

P2607: PROphetNSCLC maintains predictive performance in longitudinal sampling beyond baseline in advanced NSCLC

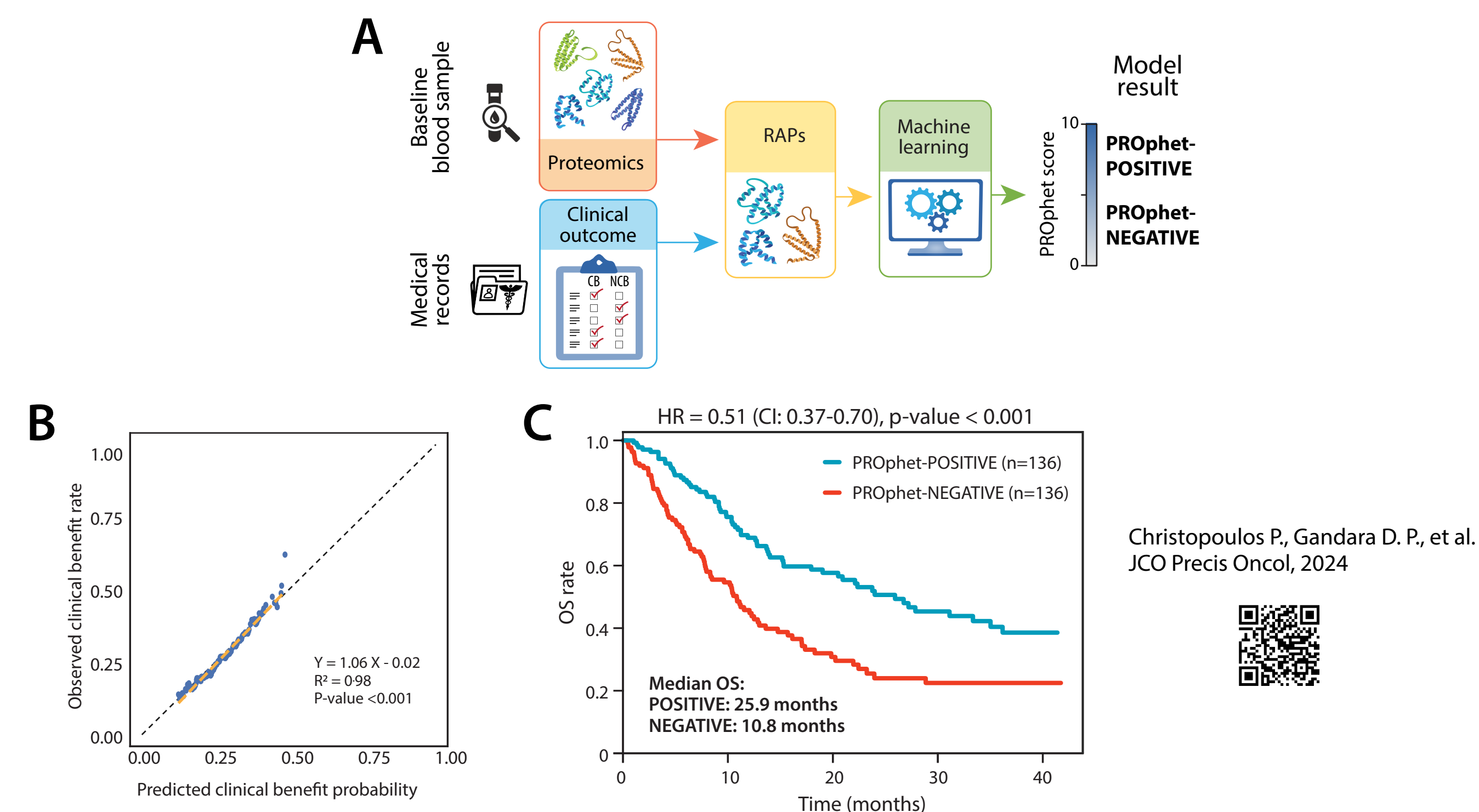
D. P. Gandara¹, F. Hirsch², P. Christopoulos³, E. Dudnik⁴, T. Muley³, M. Schneider³, O. Itzhaki⁵, S. Raveh Shoval⁵, M. Harel⁵, A. P. Dicker⁶, Y. Elon⁵

(1) UC Davis Medical Center, Sacramento/CA/USA, (2) Tisch Cancer Institute at Mount Sinai, New York/NY/USA, (3) Thoraxklinik, Heidelberg University Hospital, Heidelberg/DE, (4) Assuta Medical Centers, Tel Aviv/IL, (5) OncoHost, Binyamina/IL, (6) Thomas Jefferson University, Philadelphia/PA/USA

INTRODUCTION

PROphetNSCLC is a plasma proteomics-based test developed to guide immune checkpoint inhibitor (ICI) treatment decision-making in advanced NSCLC based on a pre-ICI sample. It generates a score that classifies patients as PROphet-POSITIVE or PROphet-NEGATIVE, reflecting the probability of clinical benefit from ICI-based therapy by measuring 388 resistance-associated proteins (RAPs) in blood plasma. However, real-world clinical constraints often preclude baseline sampling. Here, we investigate whether the plasma proteome remains sufficiently stable under serial sampling to preserve the predictive performance of PROphetNSCLC beyond the pre-treatment time point.

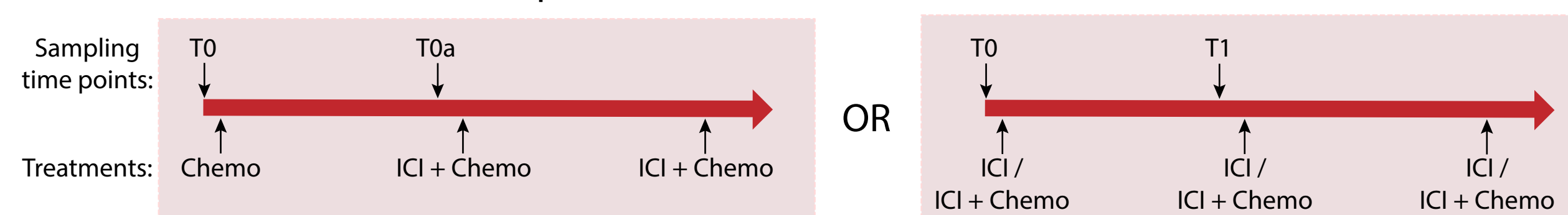
PROphetNSCLC predicts clinical benefit and survival outcomes in NSCLC patients receiving PD(L)1 inhibitor-based therapies



Predictive performance of PROphetNSCLC is shown in a validation cohort of 272 NSCLC patients: (A) PROphet model overview. (B) Observed clinical benefit (CB) rate versus predicted CB probability. (C) Kaplan-Meier plots showing overall survival (OS) for patients classified as PROphet-POSITIVE or PROphet-NEGATIVE.

METHODS

1. Plasma samples were collected from advanced NSCLC patients receiving ICI-based therapies at baseline (T0) and at serial timepoints (T0a or T1):



2. Proteomic profiling was performed using an aptamer-based platform, providing coverage of 7289 proteins.

3. Proteome stability was assessed by analyzing:

- Differentially expressed proteins between matched samples.
- Correlation between RAP expression levels.

4. Predictive performance was evaluated by statistical approaches to evaluate:

- PROphet classification consistency between matched samples.
- Non-inferiority assessment using overall survival (OS) hazard ratios (HRs) between PROphet-POSITIVE and PROphet-NEGATIVE subgroups.

RESULTS

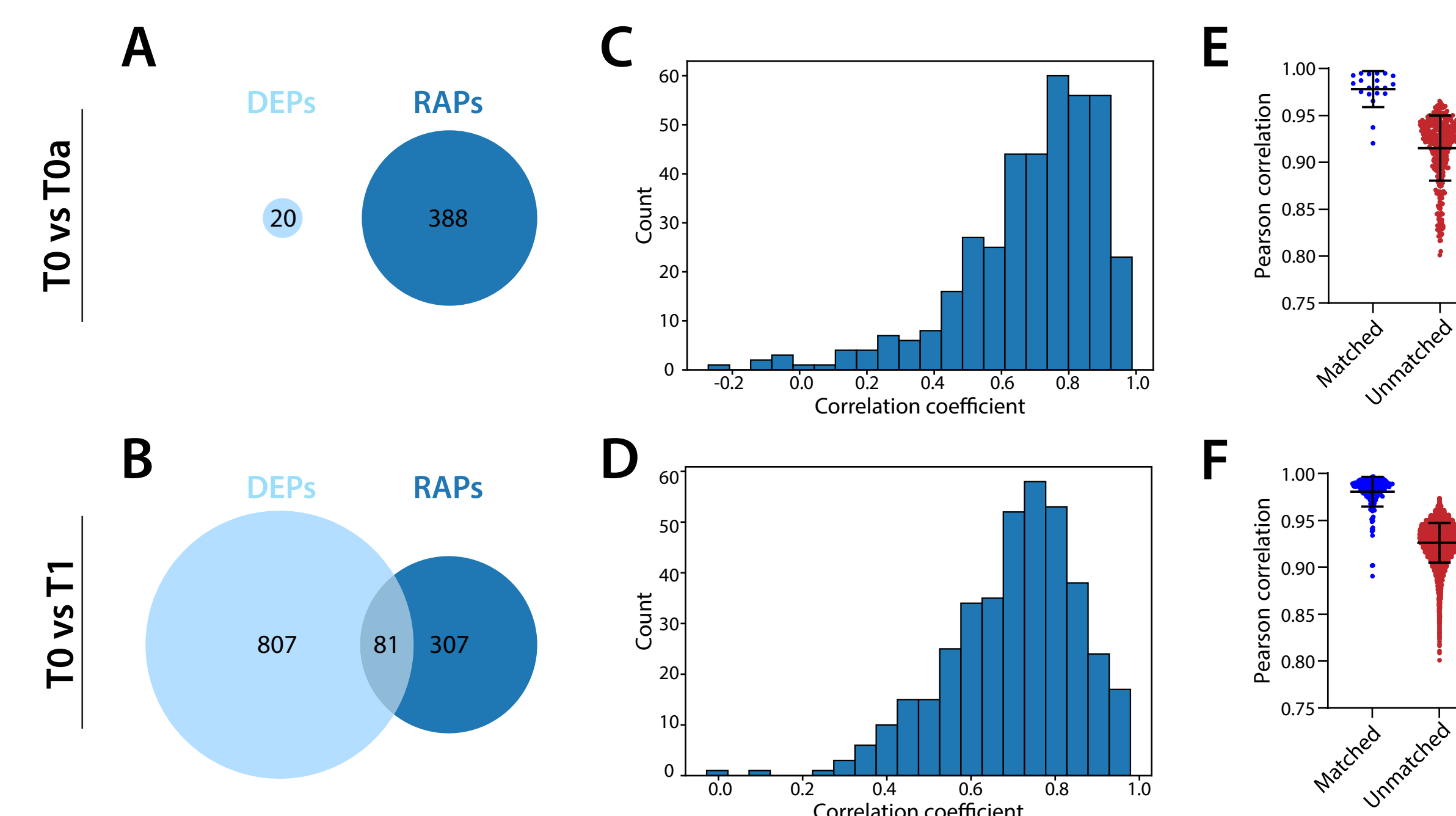
1 Cohort description

Table 1: Patient Characteristics

Characteristic	T0a cohort Number (%)	T1 cohort Number (%)
Sex		
• Male	17 (85)	128 (68.1)
• Female	3 (15)	60 (31.9)
Treatment type		
• PD(L)1 inhibitor	0 (0)	65 (34.6)
• PD(L)1 inhibitor + chemotherapy	13 (65)	123 (65.4)
• PD1 + CTLA4 inhibitor + chemotherapy	7 (35)	0 (0)
Treatment line		
• First	20 (100)	188 (100)
Clinical benefit *		
• Yes	5 (25)	48 (25.5)
• No	9 (45)	117 (62.2)
• Unknown	6 (30)	23 (12.2)
Age, mean (SD)	64.4 (7.1)	67.5 (9.4)
Total	20	188

* Defined as progression-free survival at 12 months

2 The RAP proteome remains stable over time

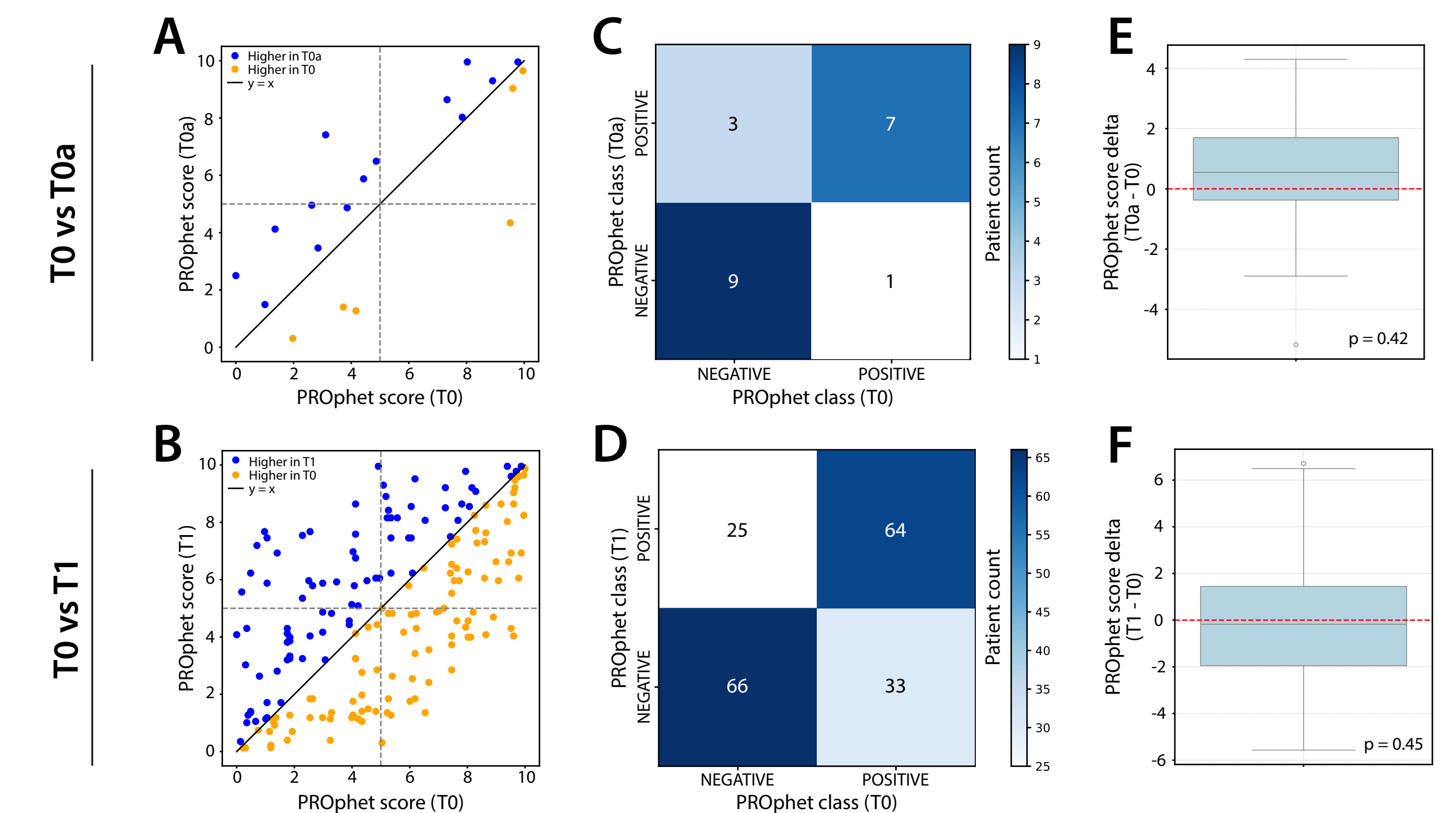


A-B. Differentially expressed proteins (DEPs) among 7289 plasma proteins were identified by comparing T0 samples to matched T0a (A) or T1 (B) samples. The Venn diagrams show the number of RAPs among the DEPs.

C-D. Distribution of Pearson correlations between RAPs in matched T0-T0a (C) and T0-T1 (D) samples. The majority of RAPs (>73%) showed strong correlation (≥ 0.6).

E-F. Correlations between sample pairs across RAPs were significantly higher in matched versus unmatched samples (Mann Whitney test).

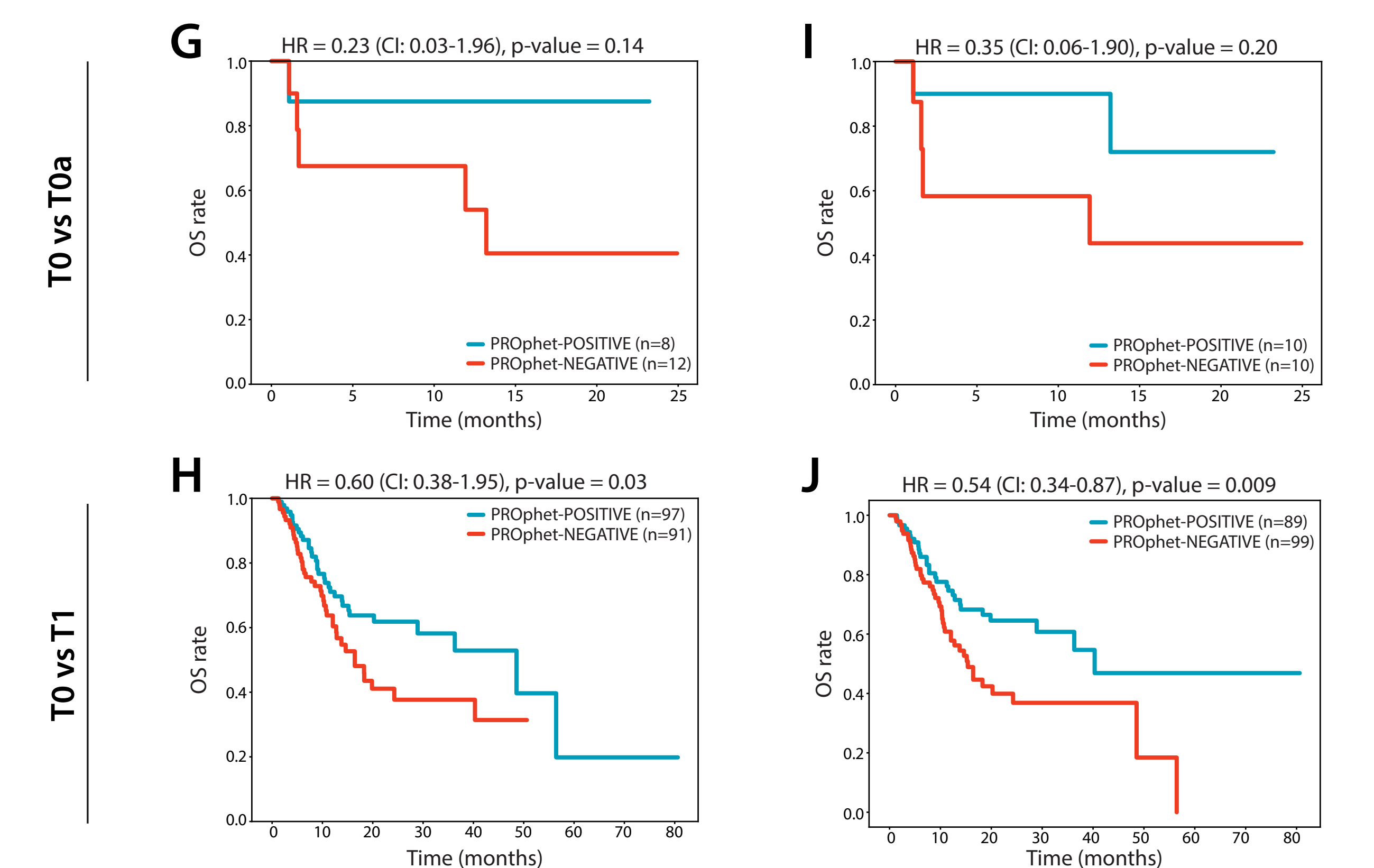
3 PROphetNSCLC retains longitudinal predictive ability



A-B. PROphet score based on T0 samples versus matched T0a (A) or T1 (B) samples.

C-D. PROphet classification based on T0 samples versus matched T0a (C) or T1 (D) samples. Consistency was analyzed with a one-sided binomial test. T0a: 16/20 (80%, $p=0.0059$); T1: 130/188 (69%, $p<0.0001$).

E-F. Classification bias was not significant (one sample t-test).



G-J. Kaplan-Meier plots showing OS of patients classified as PROphet-POSITIVE or PROphet-NEGATIVE based on T0 samples (G,H) versus matched T0a (I) or T1 (J) samples.

CONCLUSIONS

- PROphetNSCLC maintains its predictive ability across time points, supporting reliable application beyond baseline sampling.
- These findings support its use in real-world settings where pre-ICI samples may be unavailable.

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Correspondence:
drgandara@ucdavis.edu