625 IMMUNE PRIMING IFX-HU2.0 PROMOTES ANTIBODY RESPONSES NECESSARY FOR ANTI-PD1 RESPONSES IN PD-1 REFRACTORY MELANOMA PATIENTS

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Background IFx-Hu2.0 is a plasmid encoding the streptococcal Emm55 protein formulated for transfection into mammalian cells. Previous work demonstrated that IFx-Hu2.0 stimulates adaptive and innate immunity without the associated rheumatological-promoting activities of serotyping streptococcal proteins. Our first-in-human study[1] showed that IFx-Hu2.0 monotherapy is safe and feasible for patients with melanoma refractory to anti-PD1-based therapies. We now report on correlative biomarker analysis from the study and the updated survival information to post-protocol anti-PD1-based treatment to understand why patients responded to anti-PD1-based treatments when they were previously refractory to such treatments.

Methods IFx-Hu2.0 was injected subcutaneously in patients with stage III/IV melanoma, and peripheral blood and tumor specimens were collected before and approximately 1-month post-therapy. All seven patients on trial had specimens available for correlative analyses. The Olink® Inflammation (INF, v.3022) and Immunooncology (IO, v.3111) panels were used to identify cytokines and chemokines in patients' plasma. The PEPperPRINT® assay detected IgG and IgM response to melanoma antigens and parts of the Emm55 peptide used in IFx-Hu2.0. RNA (pre and post-injection) from trial subjects was profiled using Nanostring® (PanCancer IO360 Expression Panel). The output of these assays was subjected to bioinformatics analysis using Ingenuity® Pathway Analysis software. The efficacy of progression on post-protocol anti-PD1-based therapy was recorded as the time to the subsequent treatment/need for subsequent treatment for progression.

Results Plasma analysis showed different increased cytokines for each patient, highlighting that IFx-Hu2.0 produces an individualized response. The PEPperPRINT assay demonstrated IgG and IgM antibodies directed against different melanoma and Emm55-directed antigens in the plasma post-study treatment across patients. However, multiple sequence alignment of peptides using the demonstrated common motifs of peptides in individual patients. Using bioinformatics analyses on mRNA data, a strong interferon response/DC migration/viral process-like immune response was observed in paired samples. Three out of four patients responded to subsequent anti-PD-1-based therapy after prior progression on such treatment. The updated clinical information for the three patients includes: stable disease that was resected after two years without recurrence at > 3.7 years, partial response (PR) lasting 1.1 years, and PR that was resected but then recurred at 1.5 years.

Conclusions Antigenic Emm55-derived peptides provoke individual immune responses via an antigen/interferon-dependent process in those patients with the longest survival after subsequent anti-PD1 treatment. Subsequent studies are being planned for the clinic.

REFERENCE

1. Markowitz J, Shamblott M, Brohl AS, Sarnaik A, Eroglu Z, Khushalani NI, Chen P-L, De-Aquino DB, Sondak VK, Tarhini AA, Kim Y, Pilon-Thomas S. Fx-Hu2.0 phase I first in human study for unresectable melanoma for an intralesional 'in-situ vaccine' approach. *Journal of Clinical Oncology* 2022;**40**(16_suppl):e21542.

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