1104 IDENTIFICATION OF EFFECTIVE TREATMENT REGIMENS FOR OVARIAN CANCER USING TUMOR HISTOCULTURE PLATFORM

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Background The prognosis of ovarian cancer (OvCa) is poor, with a 5-year survival rate in patients of 59.60% (95% CI, 56.06–63.13).[1] Personalized treatment regimens could improve treatment outcome and quality of life. We developed the Farcast™ TruTumor Ovarian Cancer histoculture platform to predict response to therapies enabling personalized treatment options for every patient.

Methods Freshly resected OvCa tissue samples (n=10) along with matched blood were collected from consented patients. Tissue explants were generated and distributed into arms and cultured for 72 h. The functional fidelity of immune components was assessed by stimulating these with anti-CD3 (0.01 µg/ml) + Interleukin-2 (IL2, 100 µg/ml), or with Lipopolysaccharides (LPS, 1 µg/ml). Response was characterized through cytokine release assay and flow cytometry (n=3). Tumor cytotoxic response on treatment with Platin (Cisplatin:3.3 µg/ml, or Carboplatin: 37.1 µg/ml) and/or Taxane (Docetaxel:2 µg/ml, or Paclitaxel:2.7 µg/ml), or Nivolumab (132 µg/ml) was evaluated by quantifying the decrease in tumor content and/or increase in the tumor expression of cleaved caspase 3 (CC3).

Results At baseline OvCa samples (n=4) exhibited a higher proportion of lymphocytes (79.88±8.05%) than myeloid subpopulation, with a high Programmed cell death protein1, PD1 + T-cell population (43.13±11.97%). Baseline immune content in OvCa was lower in comparison to head and neck cancer but similar to renal cell cancer samples. Post-culture explants exhibited preserved tumor morphology with no significant changes across major immune cell sub-populations. Stimulation with anti-CD3+IL2 resulted in notable increase in proliferating (>2.5-fold) and active (>2.8-fold) cytotoxic-T cells across samples. Additionally, anti-CD3+IL2 stimulation led to substantial fold release of Interferon-γ (15.1±7) and Granzyme-B (2.5±1), while LPS stimulation induced higher fold release of Tumor Necrosis Factor-α (11.3±4.6) and Interleukin-10 (5.5±0.8) with respect to control.

OvCa cohort (n=7) receiving Platin and Taxane combination treatment, showed variable treatment response with six of the seven samples showing significant decrease in tumor content ($p<0.05$). The seventh sample that did not show response to combination treatment but exhibited significant fold increase in tumoral CC3 expression ($p<0.01$) with Cisplatin treatment.

Given the high PD1 expression at baseline, we attempted to check efficacy of Nivolumab (n=3). Effective masking of PD1 receptor indicated drug binding to target. Differential T-cell reinvigoration was observed across samples. None of the treated samples, however, exhibited a significant tumor cell cytotoxicity.

Conclusions The Farcast™ OvCa TruTumor platform facilitates simultaneous investigation with multiple drug treatment regimens enabling personalized treatment decision making for patients.

REFERENCE

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Ethics Approval The Institutional Ethics Committee (IEC) from the sample collection centers approved the protocol (protocol # FCB-PROTOCOL-01) and informed consent for participation in the approved study was obtained from every donor.

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