of the scalp with lymph node metastases and glucagonoma, respectively. Both patients remain on zalifrelimab with no evidence of disease progression. Additionally, durable disease stabilization was observed in a patient with spindle-cell sarcoma. Patients with chondrosarcoma and fibroblastic sarcoma progressed on therapy. Zalifrelimab was well tolerated with the most commonly reported treatment-related adverse events including fatigue, nausea, anemia, diarrhea and vomiting, consistent with the drug class. Most events were mild or moderate and resolved with standard treatments.

Conclusions Our data demonstrates the potential for Zalifrelimab to promote meaningful clinical benefit in difficult to treat tumors, including patients that progress on prior PD-1/PD-L1 therapy or chemotherapy. Notably, responses were observed in rare tumor types such as recurrent cutaneous angiosarcoma and glucagonoma. Treatment with zalifrelimab is safe and well tolerated in patients with advanced malignancies.

Trial Registration NCT03104699.

REFERENCE

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**Clinical trials completed**

**257** DEVELOPMENT OF A DIAGNOSTIC PLATFORM WHICH MATCHES THERAPIES TO THE TUMOR MICROENVIRONMENT DOMINANT BIOLOGY

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**Background** Tumor microenvironment (TME)-targeting agents such as anti-angiogenic therapies and check-point inhibitors (CPIs), have shown both promise and variability in effectiveness depending on the tumor type. For immune-targeting agents like CPIs, efforts to identify features or biomarkers that predispose responding patients include but are not limited to genomic stability, tumor mutation burden, and PD-L1 expression. Oncologie is developing a RNA-based platform that identifies subsets of patients based on multiple aspects of the biological processes (dominant biology) existing within the tumor microenvironment.

**Methods** RNA data from publicly available sources including microarray, RNASeq exome and whole RNA were analyzed with respect to gene signatures that describe four different microenvironmental phenotypes. Phenotypes were then evaluated for relationships to clinical efficacy endpoints. From these RNA signatures and driven by machine learning methodologies, drug-specific algorithms were developed and applied to retrospectively to clinical data. Comparative analyses were explored between gene signatures, commonly used biomarkers (eg. presence of microsatellite DNA, expression levels of PD-L1, etc) and within-patient metadata to better understand better how this approach can be utilized in prospective clinical studies.

**Results** Attributes in RNA expression identified using Oncologie’s platform have retrospectively characterized responders to CPIs or anti-angiogenic drugs, demonstrating a relationship between clinical response and biomarker positive and negative patient populations. Exploratory data summarizing the use of the this platform demonstrates its utility for enriching...
response to both immune- and angiogenesis-targeting drugs. Relative expression changes between archival and fresh biopsies demonstrate changes in the TME with time and/or following targeted therapy. Lastly, cross-tumor comparisons support a tumor-agnostic utility of this approach. Detailed comparisons of this biomarker approach relative to other available biomarkers will be presented for standard of care drugs and those in the Oncologie pipeline based on retrospective analyses.

Conclusions RNA based descriptors of biology may be a useful approach to enrich for response to targeted therapies whose mechanism of action is to modify the TME biology.

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258 SCIENTIFIC CORRELATIVES FROM LCCC 1525: A PHASE II STUDY OF A PRIMING DOSE OF CYCLOPHOSPHAMIDE PRIOR TO PEMBROLIZUMAB TO TREAT METASTATIC TRIPLE NEGATIVE BREAST CANCER

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Background In metastatic triple negative breast cancer (mTNBC), median progression-free survival (PFS) with chemotherapy alone is approximately 2–4 months1 and improvements with single agent checkpoint inhibitors (CI) are limited by modest response rates. Murine breast cancer models have demonstrated a role for intratumoral regulatory T cells (Tregs) in modulating response to CIs.2 A phase II clinical trial was conducted to test the hypothesis that a single, priming dose of cyclophosphamide prior to pembrolizumab would improve

Abstract 258 Figure 1 Gene set enrichment and immune gene signatures in preliminary RNA-Seq samples. Demonstrating pathways (A) and gene signatures (B) associated with B cell activation as significant in patients with clinical benefit on checkpoint inhibitor therapy

Abstract 258 Figure 2 Tumor genomic and immune features. A-B: Differential gene expression (A) and gene set enrichment (B) results in non-nodal tumor samples, by treatment response. Genes in (A) passing FDR correction (Benjamini Hochberg) are labeled and in red. C: Frequently mutated genes implicated in breast cancer, samples sorted by response. Raw tumor mutational burden is noted at the top of each sample column. Treatment response and tumor PAM50 subtype for each sample is listed at bottom of each column. D-E: Sample PD-L1 was not significantly associated with either clinical benefit (D) or response (E) to therapy (T-test; proportion of sample staining with 22C3 antibody). F-G: Immune gene signatures significantly associated with clinical benefit (F) and response (G) in non-nodal tumor samples