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Safety, efficacy and biology of the gp100 TCR-based bispecific T-cell redirector, IMCgp100 in advanced uveal melanoma

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Uveal melanoma (UM) is characterized by low PD-L1 expression, low mutational burden and limited efficacy with checkpoint inhibition. IMCgp100 is a bispecific T cell redirector with an affinity-enhanced TCR recognizing gp100 and an anti-CD3 scFV. Two phase 1 trials evaluated safety, pharmacokinetics, pharmacodynamics and efficacy for IMCgp100 administered IV weekly in HLA-A2 patients: a first in human study enrolling patients with melanoma including a cohort with advanced UM (n=16) and a second study of an intra-patient dose escalation (IE) regimen for pts with advanced UM (n=19). The intra-patient escalation regimen was designed during the course of the FIH Phase 1 study to mitigate T cell-mediated toxicities that were observed. Endpoints of the two studies included overall response rate by RECISTv1.1, progression free survival and overall survival. The safety profile of IMCgp100 was consistent between trials with the most frequent adverse events including rash, pruritus, and edema. Durable, objective responses were observed in both trials. Within 3 doses of IMCgp100, immunofluorescence studies reveal an influx of PD-1+/CD8+ T cells in the tumor bed with PD-L1 expression. Peripheral cytokines indicate activation of immune responses within 24 hours of the first dose. These studies demonstrate preliminary immune biology, safety and promising efficacy in advanced UM.

Biography

Christina Coughlin joined Immunocore as Chief Medical Officer in April 2015. She has extensive experience in Oncology Drug Development, with expertise in both clinical development and translational medicine. Prior to joining Immunocore, she led two early development programs at Novartis in checkpoint inhibition and PI3 kinase inhibition. She has also served as International Project Team Leader at Morphotek Inc., the monoclonal antibody company acquired by Eisai Co. Ltd in 2007, where she led the early clinical development team responsible for monoclonal antibody development against novel targets. She graduated with an MD and PhD from the University of Pennsylvania, where she studied patient responses to tumour antigens with Dr. Robert Vonderheide in the division of Translational Research under the direction of Dr. Carl June.

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