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Poster #5563

Ex vivo tumor testing platform for predicting clinical response to platinum-based therapy in high grade serous ovarian cancer patients

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VitroScan
PREDICTING TREATMENT OUTCOME

BACKGROUND

Precision medicine has brought effective novel therapy options over the past decades for cancer patients. However, treatment for high-grade serous ovarian cancer (HGSOC) is still based on platinum-containing chemotherapy. Approximately 30% of the patients with primary disease do not respond to this treatment, and the efficacy of systemic treatment drops steeply for patients with recurrent disease. We present the establishment of a novel chemo sensitivity score for ovarian cancer patients, using an ex vivo 3D tumor testing platform, that classifies the predicted patients' response to chemotherapy prior to the start of treatment.

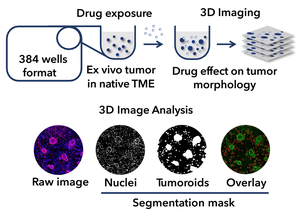


Figure 1: Assay overview, process from seeding to multiparametric image analysis

Table 1: Patient characteristics

Parameter	Data		
Age (mean, SD, range), years	67.5	8.8	41 - 80
Current diagnosis (n, %)			
- High-Grade Serous Ovarian Carcinoma	26	87%	
- Ovarian Adenocarcinoma	3	10%	
- Ovarian Mucinous Adenocarcinoma	1	3%	
Treatment (n, %)			
- Carboplatin / Paclitaxel	30	100%	
Sample origin (n, %)			
- Ascites	30	100%	
FIGO stage (n, %)			
IIIa	1	3%	
IIIc	21	70%	
IV	8	27%	
Surgery (n, %)			
- No surgery	10	33%	
- Interval debulking	19	63%	
- Unknown	1	3%	
BRCA status (n, %)			
- BRCA1 mutant	2	7%	
- BRCA2 mutant	1	3%	
- Wild-type	19	63%	
- Not tested	8	27%	
CA125 (mean, SD, range)			
- Baseline	2774	4792	140 - 25000
- Interval	505	879	12 - 3469
Interval CA125 measurement (n, %)			
- after 1 cycle	1	3%	
- after 2 cycles	11	37%	
- after 3 cycles	18	60%	
Interval in days (mean, SD, range)	56	26.5	19 - 170

METHODS

TUMOVCA trial: Patients with mucinous or HGSOC, eligible for platinum-based neoadjuvant chemotherapy (NACT), were included in the trial between 2019 and 2022 in the Netherlands (IRB P18.032). Clinical data was collected including CA125 levels at baseline and after 2-4 courses of NACT.

Ex vivo 3D tumor testing platform: Tumor clusters enriched from fresh ascites were embedded in hydrogel and exposed to first-line (carboplatin, paclitaxel) and second-line therapies (doxorubicin, gemcitabine, topotecan and olaparib). Assay plates were imaged in a high content screening 3D platform, see infographic above. Morphological features were extracted after image analysis and fitted as dose-response (Hill) curves.

Predictive model: A Bayesian linear regression model was trained on the area under the curve (AUC) of carboplatin and paclitaxel sensitivity in the assay to predict the clinical CA125 half-life for 30 patients. The result was classified according to clinical standards: strong response (CA125 normalization to 35U/ml), moderate response (at least 50% reduction of CA125) or insensitive (less than 50% reduction or increase). For each second-line treatment the top 25% strongest responding samples were classified as sensitive while the bottom 25% were classified as resistant samples.

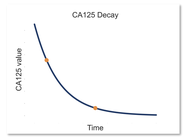


Figure 2: Example decay curve (blue), calculated based on two CA125 measurements (orange).

RESULTS

Assay performance: The technical success rate for ascites samples with sufficient tumor content is 89%. The assay duration is 2-3 weeks from receipt of the fresh tissue sample.
Predictive performance: The correlation coefficient between the predicted and actual CA125 half-life is 0.739 (R^2 = 0.55). This results in a classification accuracy of 80% (insensitive: 100% (n=2), moderate response: 80% (n=14), strong response: 80% (n=14)).
Response classification of other therapies: Out of the samples that showed a strong response to standard-of-care, 58% (8/14) responded to at least one second-line therapy. For the moderate responders and insensitive patients, these percentages are 29% (4/14) and 50% (1/2), respectively. For olaparib the equivalent results are strong responders: 36% (5/14), moderate responders: 21% (3/14) and insensitive: 0% (0/2).

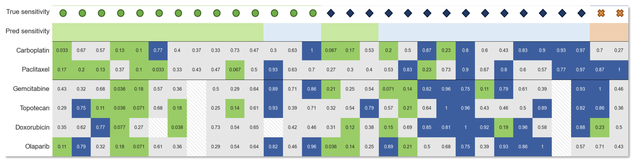


Figure 3: Relative (quantile) sensitivity of 30 patients to monotherapy treatments. Sensitive patients (green) are those with a bottom 25% ranking, while resistant patients have a top 25% ranking

CONCLUSION

The presented model based on ex vivo 3D tumor testing predicts clinical response to NACT with carboplatin and paclitaxel for mucinous and HGSOC patients. In parallel, relative sensitivity to other systemic therapies is quantified.

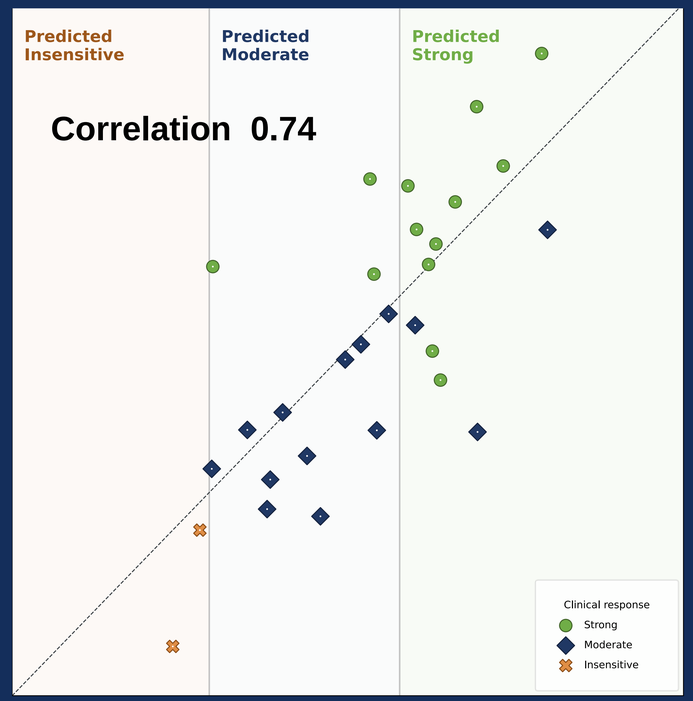
The platform enables better stratification of responders vs non-responders, and can support informed treatment decisions for first-line and second-line therapies. The value of integration of the chemo sensitivity score in the clinical routine will be assessed in an upcoming prospective trial for patients with suboptimal response and recurrent disease.

ONLINE POSTER

Leids Universitair Medisch Centrum
Radboudumc university medical center

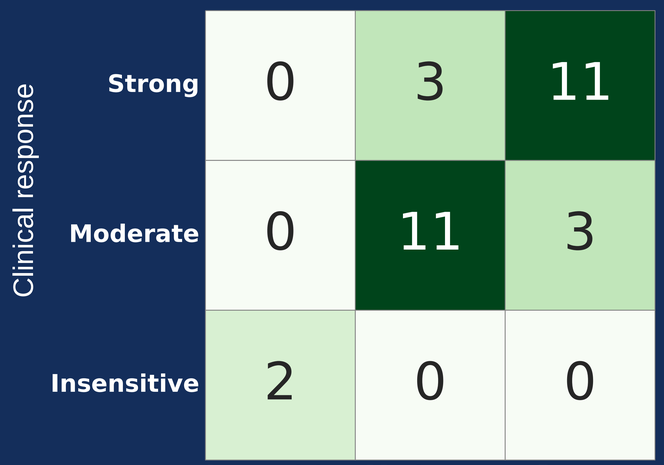
Ex vivo functional assay **predicts clinical response** to carboplatin-paclitaxel for **ovarian cancer** patients

Correlation



Response Classification

- according to clinical standard -



Accuracy 80%

Negative Predictive Value 81% - 100%

30% of the patients were classified as **strong responders** to other systemic therapy options

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