



P1.277: Clinical Predictors of Immune-Checkpoint Inhibitor-Induced Thyroiditis in Lung Cancer: Evidence from a Real-World Cohort

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INTRODUCTION

Immune checkpoint inhibitors (ICIs) have transformed the treatment landscape of lung cancer but are frequently associated with immune-related adverse events (irAEs), including thyroiditis. Despite the increasing use of ICIs, risk factors for ICI-associated thyroid dysfunction in patients with lung cancer remain incompletely characterized. Prior studies have often been limited by small sample sizes, evaluation of specific ICI agents or non-pulmonary malignancies, and limited ability to predict clinically relevant outcomes. In this study, we aimed to develop a predictive model incorporating clinically relevant baseline biomarkers to stratify the risk of ICI-induced thyroiditis in patients with non-small cell lung cancer (NSCLC).

METHODS

A retrospective cohort of 4,648 patients with NSCLC who received ICI at Mayo Clinic was identified. All patients had a minimal follow-up of 2 years from ICI initiation. Baseline predictors were assessed from 12-month window preceding ICI initiation and included thyroid biomarkers (TSH, Free T4, thyroid peroxidase (TPO) antibodies), ICI regimen, prior chemotherapy exposure, age, gender, history of hypothyroidism, and use of steroids, statins and antibiotics. Time-to-event was defined as days from first ICI administration to thyroiditis diagnosis. Cox model performance was evaluated using 5-fold cross-validated C-index and compared against three machine learning-based models including Gradient Boosting Survival (GBS), Random Survival Forest (RSF), and DeepSurv.

CONCLUSIONS

- Elevated baseline thyroid peroxidase (TPO) antibodies and thyroid-stimulating hormone (TSH) are the strongest predictors of ICI-associated thyroiditis in patients with lung cancer.
- Clinical suspicion of pre-existing thyroid disease prompting baseline thyroid evaluation is independently predictive of ICI-associated thyroiditis, regardless of baseline test results, supporting routine assessment before ICI initiation.
- Dual immune checkpoint blockade is associated with a clinically higher risk of thyroiditis compared with ICI monotherapy.

RESULTS

Among 4,648 patients with NSCLC who received ICI, 802 (17.3%) developed ICI-related thyroiditis. Our Cox model using selected baseline biomarkers outperformed complex machine learning alternatives.

The following variables were NOT significantly associated with development of ICI thyroiditis:

- Demographic variables: age, sex, race
- fHistory o hypothyroidism or diabetes
- Selected medications: corticosteroids, NSAIDs, PPI, antibiotics
- Prior malignancy history
- Proxy labs including hemoglobin and albumin

REFERENCES & ACKNOWLEDGEMENTS

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Artificial Intelligence (AI) Use Disclaimer
Machine learning software was used for statistical analysis as described in the methods section. AI was not used in the creation of this poster.

RESULTS (CONTINUED)

The most clinically significant predictors of ICI-related thyroiditis include:

- Elevated TPOAb
- Having been tested for TPOAb with a normal result
- TSH level
- Free T4 level
- Prior testing for TSH and T4
- Combination treatment with anti-PD-1/PD-L1 with anti-CTLA4

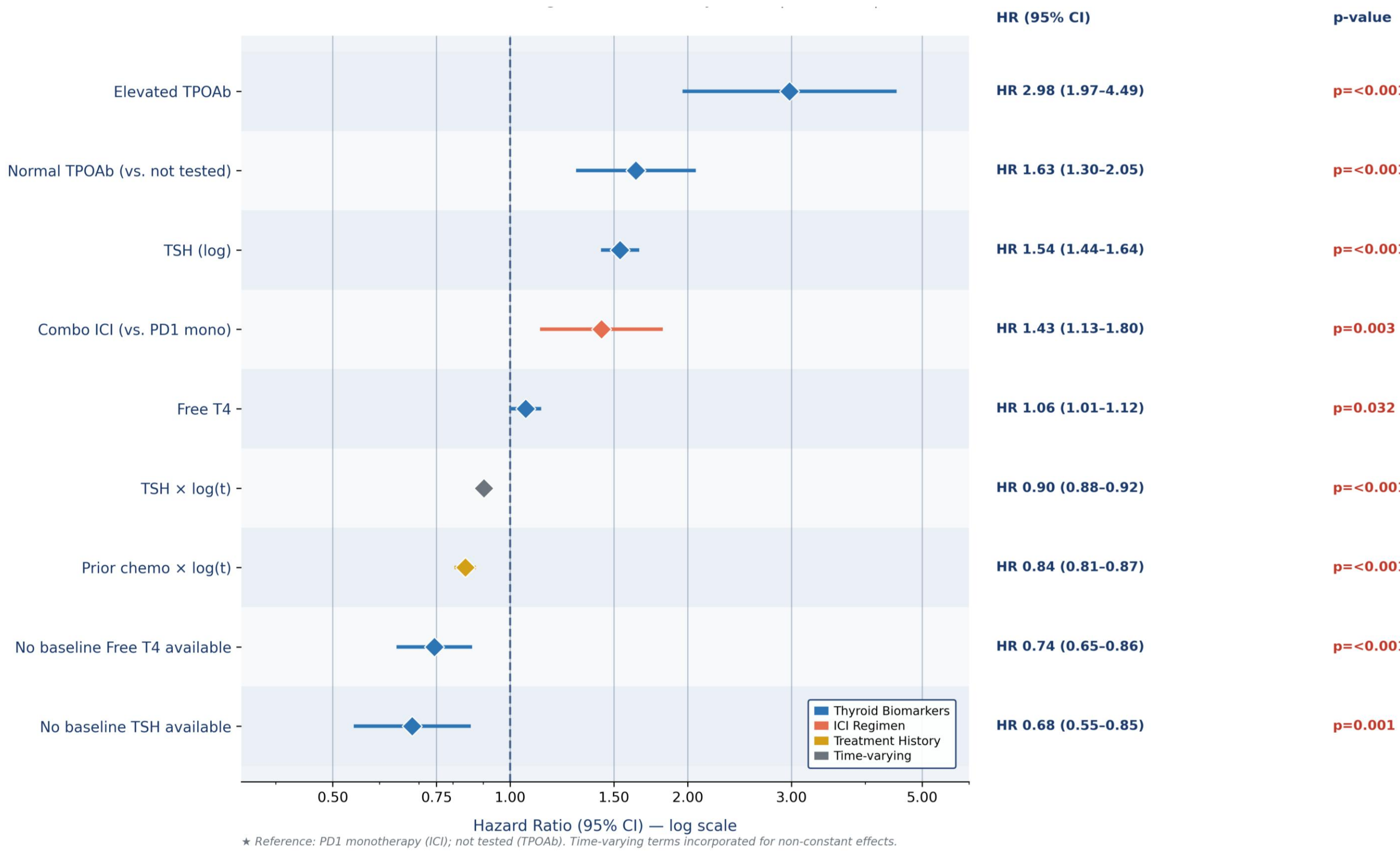


Figure 1: Statistically significant predictors of developing ICI-related thyroiditis. Variables denoted as “x log(t)” represent the predictive value of that variable over time. For example, the predictive value of a TSH measurement is strongest in the early period after starting immunotherapy and weakens as more time passes without the development of thyroiditis. Prior chemo: receipt of chemotherapy in the year before starting immunotherapy.

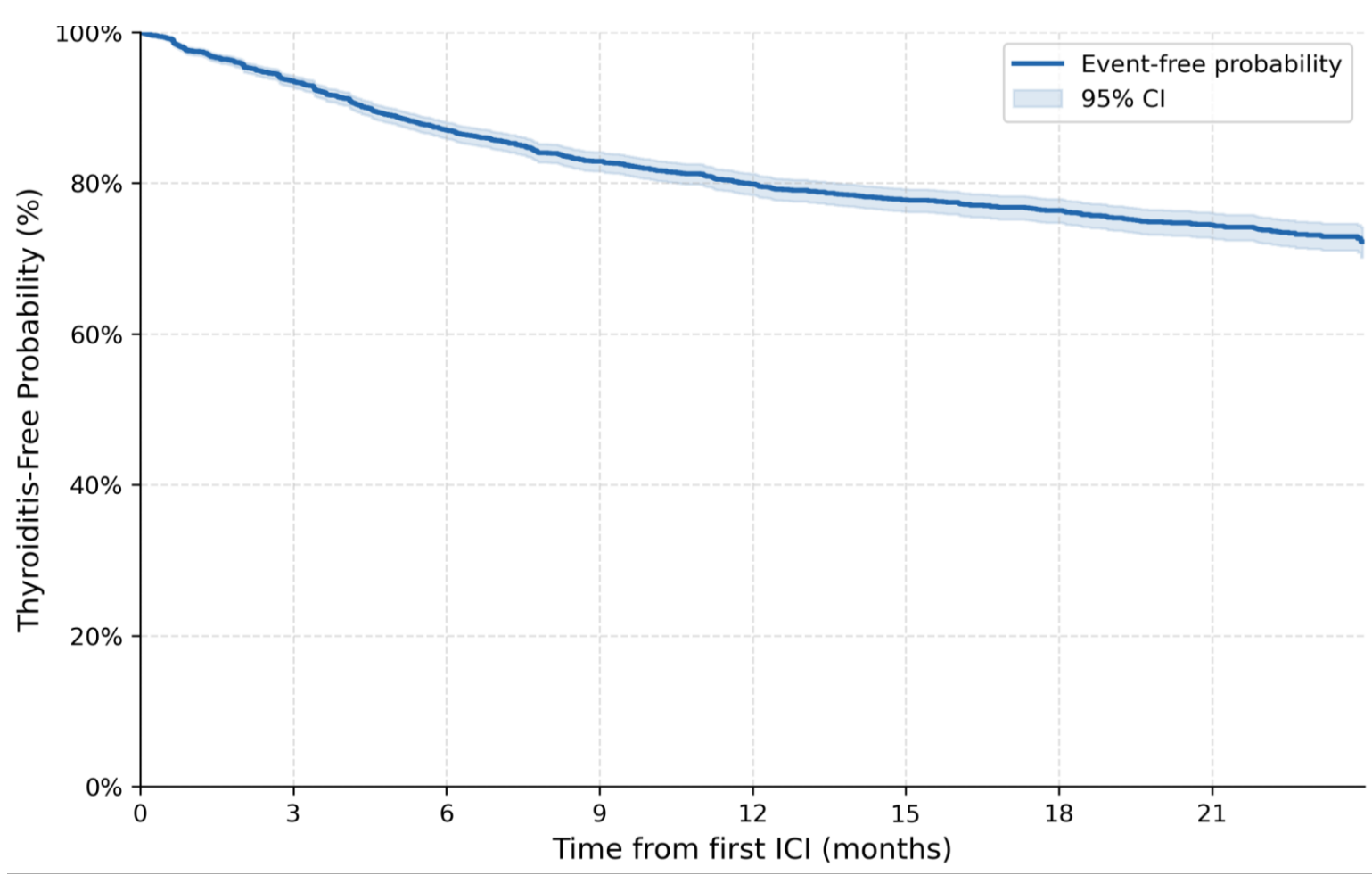


Figure 2: Kaplan-Meier curve of thyroiditis-free patients over time in NSCLC patients treated with ICI. Although incidence of ICI thyroiditis is greatest soon after the first ICI dose, it is widely distributed over time. By 24 months, approximately 27.5% of evaluable patients had ICI thyroiditis.

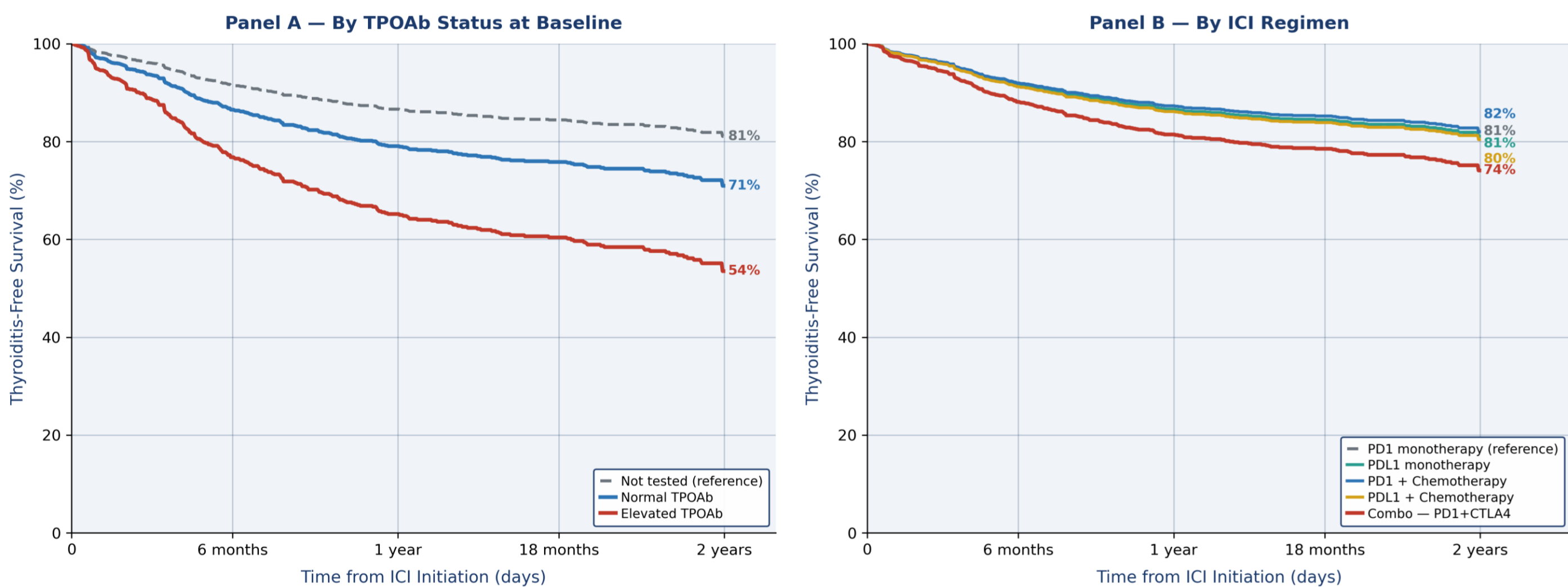


Figure 3: Cox proportional hazards model of predicted thyroiditis-free survival by key subgroups. A) Patients with elevated baseline TPOAb were 3 times more likely to develop ICI thyroiditis. Normal TPOAb was also predictive, suggesting that the clinical concern that prompts testing does select for those more likely to develop thyroiditis. B) The only regimen with significantly increased thyroiditis incidence was combination anti-PD-1/PD-L1 and anti-CTLA-4 therapy (n = 241), with a 43% higher risk compared to anti-PD-1 monotherapy (n = 714).