currently one standard-of-care therapy option in women with early, high-risk or locally advanced breast cancer. While some patients respond excellently to preoperative therapy, in other patients significant tumor shrinkage cannot be achieved. We investigated the impact of NAC on circulating immunomodulatory parameters. We also examined whether changes in these parameters correlate with the response to NAC measured by the Residual Cancer Burden (RCB) score determined after neoadjuvant treatment.

Materials and Methods To detect drug-specific effects, two different NAC regimens in primary breast cancer patients scheduled to pre-operative therapy were compared. 39 patients with conventional anthracycline/taxane sequence (E/C->D, n=39) and 40 patients with reverse sequence (D->E/C) were included. Blood plasma samples were collected at three time points - 'baseline' (before NAC), 'midterm' (after the first six cycles of NAC) and 'surgery' (after NAC before operation). The plasma levels of uPA, uPAR, TIM-3, MCP-1, MCP-2, OPG, IP-10, CD 27, Eotaxin, Tweak, TRAIL, PD-L2, M-CSF and VEGF-A were determined either by using ELISA or a multiplex bead array immunoassay.

Results OPG, CD27, MCP-1, MCP-2, CCl19, Tweak, TRAIL, PD-L2 and M-CSF decreased between baseline and midterm in E/D->D patients. However, the majority of patients treated with the reverse sequence showed no such effect. These drug-induced changes correlated with the RCB score. Non-responders (RCB $\geq$ 1.36) showed a significantly different pattern than responders.

Conclusion These data confirm that NAC affects the immune system in a drug-specific manner. Factors correlating with the RCB-score might represent promising biomarkers to predict the response to therapy.

Disclosure Information K. Wimmer: None. **M. Sachet:** None. **R. Exner:** None. **F. Fitzal:** None. **M. Filipits:** None. **R. Oehler:** None.

P06.09 ANTI-HPSMA CAR ENGINEERED NK-92 CELLS: AN OFF-THE-SHELF CELLULAR THERAPEUTIC FOR TARGETED ELIMINATION OF PROSTATE CANCER CELLS

[1]G Zuccolotto*, [2]A Penna, [2]IM Montagner, [2]D Carpanese, [1]A Rosato. [1]*Università Degli Studi di Padova, Padova, Italy*; [2]*Istituto Oncologico Veneto, Padova, Italy*

10.1136/jitc-2020-ITOC7.88

Background Adoptive cell therapy of malignant diseases takes advantages of the cellular immune system to recognize and destroy cancer cells. Despite the remarkable success in B cell malignancies after adoptive transfer of CD19 CAR T cells, CAR T cell therapy in solid tumors has shown less encouraging clinical results, above all caused by tumor escape mechanisms.In order to overcome such limitations, NK-92, a permanent and IL-2-dependent cell line with a high cytotoxicity *in vitro*, has been engineered in preclinical models with CAR. In this project, we exploited a CAR directed against the human antigen hPSMA that is overexpressed in prostate tumors. This project aimed at transducing NK-92 cell line to obtain a hPSMA-specific CAR NK-92 cell population, to be thereafter characterized *in vitro* and *in vivo* for antigen-specific functional activity.

Materials and Methods NK-92 cell line was transduced with a lentiviral vector (LV) carrying a CAR anti-hPSMA. The cell population obtained was then sorted and analyzed for degranulation capacity, IFNγ production and lytic activity against $hPSMA^+$ (PC3-hPSMA, LNCaP) or $hPSMA^-$tumor cell lines. *In vivo* therapeutic efficacy of CAR-transduced NK-92 was evaluated initially using Winn-Assay and than in subcutaneous and orthotopic tumor models.

Results CAR-expressing LV efficiently transduced NK-92 cells, which in turn produced cytokines, degranulated and exerted a relevant cytotoxic upon challenge with PSMA+ prostate tumor cells, irrespective of 10 Gy γ-irradiation. In all the *in vivo*, tumor models CAR-transduced NK-92 shown a statistically significant inhibition of tumor growth.

Conclusions Chimeric antigen receptor-engineered NK-92 could offer a valid and cost-effective alternative to primary CAR NK or T cells, in particular in cases, where a suitable donor is not available or the sophisticated infrastructure needed for cell isolation, expansion and genetic modification is missing. This work demonstrates that CAR-engineered NK-92 cells display a high and specific recognition of hPSMA+ PC both *in vitro* as is *in vivo*, and could represent an efficient strategy as a new therapeutic intervention against prostate carcinoma, thus paving the way to an Off-The-Shelf cellular therapeutic for targeted elimination of cancer cells and induction of protective antitumor immunity.

Disclosure Information G. Zuccolotto: None. **A. Penna:** None. **I.M. Montagner:** None. **D. Carpanese:** None. **A. Rosato:** None.

P06.10 SHORT TERM INHIBITION OF CHECKPOINT PROTEINS INCREASES EX VIVO EXPANSION OF TUMOUR INFILTRATING LYMPHOCYTES IN HIGH GRADE SEROUS OVARIAN CANCER

[1]CA Waddell*, [1]MJ Price, [1]P Johnson, [1,2]RJ Edmondson, [1,2]GL Owens. [1]*University of Manchester, Manchester, UK*; [2]*Saint Mary's Hospital, Manchester, UK*

10.1136/jitc-2020-ITOC7.89

Background Ovarian cancer is the most lethal gynaecological malignancy, accounting for approximately 185,000 deaths worldwide in 2018. The majority of patients will experience recurrence of disease. Therefore, there is an urgent need for the development of further therapies to improve patient survival. Tumour infiltrating lymphocyte (TIL) therapy has shown clear efficacy in immunogenic cancers, and TIL can be readily expanded ex vivo from samples of high grade serous ovarian cancer (HGSOC). Key indicators of effective TIL products for infusion are high TIL yield and functionality against autologous tumour. Blockade of checkpoint proteins is effective in increasing TIL yield and functional response from ovarian cancer TIL cultures. However, it is unknown whether blockade of other key checkpoints, including programmed death ligand-1 (PD-1), T cell immunoglobulin mucin-3 (TIM-3) and lymphocyte activation gene-3 (LAG-3) increase TIL yield in ex vivo cultures from HGSOC samples.

Materials and Methods TIL cultures were generated from surgically resected HGSOC tumour samples and were incubated with CD3/CD28 Dynabeads. 3000IU/mL recombinant interleukin-2 (IL-2) was added on alternate days for 7 days before beads were removed. 1000IU/mL IL-2 was added on alternate days for a further 12 days of culture. In cohort 1, 10μg/mL αPD-1, αTIM-3 or αLAG-3 antibodies were added at initiation of TIL cultures only. In cohort 2, 10μg/mL αPD-1, αTIM-3 or αLAG-3 antibodies were added on alternate days

until Day 19. Interferon gamma (IFN-γ) release in response to TIL co-culture with autologous tumour cultures was measured with 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 culture treated 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.

Disclosure Information C.A. Waddell: None. **M.J. Price:** None. **P. Johnson:** None. **R.J. Edmondson:** None. **G.L. Owens** None.

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

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

10.1136/jitc-2020-ITOC7.90

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.[1,2] 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.[3] 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.[2] 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.[4]

Results Our data shows that CD98-redirected 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

1. Linge A, *et al*., Low Cancer Stem Cell Marker Expression and Low Hypoxia Identify Good Prognosis Subgroups in HPV(-) HNSCC after Postoperative Radiochemotherapy: A Multicenter Study of the DKTK-ROG. *Clin Cancer Res* 2016. **22**(11): 2639–49.
2. Digomann D, *et al*., The CD98 Heavy Chain Is a Marker and Regulator of Head and Neck Squamous Cell Carcinoma Radiosensitivity. *Clin Cancer Res* 2019. **25** (10): 3152–63.
3. Bachmann M, *et al*., The UniCAR system: A modular CAR T cell approach to improve the safety of CAR T cells. *Immunol Lett* 2019;**211**:13–22.
4. Arndt C, *et al*., UniCAR T Cell Immunotherapy Enables Efficient Elimination of Radioresistant Cancer Cells. *Oncoimmunology* 2020.**9**(1): 1743036.

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; GEMoaB.

P06.12 COMBINATION THERAPY OF CAR-NK-CELLS AND ANTI-PD-1 ANTIBODY RESULTS IN HIGH EFFICACY AGAINST ADVANCED-STAGE GLIOBLASTOMA IN A SYNGENEIC MOUSE MODEL AND INDUCES PROTECTIVE ANTI-TUMOR IMMUNITY *IN VIVO*

[1,2,3]F Strassheimer, [1,2,3]MI Strecker, [4,2]T Alekseeva, [5,2]J Macas, [6,2]MC Demes, [1,7]IC Mildenberger, [8]T Tonn, [6,2]PJ Wild, [4,2,3]L Sevenich, [5,2,3]Y Reiss, [5,2,3]PN Harter, [5,2,3]KH Plate, [4,2,3]WS Wels, [1,2,3]JP Steinbach, [1,2,3]MC Burger*. *[1]Dr. Senckenberg Institute of Neurooncology, Goethe University Hospital, Frankfurt, Germany; [2]Frankfurt Cancer Institute (FCI), Frankfurt, Germany; [3]German Cancer Consortium (DKTK), partner site Frankfurt/Mainz, and German Cancer Research Center (DKFZ), Heidelberg, Germany; [4]Georg-Speyer-Haus, Institute for Tumor Biology and Experimental Therapy, Frankfurt, Germany; [5]Institute of Neurology (Edinger Institute), Goethe University Hospital, Frankfurt, Germany; [6]Dr. Senckenberg Institute of Pathology, Goethe University Hospital, Frankfurt, Germany; [7]Department of Neurology, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany; [8]Institute for Transfusion Medicine, German Red Cross Blood Donation Service North-East and Medical Faculty Carl Gustav Carus, TU Dresden, Dresden, Germany*

10.1136/jitc-2020-ITOC7.91

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 FOX-P3 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.