

A phase Ib, open-label trial of MOv18 IgE in patients with advanced ovarian cancer.

Rebecca Kristeleit, Bristi Basu, Rowan Miller, Jose Luis Iglesias, Andrew Calam, Rachel Nirsimloo, Clare E. Green, Axel Walther, Chris Twelves, James F. Spicer; Department of Oncology, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; University of Cambridge, Cambridge, United Kingdom; University College Hospital-London, London, United Kingdom; APEX Oncology Consulting, Inc., Oakville, ON, Canada; Epsilogen, London, United Kingdom; Edinburgh Cancer Centre, Edinburgh, United Kingdom; Southampton University NHS Trust, Brockenhurst, United Kingdom; University Hospitals Bristol, Bristol, United Kingdom; Leeds Institute of Molecular Medicine, University of Leeds, Leeds, United Kingdom; King's College London, London, United Kingdom

Background: All antibodies currently approved for cancer therapy are monoclonal IgGs. MOv18 IgE is a first-in-class therapeutic IgE antibody to have entered the clinic, successfully completing a Phase I trial in patients with advanced solid tumours. MOv18 IgE targets folate receptor alpha (FRA), an antigen present on a variety of cancers including ovarian, endometrial, lung and triple negative breast cancer. In the first-in-human Phase I trial, MOv18 IgE was well tolerated (up to 12 mg), with urticaria the most frequent toxicity [Spicer, J., *et al. Nat Commun* 14, 4180 (2023)]. These results demonstrated the potential of MOv18 IgE as an anti-cancer therapy supporting further clinical development. MOv18 IgE's unique mechanism of action includes high affinity binding to its main cognate receptor, FcεR1, enabling immunosurveillance and potent myeloid cell driven tumour FRA killing. Additionally, IgE antibodies drive modulation of the tumour immune microenvironment to a more pro-inflammatory phenotype, increasing intra-tumoral levels of activated T cells and tumour killing macrophages. **Methods:** EPS101-10-02 is a two-part, Phase Ib, open-label, dose escalation and expansion trial in patients with PROC, whose disease has progressed after ≤ 4 prior regimens of anti-cancer therapy. Tumours must express FRA at $\geq 5\%$, (1+, 2+ or 3+ membrane staining on at least 5% of tumour cells by IHC using the BN3.2 antibody), and patients must have a negative basophil activation test to stimulation with MOv18 IgE prior to Cycle 1, Day 1. Approximately 45 patients with measurable disease will be recruited. MOv18 will be given by IV infusion (starting dose 3 mg) on Days 1, 8 and 15 of a 21-day cycle. Treatment will continue until disease progression, unacceptable toxicity, withdrawal of consent or death. A range of translational endpoints will be evaluated. Primary objectives are to evaluate the safety and tolerability of MOv18 IgE and make a preliminary assessment of efficacy in PROC. Clinical trial information: NCT06547840. Research Sponsor: None.