

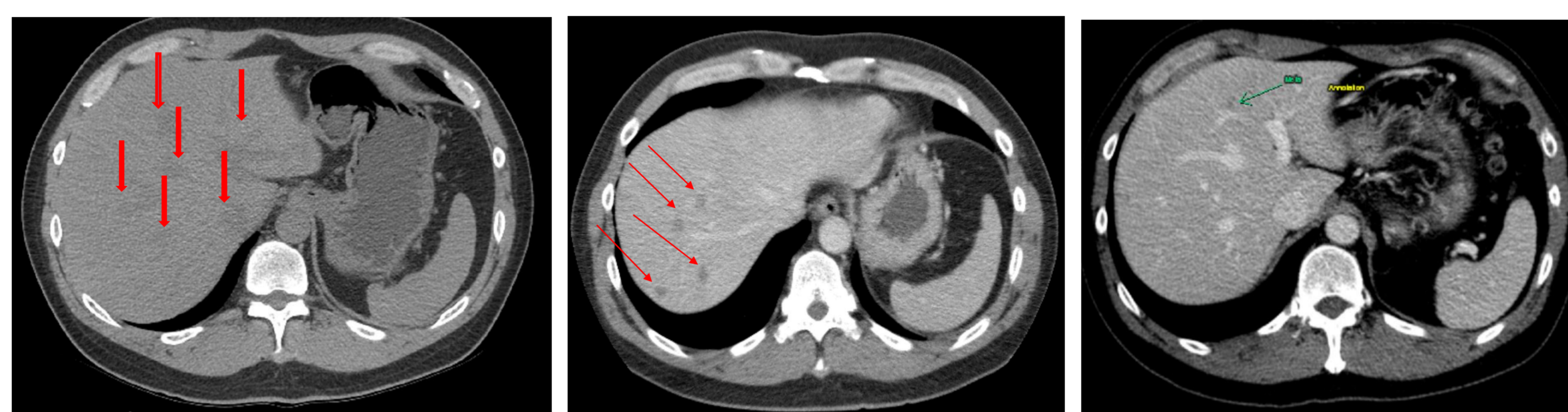
Complete response of stage IV pancreatic cancer combining dose adapted checkpoint inhibitors with interleukin-2 (IL-2) and fever range hyperthermia

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INTRODUCTION

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 significant 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.

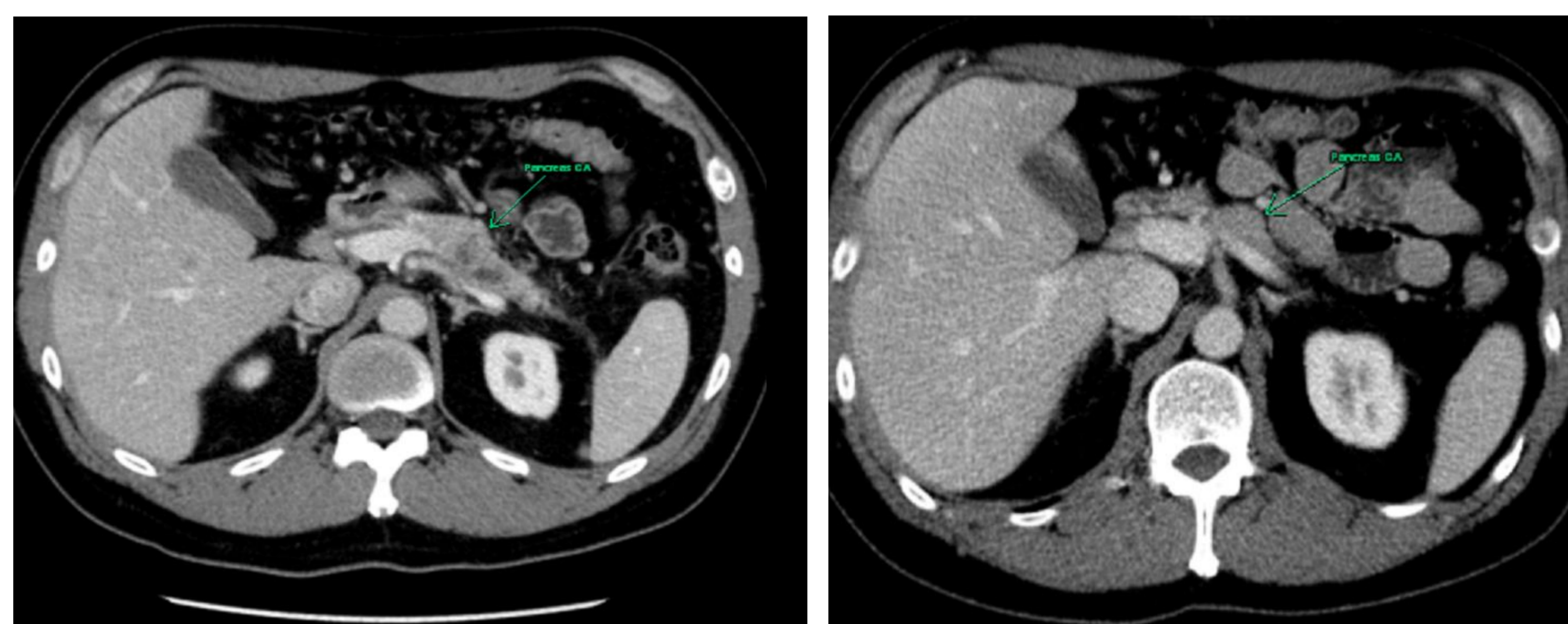
STAGING



05/2017

07/2017

11/2018



05/2017

11/2018

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. Third restaging 11/2018 16 months following initiation of therapy with CT of the abdomen and thorax indicated complete remission. Follow-up time now is 26 months. Patient is healthy and free of any symptoms.

CONCLUSION

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.

MATERIALS & METHODS

Dose adapted PD-1 immune checkpoint (IC) inhibitor nivolumab (0.5 mg/kg) with CTLA-4 IC inhibitor ipilimumab (0.3 mg/kg) was 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 400W) over the tumor region in combination with high dose vitamin C (0.5 g/kg) and alpha lipoic acid (600mg) over three weeks. This was followed by long duration fever range whole body hyperthermia (using the Heckel HT3000 device) in combination with low dose chemotherapy using cyclophosphamide 300 mg/m² to down modulate TReg 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 500mg/m² two times.

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 Declaration of conflict of interest: RK has international patent pending