

Background

- 5-year survival for stage III melanoma ranges from 93% to 32% based on tumour burden¹.
- Adjuvant anti-PD-1 therapy improves recurrence-free survival by ~17%, yet ~43% of patients still recur within 1 year².
- Accurate biomarker models that identify patients at a high risk of disease recurrence can be used to alter treatment and monitoring strategies³.

Objectives

- Develop multi-omics models (genomic, transcriptomic, tumour microenvironment [TME] immune infiltrate) that identify patients that recur <12 months from start of treatment with adjuvant immunotherapies.
- Identify combinations of clinical and omics that identify high-risk disease.
- Improve patient stratification to support personalised treatment decisions.

Cohort and Methods

Eligibility:

- Patients with stage III resectable melanoma who received adjuvant anti-PD-1.
- Pre-treatment tumour biopsies collected within the last 2 years.

Multi-omics assays performed on pre-treatment tumour specimen:

- Tumour mutational burden (TMB): QIAsSeq TMB Panel (DHS-6600Z, QIAGEN).
- Gene expression profiling (GEP): TruSeq RNA Exome (Illumina).
- TME: Multiplex IF (Opal, Akoya Biosciences).

- Machine learning models** integrating clinical and multi-omics features were used to predict 12-months recurrence status.

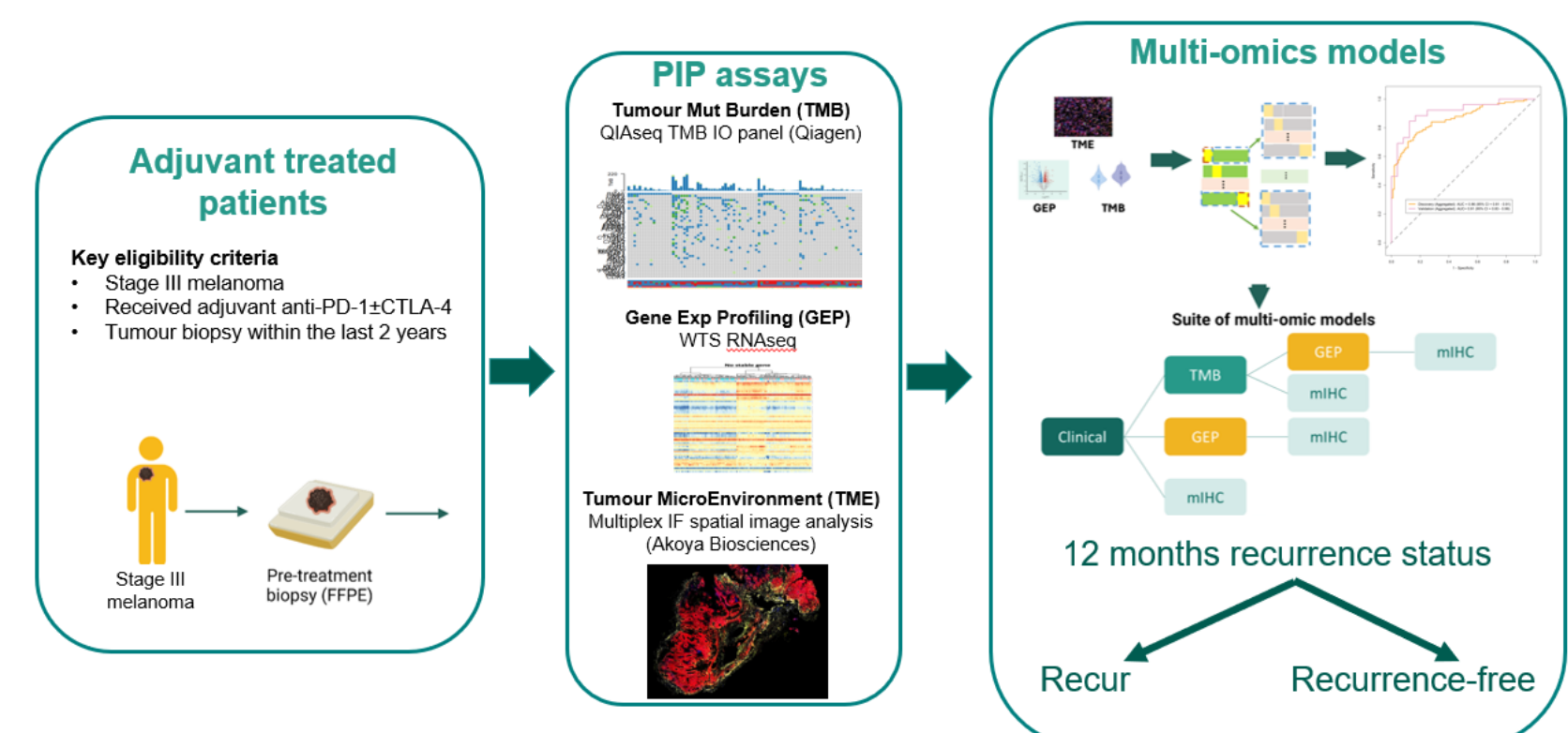


Figure 1: Multi-omics machine learning approach to identify patients with stage III melanoma at high risk of recurrence following adjuvant immunotherapies.

Conclusions

- Multi-omics data accurately predicted risk of recurrence in stage III melanoma patients treated in the adjuvant setting.
- Tumour mutation burden, gene expression profiling of NK-cell and IFN γ signatures and macrophage populations within the stroma significantly add to the accuracy of identifying patients that recur within 12 months of receiving adjuvant immunotherapy.
- Findings may improve clinical outcomes by guiding biomarker-informed therapeutic decisions.

Table 1: Patient Clinical Characteristics

	Non-recurrence (N=85)	Recurrence (N=46)	Total (N=131)	p value
Treatment				0.5295
Anti-PD-1	70 (82.4%)	35 (76.1%)	105 (80.2%)	
Anti-PD-1+anti-CTLA-4	15 (17.6%)	11 (23.9%)	26 (19.8%)	
Age				0.8508
Median (Range)	61.40 (22.91, 82.90)	61.79 (30.35, 82.75)	61.74 (22.91, 82.90)	
Sex				0.9379
Female	26 (30.6%)	13 (28.3%)	39 (29.8%)	
Male	59 (69.4%)	33 (71.7%)	92 (70.2%)	
Primary melanoma				0.0246
Scalp Face Neck	15 (17.6%)	16 (34.8%)	31 (23.7%)	
Occult	14 (16.5%)	2 (4.3%)	16 (12.2%)	
Other	56 (65.9%)	28 (60.9%)	84 (64.1%)	
Cutaneous primary				0.807
Yes	81 (95.3%)	45 (97.8%)	126 (96.2%)	
No	4 (4.7%)	1 (2.2%)	5 (3.8%)	
Previous MAPKi				
No	85 (100.0%)	46 (100.0%)	131 (100.0%)	
Baseline LDH				0.231
Elevated	2 (2.4%)	0 (0.0%)	2 (1.5%)	
Normal	83 (97.6%)	45 (97.8%)	128 (97.7%)	
Missing	0 (0.0%)	1 (2.2%)	1 (0.8%)	
Stage				0.071
IIIB	45 (52.9%)	16 (34.8%)	61 (46.6%)	
IIICD	40 (47.1%)	30 (65.2%)	70 (53.4%)	

Results

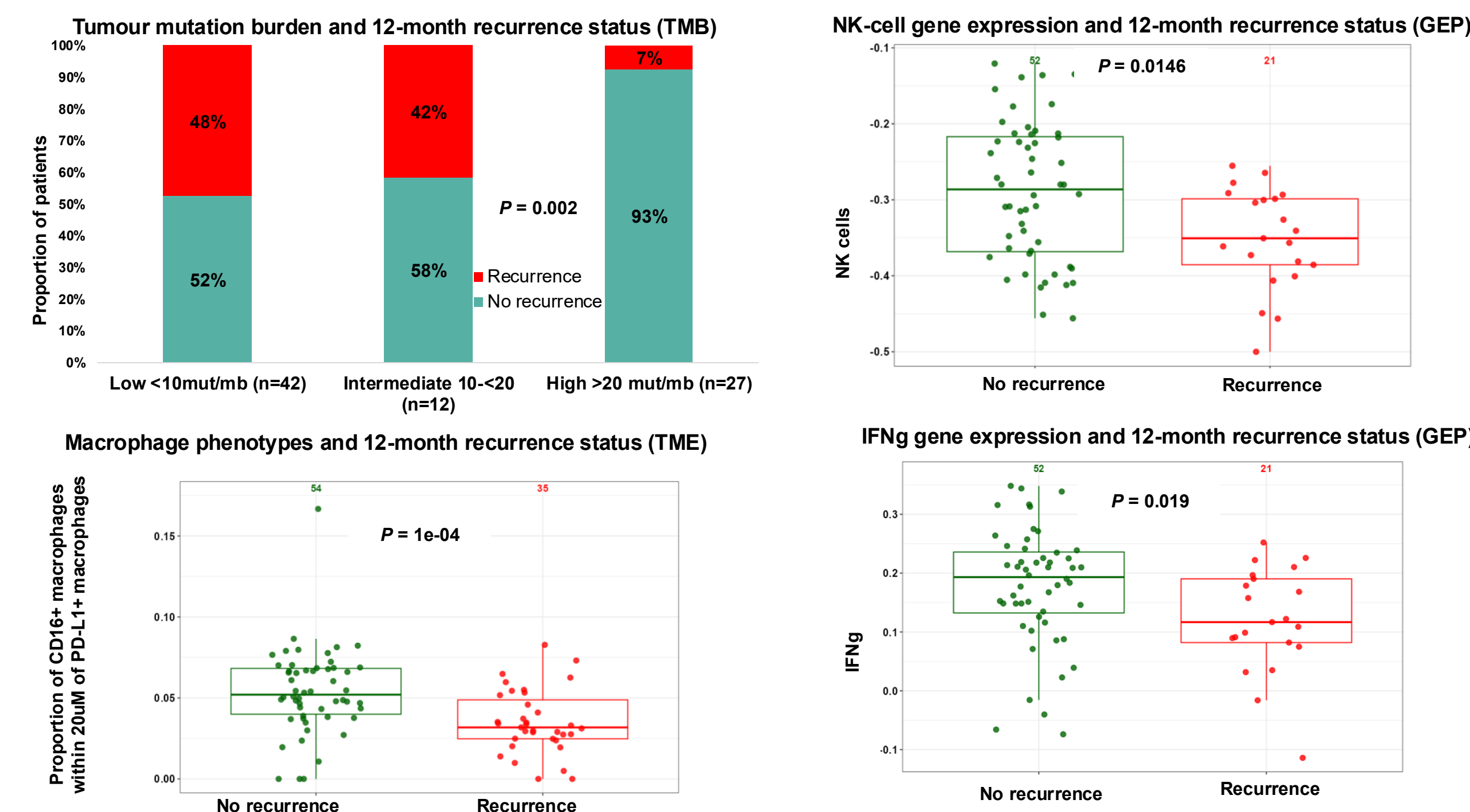


Figure 2: 12-month recurrence status is linked to higher TMB, more CD16⁺ macrophages within 20 μ m of PD-L1⁺ cells (TME), and elevated NK-cell and IFN γ expression in non-recurrent patients.

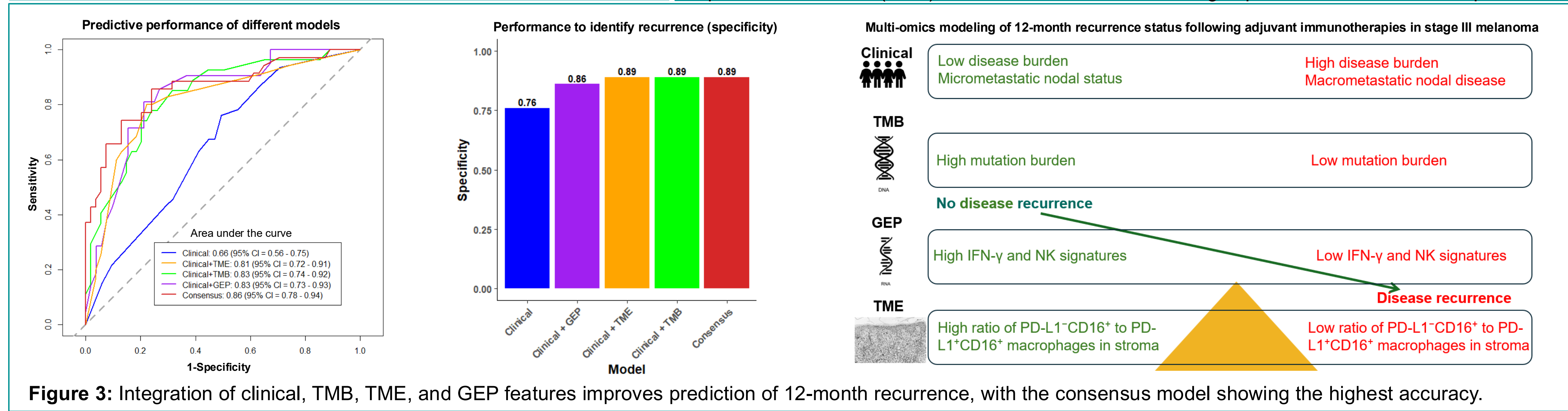


Figure 3: Integration of clinical, TMB, TME, and GEP features improves prediction of 12-month recurrence, with the consensus model showing the highest accuracy.

References

- Gershenwald JE, et al. CA Cancer J Clin 2017.
- Eggermont AMM, et al. N Engl J Med 2018.
- Gide TN, et al. Cancer Cell 2019.

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