

DATA SUPPLEMENT - APPENDIX

FIGURES AND TABLES

Data Supplement, Figure A1

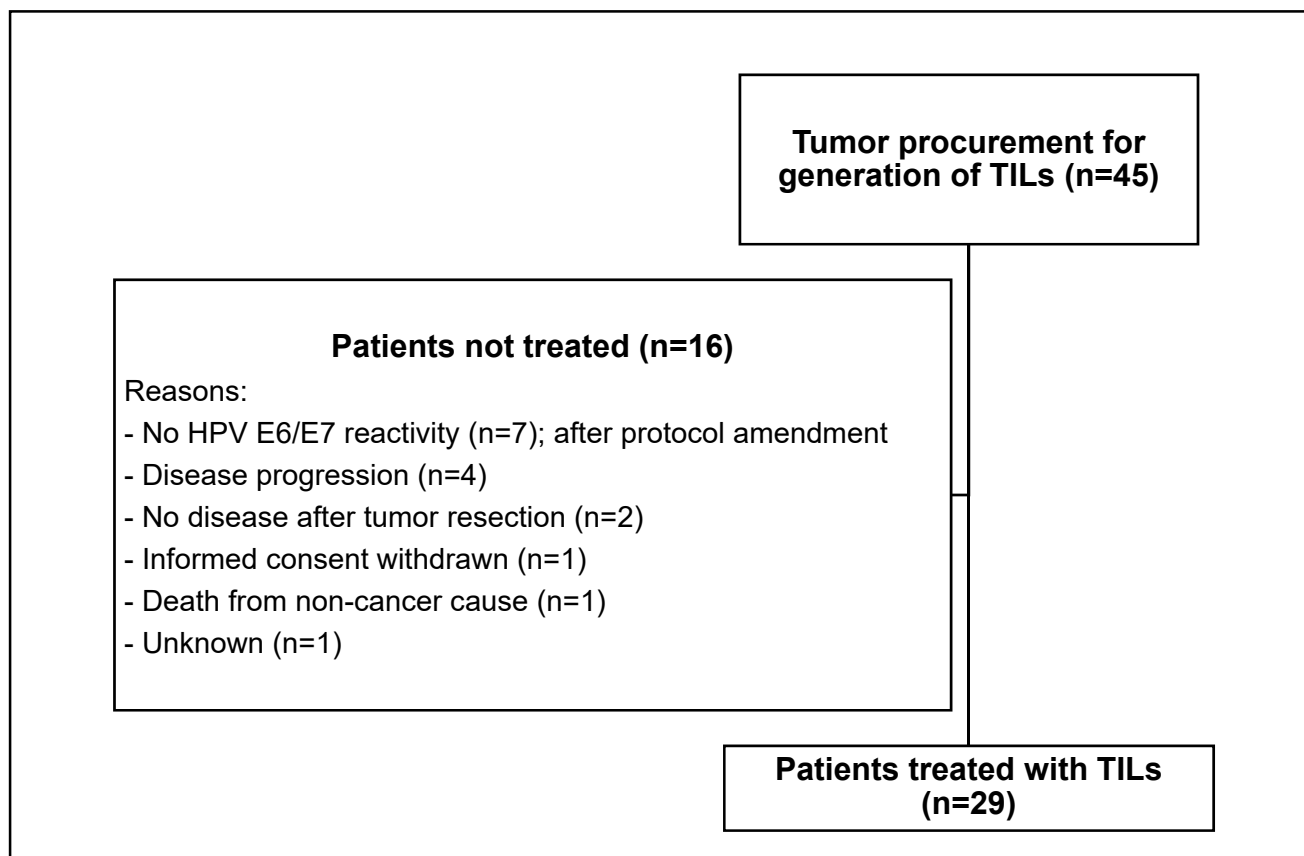


Fig A1. Trial diagram. Surgery for tumor procurement and generation of tumor-infiltrating lymphocytes (TILs) was performed for 45 patients. Sixteen patients were not treated for above indicated reasons. A total of 29 patients were treated with TILs.

Data Supplement, Figure A2

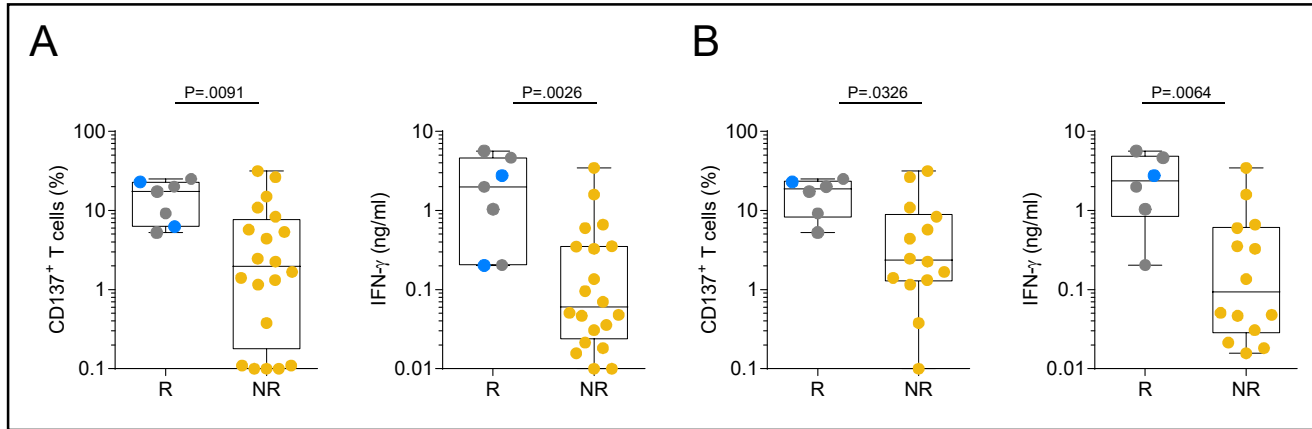


Fig A2. HPV-reactivity of administered TILs from responding and nonresponding patients. (A) Frequency of T cells upregulating CD137 (*Left*) and magnitude of interferon gamma (IFN- γ) release (*Right*) in infused TILs from responding (n=7) and nonresponding (n=20) patients. (B) Frequency of T cells upregulating CD137 (*Left*) and magnitude of IFN- γ release (*Right*) in infused TILs from responding (n=6) and nonresponding (n=14) patients who would have met the amended criteria for treatment in retrospective analysis based on HPV-reactivity in TIL subcultures. One patient who experienced a complete response is not shown in panel B as the TIL demonstrated HPV reactivity in fewer than three subcultures. R, responding patients (objective complete or partial response); NR, nonresponding patients (no objective tumor response). Color denotes type of tumor response (blue, complete response; grey, partial response; gold, no response). Box and whisker plots show median (line), first and third quartiles, and minimum and maximum values. The Mann-Whitney U test was used to test for correlations between the responding and nonresponding patients. Reported P values are two tailed and not adjusted for multiple comparisons. P values < .05 were considered statistically significant.

Data Supplement, Figure A3

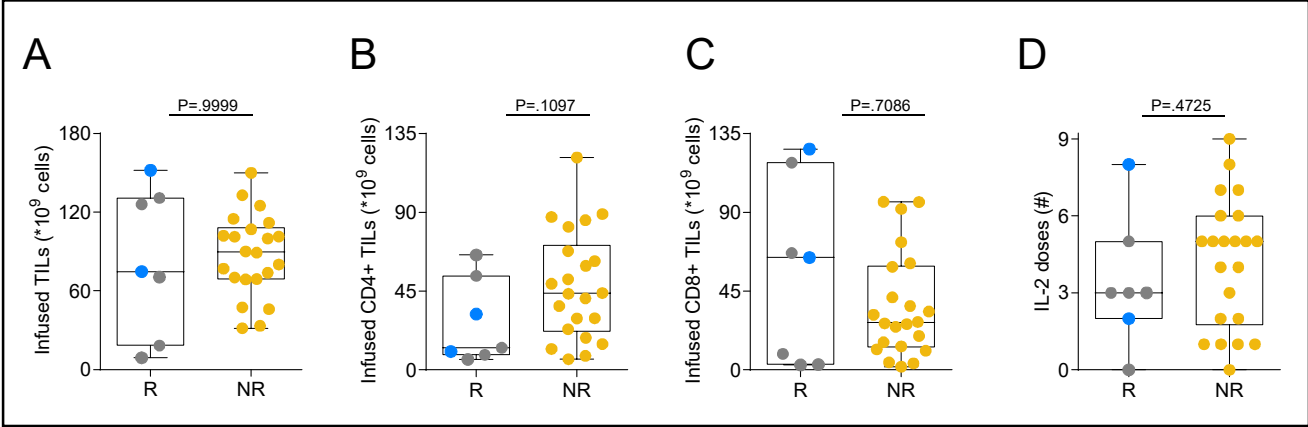


Fig A3. Characteristics of administered TILs in responding and nonresponding patients. (A) Number of CD3⁺ T cells infused. (B) Number of CD4⁺ T cells infused. (C) Number of CD8⁺ T cells infused. (D) Number of IL-2 doses administered. R, responding patients (objective complete or partial response; n=7); NR, nonresponding patients (no objective tumor response; n=22). Color denotes type of tumor response (blue, complete response; grey, partial response; gold, no response). Box and whisker plots show median (line), first and third quartiles, and minimum and maximum values. The Mann-Whitney U test was used to test for correlations between responding and nonresponding patients. Reported P values are two tailed and not adjusted for multiple comparisons. P values < .05 were considered statistically significant.

Data Supplement, Figure A4

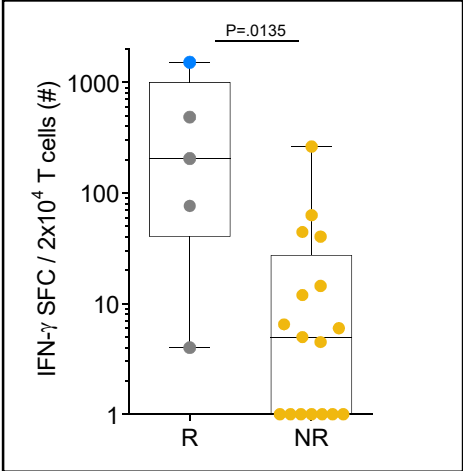


Fig A4. HPV-reactivity in peripheral blood T cells after treatment in responding versus nonresponding patients. Peripheral blood T cells one-month after treatment were assessed by IFN- γ enzyme-linked immunospot assay for reactivity against HPV-oncoproteins in 5 responding (R) and 17 nonresponding (NR) patients (Figure 2C). Color denotes type of tumor response (blue, complete response; grey, partial response; gold, no response). Box and whisker plots show median (line), first and third quartiles, and minimum and maximum values. The Mann-Whitney U test was used to test for correlations between the responding and nonresponding patients. Reported P values are two tailed and not adjusted for multiple comparisons. P values < .05 were considered statistically significant. SFC, spot-forming cells.

Data Supplement, Figure A5

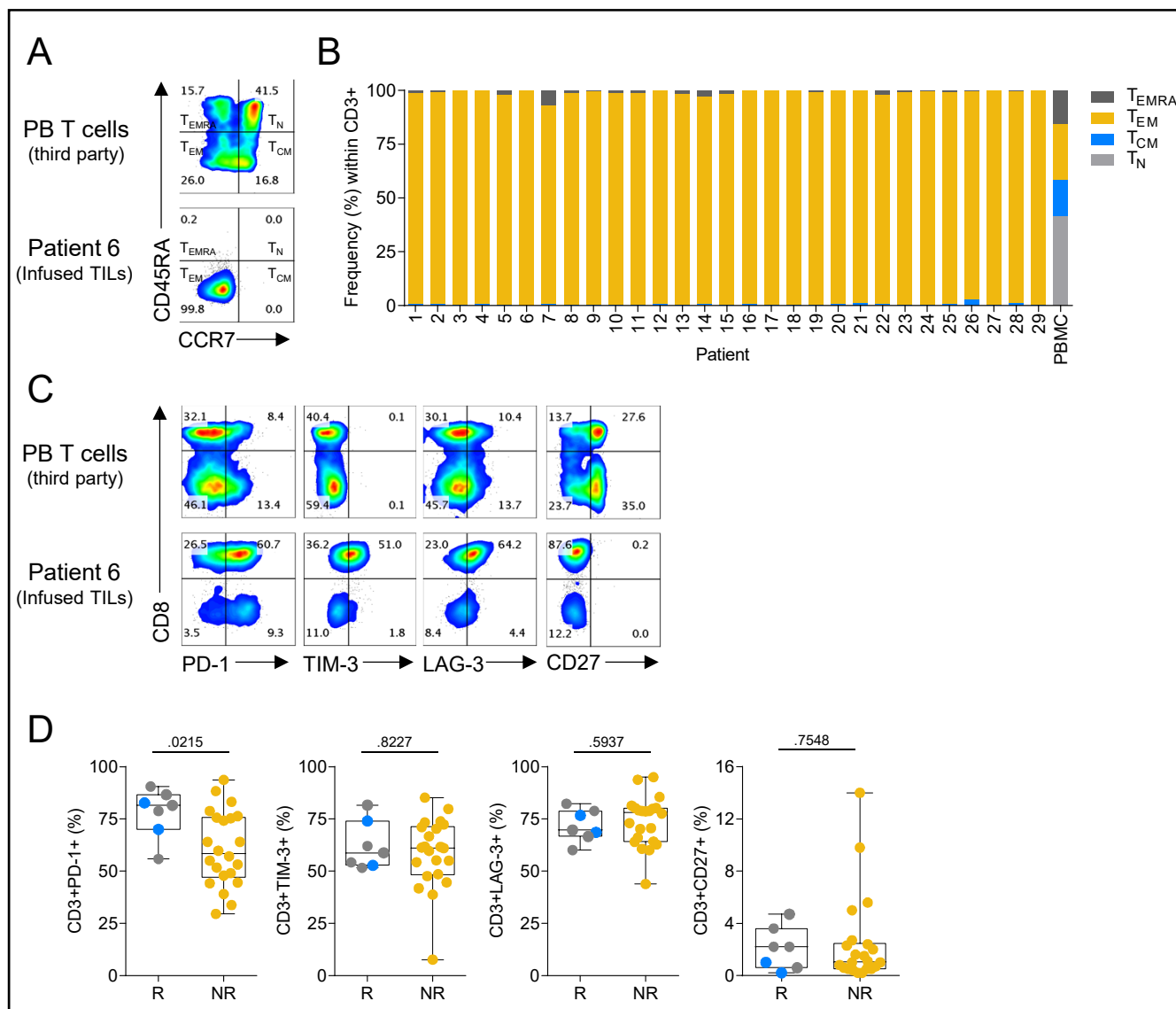


Fig A5. Phenotype of administered TILs in responding and nonresponding patients. (A) Example of flow cytometric staining for CD45RA and CCR7 on infused TILs from Patient 6 and third party peripheral blood T cells (PB T cells) defining naïve (T_N , $CD45RA^+CCR7^+$), central memory (T_{CM} , $CD45RA^+CCR7^+$), effector memory (T_{EM} , $CD45RA^+CCR7^-$) and terminally differentiated effector memory (T_{EMRA} , $CD45RA^+CCR7^-$) T cell subsets. Cells are pre-gated on live, $CD3^+$ T cells. (B) Frequency of T_N (grey), T_{CM} (blue), T_{EM} (gold) and T_{EMRA} (dark grey) T cell subsets in infused TILs as assessed in A. Third party PB T cells are shown as PBMC. (C) Example of flow cytometric staining for PD-1, TIM-3, LAG-3 and CD27 infused TILs from Patient 6 and third party peripheral blood T cells (PB T cells). Cells are pre-gated on live, $CD3^+$ T cells. (D) Frequency of PD-1⁺, TIM-3⁺, LAG-3⁺ or CD27⁺ within $CD3^+$ T cells is shown. R, responding patients (objective complete or partial response; n=7); NR, nonresponding patients (no objective tumor response; n=22). Color denotes type of tumor response (blue, complete response; grey, partial response; gold, no response). Box and whisker plots show median (line), first and third quartiles, and minimum and maximum values. The Mann-Whitney U test was used to test for correlations between responding and nonresponding patients. Reported P values are two tailed and not adjusted for multiple comparisons.

Data Supplement, Figure A6

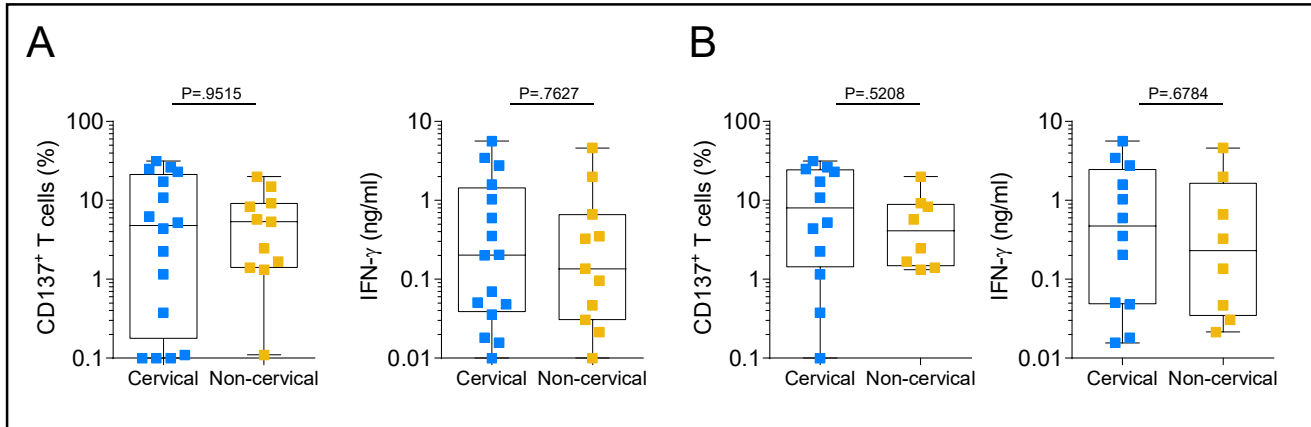


Fig A5. HPV-reactivity of infused TILs in the cervical versus non-cervical cancer cohort. (A) Frequency of T cells upregulating CD137 (*Left*) and magnitude of interferon gamma (IFN-gamma) release (*Right*) in infused TILs from evaluable patients (n=27) from the cervical cancer cohort (n=16) and the non-cervical cancer cohort (n=11). (B) Frequency of T cells upregulating CD137 (*Left*) and magnitude of IFN-gamma release (*Right*) in infused TILs from 20 patients (n=12 from the cervical cancer cohort and n=8 from the non-cervical cancer cohort) who, in retrospective analysis, would have met the amended criteria for treatment based on HPV-reactivity in TIL subcultures. Color denotes cohort (blue, cervical cancer cohort; gold, non-cervical cancer cohort). Box and whisker plots show median (line), first and third quartiles, and minimum and maximum values. The Mann-Whitney U test was used to test for correlations between the two cohorts. Reported P values are two tailed and not adjusted for multiple comparisons. P values < .05 were considered statistically significant.

Data Supplement, Figure A7

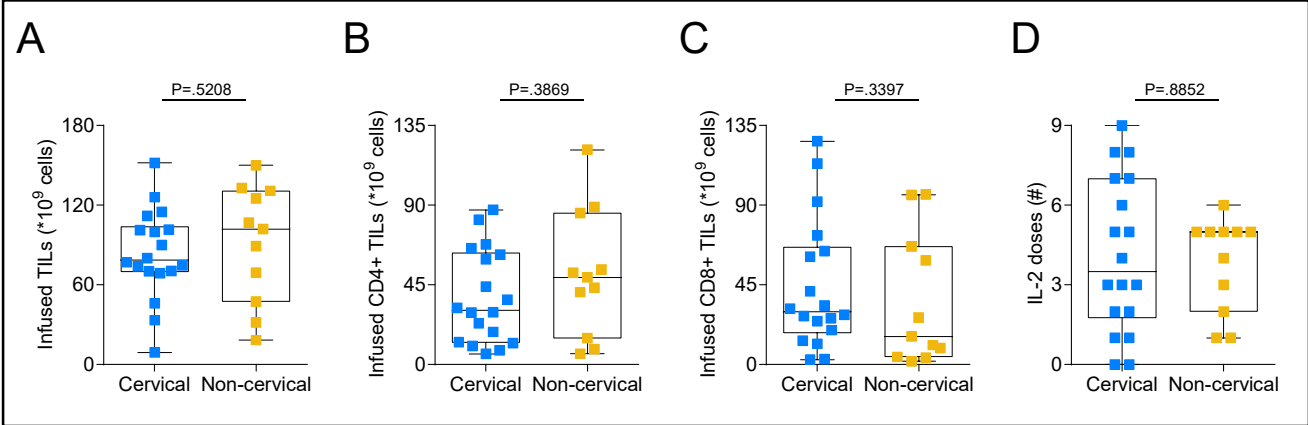


Fig A6. Characteristics of administered TILs in the cervical versus non-cervical cancer cohort. (A) Number of CD3⁺ T cells infused. (B) Number of CD4⁺ T cells infused. (C) Number of CD8⁺ T cells infused. (D) Number of IL-2 doses administered. Color denotes cohort (blue, cervical cancer cohort (n=18); gold, non-cervical cancer cohort (n=11)). Box and whisker plots show median (line), first and third quartiles, and minimum and maximum values. The Mann-Whitney U test was used to test for correlations between the two cohorts. Reported P values are two tailed and not adjusted for multiple comparisons. P values < .05 were considered statistically significant.