ADAPT-M: A tool to predict individualised benefit from adjuvant anti-PD1 (PD1) in resected high-risk melanoma

Ines Pires da Silva[1,2], Susana Puig[3], Josep Malvehy[3], Sebastian Podlipnik[3], Ronen Stoff[4], Tina J. Hieken[4], Celeste Lebbe[5], Laetitia Da Meda[5], Ulrike M. Leiter[6], Vincent T. Ma[7], Katharina C. Kaehler[8], Rishitha Nalabothu[9], Karam Khaddour[10], Andrea Boutros[11], Luis Paul Del Carpio Huerta[12], Shirly Grynberg[13], Matteo S. Carlino[1,14], Nurudeen A. Adegoke[1], Alexander M. Menzies[1,15], Georgina V. Long[1,15]

1. Melanoma Institute Australia, The University of Sydney, Sydney, Australia; 2. Champalimaud Foundation, Lisbon, Portugal; 3. Dermatology Department, Hospital Clínic de Barcelona, Barcelona, Spain; 4. Mayo Clinic Hospital, Methodist Campus, Rochester, MN; 5. Université de Paris, AP-HP Hôpital Saint-Louis, Paris, France; 6. Department of Dermatology, Center for Dermatooncology, Eberhard Karls University of Tübingen, Tübingen, Germany; 7. Division of Hematology, Medical Oncology, and Palliative Care, Department of Medicine, University of Wisconsin, Madison, WI; 8. University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany; 9. Vanderbilt University Medical Center, Nashville, TN; 10. Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; 11. University of Genoa, Genova, Italy; 12. Medical Oncology Department, Catalan Institute of Cancer (ICO). Cancer Immunotherapy Group (CIT), Bellvitge Biomedical Research Institute (IDIBELL) —OncoBell; L'Hospitalet De Llobregat, Barcelona, Spain; 13. Ella Lemelbaum Institute for Immuno-Oncology and Melanoma, Tel Aviv, Israel; 14. Westmead and Blacktown Hospitals, Wentworthville, Australia; 15. Mater and Royal North Shore Hospitals, Sydney, Australia

Background

- ❑ Resected stage IIB/C and microscopic stage IIIA/B/C/D melanoma present a significant risk of recurrence risk (from 37% to 62%) at 5 years[1,2,3,4].
- ❑ While one year of adjuvant anti-PD1 (PD1) therapy reduces this risk by approximately half, the individual patient's baseline risk without treatment and their specific benefit from adjuvant PD1 remain unknown.

Objectives

We aimed to generate two separate predictive models for recurrence: one for untreated and one for treated patients, to calculate the individualised benefit of adjuvant PD1.

Methods

- ❑ Patients with resected stage IIB/C or microscopic stage IIIA/B/C/D melanoma, either treated with adjuvant PD1 or untreated from 13 melanoma centres (Australia, Europe, United States and Israel), and with at least 2 years of follow-up from surgery were included.
- ❑ We analysed patients' demographics, disease characteristics, blood parameters, pathological and imaging data at baseline, and clinical outcomes.
- ❑ Stabilised inverse-probability-of-treatment weights were derived from a logistic propensity model (covariates with univariate p<0.05); balance confirmed by standardised mean differences <0.10.
- ❑ Two weighted penalised Cox proportional hazards models (elastic net) were fitted separately for treated and untreated patients within stratified discovery/validation splits; tuning by repeated 10-fold cross-validation (10 repeats) with ≥80% stability selection.
- ❑ Individualised absolute benefit was computed as S_treated(t) - S_untreated(t) at 12 and 24 months with 1,000-bootstrap 95% CIs, and deployed as the ***ADAPT-M*** clinical tool.

Results

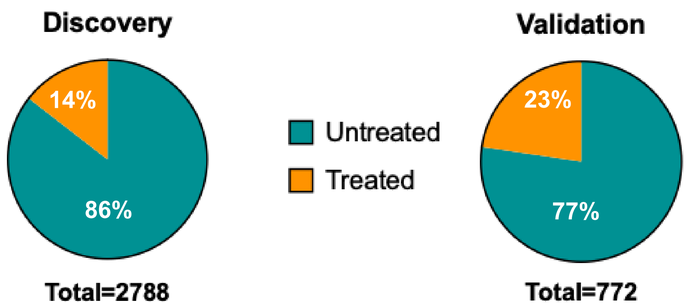

Figure 1. A total of 3560 patients were included in this study, divided into discovery and validation cohorts.

Results

Table 1. Model to predict recurrence for untreated patients

Variables	Age, gender, primary site, histological subtype, Breslow thickness, ulceration, mitosis, number and site of regional lymph nodes (LN), mutation status, and LDH
AUC	**0.70 in discovery, 0.69 in validation**

Table 2. Model to predict recurrence for treated patients

Variables	Age, gender, Breslow thickness, site of regional LN, and mutation status
AUC	**0.69 in discovery, 0.61 in validation**

Patient A, a woman ≤45 years old with a primary head & neck melanoma (superficial spreading, thickness >1-2 mm, no ulceration, 1 mitosis/mm^2), 2 clinically occult LN metastases in the neck, NRAS mutant, and normal LDH.

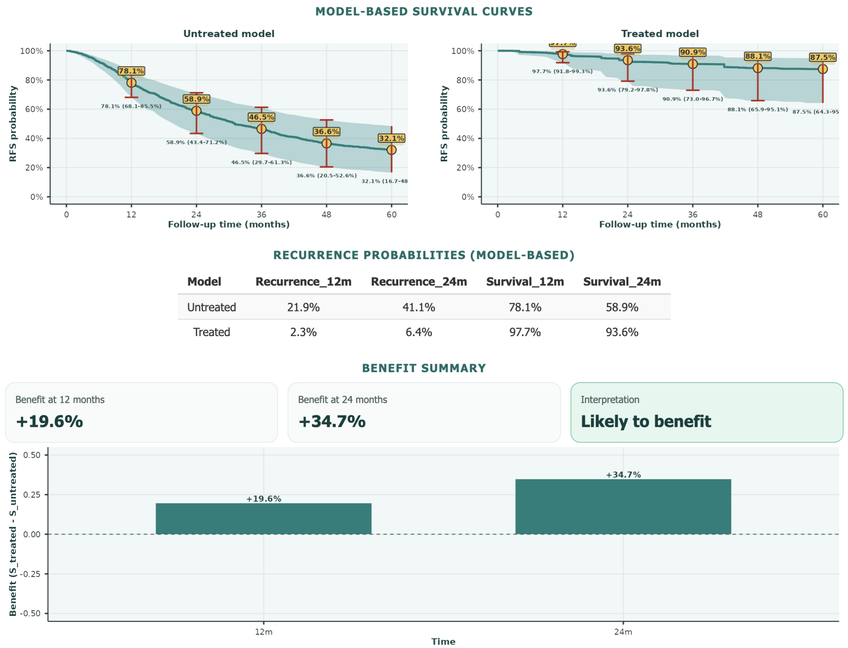

Figure 2. Absolute **r**ecurrence-free survival benefit of adjuvant treatment for a representative clinical example ***Patient A***.

Patient B, a man ≤45 years old with a primary melanoma in the lower limb (nodular, thickness >1-2 mm, no ulceration, 1 mitosis/mm^2), 2 clinically occult LN metastases in the groin, BRAF V600 mutant, and normal LDH.

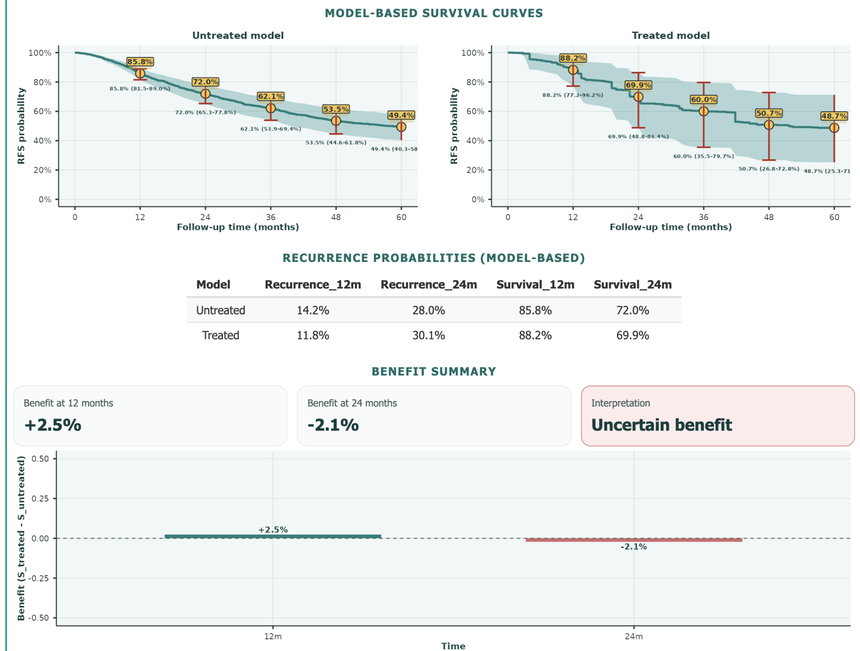

Figure 3. Absolute **r**ecurrence-free survival benefit of adjuvant treatment for a representative clinical example ***Patient B***.

Conclusions

ADAPT-M, a clinical tool that estimate individualized recurrence risks with and without adjuvant anti-PD1 therapy, quantifies the absolute benefit of treatment for patients with high-risk resected melanoma, facilitating personalized adjuvant therapy decisions.

References

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Ines.silva@melanoma.org.au