Supplementary figures

Figure S1

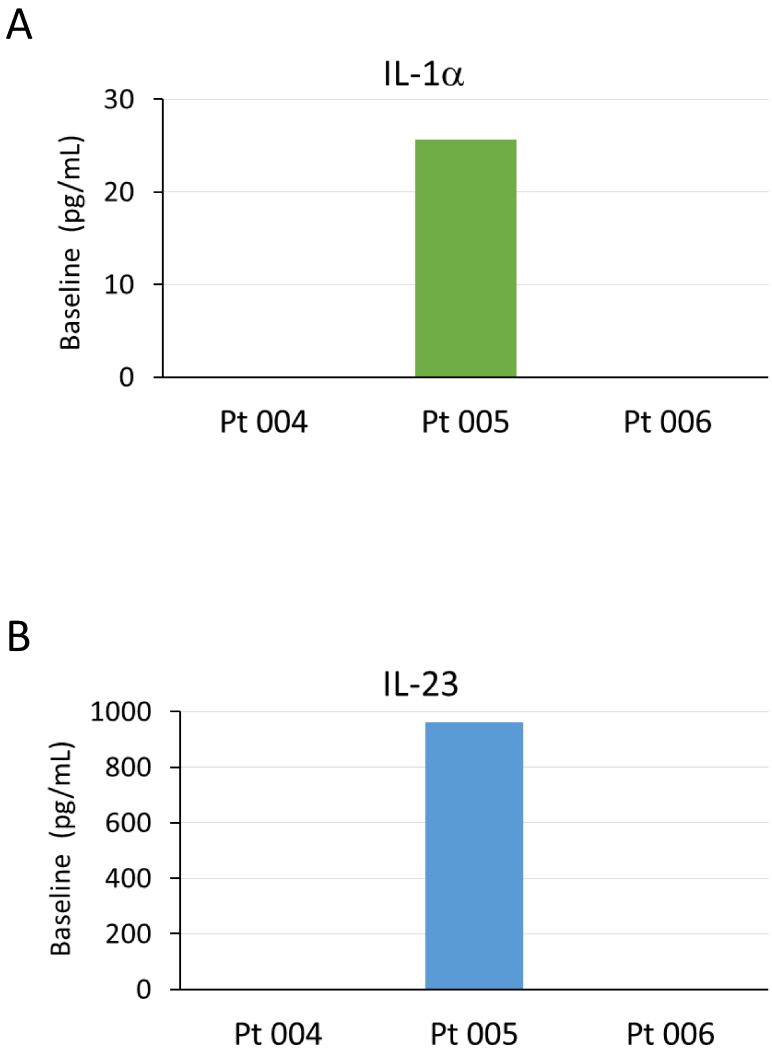


Figure S1. Baseline plasma IL-1α (A) and IL-23 (B) concentrations for the three participants receiving 50 mg of pixatimod/240 mg of nivolumab, including Pt 005 who experienced multi-organ failure.

Figure S2

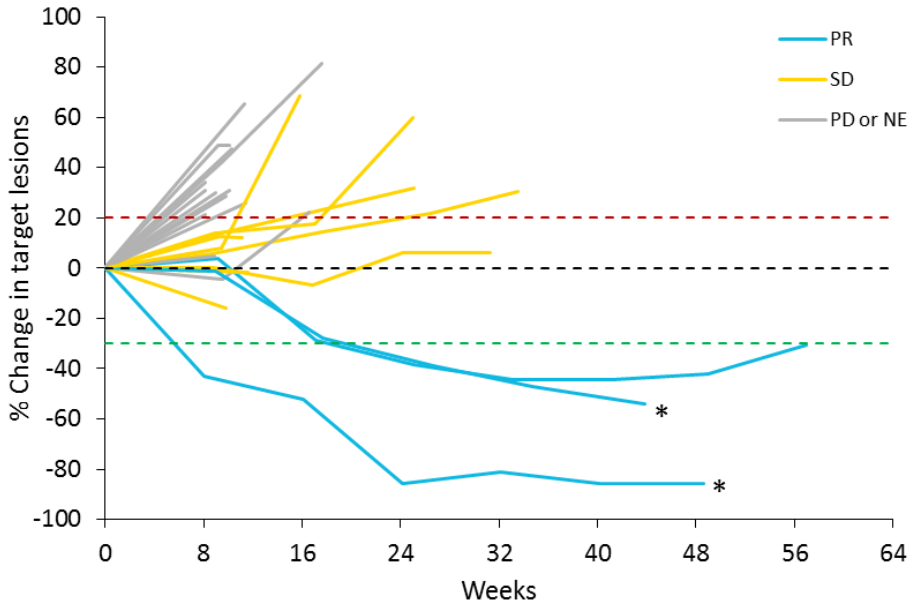
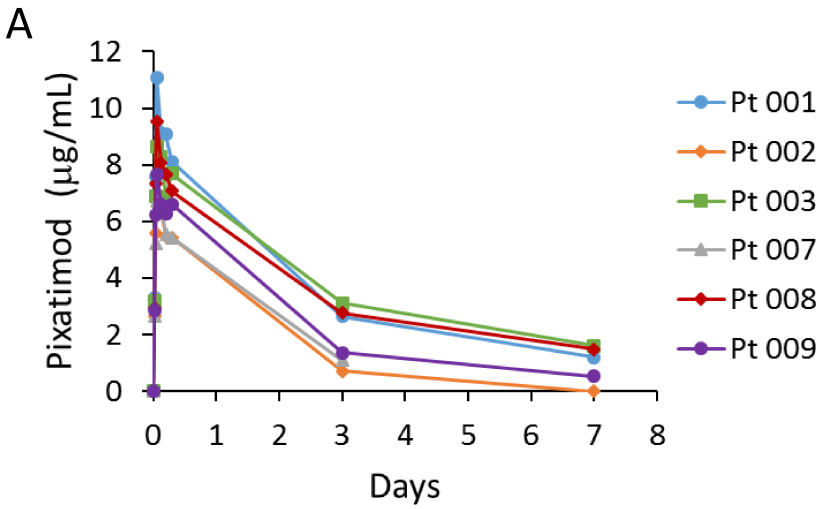
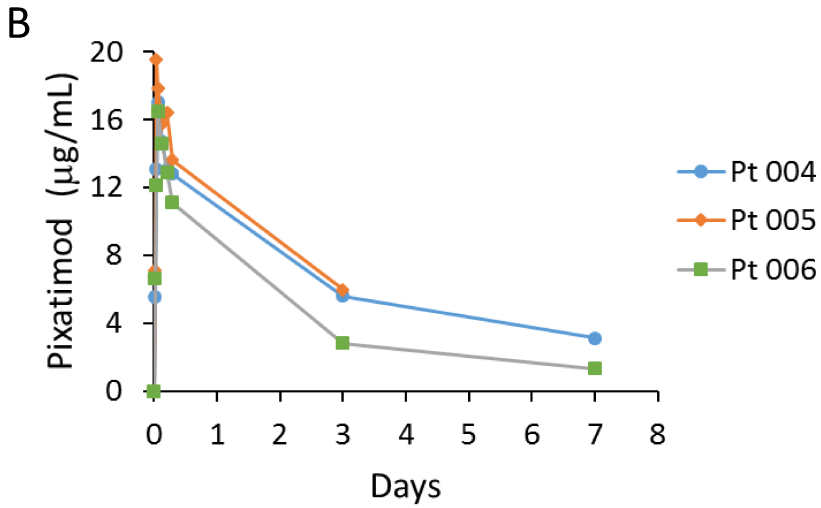


Figure S2. Spider plot showing the percentage change in target lesions during treatment for the mCRC participants. Data are colored by clinical outcome, PR (blue), SD (yellow), PD or NE (grey). The two participants indicated (*) came off the trial due to SAE not disease progression by RECIST.

Figure S3





C

Dose	Cmax (µg/mL)	AUC0-last (h*µg/mL)
25 mg	8.4 (9.6)	457 (463)
50 mg	17.7 (15.6)	855 (709)

Note: Numbers in parentheses refer to previous PK data in monotherapy study (Dredge *et al, Br J Cancer* 2018)

Figure S3. Time versus concentration curves of plasma pixatimod (in combination with nivolumab) for 25 (A) and 50 mg (B) cohorts following first dose. Systemic exposure of pixatimod as determined by Cmax and AUC0-last using NCA following treatment (C).

Figure S4

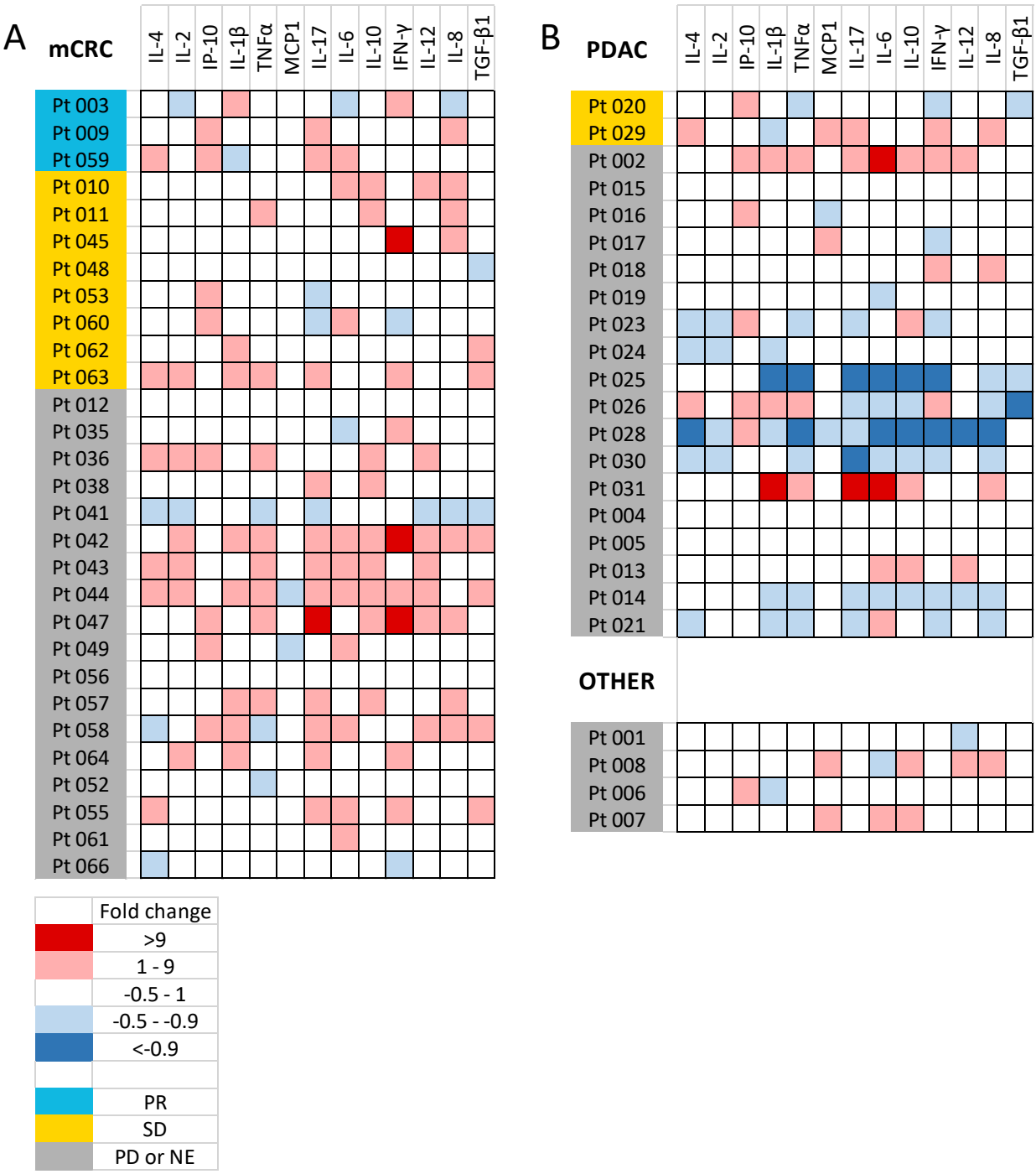


Figure S4. Maximum fold change in plasma protein biomarker concentration following treatment commencement are presented as heat maps for mCRC (A) and mPDAC and other cancer types (B). Increased biomarker concentrations are shown with shades of red and decreased concentrations with blue. Participant clinical response indicated by color: PR, blue; SD, yellow; PD or NE, grey.

Figure S5

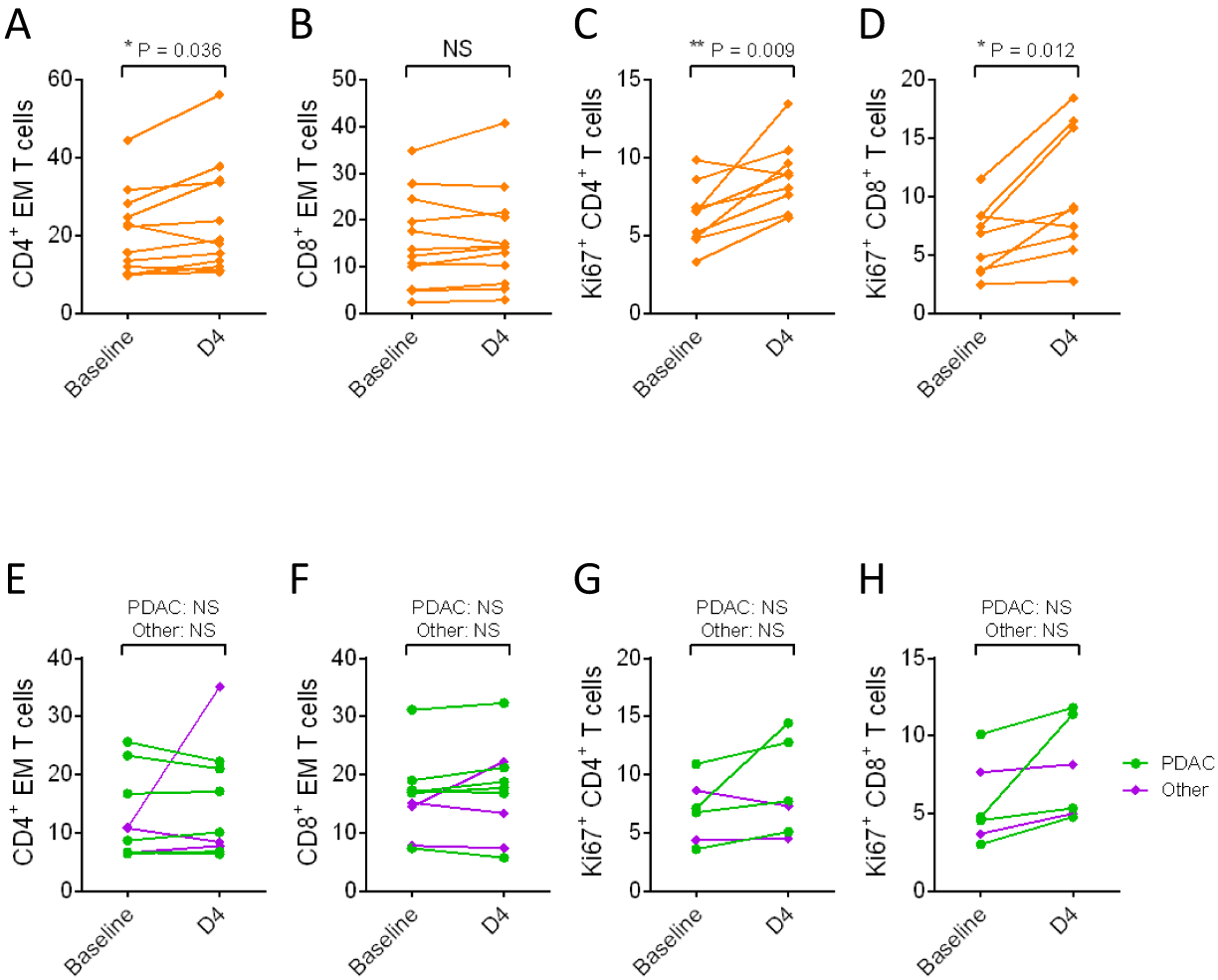


Figure S5. Pixatimod and nivolumab treatment drives expansion of peripheral T cells in mCRC participants but not in mPDAC participants. Data for mCRC participants in panels A-D and mPDAC and other cancer types in panels E-H. Increased numbers of $CD4^+$ (A) although not $CD8^+$ (B) effector memory (EM) T cells were present in PBMC from mCRC participants on D4 after treatment commencement. Increased Ki67 expression on $CD4^+$ (C) and $CD8^+$ (D) T cells was also noted in majority of mCRC participants. In contrast, no significant changes in these T cell parameters were observed in mPDAC or participants with other tumor types. PBMC samples were collected on D1 before treatment (Baseline) and on D4. Comparisons performed with paired t-tests (*$p < 0.05$, **$p < 0.01$).

Figure S6

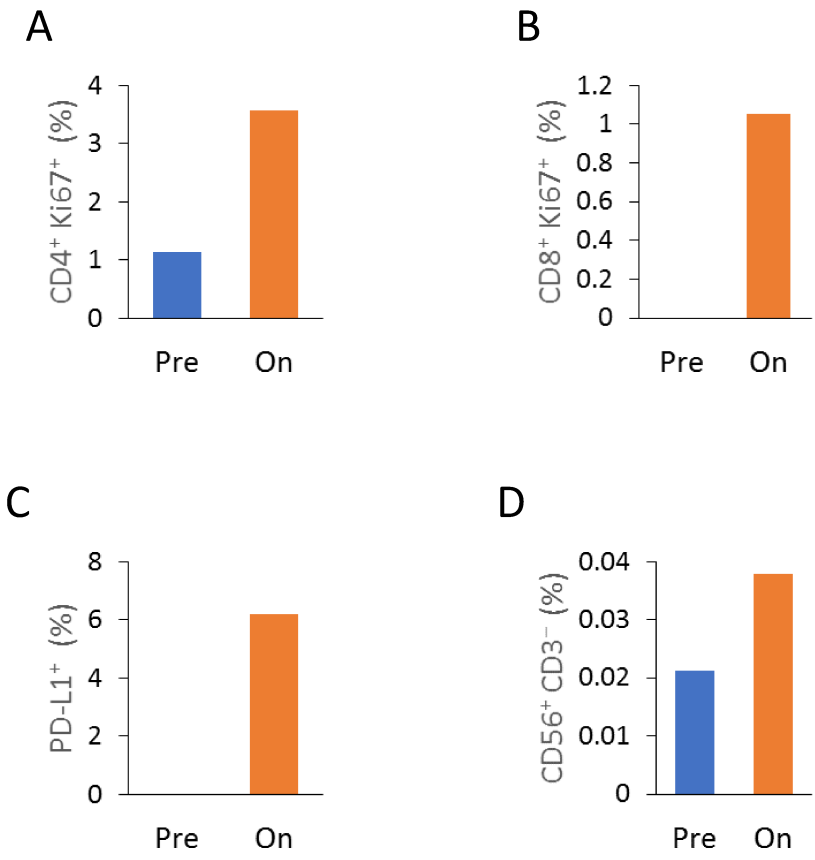


Figure S6. Analysis of pre and on-treatment liver lesion biopsies of a PR participant (Pt 059) by fluorescence multiplex microscopy. In addition to the data presented in Figure 4, data for $CD4^+$ $Ki67^+$ cells (A); $CD8^+$ $Ki67^+$ cells (B); $PD\text{-}L1^+$ cells (C) and $CD56^+$ $CD3^-$ cells (D) are presented.