1309TiP Trial in progress: First-in-human study of a novel anti-NY-ESO-1–anti-CD3, TCR-based bispecific (IMCnyeso) as monotherapy in NY-ESO-1/LAGE-1A-positive advanced solid tumours (IMCnyeso-101)

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Background: ImmTAC® bispecific molecules are unique TCR–anti-CD3 agents that redirect T cells against intracellular antigens, in contrast to antibody-based therapies, which are limited to extracellular antigens. The most advanced ImmTAC, tebentafusp (IMCgp100), against melanocyte-associated lineage antigen gp100, has shown monotherapy responses in advanced melanoma, a solid tumor. In contrast, bispecific antibodies have shown activity in hematologic cancers but appear less active in solid tumors. ImmTAC molecules recognize a specific peptide presented on a defined Class I HLA molecule via an affinity enhanced, engineered, soluble TCR. Through the addition of an anti-CD3 scFv domain fused to the TCR targeting domain, an ImmTAC can redirect T cell activity against cancer cells, regardless of the specificity of the T cell. IMCnyeso is an ImmTAC against NY-ESO-1/LAGE-1A, which are cancer testis antigens expressed in a variety of solid malignancies, but with very low or absent normal tissue expression.

Trial design: IMCnyeso-101 is a multi-center, open-label, first-in-human study of IMCnyeso in HLA-A*02:01-positive patients with NY-ESO-1- and/or LAGE-1A-positive advanced NSCLC, synovial sarcoma, melanoma, or urothelial carcinoma. The study includes dose escalation (Bayesian logistic regression models) and expansion for IMCnyeso monotherapy (QW), followed by expansion into indication specific arms to test for signs of efficacy in defined patient cohorts. Primary endpoints are establishing MTD/RP2D and safety and tolerability. Secondary endpoints include: characterization of PK and ADA, efficacy by RECIST v1.1 (PFS, ORR and DOR) and OS. The dose escalation portion of the study is in progress. The trial continues to enroll; NCT number NCT03515551.

Clinical trial identification: NCT03515551.

Legal entity responsible for the study: Immunocore.

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