Results summary

A phase II-study of electroporation potentiated immunotherapy in liver metastatic pancreatic cancer

Baseline characteristics

Eight patients in PS 0 (n=3) or 1 (n=5) with liver-metastatic pancreatic adenocarcinoma were include from May 27th to December 3rd, 2021. The median age was 61 (range 39-71) years and the median time from diagnosis was 13.2 (range 4.4-47.6) months. Six patients were included due to progression on previous treatment while the last two had developed intolerability to treatment. Patients were previously treated with surgery (n=2), FOLFIRINOX (n=7), gemcitabine + nab-paclitaxel (n=7), FOLFIRI (n=1), 5-flourouracil (n=1) and gemcitabine (n=2).

Safety outcomes

All patients received the first dose of pembrolizumab (400mg) and were subsequently treated with irreversible electroporation of a single liver metastasis. Only one patient received the second dose of pembrolizumab. No dose-limiting toxicities were observed during follow-up. A total of six SAEs were registered. None were attributed to treatment. On-treatment AEs (grade 1-3) included fatigue (n=7), nausea (n=4), vomiting (n=2), anorexia (n=5), diarrhea (n=4), constipation (n=2), anemia (n=5), dizziness (n=3), dyspnea (n=4), edema (n=2), cough (n=1), arthralgia (n=1), myalgia (n=1), abdominal pain (n=7), pruritus (n=3), peripheral motor neuropathy (n=1), peripheral sensory neuropathy (n=4), back pain (n=1), eczema (n=1), venous thrombo-embolism (n=1), thrush (n=1). Most observed AEs were unchanged from baseline while pruritus (3 cases of grade 1) and anemia (1 case of grade 2 and 1 case of grade 3) were deemed possible treatment effect.

Efficacy outcomes

No clinically relevant effect was observed. The objective response rate was 0%. The median progression-free survival was 1.8 months, and the overall survival was 2.0 months.

Biomarker outcomes

No CA 19-9 response was observed during follow-up.

No significant changes were observed in circulating monocytic MDSCs ten days after pembrolizumab injection, but an increase was observed immediately after irreversible electroporation. No significant changes in circulating monocytic MDSCs were observes.

The mean number of plasmacytoid DCs dropped significantly ten days after pembrolizumab injection and tended to be even lower immediately after irreversible electroporation. The mean number of circulating cDC1s and cDC2s and PD-L1 expression in these were unchanged during treatment.

No significant changes were observed in circulating CD8 or CD4 T-lymphocytes or Tregs. No significant changes were observed in circulating CD4/CD8 ratio or Treg/CD8 ratio. No significant changes were observed in circulating CTLA4+, LAG3+ or TIM3+ CD4 or CD8 cells.