Anti-tumor activity of PEGylated human IL-10 (AM0010) in patients with Pancreatic or Colorectal Cancer.

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Background and Purpose
- Time to objective response in pancreatic cancer (TOMP) (9%)
- OS in CRC (7%)
- Grade 4 hypokalemia
- Grade 3 rash
- Grade 2 pain
- Grade 1 and 2 CA19-9: 5 patients had stable disease at 8 weeks of treatment with AM0010 monotherapy
- mPFS in CRC (10.2 months)
- OS in CRC (11.4 months)
- TGFβ receptor 1 (TGFβR1) knockdown enhances IL-10-induced PD-L1 expression
- TGFβ and IL-10 are known to be autocrine and paracrine cytokines to stimulate the growth and survival of cancer cells

Treatment related Adverse Events
- AM0010 monotherapy in pancreatic cancer patients
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  - Grade 2 pain
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Summary and Outlook
- Acceptable tolerability profile [up to 16 months]
- Tolerated on continuous dosing without autoimmune AEs
- Selected patients on AM0010 for more than one year, including patients with PDAC for 13.5 mos, melanoma for 16.6 mos, and with CRC for 10.4 mos.

Encouraging Efficacy Profile
- (Cancer Cell 2011; Emmerich et al. Cancer Research 2012)
- Phase 2 (n=17): ORR 47% at 4 weeks, reduction in CA223-10 46% at 47 mos.

Sustained TLR3/IL-23 T-cell-mediated immune activation
- Increase in Th1/Th17 cytokines / Immune suppression
- Reduction in CA19-9 and growth in tumors
- Increase in activated tumor infiltrating CD8+ T cells
- Regression of preexisting PD-1+ PD-L1+ T cells
- Disappearance of novel T cells in systemic circulation

Mechanism Based Combinations with AM0010
- (Cancer Research 2012; 2015)
- Preclinical and clinical data
- Increased antitumor efficacy
- Reduced toxicities
- Demonstrated in combination with multiple agents

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