UNDERSTANDING TUMOR BIOLOGY COMPLEXITY IN THE ADVANCED CANCER SETTING:
PreciGENE® platform predictions correlate with exceptional responses to cancer treatment

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BACKGROUND

Cancer is caused by an elaborate network of genetic and environmental factors. Novel high-throughput screening methods have demonstrated that tumors harbor many causative molecular alterations.

➤ **Targeting tumor-specific molecular alterations may increase treatment effectiveness and reduce iatrogenic toxicities.**

This molecular complexity makes the selection of treatment options for an individual difficult. While a myriad of anti-cancer drugs exists, the long-term efficacy of current standard-of-care regimens is still lacking.

➤ **New tools are needed to allow oncologists to quickly identify, amongst the many possible combinations, the regimens that best fit the patient's specificities and increase his/her chances of survival.**

OBJECTIVE

The focus of this study was to evaluate whether an advanced software platform using a personalized approach to oncology could predict the efficacy of systemic cancer therapies.

The PreciGENE decision-support platform integrates and analyzes patient's molecular data to provide a list of drug regimens targeting the distinct nature of his/her cancer.

Using proprietary databases of clinical evidences, the software identifies the functional impact of the aberrations observed and defines which one(s) can be pharmaceutically targeted. Relevant monotherapies and/or combination therapies are then ranked using a scoring system or 'matching score'.
Herein, we aimed at evaluating the accuracy of the PreciGENE scoring system using published cases of exceptional responders to anti-cancer therapy.

CureMatch's PreciGENE decision-support platform has been developed in collaboration with UCSD Moores Cancer Center and the San Diego Supercomputer Center. It is currently undergoing validation using retrospective data analyses and prospective clinical studies.

RESULTS

Can We Correctly Predict Cancer Therapies?

	Successful regimens	Unsuccessful regimens
Number of patients	70	
Age (median [range])	57 [29-84] years	
Gender (Female/Male)	39 / 31	
Cancer types	23	
Number of regimens	70 (35%)	132 (65%)
Single agent regimens	39 (56%)	73 (55%)
Combination regimens	31 (44%)	59 (45%)

Figure 1 – Patient demographics and description of the 202 treatment lines reviewed.
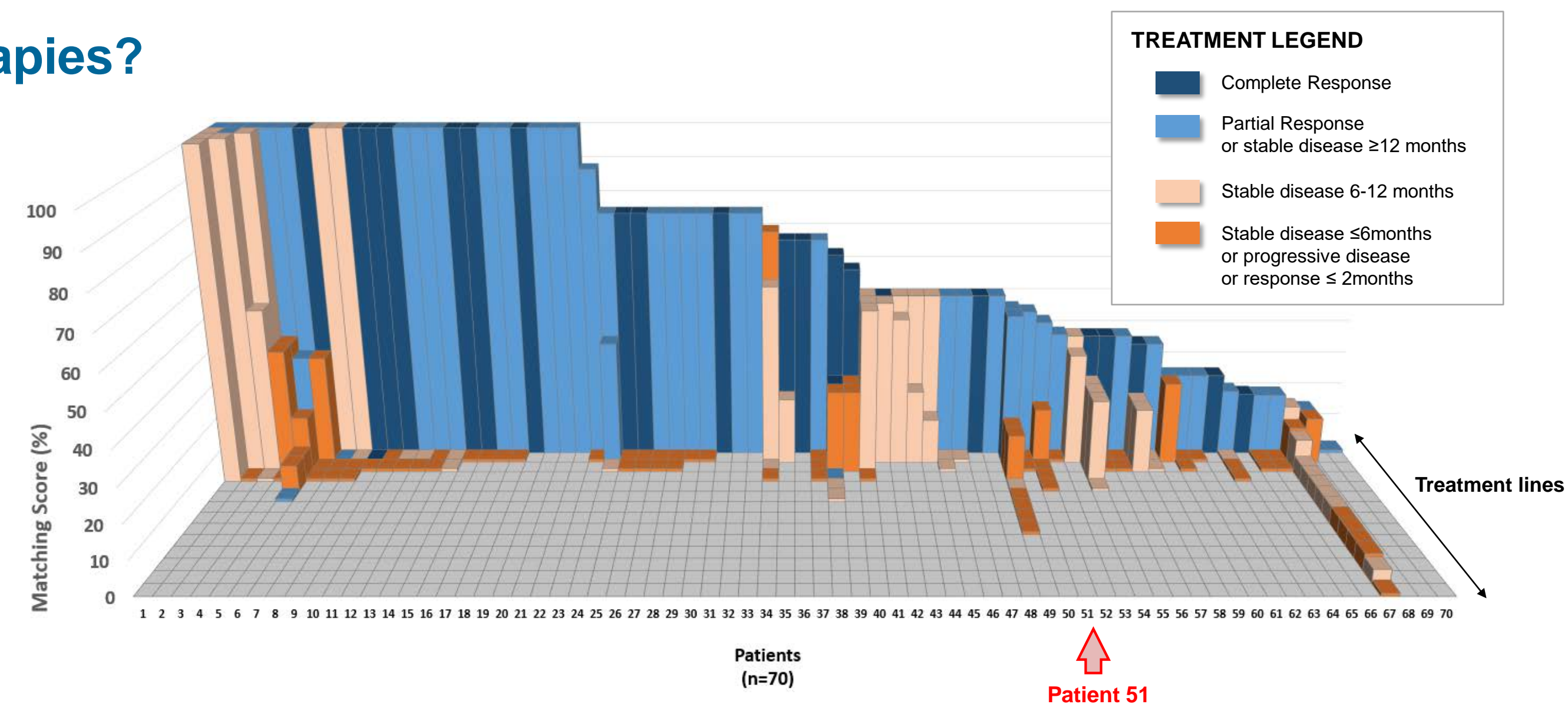

Figure 2 – Matching score distribution for the 202 treatment lines reviewed.
The 70 patients reviewed are represented on the X-axis of the 3-D graph. For each patient, columns/squares correspond to the various treatment regimens that each individual patient was treated with. The height of each column/square is proportional to the matching score retrospectively calculated. Patient 51 is described in Figure 3.
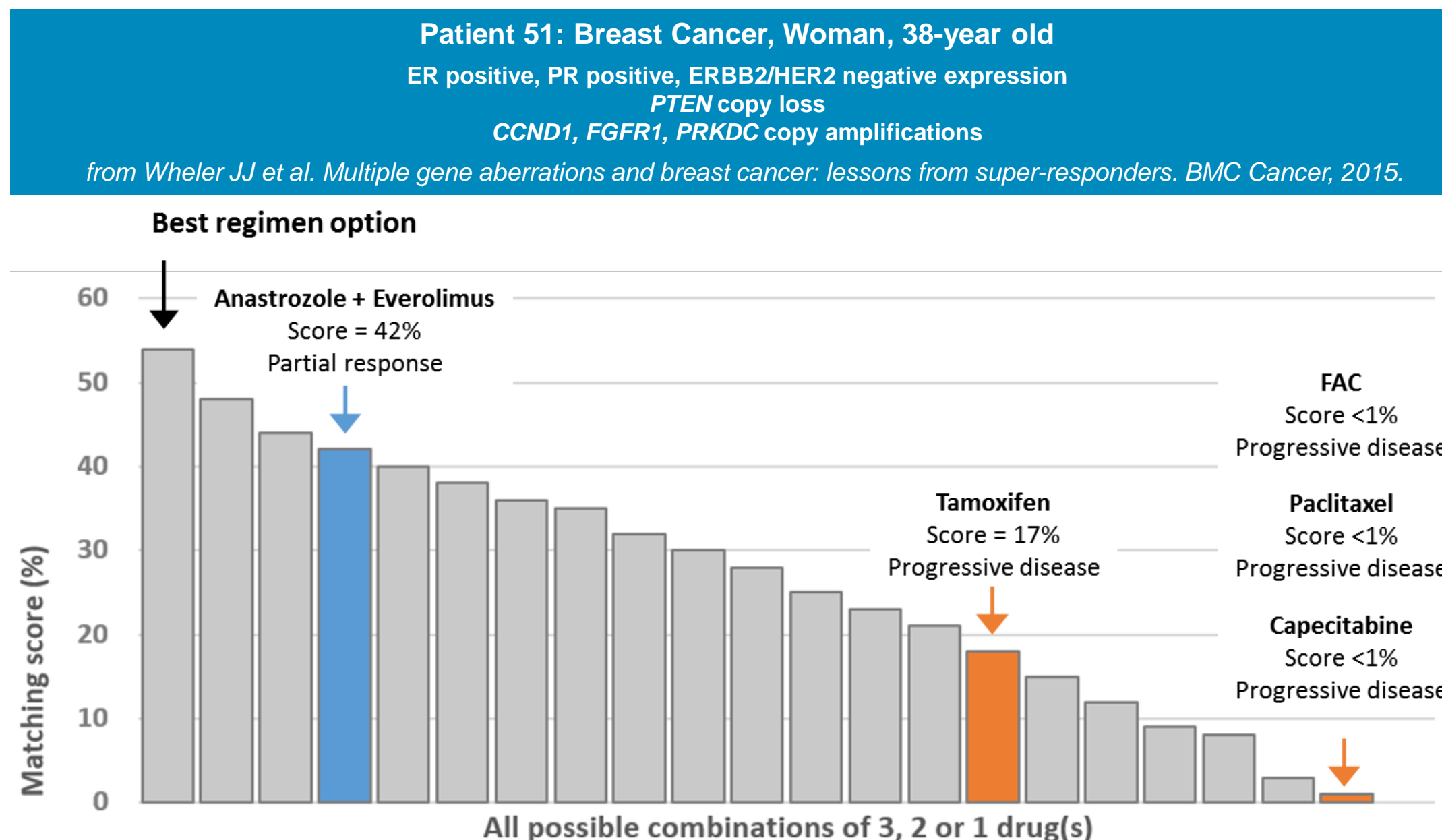
TREATMENT LEGEND
- Complete Response
- Partial Response or stable disease ≥12 months
- Stable disease 6-12 months
- Stable disease ≤6months or progressive disease or response ≤ 2months

Patient 51: Breast Cancer, Woman, 38-year old
ER positive, PR positive, ERBB2/HER2 negative expression
PTEN copy loss
CCND1, FGFR1, PRKDC copy amplifications
from Wheler JJ et al. Multiple gene aberrations and breast cancer: lessons from super-responders. BMC Cancer, 2015.

Best regimen option

Anastrozole + Everolimus
Score = 42%
Partial response

Tamoxifen Score = 17% Progressive disease

FAC Score <1% Progressive disease

Paclitaxel Score <1% Progressive disease

Capecitabine Score <1% Progressive disease

All possible combinations of 3, 2 or 1 drug(s)

Figure 3 – Comprehensive analysis of a breast cancer patient.
Regimens and molecular profile corresponding to patient 51 were entered into the PreciGENE decision-support platform and the corresponding matching score was computed.
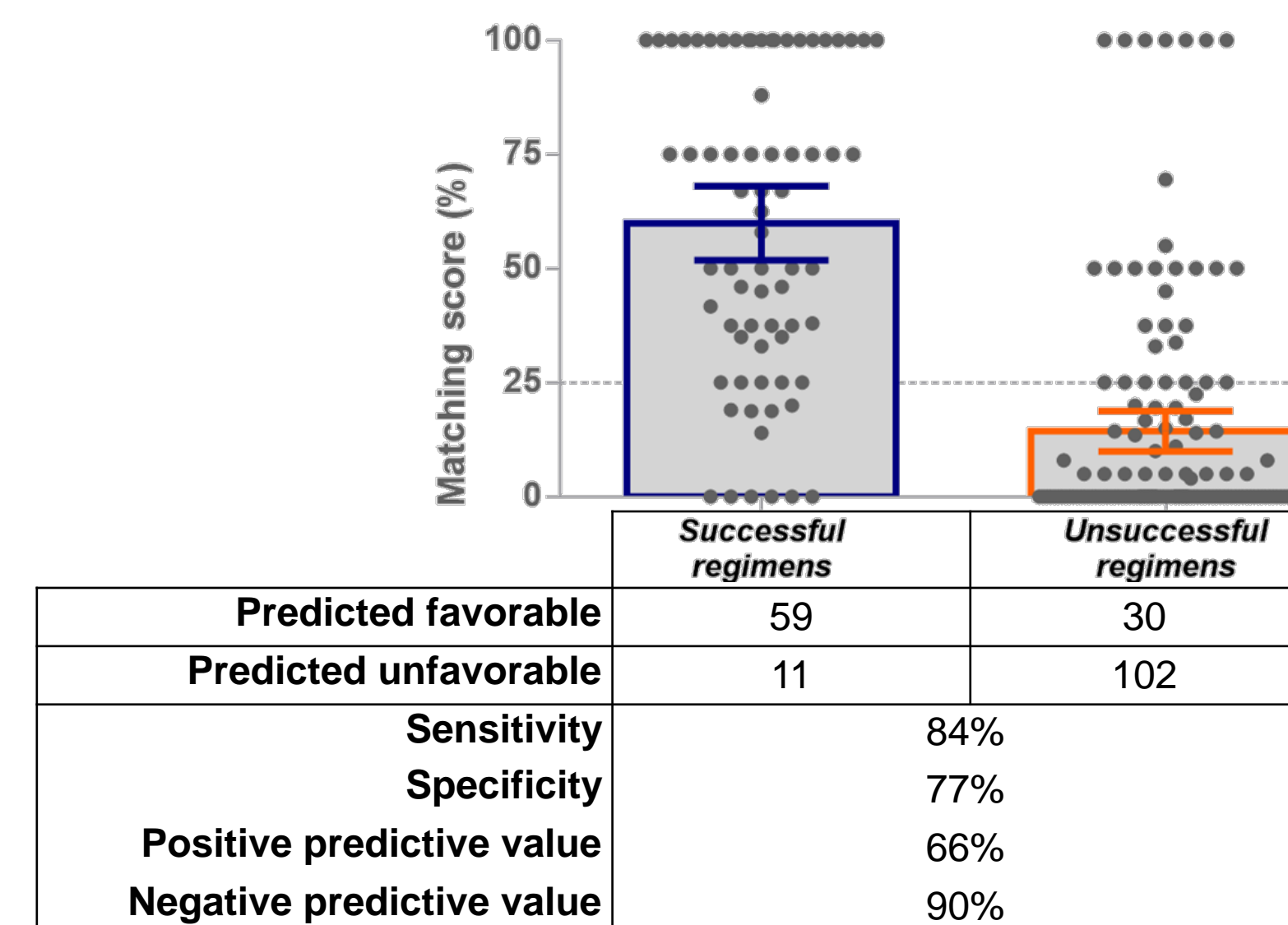

	Successful regimens	Unsuccessful regimens
Predicted favorable	59	30
Predicted unfavorable	11	102
Sensitivity	84%	
Specificity	77%	
Positive predictive value	66%	
Negative predictive value	90%	

Figure 4 – Matching score distribution between successful and unsuccessful regimens and performance evaluation of the decision-support platform.

METHODS

CONCLUSIONS

✓ The algorithm used by the decision-support platform correctly ranked the drug regimens received by 70 published cancer patients with available treatment outcomes and molecular profiling.

A total of 202 different treatment lines were evaluated, including prior treatments which failed to be effective in the individuals with exceptional responses.

✓ The matching scores obtained for regimens that led to a positive outcome were significantly higher than those obtained for regimens that failed (p<0.0001).

✓ Using a threshold of 25% (that optimizes sensitivity and specificity and has been selected using a ROC curve), the decision-support platform presented a sensitivity of 84% and a specificity of 77% for the prediction of the clinical response to anti-cancer treatment.

By integrating multi-disciplinary expertise, the PreciGENE computational platform empowers oncologists in their choice of successful therapeutic options.

Facilitating the application of Precision Oncology concepts in the daily practice not only provides significant increases in positive outcomes, but also improves the patient quality of life by reducing the burden of unsuccessful and unnecessary treatments.

The PreciGENE Analysis is currently available to oncologists and sequencing lab partners.