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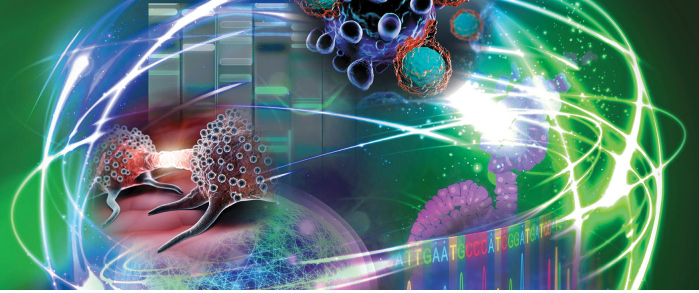

Validation of a 27-gene immuno-oncology algorithm in metastatic urothelial carcinoma treated with an immune checkpoint inhibitor

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Disclosure Information

Robert S. Seitz

I have the following financial relationships to disclose:

I am an employee and stockholder of Oncocyte Corporation and have a financial interest in the subject of today's presentation.

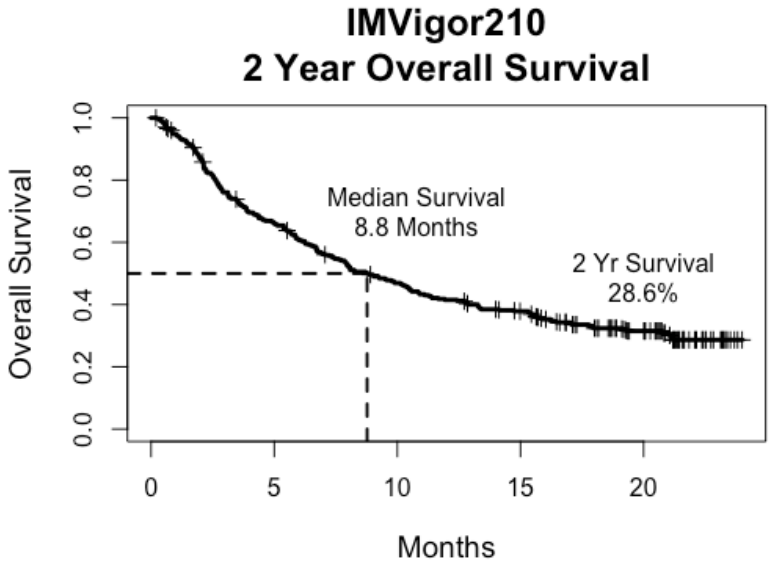
Bladder Cancer and Immune Checkpoint Inhibitors

- Bladder (Urothelial) Cancer is the 10th most common cancer in the world with more than 210k deaths in 2020[1].
- Immune Checkpoint Inhibitors (ICIs) are approved for advanced bladder cancer in certain circumstances including:
  - The patient is deemed unable to tolerate cisplatin and is PD-L1 IHC+.
  - The patient has progressed/recurred since prior platinum therapy.

[1] https://gco.iarc.fr/today/data/factsheets/cancers/30-Bladder-fact-sheet.pdf

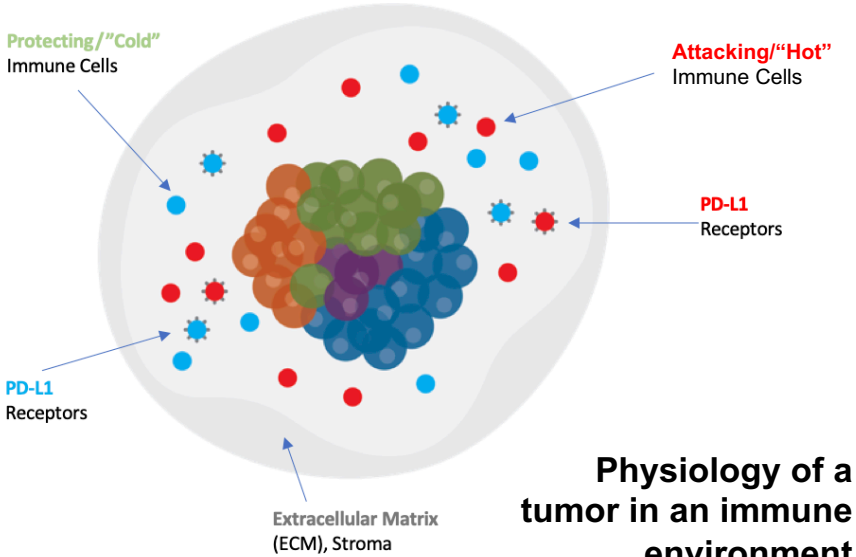
IMVigor210 Trial Results

- IMVigor210 in mUC with the ICI Atezolizumab
- Primary endpoint was overall response rate > 10%
  - Cohort 1 - 119 patients platinum ineligible
  - Cohort 2 - 310 patients progressed after platinum
- Both indications granted accelerated approval
  - Platinum ineligible: IC PD-L1 ≥ 5%
  - Progressed post-platinum: no Biomarker
    - Indication withdrawn in March 2021
- Secondary endpoints included OS
- Biomarker Data
  - Rosenberg, 2016
  - Balar, 2017
  - Mariathasan, 2018



27 Gene Predictor

- Gene expression signature run as algorithm on whole transcriptome RNAseq data
  - Also translated to RTPCR assay
  - Nielsen, 2021 provides details including gene IDs.
- Measures three distinct components of the tumor immune microenvironment:
  1. Immune Infiltrates (“Hot”)
  2. Fibroblasts /ECM (“Cold”)
  3. Epithelial-Mesenchymal Transition (“Cold”)



Physiology of a tumor in an immune environment

27-Gene Predictor: Validation

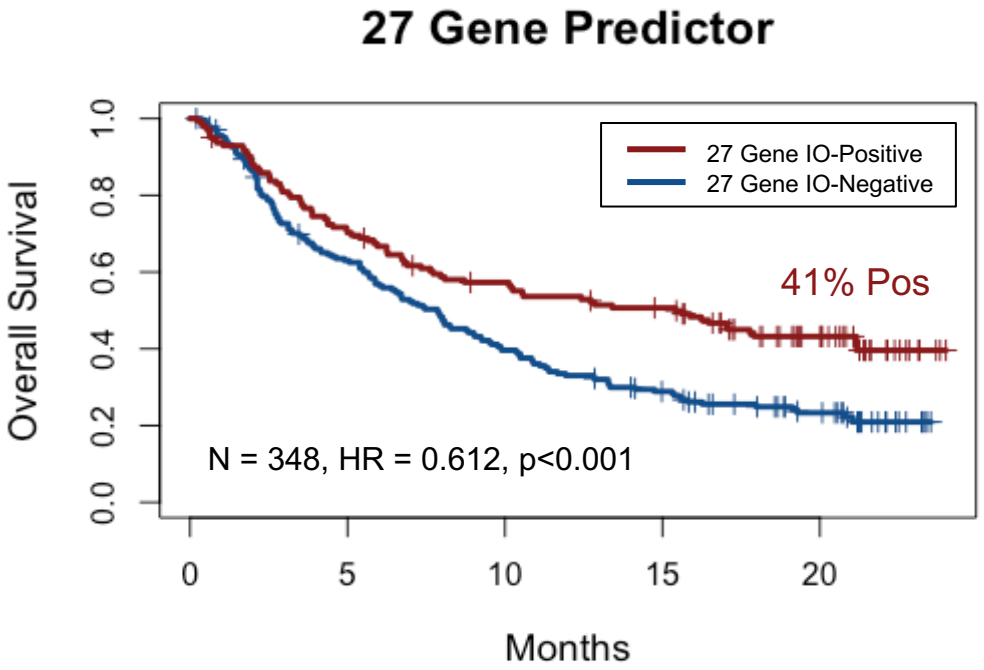
The assay was developed in TNBC and given a pre-defined threshold to allow for binary positive/negative calls.

It was then validated in:

- NSCLC (Ranganath, SITC, 2019)
- Neoadjuvant treatment of TNBC (Iwase, ASCO, 2020, *manuscript submitted*)

The (unchanged) algorithm and threshold were validated as a classifier on TCGA Bladder Cancer (AACR 2021, Poster #175)

Applying the 27 Gene Predictor to IMVigor210 – Results: Primary endpoint, OS (all patients)

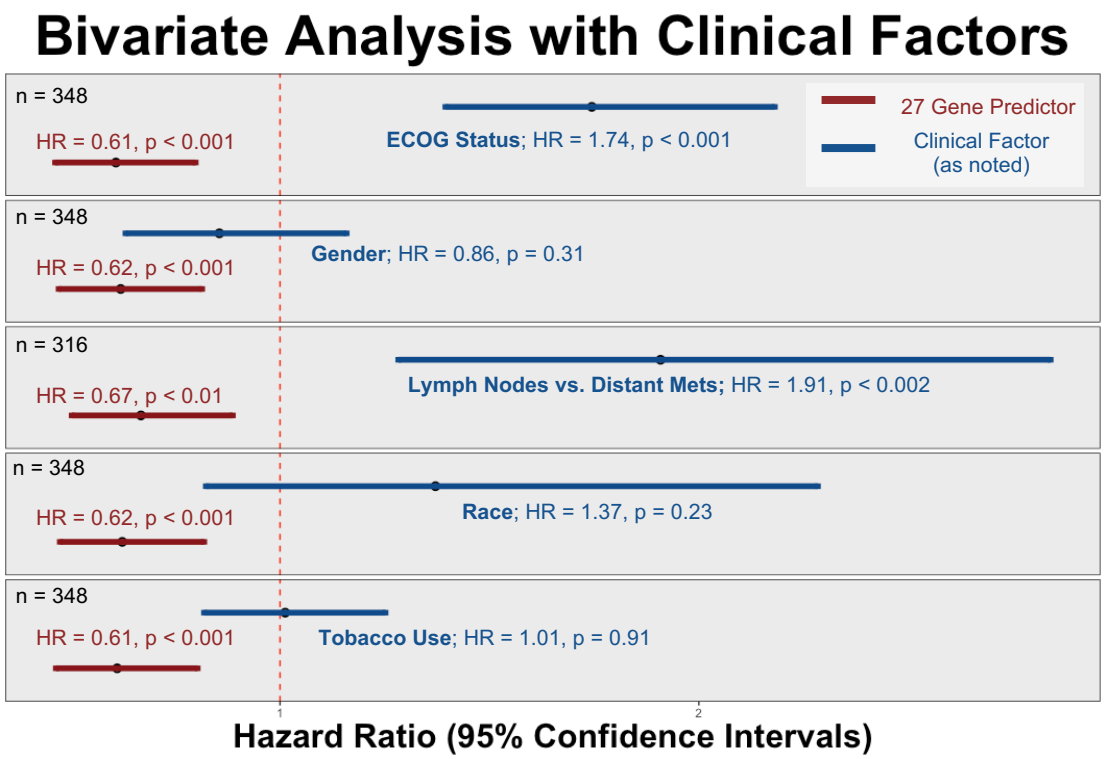


	Median OS (mos)	2 Year OS
27 Gene IO-Positive	15.4	39.6%
27 Gene IO-Negative	7.9	20.9%

Comparison to Clinical Trial Endpoint:
27 Gene Predictor met Primary Endpoint of IMVigor210 Trial (ORR > 10%):

32% ORR (24 - 41 % CI); Δ10% p < 0.001

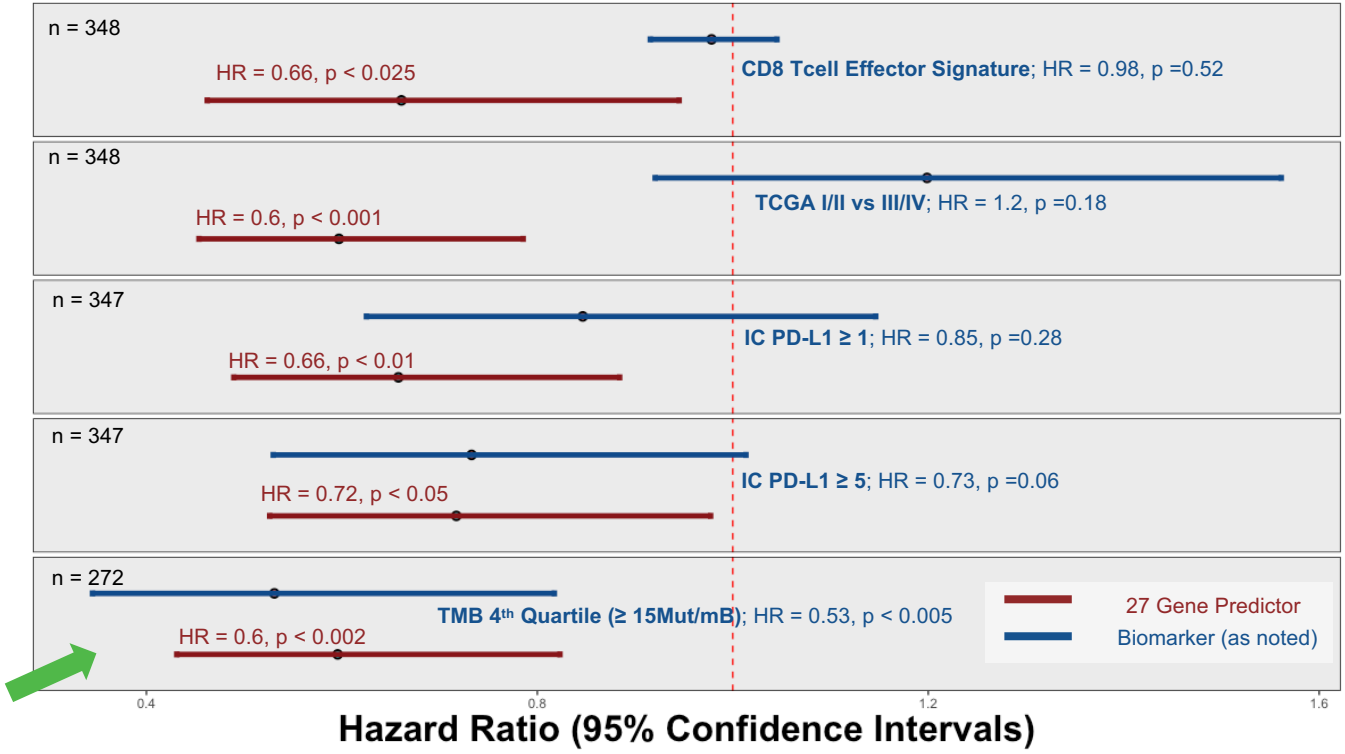
Independence From Clinical Factors



27 Gene Signature was independent of standard clinical factors

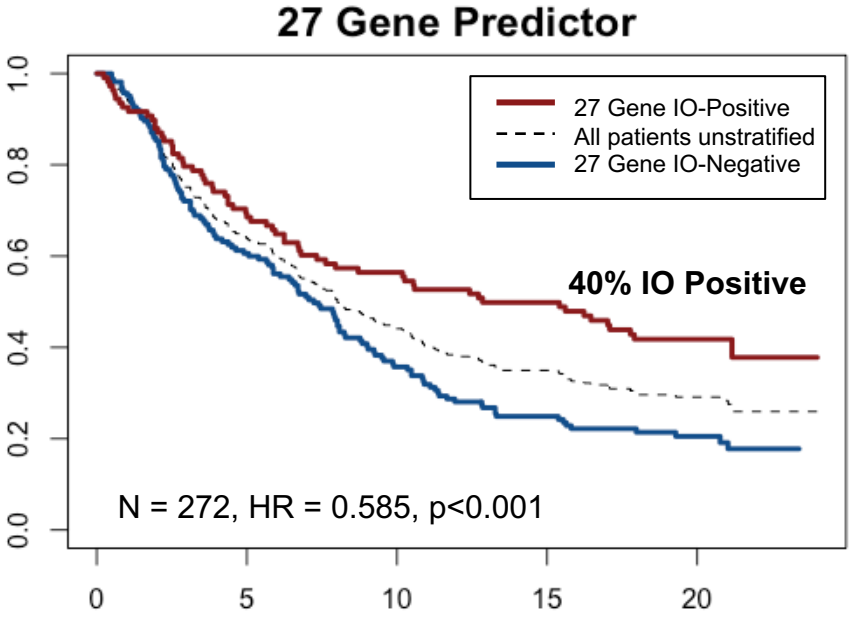
Independence from TMB and IC PD-L1 (Rosenberg, 2016; Balar, 2017)

Bivariate Analysis with Various Biomarkers



27 Gene IO Predictor – Results in Cohort 2
(Patients that Progressed on Platinum Treatment)

Focusing on the patients that progressed on platinum treatment (Cohort 2):



Results:

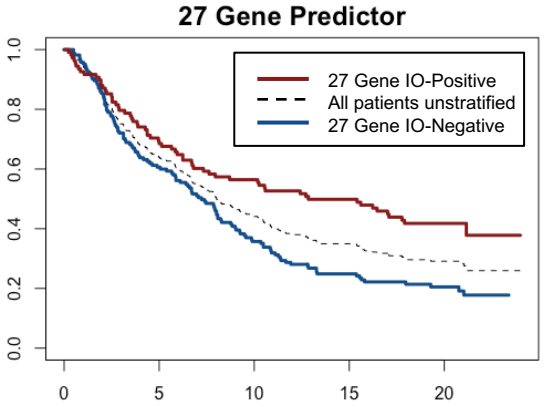
	n	%
27 Gene IO-Positive	108	40%
27 Gene IO-Negative	164	60%

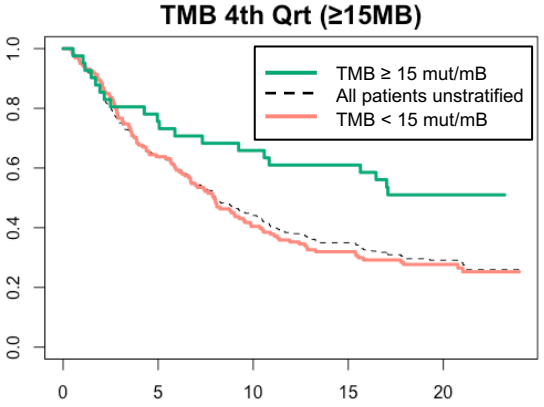
	Median OS (mos)	2 Year OS
27 Gene IO-Positive	12.9	37.8%
All Patients Unstratified	8.0	25.9%
27 Gene IO-Negative	7.2	17.8%

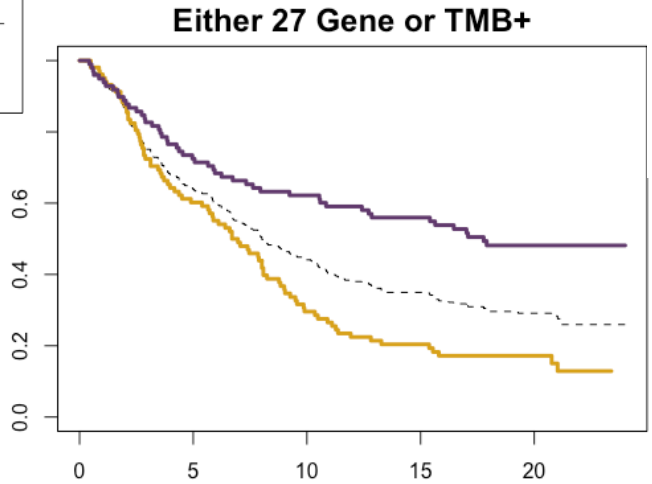
Combining the 27 Gene Predictor with TMB

Cohort 2:
Progressed on Platinum (n=272)

TMB Measure 1:
4th Quartile (≥ 15 mut/mB)





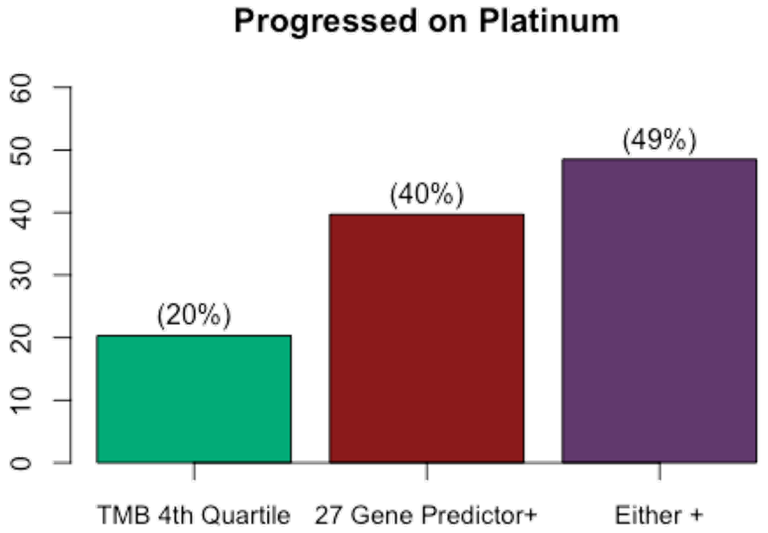


Identifying Additional Patients with 27 Gene Predictor – TMB ≥ 15 Mut/mB

Cohort 2: Progressed on Platinum (TMB+, n = 202)

TMB Threshold: 4th Quartile (≥ 15 mut/mB)

Results:	Median OS (mos)	2 Year OS
TMB 4th Quartile or 27 Gene+	17.8	48.1%
27 Gene +	17.8	47.1%
TMB 4th Quartile (≥ 15 Mut/mB)	NA	51%
Unstratified (w/TMB; n=202)	8.8	30.5%
Unstratified (all n=272)	8.0	28.6%
TMB 4th Quartile **AND** 27 Gene+ (11.9%)	17.08	49.0%



Adding the results of the 27 Gene Predictor to the TMB 4th Quartile population results in positive identification of 29% more patients

Conclusions

- The 27 Gene predictor:
  - Pre-specified endpoint – Identifying responders to Atezolizumab in overall survival (HR = 0.612, p<0.001)
  - Bivariate analyses demonstrated independence from other biomarkers and gene signatures
  - Shows the potential to identify additional patients who may respond to ICI therapy when combined with other biomarkers, notably TMB, in patients who progressed on platinum
- This represents the third tissue type (TNBC, NSCLC, and mUC) where the 27-gene predictor, using the same algorithm and threshold, has shown a significant association with response to immune checkpoint inhibitors
  - These studies included four different ICI agents (two anti-PD-L1 and two anti-PD1)
- Taken together, these data begin to establish the 27-gene predictor as a pan-cancer predictor of response to ICI therapy

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