**Supplementary Figure S1.** Flow diagram for patient selection.

**Supplementary Figure S2.** Changes in PD-L1 expression in both tumor and tumor-infiltrating immune cells as well as ICI efficacy with regard to PD-L1 expression. (**A** and **B**) Changes in PD-L1 expression status of tumor cells between before (pre) and after (post) EGFR-TKI treatment for patients classified according to smoking status (A) or type of *EGFR* activating mutation at baseline (B). PD-L1 expression in tumor cells is classified as ≥50%, 1% to 49%, or <1%. (**C**) Changes in PD-L1 expression status of tumor-infiltrating immune cells between before (pre) and after (post) EGFR-TKI treatment. PD-L1 expression in immune cells is classified as ≥10%, 5%≤ and <10%, 1%≤ and <5%, or <1%. The *P* value for the changes in the proportions of patients with different PD-L1 expression levels was determined with Bowker’s test of symmetry. (**D**) Kaplan-Meier curves of PFS for patients treated with antibodies to PD-1 after disease progression during EGFR-TKI treatment. PFS is plotted according to PD-L1 expression level with a cutoff of 50% in tumor samples obtained before EGFR-TKI treatment. Tick marks represent censored data. CI, confidence interval; NR, not reached.

**Supplementary Figure S3.** ICI efficacy with regard to PD-L1 expression and T790M status. (**A** and **B**) Kaplan-Meier curves of OS for patients treated with antibodies to PD-1 after disease progression during EGFR-TKI treatment according to PD-L1 expression level with a cutoff of 50% in tumor samples obtained after (A) or before (B) EGFR-TKI treatment. (**C** and **D**) PFS (C) and OS (D) stratified on the basis of both T790M status and PD-L1 expression in post–EGFR-TKI treatment samples. Tick marks represent censored data. CI, confidence interval; NR, not reached.

**Supplementary Figure S4.** ICI efficacy with regard to PD-L1 expression status in both tumor and tumor-infiltrating immune cells. Kaplan-Meier curves of PFS for patients treated with antibodies to PD-1 after disease progression during EGFR-TKI treatment. PFS is plotted according to PD-L1 expression level in immune cells (IC) classified as ≥10%, 1%≤ and <5%, or <1% in tumor samples obtained after EGFR-TKI treatment (A), or according to PD-L1 expression level in tumor cells (TC) and immune cells (IC) with a cutoff of 1% in tumor samples obtained after EGFR-TKI treatment (B). Tick marks represent censored data. CI, confidence interval; NR, not reached.

**Supplementary Figure S5.** ICI efficacy with regard to type of *EGFR* activating mutation. Kaplan-Meier curves of PFS (A) and OS (B) are plotted according to type of *EGFR* activating mutation for patients treated with antibodies to PD-1 after disease progression during EGFR-TKI treatment. Tick marks represent censored data. CI, confidence interval; NR, not reached.

**Supplementary Figure S6.** Association between FOXP3 and CD73 expression in TILs. CD73+ TIL density in post–EGFR-TKI treatment samples according to FOXP3+ TIL density with a cutoff of median FOXP3+ TIL density from all study patients (150.4 /mm2). Each box plot shows the full range of variation, the median, and the interquartile range (top and bottom borders of the box). The *P* value was determined with the Mann-Whitney U test.