



**Supplementary Figure 1.** Plot of DMFS and OS for all patients according to the densities of CD45RO+ cells (A, B), CD8+ cells (C, D), and CD3+ cells (E, F) in combined tumor regions (CT and IM) ( $n = 288$ ). For each marker, high densities in the CT and IM (HiHi, red curve), low densities in the CT and IM (LoLo, blue curve), and heterogeneous densities with CT<sup>Lo</sup> and IM<sup>Hi</sup> or CT<sup>Hi</sup> plus IM<sup>Lo</sup> (Het, green curve) are presented, respectively.

CT, center of the tumor; DMFS, distant metastasis-free survival; IM, invasive margin; OS, overall survival.

**Supplementary Table 1. Previous studies on the association of TILs with clinical outcome and establishment of IS in NSCLC**

| Study               | Patients                 | T-cell subtype | Compartment                           | Localization<br>(CT vs IM)           | Main findings  |
|---------------------|--------------------------|----------------|---------------------------------------|--------------------------------------|--|
| Schalper et al.[19] | 552 pts<br>Stage I-IV    | CD3, CD8, CD20 | Intraepithelial,<br>stromal and total | No                                   | CD8+ TILs have independent positive PI.  |
| Donnem et al.[21]   | 797 pts<br>Stage I-III A | CD8            | Stromal                               | Yes, only in one<br>cohort (178 pts) | Stromal CD8+ T cells have independent positive PI and were<br>candidate for TNM-Immunoscore.   |
| Paulsen et al.[22]  | 536 pts<br>Stage I-III A | CD45RO, CD8    | Intraepithelial,<br>stromal           | No                                   | In SCC group, intraepithelial CD45RO+ TILs have independent<br>positive PI and combining the intraepithelial CD45RO score<br>with stromal CD8 score, the PI increased. |
| Ishii et al.[32]    | 36 pts<br>Stage II-III   | CD3, CD8       | No                                    | Yes                                  | IS (CD3+ and CD8+ TILs in CT and IM) have positive PI.   |

TILs, tumor infiltrating lymphocytes; IS, immunoscore; CT, center of the tumor; IM, invasive margin; PI, prognostic impact; SCC, squamous cell carcinoma.