Results: Seventeen pts were enrolled [11 ovarian [30 clear cell, 1 low grade serous], 4 high grade and 2 endometrial and 2 non small cell lung cancer]. Median number of previous therapies was 1 (range 0-2); 8 pts were chemotherapy naive. Median age was 52 (range 34-71). Four pts were treated at G 95 mg/m², 8 at 110 mg/m² and 5 at 130 mg/m². Median number of administered cycles was 6 (range 2-16). Dose limiting toxicity (DLT) occurred in 4/16 evaluable pts; 2 (delay in starting cycle 2 due to G2 and G3 neutropenia) at 110 mg/m² (initial schedule), 2 at 130 mg/m² (G2 and G3 mucositis) and no DLT at 110 mg/m² at amended schedule. G 3 treatment-emergent adverse events were neutropenia (6 pts), anemia (3 pts), mucositis (2 pts) and fatigue, nausea, peripheral neuropathy, thrombocytopenia, hypokalemia, hypomagnesemia, infective colitis and aortic intramural hematoma (one pt each). All pts were evaluable for response: 11/17 (65%) achieved an objective response (8 partial and 3 complete) and 3 SD (17%). Among clear cell ovarian cancer (CCODC) pts, 8/10 had an evaluable response.

Conclusions: G has a tolerable safety profile when combined with C and weekly P. The RP2D is G 110 mg/m² on d1, 8, 15 and 22 with CAU 5 on d1 and P 80 mg/m² on d1, 8 and 15 in 28 days cycles. Preliminary antitumor activity was observed especially in the COC pts.

Clinical trial identification: NCT02069158.

Legal entity responsible for the study: Oncology Institute of Southern Switzerland (OISI).

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Intratumoral injection of allogeneic pro-inflammatory dendritic cells (ilixadencel) in combination with anti-CTLA-4 treatment induce complete tumour responses and anti-tumour immune memory in a mouse tumour model

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Background: ilixadencel, a cell-based allogeneic immune primer consisting of pro-inflammatory monocyte-derived dendritic cells (DCs) that are injected intratumorally (i.t) recently received Regenerative Medicine Advanced Therapy (RMAT) designation making it a promising treatment for metastatic renal cell cancer (mRCC). Ilixadencel is produced from C57BL/6 mice. Cryopreserved and subsequently thawed cells were injected i.t (2 doses) as monotherapy or in combination with anti-VEGF (4 doses), anti-PD-1 (4 doses) or anti-CTLA-4 (2 doses) given i.p. in Balb/c mice, starting treatment when CT-26 tumour mice reached an average size of 100 mm³.

Results: Monotherapy with mouse-ilixadencel, anti-PD-1 or anti-VEGF had no or only marginal effect on tumour growth while monotherapy with anti-CTLA-4 significantly delayed tumour growth without inducing any complete tumour responses. Mouse-ilixadencel in combination with anti-PD-1 or anti-VEGF trended to delayed tumour growth without inducing any complete responses. When ilixadencel was combined with anti-CTLA-4, 50-70% of the treated animals (data from 2 independent experiments) had a complete tumour response. Notably, animals with complete tumour response where protected from tumour growth upon subsequent tumour re-challenge.

Conclusions: Intratumoral administration of allogeneic pro-inflammatory DCs induce a synergistic anti-tumour response when combined with anti-CTLA-4, including complete responses and signs of systemic anti-tumour immune memory.

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Phase I dose escalation study of the dual PI3K/mTORC1/2 inhibitor Gedatolisib (PF-05212384) in combination with paclitaxel (P) and carboplatin (C) in patients (pts) with advanced solid tumours

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Background: Inhibition of the PI3K pathway may overcome resistance to chemotherapy. The PI3K/mTORC1/2 dual inhibitor Gedatolisib (G) has an acceptable safety profile as single agent. This phase I study aimed to define safety, recommended phase II dose (RP2D), pharmacokinetics and preliminary activity of G in combination with C and weekly P.

Methods: Adult pts with selected advanced solid tumours previously treated with 0-2 lines of palliative chemotherapy were eligible. G was administered intravenously on days (d) 1, 8, 15 and 22 at increasing doses (95, 110 and 130 mg/m²) following a 3+3 design. G was initially administered at AUCs on d8 and P at 80 mg/m² on d8, 15 and 22 and after a protocol amendment on d1 and d8 and 15 respectively, in 28 days cycles. Pts responded or on stable disease (SD) (or cycle 6 continued on weekly G maintenance.

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