibitors as well as adoptive cell therapy hold great promise for cancer therapy and encouraging treatment responses have already been demonstrated in different cancer indications. Glioblastoma (GB) is the most common and aggressive primary brain tumor. Standard therapy has very limited efficacy in the majority of patients. Analysis of the GB tumor microenvironment (TME) has shown prominent immunosuppressive features including expression of PD-L1 on tumor cells and increased frequency of FOXP-3 positive regulatory T cells. While the surrounding brain is HER2-negative, GB tumors are frequently HER2-positive, suggesting HER2 as a promising target for adoptive immunotherapy.