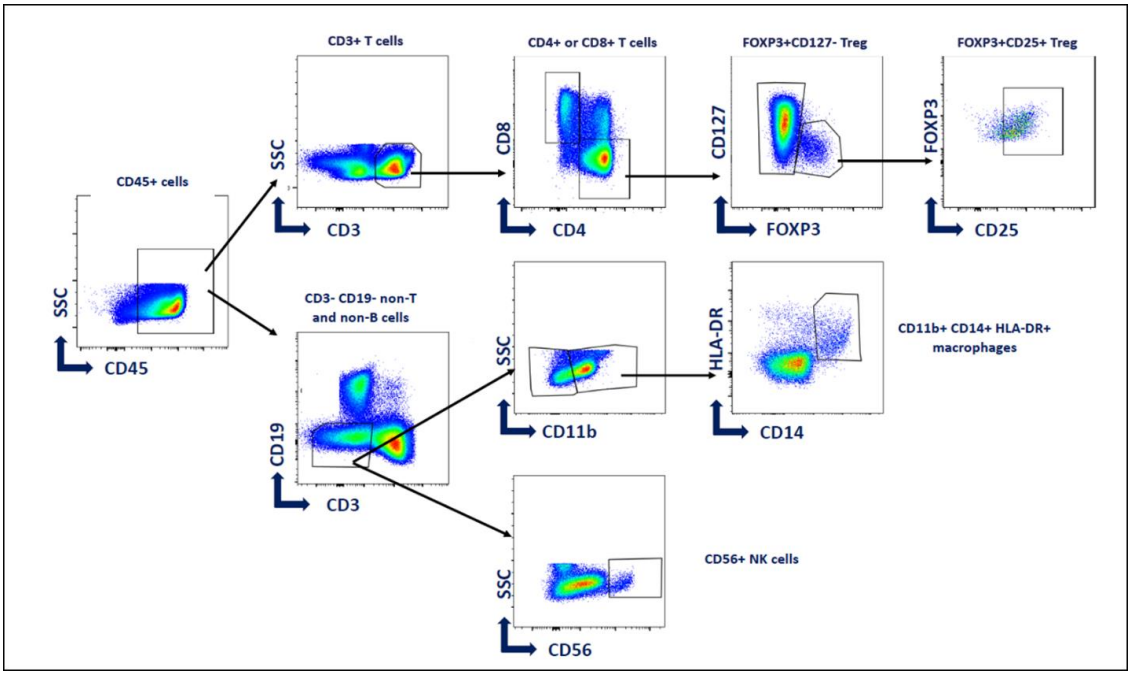
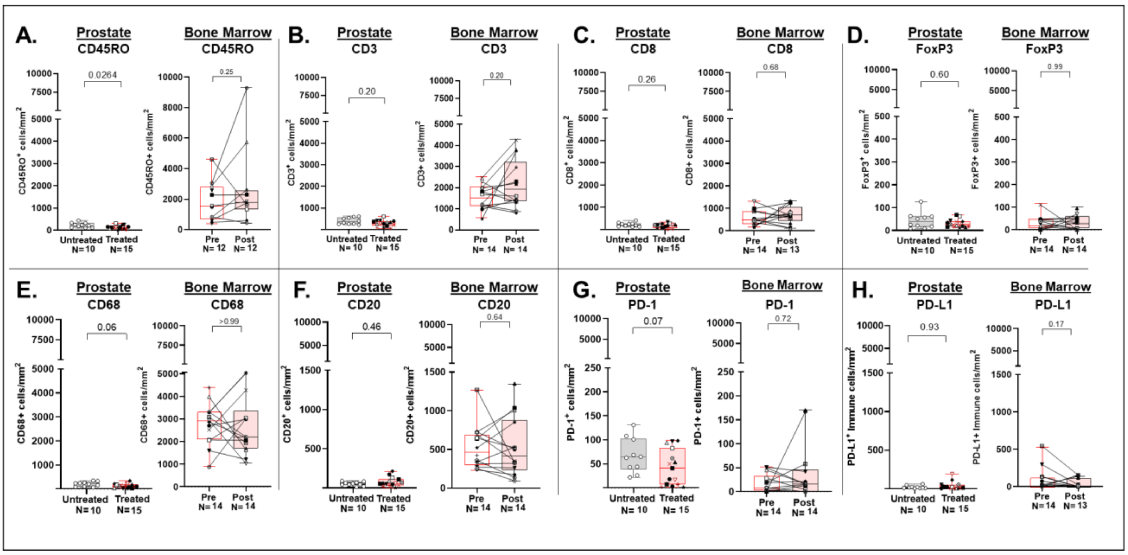
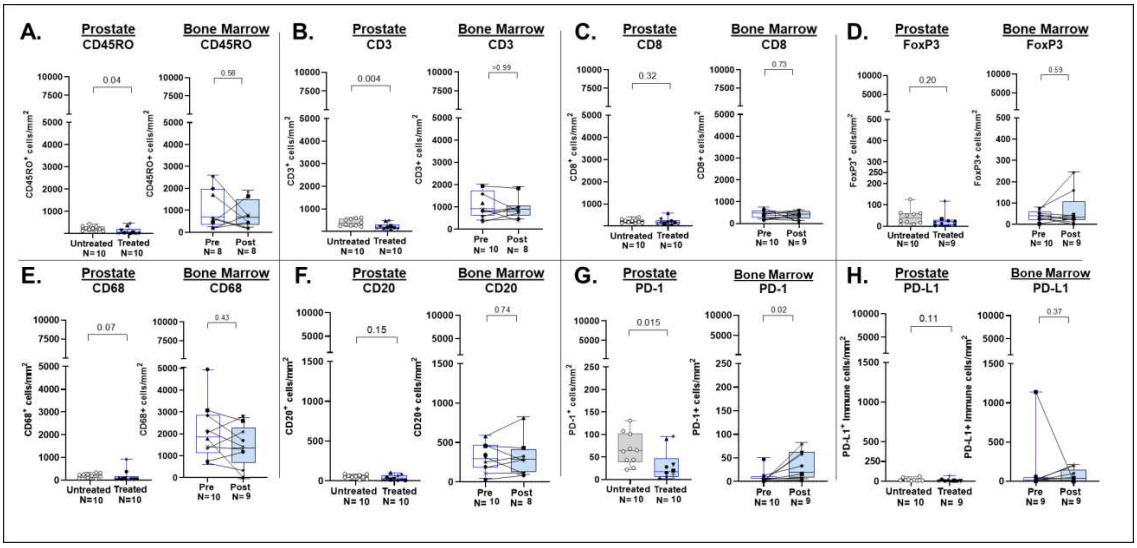


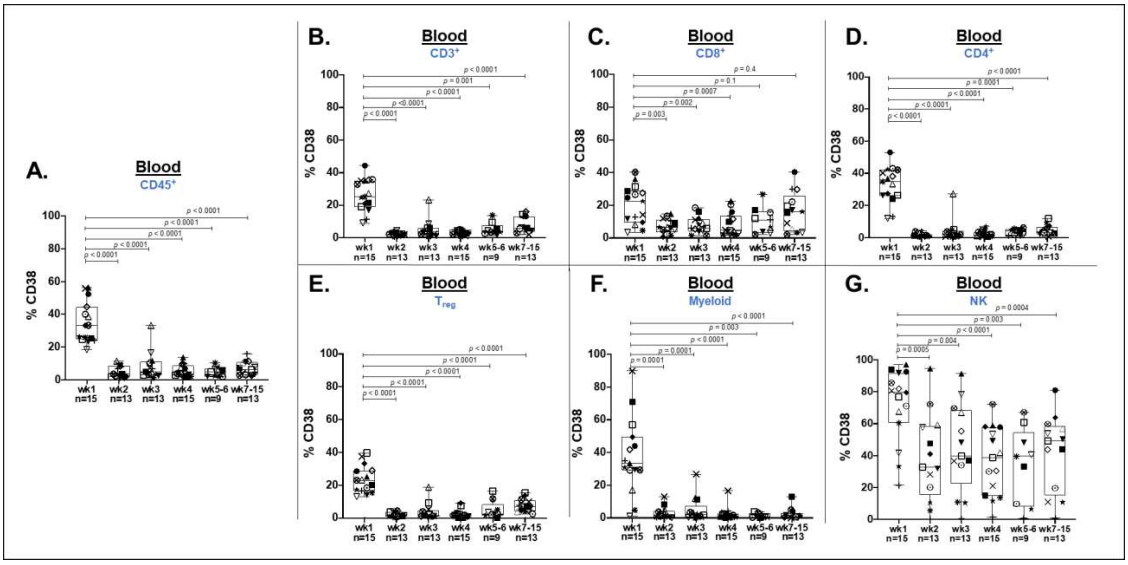
Supplementary Figure 1. Flow cytometry gating strategy.



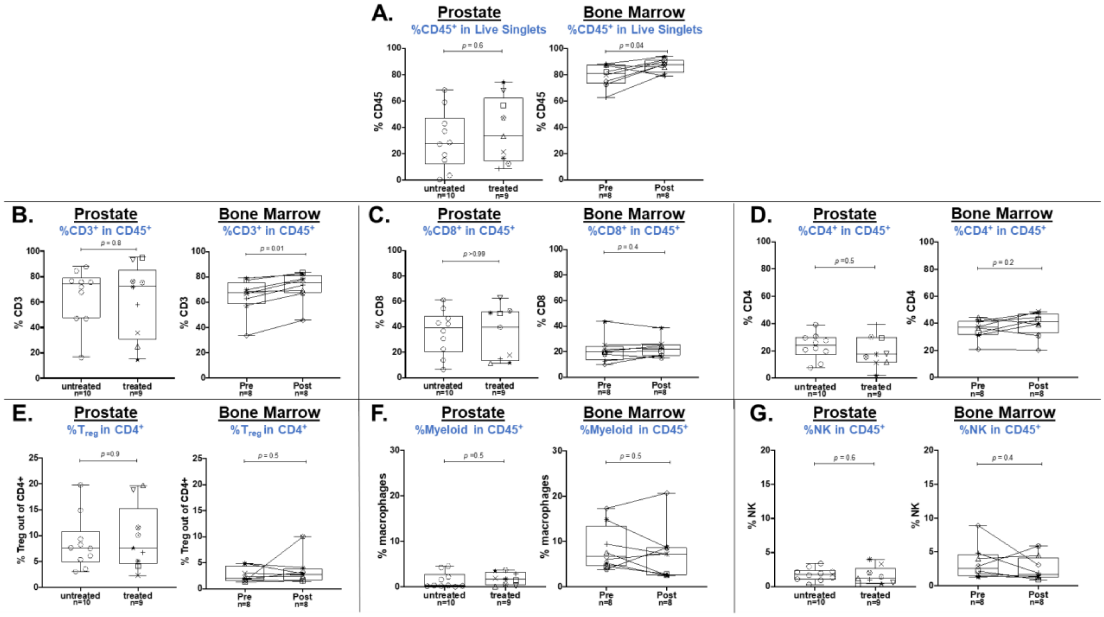
Supplementary Figure 2. Changes in immune cell subsets and PD-1/PD-L1 in prostate tumors and bone marrow with daratumumab as assessed by IHC. Quantitative IHC of **A.** CD45RO**; B.** CD3**; C.** CD8**; D.** FoxP3**; E.** CD68**; F.** CD20; **G.** PD-1; **H.** PD-L1. Daratumumab-treated vs. untreated prostate tumors and patient-matched pre-daratumumab and post-daratumumab bone marrow cores were assessed.



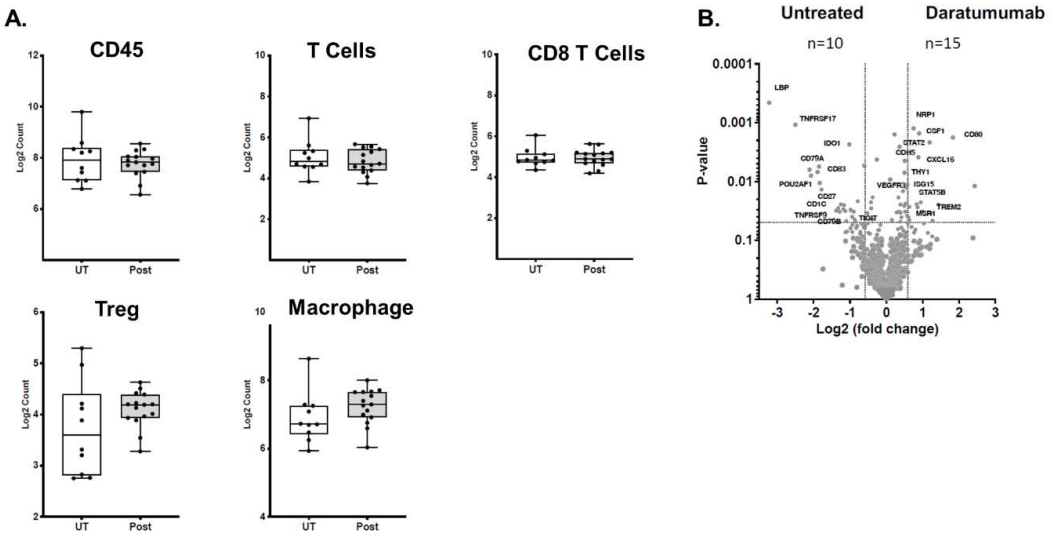
Supplementary Figure 3. Changes in immune cell subsets and PD-1/PD-L1 in prostate tumors and bone marrow with edicotinib as assessed by IHC. Quantitative IHC of **A.** CD45RO**; B.** CD3**; C.** CD8**; D.** FoxP3**; E.** CD68**; F.** CD20; **G.** PD-1; **H.** PD-L1. Edicotinib-treated vs. untreated prostate tumors and patient-matched pre-edicotinib and post-edicotinib bone marrow cores were assessed.



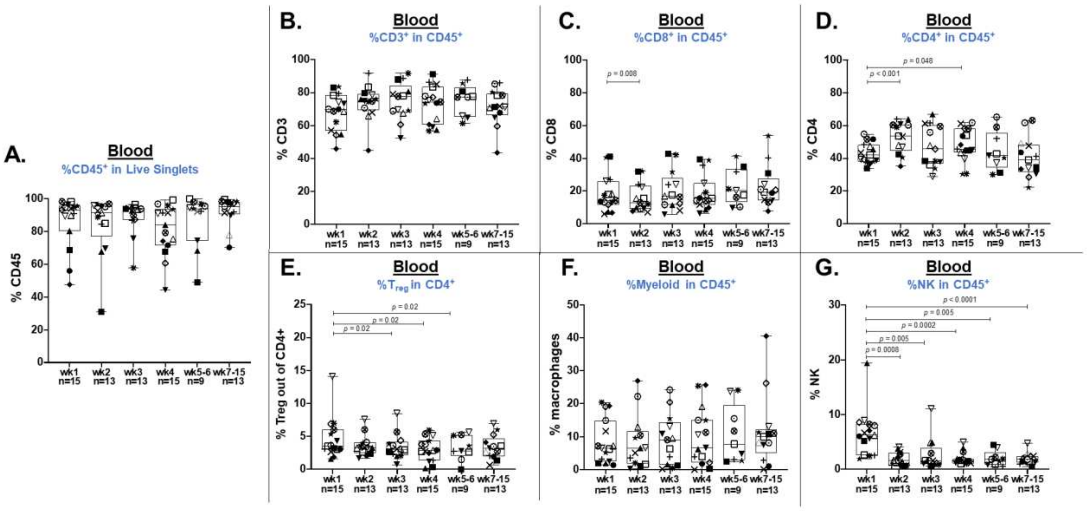
Supplementary Figure 4. Target modulation by daratumumab in blood as assessed by flow cytometry. Flow cytometric analysis gated on $CD45^+$ live cells showing frequency of $CD38^+$ cells in: **A.** $CD45^+$ immune cells; **B.** $CD3^+$ T cells; **C.** $CD8^+$ T cells; **D**. $CD4^+$ T cells; **E.** $CD4^+CD25^+FoxP3^+$ Treg cells; **F.** $CD11b^+CD14^+HLA\text{-}DR^+$ myeloid cells; **G.** $CD3^-CD19^-CD56^+$ NK cells. Peripheral blood mononuclear cells (PBMCs) from daratumumab-treated patients were assessed at the timepoints indicated.



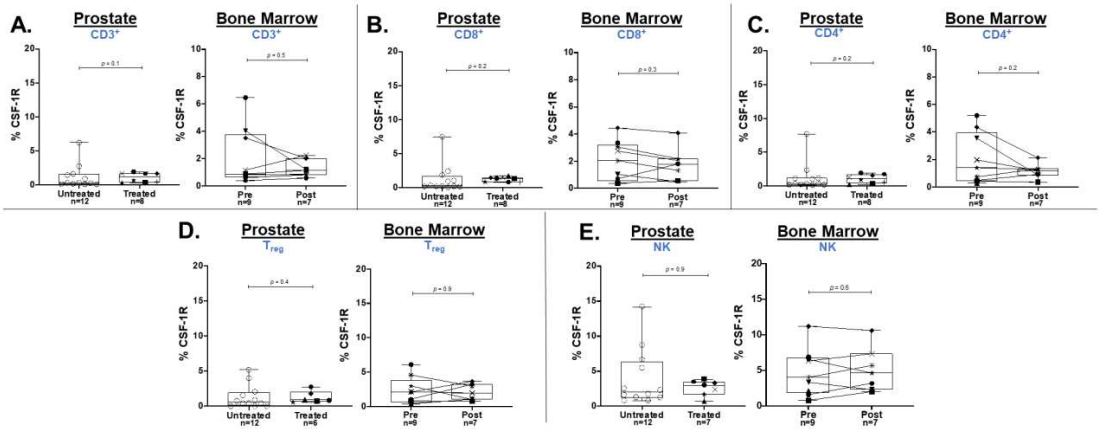
Supplementary Figure 5. Changes in total immune cell subsets with daratumumab in prostate tumors and bone marrow as assessed by flow cytometry. A. Flow cytometric analysis showing frequency of CD45 cells in live singlets. **B-F:** Flow cytometric analysis gated on $CD45^+$ live cells showing frequency of: **B.** $CD3^+$ T cells; **C.** $CD8^+$ T cells; **D.** $CD4^+$ T cells; **E.** $CD25^+FoxP3^+$ Treg cells out of $CD4^+$ T cells; **F.** $CD11b^+CD14^+HLA\text{-}DR^+$ myeloid cells; **G.** $CD3\text{-}CD19^-CD56^+$ NK cells. Daratumumab-treated vs. untreated prostate tumors and patient-matched pre-daratumumab and post-daratumumab bone marrow aspirates were assessed.



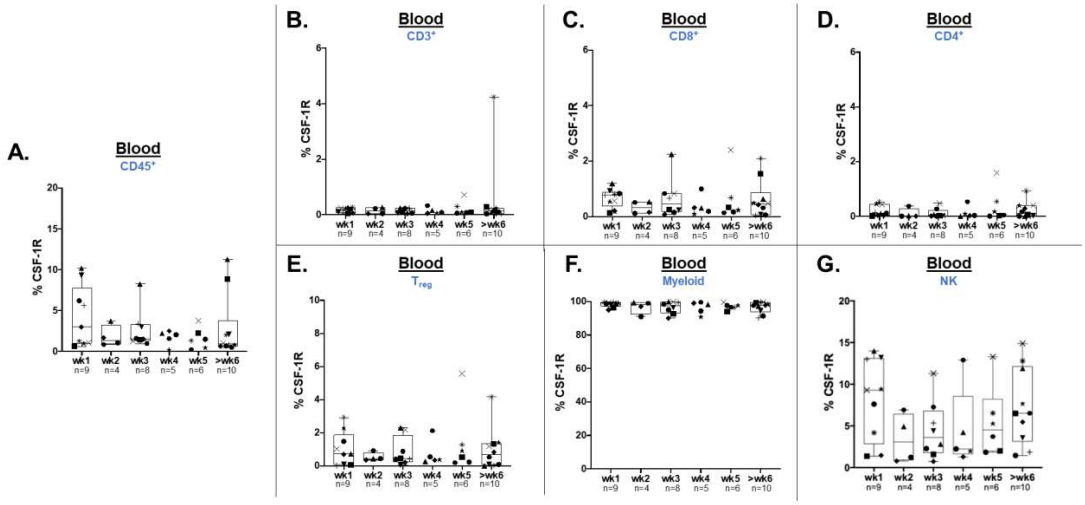
Supplementary Figure 6. Transcriptional analysis of daratumumab-treated versus untreated prostate tumors by NanoString. A. Scatter plots of immune cell phenotypes identified by transcriptional signatures and CD38 expression**. B.** Volcano plot of differentially expressed genes in daratumumab-treated vs. untreated prostate tumors. Dara=daratumumab.



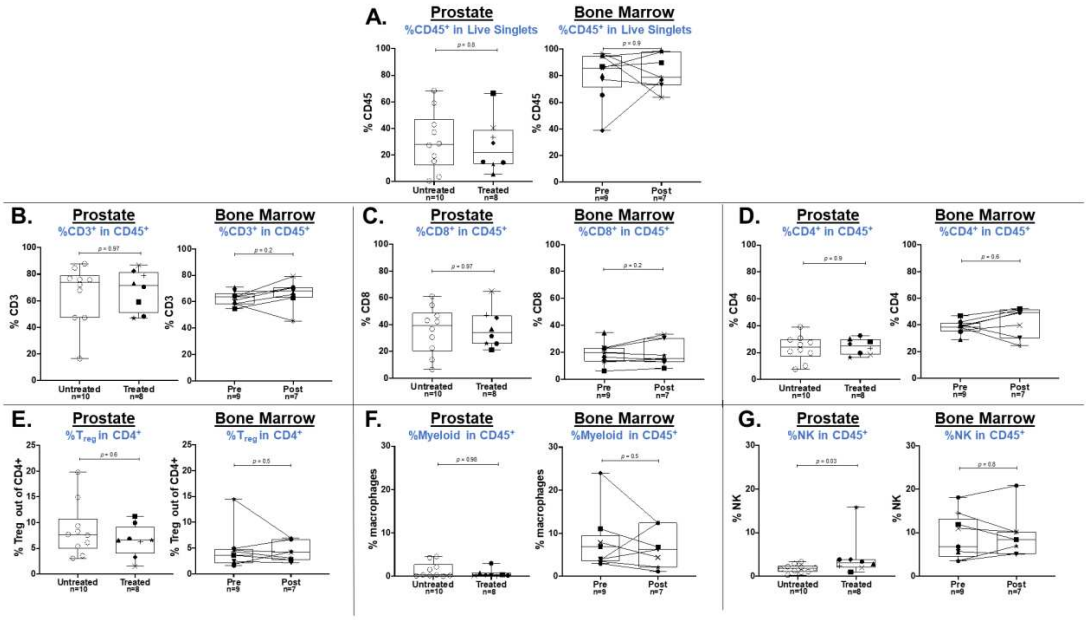
Supplementary Figure 7. Changes in total immune cell subsets with daratumumab in blood as assessed by flow cytometry. A. Flow cytometric analysis showing frequency of CD45 cells in live singlets. **B-F:** Flow cytometric analysis gated on $CD45^+$ live cells showing frequency of: **B.** $CD3^+$ T cells; **C.** $CD8^+$ T cells; **D.** $CD4^+$ T cells; **E.** $CD25^+FoxP3^+$ Treg cells out of $CD4^+$ T cells; **F.** $CD11b^+CD14^+HLA\text{-}DR^+$ myeloid cells; **G.** $CD3^-CD19^-CD56^+$ NK cells. Peripheral blood mononuclear cells (PBMCs) from daratumumab-treated patients were assessed at the timepoints indicated.



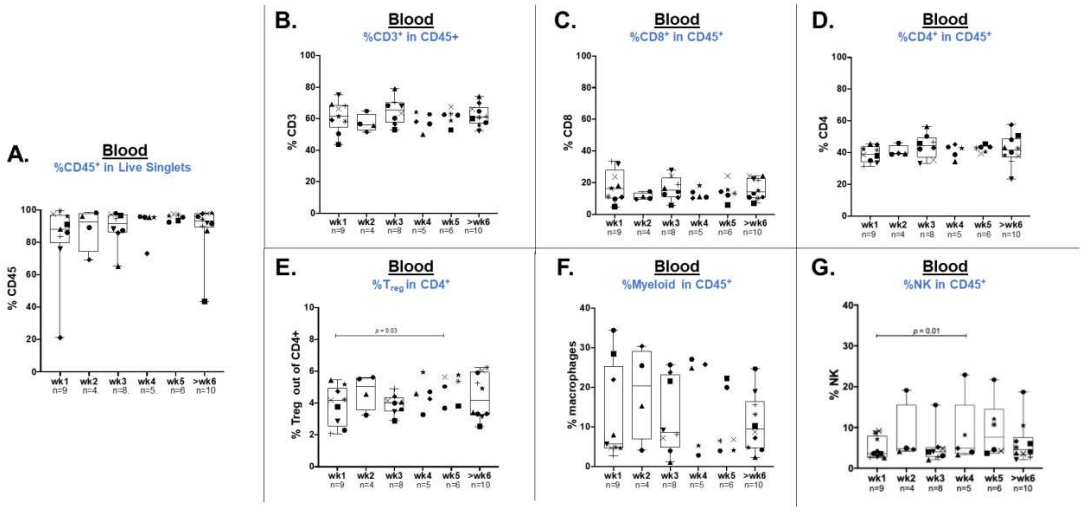
Supplementary Figure 8. Assessment of target modulation on non-myeloid populations with edicotinib by flow cytometry in evaluable prostate tumors and bone marrow as assessed by flow cytometry. Flow cytometric analysis gated on CD45+ live cells showing frequency of CSF-1R+ cells in: **A.** $CD3^+$ T cells; **B.** $CD8^+$ T cells; **C.** $CD4^+$ T cells; **D.** $CD4^+CD25^+FoxP3^+$ T_{reg} cells; **E.** $CD3^-CD19^-CD56^+$ NK cells.



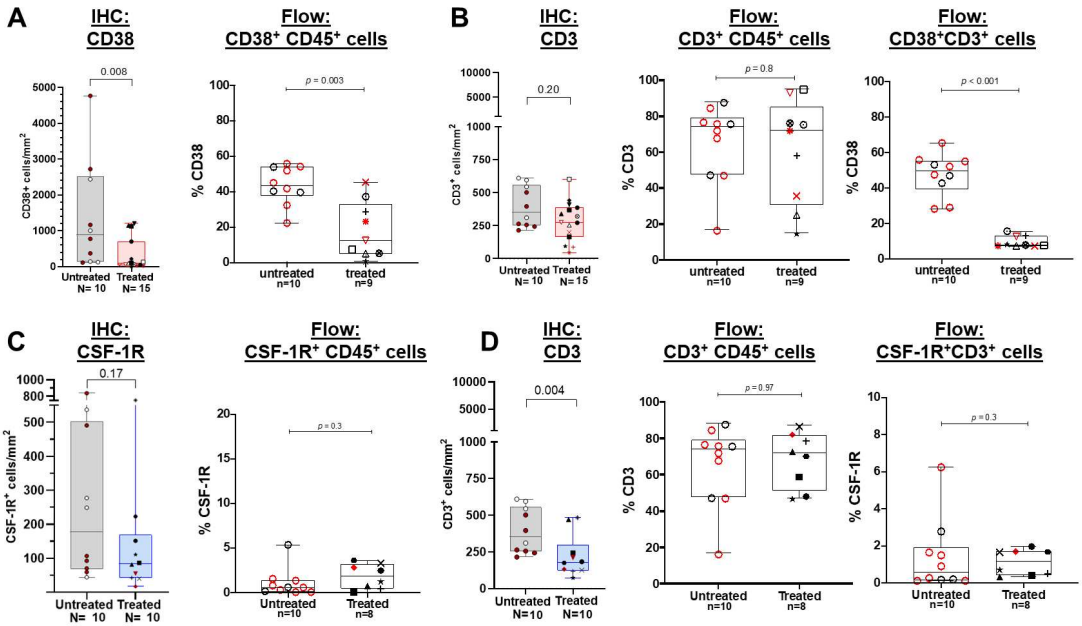
Supplementary Figure 9. Absence of target modulation by edicotinib in blood as assessed by flow cytometry. Flow cytometric analysis gated on $CD45^+$ live cells showing frequency of $CSF\text{-}1R^+$ cells in: **A.** $CD45^+$ immune cells; **B.** $CD3^+$ T cells; **C.** $CD8^+$ T cells; **D.** $CD4^+$ T cells; **E.** $CD4^+CD25^+FoxP3^+$ Treg cells; **F.** $CD11b^+CD14^+HLA\text{-}DR^+$ myeloid cells; **G.** $CD3^-CD19^-CD56^+$ NK cells. Peripheral blood mononuclear cells (PBMCs) from edicotinib-treated patients were assessed at the timepoints indicated.



Supplementary Figure 10. Changes in total immune cell subsets with edicotinib in prostate tumors and bone marrow as assessed by flow cytometry. A. Flow cytometric analysis showing frequency of CD45 cells in live singlets. **B-F:** Flow cytometric analysis gated on $CD45^+$ live cells showing frequency of: **B.** $CD3^+$ T cells; **C.** $CD8^+$ T cells; **D.** $CD4^+$ T cells; **E.** $CD25^+FoxP3^+$ Treg cells out of $CD4^+$ T cells; **F.** $CD11b^+CD14^+HLA\text{-}DR^+$ myeloid cells; **G.** $CD3^-CD19^-CD56^+$ NK cells. Edicotinib-treated vs. untreated prostate tumors and patient-matched pre-edicotinib and post-edicotinib bone marrow aspirates were assessed.



Supplementary Figure 11. Changes in total immune cell subsets with edicotinib in blood as assessed by flow cytometry. A. Flow cytometric analysis showing frequency of CD45 cells in live singlets. **B-F:** Flow cytometric analysis gated on $CD45^+$ live cells showing frequency of: **B.** $CD3^+$ T cells; **C.** $CD8^+$ T cells; **D.** $CD4^+$ T cells; **E.** $CD25^+FoxP3^+$ Treg cells out of $CD4^+$ T cells; **F.** $CD11b^+CD14^+HLA\text{-}DR^+$ myeloid cells; **G.** $CD3^-CD19^-CD56^+$ NK cells. Peripheral blood mononuclear cells (PBMCs) from edicotinib-treated patients were assessed at the timepoints indicated.



Supplementary Figure 12. No differences in immune infiltrates between Gleason 7 and Gleason 8-10 prostate tumors as assessed at time of prostatectomy by IHC and flow cytometry. **A**. $CD38^+$ cells in daratumumab-treated vs. untreated prostate tumors; **B**. $CD3^+$ T cells in daratumumab-treated vs. untreated prostate tumors; **C.** $CSF\text{-}1R^+$ cells in edicotinib-treated vs. untreated prostate tumors; **D**. $CD3^+$ T cells in edicotinib-treated vs. untreated prostate tumors. Red symbols indicate Gleason score 7 at prostatectomy.