Poster # 773

Evaluating clinical features and prognostic factors associated with response to immune checkpoint blockade in metastatic NSCLC

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BACKGROUND

In the past decade, immune checkpoint blockade (ICB) has become standard of care for patients with metastatic non- small cell lung cancer (mNSCLC). Biomarkers of response, such as PD-L1 status, help identify suitable candidates for ICB. However, differences in the underlying clinical features of patients and the association of such features with ICB outcomes have not received significant attention. We sought to evaluate clinical features in the de-identified health records of patients with mNSCLC and determine their prognostic value.

METHODS

Real world cohort design

De-identified health records of patients with mNSCLC and non-squamous histology who received first-line FDA-approved treatment for mNSCLC were included in this study. The clinical endpoint of this study, time to progression (TTP), was calculated as the time from initiation of treatment to the first recorded progression event, censored on last-known date or death date.

Survival-SVM algorithm

A survival-SVM algorithm from the scikit-survival package (Polsterl et al, 2016) was applied to model progression risk based on TTP. This model treats survival analysis as a ranking problem, and assigns lower ranks to patients with a shorter TTP. The output of the final trained model is a risk score, which is positively correlated with progression risk.

Prognostic score model development

The Tempus mNSCLC development cohort (n=1426) was used for model development, with 70% (n = 988) of the cohort assigned for model training and 30% (n = 438) for testing. Clinically relevant features such as age, sex, comorbidity information, smoking status, and self-reported race/ethnicity were considered as potential prognostic factors. Features retained after filtering for high correlation and low frequency were used to train the final model with the tuned hyperparameter alpha=0.025. Following model training, the resulting feature weights of the model and the predictions of the model in the test set and validation cohorts were evaluated.

Prognostic score model evaluation

The perfomance of the prognostic score was evaluated in two independent cohorts: ASCO CancerLinQ cohort of 3217 mNSCLC records treated with first-line therapy and a Tempus cohort of 512 mNSCLC records treated with ICB at any line. The top 15th percentile was defined as high risk for progression. Additionally, the utility of the prognostic score in supporting known biomakers of ICB response was assessed in the Tempus mNSCLC ICB cohort by comparing high risk groups defined by PD-L1 positive (TPS >1%) IHC status alone and in combination with the prognostic score.

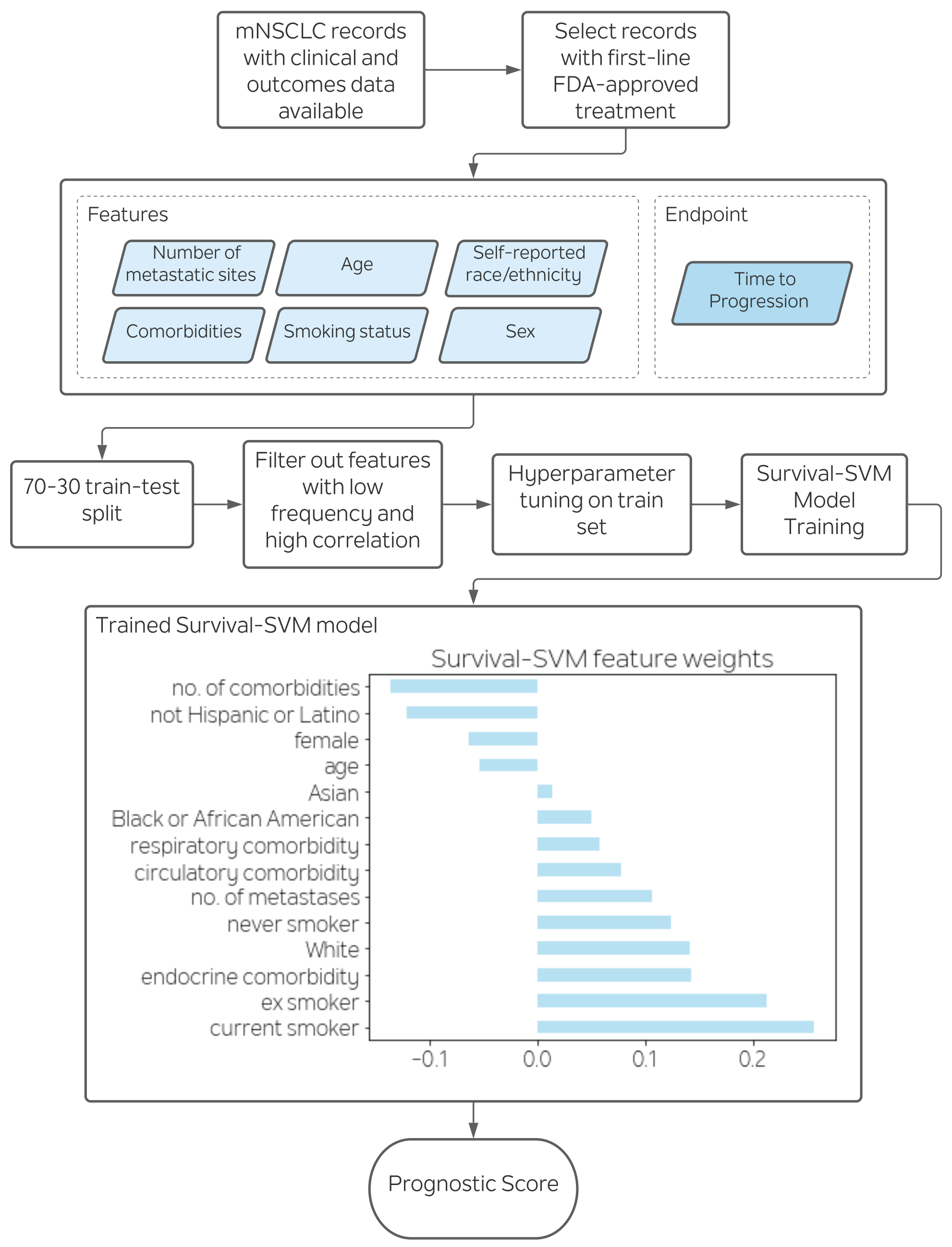
RESULTS

Table 1: Cohort Characteristics

		Tempus mNSCLC development (n = 1426)	ASCO CancerLinQ (n = 3217)	Tempus mNSCLC ICB (n = 512)
Age group	*>= 40*	26 (1.8%)	52 (1.6%)	6 (1.2%)
	41-60	403 (28.3%)	961 (29.9%)	141 (27.5%)
	61-80	877 (61.5%)	1927 (59.9%)	330 (64.5%)
	>= 81	120 (8.4%)	277 (8.6%)	35 (6.8%)
Gender	*Female*	739 (51.8%)	1522 (47.3%)	266 (52.0%)
	Male	687 (48.2%)	1695 (52.7%)	246 (48.0%)
Line of therapy	*1*	1426 (100.0%)	3217 (100.0%)	258 (50.4%)
	2+			254 (49.6%)
Treatment	*Immunotherapy*	137 (9.6%)	275 (8.5%)	512 (100.0%)
	Antineoplastic agents	350 (24.5%)	728 (22.6%)	
	Platinum	540 (37.9%)	1721 (53.5%)	
	Targeted therapy	399 (28.0%)	493 (15.3%)	

Table 1: The prognostic score model was developed using a de-identified Tempus mNSCLC dataset with first-line treatments and validated in two independent mNSCLC cohorts: ASCO CancerLinQ records with first-line treatments and Tempus records with ICB treatment at any line.

Figure 1: Model training results


mNSCLC records with clinical and outcomes data available

Select records with first-line FDA-approved treatment

Features

Number of metastatic sites

Age

Self-reported race/ethnicity

Comorbidities

Smoking status

Sex

Endpoint

Time to Progression

70-30 train-test split

Filter out features with low frequency and high correlation

Hyperparameter tuning on train set

Survival-SVM Model Training

Trained Survival-SVM model

Prognostic Score

Figure 1: The output of the survival-SVM model is a prognostic risk score. The weights for features contributing to the prognostic score were positively correlated with progression risk. Positive correlation of expected factors such as number of metastases, presence of respiratory and circulatory comorbidities, or male sex with progression risk was observed.

Figure 2: The prognostic score is an effective combination of clinical features

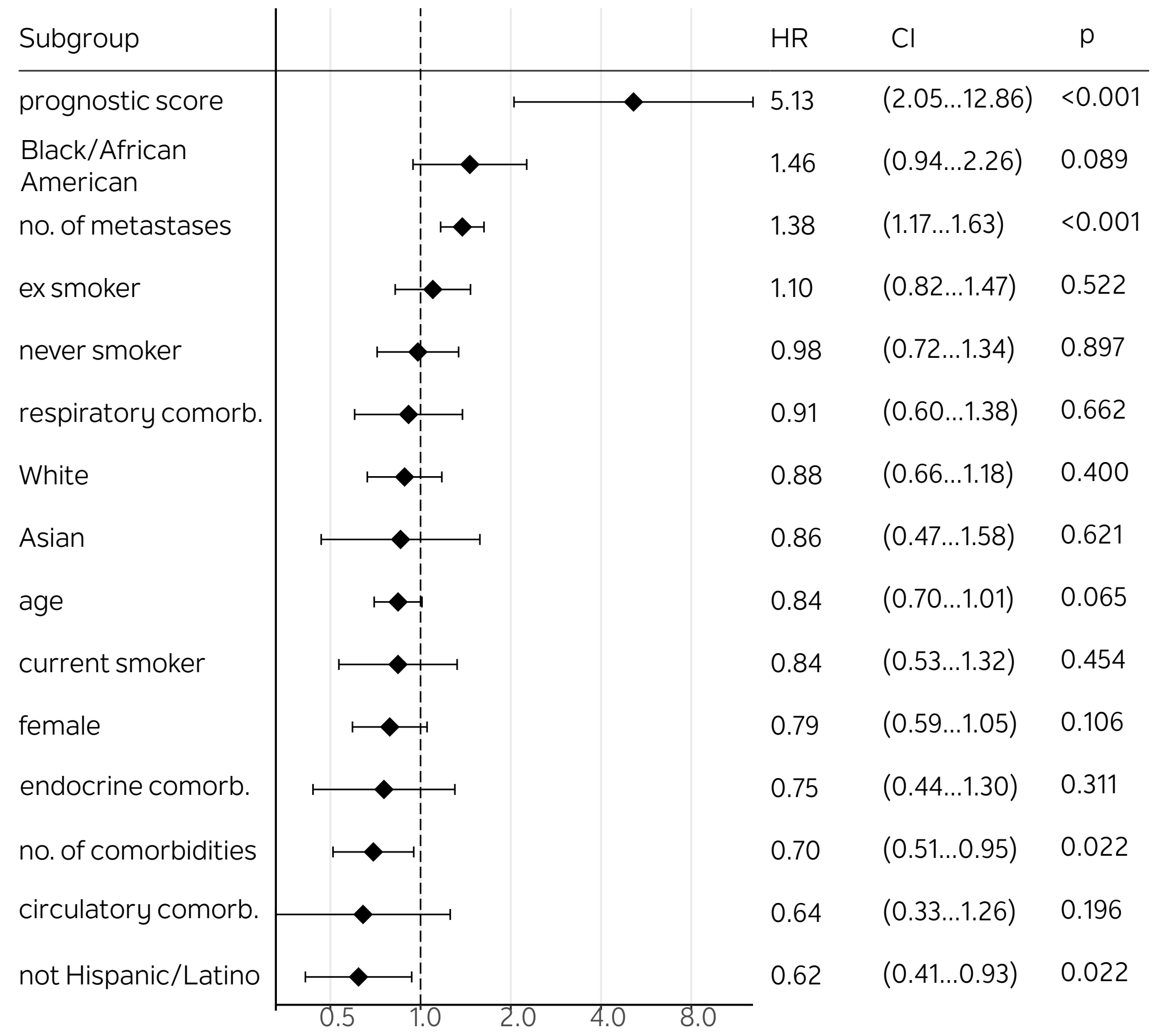
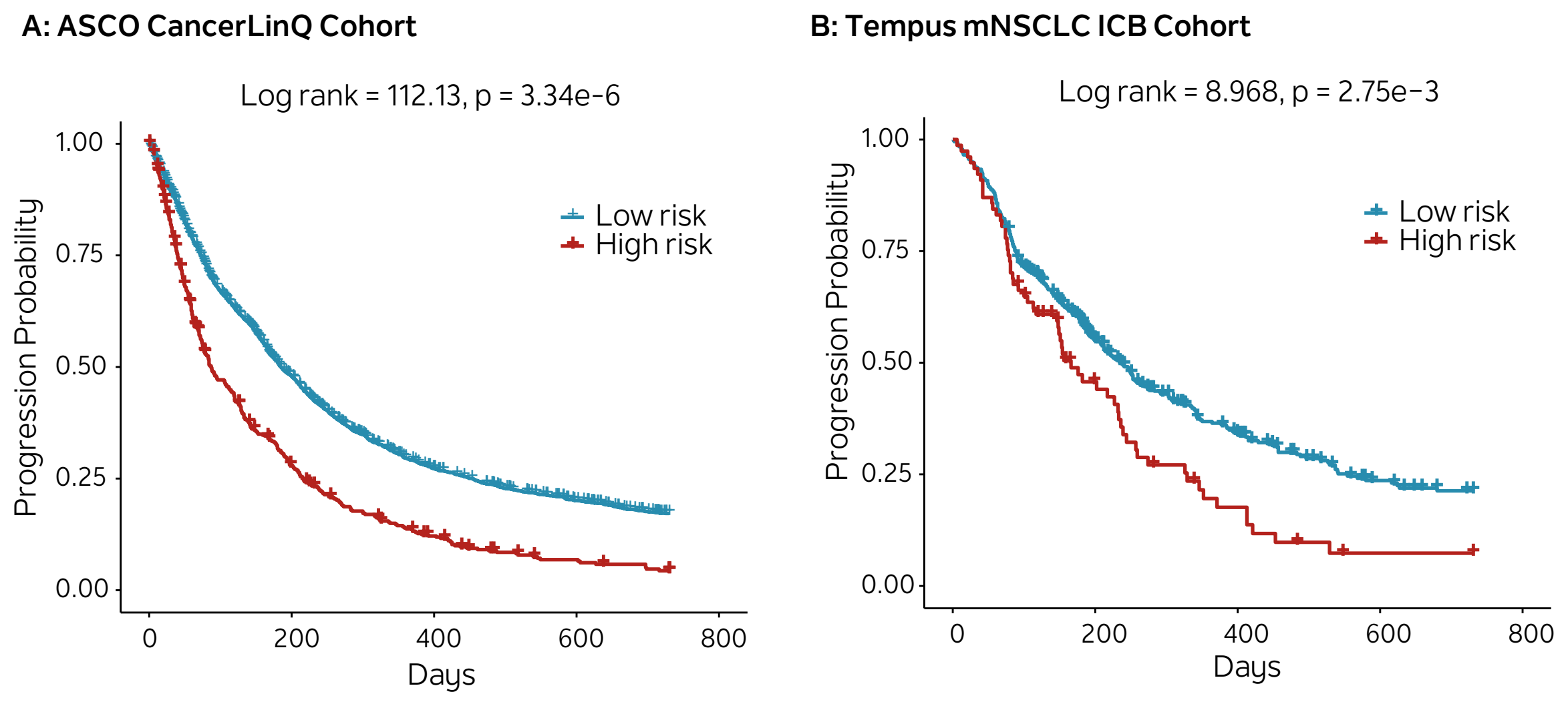


Figure 2.Forest plot for the test set (n = 438) showing hazard ratios and 95% CIs from univariate cox regression of prognostic scores and clinical features used as model inputs against TTP. The combined use of all clinical features produced a more accurate prognostic score for predicting TTP compared to individual clinical features.

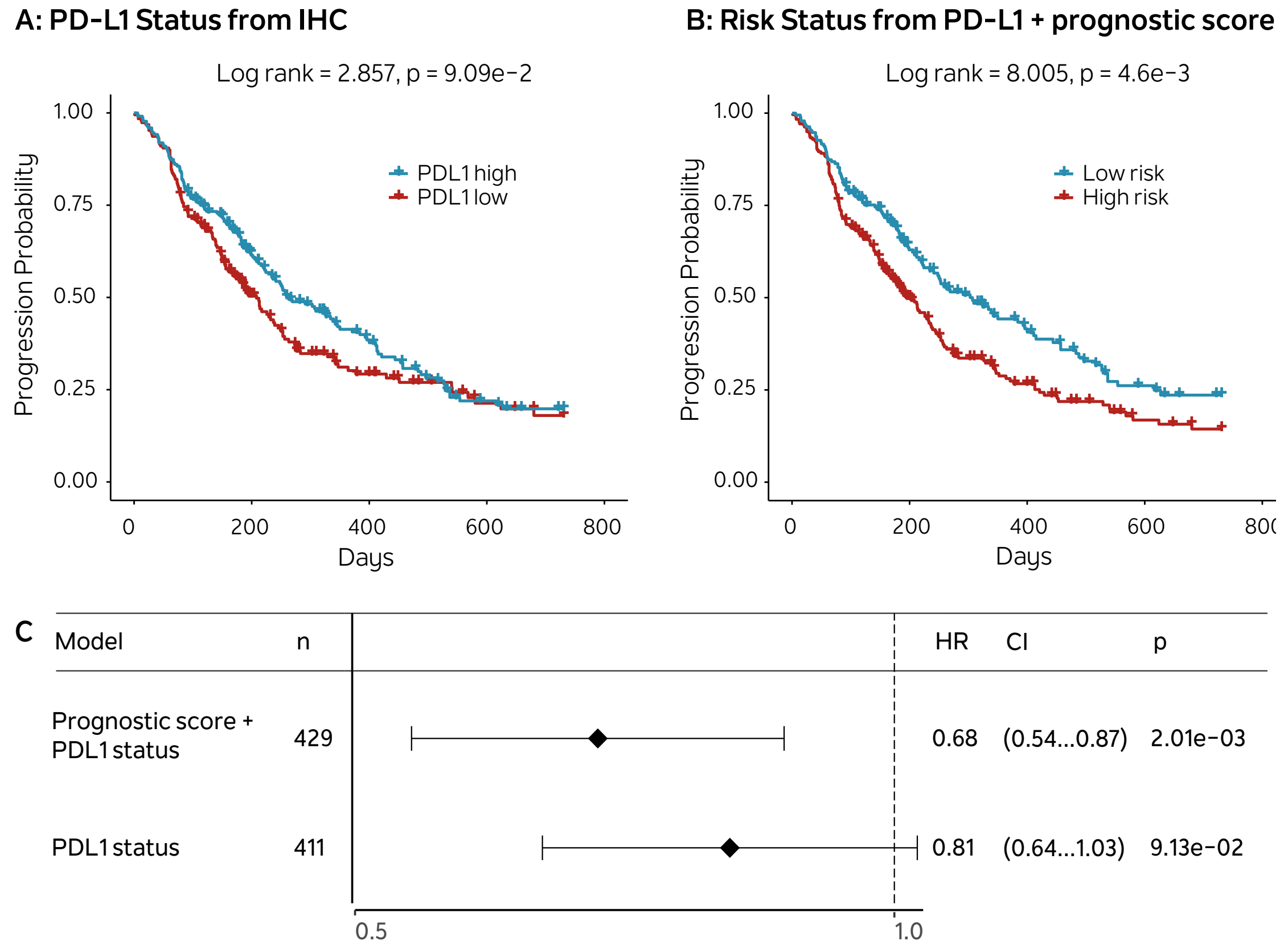
Figure 3: The prognostic score identifies high-risk groups in independent validation cohorts


A: ASCO CancerLinQ Cohort

B: Tempus mNSCLC ICB Cohort

Figure 3: The prognostic score stratifies high risk and low risk patients in the (A) ASCO CancerLinQ (n=3217) and (B) Tempus mNSCLC ICB (n =512) cohorts. Kaplan-Meier (KM) plots were generated using TTP as an endpoint and the log-rank statistic was calculated to assess the difference in TTP between high risk and low risk groups. Significant stratification (log-rank p-value < 0.05) between high risk and low risk groups was observed for both cohorts.

Figure 4: Integration of prognostic score with PD-L1 IHC status improves ICB response prediction


A: PD-L1 Status from IHC

B: Risk Status from PD-L1 + prognostic score

Figure 4: In the Tempus mNSCLC ICB cohort, high risk cases were determined by combining risk status from the prognostic scores and PD-L1 IHC status. The figure depicts KM plots for (A) positive PD-L1 IHC status and (B) risk status from the prognostic score and PD-L1 positive IHC status, and (C) a forest plot showing HRs and 95% CIs for both outputs. Overall, the prognostic score improved prediction of risk compared to PD-L1 IHC status. alone.

CONCLUSIONS

- These results highlight the utility of clinical and prognostic factors for identifying high risk groups in mNSCLC.
- The survival-SVM algorithm enables accomodation of statistical complexity in the context of survival analysis and was succesfully applied to aggregate clinical and prognostic factors.
- The resulting prognostic score can augment established biomarkers and improve prediction of response to immune checkpoint blockade in mNSCLC.

ACKNOWLEDGMENTS

Thanks to the Scientific Communications team for their help with the poster design, and the Immunology team for feedback on model development.