Neoadjuvant immunotherapy (neoIT) in melanoma; A prediction tool for pathological response and recurrence, and the role of adjuvant (Adj) therapy (Tx) to improve recurrence-free survival (RFS).

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Background

- NeoIT with anti-PD-1 (PD1) showed better event-free survival than adjuvant (adj)IT and is a standard of care for patients with stage IIIB–D melanoma[1].
- Many patients achieve a Major Pathological Response with neoIT (MPR; complete [pCR] or near-complete [near-pCR] pathological response) and may not require additional treatment; while patients with non-MPR (partial [pPR] or no [pNR] pathological response) are at higher risk of recurrence and may benefit from adjuvant therapy[2].

Objectives

We sought to:

1) Predict patients with non-MPR and at higher risk of recurrence with PD1-based neoIT;
2) Study the role of adjuvant therapy in patients with pNR.

Methods

- Patients with stage IIIB–D melanoma treated with PD1-based neoIT were included.
- Demographics, disease characteristics, baseline blood parameters, radiological response, and clinical outcomes were examined.
- A multivariate penalized logistic regression model was developed to predict non-MPR and recurrence.

Results

TABLE 1. Neoadjuvant treatment and Pathological response.

	Cohort (n=184)
Treatment	
PD1	30 (16%)
PD1 + anti-CTLA-4	107 (58%)
PD1 + novel immunotherapy agents	47 (26%)
Pathological response*	
pCR	95 (53%)
near-pCR	19 (11%)
pPR	20 (11%)
pNR	45 (25%)

*Five patients did not receive surgery (due to clinical progression in 4 patients).

Results

1. Model Predictive of Non-Major Pathological Response

A

Predictors	AOR	95% CI	p-value
% tumour change from baseline by RECIST	18.94	3.76 - 51.83	**0.0001**
Neutrophils count at baseline	1.29	1.00 - 1.64	**0.0476**
Lymphocytes count at baseline	1.64	1.01 - 2.52	**0.0467**
Baseline largest LN (long axis)	1.02	1.00 - 1.05	0.1056
Haemoglobin level at baseline	0.99	0.95 - 1.02	0.6728
Stage of primary tumour			
T1	1		
T2	1.22	0.61 - 2.17	0.6695
T3	1.56	0.76 - 2.86	0.2572
T4	1.83	1.01 - 3.05	**0.0457**

B

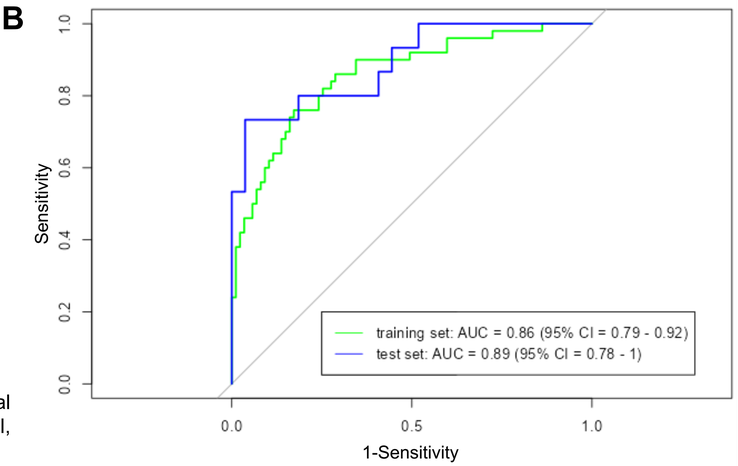
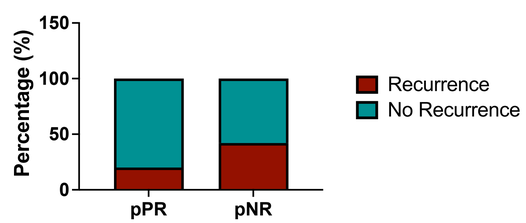


FIGURE 1. Model predictive of non-major pathological response (non-MPR). (A) Clinical, pathological and radiological predictors of non-MPR (AOR, adjusted odds ration). **(B)** The combination of clinical, pathological and imaging data can accurately predict non-MPR (training set, AUC=0.86; test set, AUC=0.89).

2. Model Predictive of Recurrence for non-MPR patients & Role of adjuvant treatment to reduce the risk of recurrence

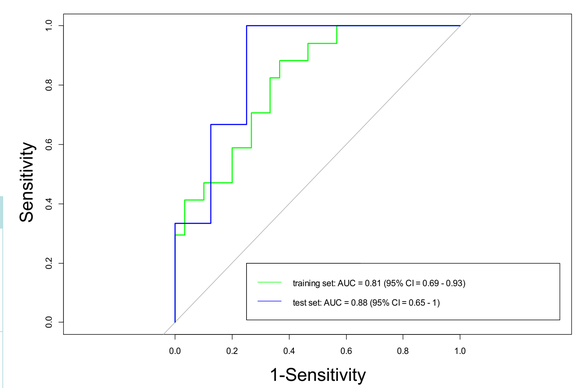
A



B

Predictors	AOR	95% CI	p-values
Mitoses in the primary tumour			
<= 1	1		
>= 2	8.23	2.93 - 19.46	**<0.0001**
% tumor change from baseline by RECIST	13.59	2.86 - 43.79	**0.0005**

C



D

	Recurrence Rate
No adjuvant therapy	64% (7/11)
Adjuvant targeted therapy	27% (3/11)
Adjuvant PD1 therapy	38% (6/16)

FIGURE 2. Model predictive of recurrence for non-MPR patients. (A) Recurrence rate in pPR *versus* pNR. The combination of mitosis (primary tumor) and % tumor change from baseline by RECIST **(B)** can accurately predict recurrence (training set, AUC=0.81; test set, AUC=0.88) **(C)**. Recurrence rate in patients with pNR who had adjuvant targeted therapy, adjuvant PD1 therapy and no adjuvant therapy **(D)**.

Conclusions

- Clinical, pathological, and radiological features can accurately predict MPR or non-MPR to neoIT (AUC=0.86), as well as recurrence (AUC=0.81), facilitating response-directed management.
- Acknowledging the small numbers of patients, these early data suggests that: (1) Adjuvant targeted therapy or PD1 reduces recurrence and should be discussed with patients with pNR; (2) De-escalation of surgery (± adjuvant therapy) should be investigated in MPR patients.

References

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Acknowledgements

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