TPS2689 Poster Session

ELEPHAS-01, ELEPHAS-02 and ELEPHAS-04: Multi-institutional observational prospective clinical trials to assess the accuracy of an ex vivo live tumor fragment platform for predicting immunotherapy response.

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Background: Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment. However, existing FDA approved companion diagnostic biomarkers like PD-L1, dMMR/MSI-H and TMB have low accuracy in predicting response. Ex vivo cytokine profiling of live tumor samples has shown promise as an improved means of predicting response to PD-1 blockade (Voabil, et al. *Nat Med.* 2021), but this approach has been limited to tumor resections given the need for large amounts of tissue. Here we present three clinical trials that leverage a novel approach using limited tissue from a single core needle biopsy (CNB) (20 gauge or larger). A sequential ex vivo treatment strategy is used, eliminating the need for a separate control arm and addressing challenges with tumor heterogeneity, particularly in CNBs where tissue is limiting. Using a specialized instrument, CNBs are cut into live tumor fragments (LTFs) which are viable in culture and retain the native tumor microenvironment, enabling cytokine profiling in response to ICI treatment ex vivo. **Methods:** ELEPHAS-01 (NCT05478538), ELEPHAS-02 (NCT05520099) and ELEPHAS-04 (NCT06349642) are observational prospective clinical trials initiated to characterize the accuracy of this approach for predicting ICI response. Over 750 patients that are being considered for standard of care (SOC) ICI therapy in the metastatic/relapse or neoadjuvant setting will be enrolled (Table). Fresh live CNBs are collected prior to treatment start and processed within 24 hrs enabling prediction of results within 72 hrs of receipt. LTFs are treated using a strategy where control (IgG) and SOC ICI treatments are performed sequentially on the same tissue in a single well. Changes in the cytokine secretion rates are then compared between ICI and control to characterize immunotherapy response. Additionally, tissue viability and tumor content measurements are used to assess tissue quality. Clinical response is measured using pathologic response in patients receiving neoadjuvant ICI therapy, while RECIST v1.1 is used in all other patients. The primary objective of these trials is to determine the platform's ex vivo accuracy (e.g., sensitivity, specificity) for predicting clinical response to ICIs and comparing it to the accuracy of PD-L1, dMMR/MSI-H and TMB. Clinical trial information: NCT06349642, NCT05478538, NCT05520099. Research Sponsor: None.

	ELEPHAS-01 (Lung)	ELEPHAS-02 (Hoosier)	ELEPHAS-04 (Mayo)
Setting	Metastatic & recurrent	Metastatic & recurrent	Metastatic, recurrent & neoadjuvant
Tumor type	Lung	Bladder, kidney, colorectal, head and neck, lung, melanoma, endometrial	Metastatic/recurrent: lung, skin, esophageal, cervical, endometrial, colon, liver, kidney, bladder Neoadjuvant: breast—TNBC, lung
Enrollment as of 1/27/2025	26	44	20
Est. total enrollment	216	216	324
Clinical endpoints	RECIST v1.1	RECIST v1.1	RECIST v1.1 & Pathologic response at surgery