



**Supplementary Figure S7.** On-treatment circulating tumor DNA (ctDNA) fraction, prostate specific antigen (PSA) responses and baseline genomic and clinical features. **(A)** Swimmers plot showing per patient progression-free survival. Bar colors indicate the ctDNA change groups following 4 weeks of treatment. Arrows indicate patients who are still on-treatment. **(B)** ctDNA fraction (ctDNA%) changes following 4 weeks of treatment. **(C)** The change in serum PSA following 4 weeks of treatment. Arrows indicate a PSA increase greater than

100%. Red bars indicate patients who did not achieve a PSA30 response at 4 weeks. **(D)** The change in serum PSA following 12 weeks of treatment. Arrows indicate a PSA increase greater than 100%. Red bars indicate patients who did not achieve a PSA50 response at 12 weeks. **(E)** Baseline patient clinical characteristics. **(F)** Potentially actionable alterations present in baseline ctDNA samples, within the homologous recombination repair (HRR) pathway, mismatch repair (MMR) pathway and phosphoinositide 3-kinase (PI3K) pathway. **(G)** Baseline *TP53* and *AR* alterations.

Abbreviations: HB, hemoglobin; LDH, lactate dehydrogenase; ALP, alkaline phosphatase; PSA, prostate-specific antigen; ECOG, Eastern Cooperative Oncology Group performance status;  $\Delta$ PSA, prostate-specific antigen change; PSA30, 30% decline in prostate-specific antigen; PSA50, 50% decline in prostate-specific antigen.