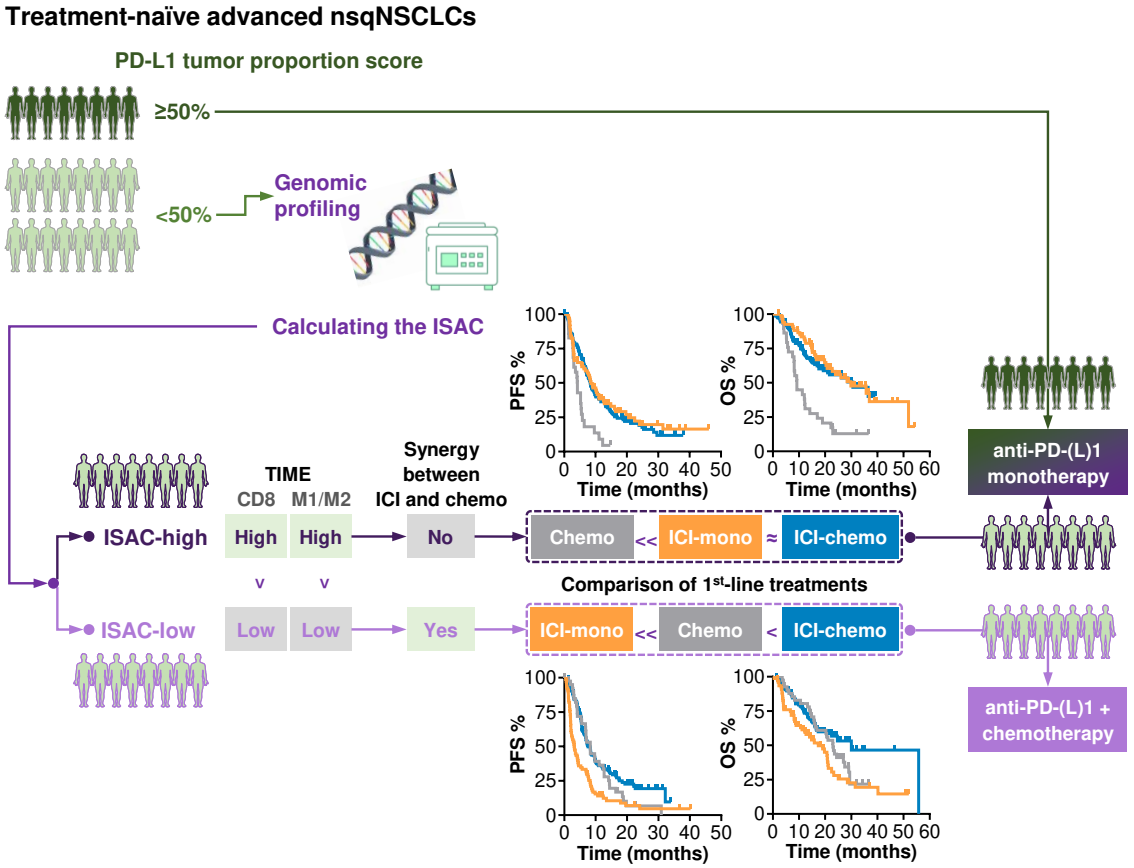
Mutation-guided chemotherapy-free strategy in first-line immunotherapy for low PD-L1-expressing non-squamous NSCLC



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In brief

- In non-squamous non-small cell lung cancer (nsqNSCLC) with programmed death-ligand 1 (PD-L1) expression on less than 50% of tumor cells, we leveraged clinical and mutational data of multiple cohorts to develop the interaction score for additional chemotherapy (ISAC) to predict the survival benefit from the addition of platinum-doublet chemotherapy to anti-PD-(L)1 in first-line treatment.
- A high ISAC was identified as a significant predictor for virtually no added value of chemotherapy to anti-PD-(L)1 and adaptive immune resistance reflected by more pro-inflammatory rather than anti-inflammatory tumor-infiltrating immune cells and high expression of immune checkpoints except PD-L1 (e.g., PD-1).
- In addition to the PD-L1≥50% nsqNSCLC where anti-PD-(L)1 monotherapy was approved and recommended as first-line therapy, the ISAC can further distinguish nearly half of PD-L1<50% nsqNSCLCs to be exempted from chemotherapy in the first-line setting, thereby reducing undue toxicity and improving quality of life.