The Tempus Immune Profile Score (IPS) is a multimodal biomarker that can be used as a prognostic indicator for adult patients with advanced pan-solid tumor disease who are already considered candidates for immune checkpoint inhibitor (ICI) based therapy. The IPS test is offered as a laboratory-developed test.

The test uses DNA and RNA sequencing data from the Tempus xT and xR tests to calculate an **IPS**, which ranges from 0 to 100, and classifies patients as either **IPS-Low** (scores 0-44) or **IPS-High** (scores 48-100). Scores between 45-47 are classified as Indeterminate.

The IPS test was developed utilizing a machine learning framework and records from 1,707 patients from the Tempus real-world database. The model includes tumor mutational burden (TMB), 8 single-gene RNA features*, and 3 RNA signatures*.

STUDY DESIGN

Clinical validation of the Tempus IPS test in Chicago, Illinois and Durham, North Carolina was performed in Tempus' CLIA-certified, CAP-accredited labs. The clinical validation cohort was evaluated in a prospective-retrospective analysis involving metastatic and/or stage IV pan-solid tumor adult patients from Tempus' real-world database. The evaluated patient population included 1,600 individuals in cancer types with ICI approvals, who were treated with ICI-containing regimens in the first line (1L) or second line (2L) of treatment. Appendix Tables 1-3 provide the full inclusion and exclusion criteria.

The primary objective of the study was to demonstrate that patients classified as IPS-High had a higher real world overall survival (rwOS) compared to those with an IPS-Low result.

RESULTS

To determine the prognostic utility of IPS pan-cancer, the study used a multivariate CoxPH model fit on IPS, controlling for treatment group, and stratified by line of therapy. rwOS was significantly higher in IPS-High patients in the study compared to IPS-Low patients in the study (HR = 0.45 [0.40, 0.52]; p< 0.01).

IPS also demonstrated prognostic utility independent of TMB, PD-L1 IHC, and MSI status. IPS-High patients had longer OS than IPS-Low patients with HR≤0.50 in subgroups of patients that were TMB-high, TMB-low, PDL1-positive, PDL1-negative, and MSS (Figure 1). IPS remained significant for OS in separate multivariable models controlling for TMB, MSI, and PD-L1, with HRs of 0.49 ([0.42-0.56] ; p<0.001), 0.47 ([0.41-0.53] ; p<0.001), and 0.45 ([0.38-0.53] ; p<0.001), respectively.

Additional subgroup analyses showed that IPS-High vs. IPS-Low hazard ratios were consistently <1 across demographics, clinically relevant subgroups, and important confounders (Figure 1).

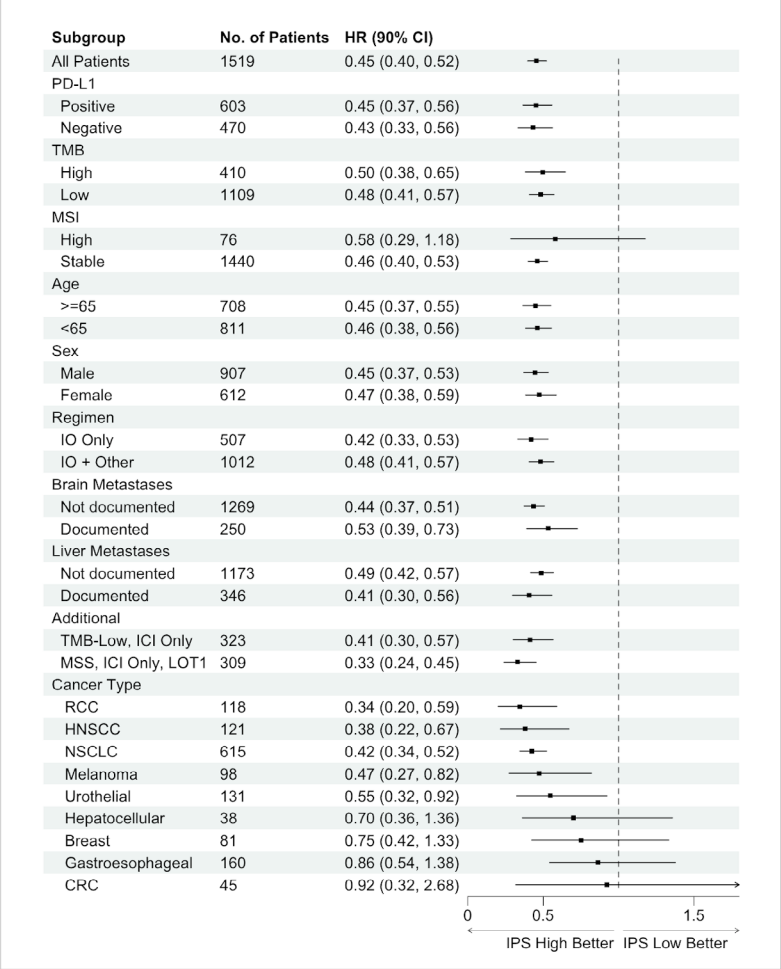

Figure 1: Forest plot showing IPS-High vs. IPS-Low hazard ratios and confidence intervals across demographics, clinically relevant subgroups, and important confounders.

*RNA-based features: CD274, SPP1, CXCL9, CD74, CD40, CD276, IDO1, PDCD1LG2, a 43-gene gMDSC signature, an 768-gene Tempus immune resistance signature developed from scRNAseq data, and a 105-gene Tempus literature-based meta-analysis signature

Appendix

INCLUDED CANCER TYPES

breast carcinoma
cervical carcinoma
cholangiocarcinoma
colorectal adenocarcinoma
endometrial serous carcinoma
endometrioid carcinoma
gastroesophageal adenocarcinoma
gastroesophageal squamous cell carcinoma
head and neck squamous cell carcinoma
hepatocellular carcinoma
lung adenocarcinoma
lung squamous cell carcinoma
melanoma
non small cell lung cancer
renal clear cell carcinoma
skin squamous and basal cell carcinoma
small cell lung carcinoma
urothelial carcinoma
urothelial neuroendocrine carcinoma

INCLUSION CRITERIA

- **Age ≥18 at metastatic dx**
- **De novo Stage IV or metastatic at sample collection**
- **IO treatment in 1L or 2L**

IO in 1L:	IO in 2L:
Metastatic dx < 7/1/2023	2L initiation < 1/1/2024
Sample date ≤ 90d of 1L initiation, and ≤ 240d for HNSCC , RCC and Cervical	If 1L initiation date < sample date < 2L initiation date: 2L initiation ≤ 90d of sample date
Metastatic dx ≤ 90d of 1L initiation, and ≤ 240d for HNSCC, RCC and Cervical	If sample date < 1L initiation date: 2L initiation ≤ 545d of sample date for all cancers

- **IO start ≤ 60d of line of treatment start, and ≤ 180d for maintenance therapy indications (Urothelial cancers)**

EXCLUSION CRITERIA

- **Prior IO treatment**
- **Unknown TMB**
- **ECOG score ≥ 3**
- **Tumor purity < 30%**
- **Samples collected from lymph node**
- **Received an investigational new drug**
- **Delayed entry >1 year from IO initiation**
- **Primary dx > 60d of metastatic dx**
- **Samples collected by 'bone marrow core biopsy', 'venipuncture', 'fine needle aspirate', 'fluid aspirate'**