The 27-gene IO score is associated with pathologic complete response (pCR) in HR+/HER2- breast cancer patients treated with pembrolizumab in the I-SPY2 Trial.

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INTRODUCTION

- Approximately 74% of all breast cancer are hormone receptor (HR) positive and human epidermal growth factor receptor 2 (HER2) negative (HR+/HER2-)
- ICIs are approved in both early-stage and metastatic triple negative breast cancer
- No such approval exists for HR+/HER2- breast cancer (BC) which typically has a lower TMB, lower PD-L1 expression, and lower numbers of tumor infiltrating lymphocytes than TNBC
- There is an unmet need for a biomarker to help identify likely responders to ICI therapy in neoadjuvant treatment of HR+ patients

The 27-Gene IO Assay (IO Score)

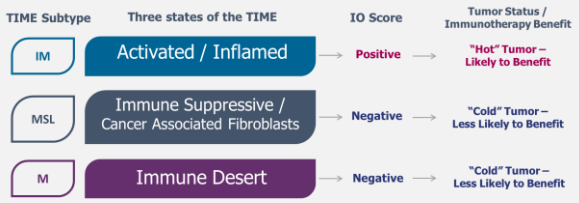
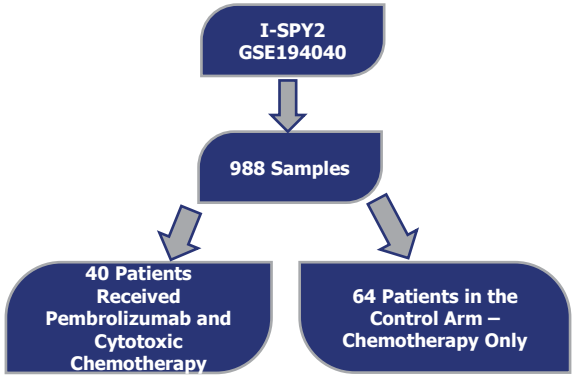


Figure 1: IM inflammatory; MSL mesenchymal stem like; M mesenchymal

- The 27-gene IO Score has previously demonstrated an association between ICI therapy and efficacy in NSCLC[1,2], mUC[3], and neoadjuvant treatment of TNBC[4,5,6]
- This marks the first time the IO Score has been tested in a cohort of HR+/HER2- breast cancer

METHODS

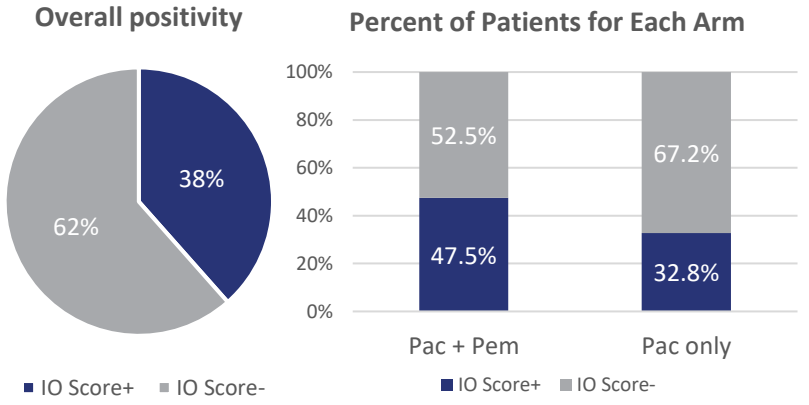
- I-SPY2 is an adaptively randomized phase 2 multicenter trial of neoadjuvant chemotherapy for early stage, high risk BC.
- This platform trial evaluates multiple investigational arms in parallel with a standard chemotherapy backbone (paclitaxel followed by AC), which served as a common control arm
- Array-based expression data were normalized, combined, batch corrected, and log-transformed by the submitting institution
- The binary IO Scores results were calculated using the previously established threshold

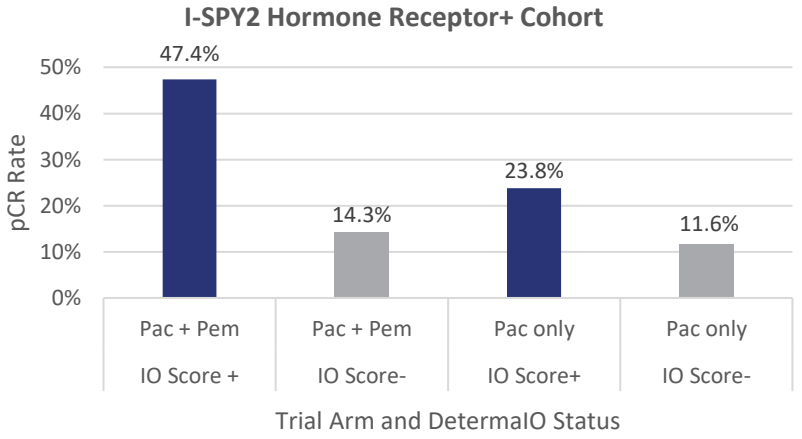


RESULTS

- A total of 40 HR+/HER2- patients received pembrolizumab and qualified for analysis
- Of these, 12 patients achieved pathologic complete response (pCR), and 28 had residual disease (RD)
- Of the 12 patients who achieved pCR, 9 were IO Score+ (75%)
- Of the 28 patients with RD, 18 were IO- (64%)

RESULTS





Arm	N= (pCR)	IO+ (pCR)	IO- (pCR)	IO Score Odds Ratio
Pac only	64 (10)	21 (5)	43 (5)	2.4 (0.6-9.3, p>0.2)
Pac + Pem	40 (12)	19 (9)	21 (3)	5.4 (1.2-24.7, **p<0.03**)

Paclitaxel + AC (Pac); Pembrolizumab (Pem)

DISCUSSION

- Despite a generally low inflammatory tumor microenvironment characteristic of the HR+/HER2- BC phenotype, the IO Score+ group was 3x more likely to achieve pCR with the addition of pembrolizumab to chemotherapy
- These data extend on previous findings supporting IO Score as predictive of pCR in TNBC but now extending to HR+/HER- BC
- Data from the TNBC arm of I-SPY2 will be released at a later date

CONCLUSION

- IO Score was significantly associated with pCR in the presence of ICI but not chemo alone suggesting it is predictive of response in HR+/HER- BC
- This is the 4th BC study demonstrating Io Score is associated with pCR in patients treated with neoadjuvant ICI therapy

BC Type	Source	Outcome	N
neoTNBC	NeoTRIP	OR 2.9, p=0.011	220
	NeoPACT	OR 5.9, p<0.01	90
	NCT02489448	OR 4.1, p=0.012	55
HR+/HER2-	NTC01042379	OR 5.4, p<0.03	40

References

1. Ranganath (2021)
2. Saltman (2022)
3. Seitz (2022)
4. Iwase (2021)
5. Bianchini (2021)
6. Sharma (2022)

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