melanoma, we studied peripheral blood mononuclear cells (PBMC) in those who developed IN-C and those who received the same immunotherapy with no autoimmune side effects (IN-NAE). We compared these samples to those from patients with active ulcerative colitis (UC) and healthy volunteers in a retrospective single-centre cross-sectional study.

Materials and methods: Cryopreserved PBMC from patients with IN-C ($N = 9$) were studied at 4 time-points: baseline, early on-treatment but before colitis, at the time of colitis and post-colitis. IN-NAE ($N = 11$) were studied at baseline and at Week 7–10 of treatment (a comparator to the IN-C "colitis" time-point). Patients with treatment-experienced active UC ($N = 6$) and healthy volunteers ($N = 17$) were studied at single time-points. Thawed PBMC were stained with a near infra-red live/dead stain and fluorochrome-conjugated antibodies to CD45RA, CD3, CD19, IgA, CD27, CD38, CD56, CD4, CD8, CD25, CD127 4-integrin, β7-integrin and HLA-DR. Cells were analysed on a five-laser LSRFortessaX20 flow cytometer (BD) and FloJo software. Differences between groups were assessed by non-parametric Mann-Whiney and Chi-square tests for continuous and categorical data, respectively (SPSS Software).

Results: There was no significant difference between IN-C and IN-NAE groups in terms of age, sex, melanoma stage, presence of visceral metastases or serum lactate dehydrogenase level. IN-C was not associated with a change in the proportion of total, CD4+ or CD8+ T-cells. Treatment with combination ipilimumab and nivolumab was associated with a rise in activated memory gut-homing CD8+ T-cells in both IN-C and IN-NAE groups. IN-C differed from active UC in that it was not associated with a rise in circulating plasmablasts. Compared with healthy volunteers, patients with melanoma had a lower proportion of total T-cells and higher proportion of NK-cells at baseline, but these changes were not predictive of colitis.

Conclusions: Treatment with combination ipilimumab and nivolumab therapy is associated with a rise in circulating activated memory gut-homing CD8+ T-cells, however this was independent of the development of colitis. Further work is needed to determine if these cells are pathogenic and/or the presence of host protective factors. IN-C was distinct from active UC in that it does not generate a significant plasmablast response. This indicates pathogenic B-cells might play less of a role in IN-C, relevant given the high expression of PD-1 on follicular-helper T-cells. We are currently running a prospective trial on TCI-associated colitis, studying PBMC, gastrointestinal tissue and microbiome. We aim to confirm if changes seen in PBMC are mirrored in the gastrointestinal tract. Our ultimate goal is to define baseline risk factors and biomarkers that can be used clinically to reduce the morbidity of this condition.

P4.03

Complete response of stage IV pancreatic cancer combining low-dose checkpoint inhibitors with interleukin-2 (IL-2) and fever range hyperthermia

R. Kleef[1], R. Nagy[1], A. Bohdjalian[2], V. Bacher[1], A. Wychera[1], S. Kekic[1], D. McKee[3], H. Bojar[4], R. Moss[5]
[1]*Ralf Kleef Immunology & Integrative Oncology, Vienna, Austria*
[2]*Rudolfinerhaus Hospital, Vienna, Austria*
[3]*Integrative Cancer Therapies, London, United Kingdom*
[4]*NextGen Oncology Group, Duesseldorf, Germany*
[5]*Cancer Decisions, Lemont, PA, United States*

Background: Advanced stage inoperable pancreatic cancer has a poor prognosis and patients rarely enjoy durable complete response to treatment; progression free survival often is limited.

Materials and methods: We previously reported several cases of complete remission of far advanced lung metastasis in triple negative breast cancer, esophageal cancer and breast cancer at ITOC3 (Munich) 2016, ITOC 4 (Prague) 2017 and ITOC 5 (Berlin) 2018 respectively; here we report a similar case.

The patient was a 45-year-old male newly diagnosed 05/2017 with adenocarcinoma of the pancreas with histological confirmation of primary invasive ductal adenocarcinoma of the pancreas with disseminated liver metastasis (>20 single lesions up to 2cm) and a single large peritoneal deposit (2.7 × 2.0 × 3.9 cm) close to the caecum. There was small volume malignant ascites. Histology revealed adenocarcinoma stage UICC IV T2 N2 M1 (hepar, peritoneum) with disseminated para-aortal and celiac lymph node metastasis. Guardant360 sequencing indicated somatic alteration burden of 9.2%. Analysis of circulating Tumor cells (CTC) revealed a high score of 236. Laboratory showed elevated transaminases and pancreatic enzymes, TM CEA/ was 3.4 ng/ml, CA19/9 4 U/ml. The patient underwent one-time neoadjuvant CHT with Gemcitabine-Abraxane prior. Clinically the patient presented with Karnofsky index of 90% with moderate weight loss of 4 kg in the last 2 months, the patient experienced mild left upper abdominal discomfort which started around 9 months ago VAS 2–3. Therapy consisted of administration of the following combination protocol: Low-dose PD-1 immune checkpoint (IC) inhibitor nivolumab (0.5 mg/kg) with CTLA-4 IC inhibitor ipilimumab (0.3 mg/kg) administered weekly, over three weeks. This was accompanied by loco regional hyperthermia with radiofrequency fields (13.56 MHz) using the Syncrotherm device 3 times per week (max output 400 w) over the tumor region in combination with high dose vitamin C (0.5 g/kg) and alpha lipoic acid (600 mg) over three weeks. This was followed by long duration fever range whole body hyperthermia (using the Heckel HT^{3000} device) in combination with low dose chemotherapy using cyclophosphamide 300 mg/m^2 to down modulate T_{reg} cells. Moderate dose i.v. Interleukin-2 (IL-2) under Taurolidine protection was administered for five days with careful titration to daily fever hyperthermia of max 39.5 °C. CHT was administered with metronomic gemcitabine 500 mg/m^2 two times.

Results: First restaging 11/2017 three month following initiation of therapy with CT of abdomen and pelvis demonstrated major partial remission with decrease of the size of disseminated liver metastasis and no measurable primary pancreatic tumour, vanishing of the previously described lymphadenopathy. At that time the patient had started gaining weight again and was free of any cancer-related symptoms. Second restaging 05/2018 nine months following initiation of therapy with CT of the abdomen and indicated complete remission. Follow-up time now is $1^1/_2$ years. Patient is healthy and free of any symptoms.

Conclusions: This is one of several cases of advanced stage cancer patients having a complete response to primary immunotherapy treatment. Clearly, this combination immune therapy warrants further clinical studies.

P4.04

Viral sensitizers potential infection of cancer cells via NF-kappaB

M. Phan[1,2], R. Krishnan[1,2], N. El Sayes[1,2], J. Mathieu[1,2], M. Selman[1,2], A. Macklin[3], M. Dornan[4], H. Groom[3], D. Patten[2], C. Davis[1,2], F. Lai[5], B. Lichty[5], M. Harper[2], R. Arulanandam[1], J. Bell[1,2], T. Alain[2,6], D. Josephy[3], J. Smith[4], C. Boddy[2], J. Diallo[1,2]
[1]*Ottawa Hospital Research Institute, Ottawa, ON, Canada*