Background MRx0518 is a novel, human gut microbiome-derived, single-strain, live biotherapeutic in clinical development for treatment of solid tumours. Preclinically, MRx0518 induced broad immunostimulatory activity and demonstrated anti-tumorigenic effects in a range of murine tumor models. MRx0518 increased CD4+ and CD8+ T cell and NK cell tumor infiltration and decreased Tregs. Activation of tumour TLR5 was observed and linked to the bacterial flagellin moiety, which was shown to strongly induce NFκB, cytokine responses and IFNγ + CD4+ and CD8+ T cells.

Methods Heavily pre-treated patients refractory to ICIs were enrolled from March 2019 to March 2020. Patients had experienced at least SD from previous ICI (monotherapy or combination) but eventually progressed as confirmed by two radiological scans ≥4 weeks apart in the absence of rapid clinical progression and within 12 weeks of last dose of ICI. Patients were treated with 1 capsule of MRx0518 (1 × 10^{10} to 1 × 10^{11} CFU) BID and pembrolizumab (200 mg every 3 weeks) for up to 35 cycles or disease progression. Tumour response was assessed every 9 weeks per RECIST 1.1. The primary objective was to evaluate safety of the combination by monitoring toxicities in the first cycle of treatment. Secondary objectives were to evaluate efficacy via ORR, DOR, DCR and PFS.

Results In Part A, patients with mRCC (n=9) and mNSCLC (n=3) were recruited. At data cut-off (21 Aug 20), 5 patients remain on study treatment. 83% of patients were male and 17% were female. Median number of prior lines of therapy was 3. 10 patients received nivolumab previously (83%), one received avelumab (8%) and one received pembrolizumab and nivolumab (8%). 83% of patients had experienced SD as best response to prior ICI and 17% had PR as best response. Of 6 patients with available PD-L1 results, 5 had a positive CPS/TPS (>1) and 1 negative (<1). The combination shows a positive safety profile with no treatment-related SAEs or toxicity-related drug discontinuations. No increase in irAEs has been reported.

On study treatment, 2 RCC patients and 1 NSCLC patient experienced a PR, with an additional 2 RCC patients experiencing durable SD (6 and 13 months), a protocol defined DCR of 42%. Median PFS is 2.14 months at data cut-off (table 1).

Conclusions This data represents first-in-class proof of concept for a live biotherapeutic in an oncology setting. The combination was tolerable and there were preliminary signals of efficacy. Part B (phase II) in NSCLC, RCC and bladder cancer is ongoing.

Trial Registration www.clinicaltrials.gov NCT03637803

Ethics Approval This study was approved by University of Texas MD Anderson’s Institutional Review Board; approval ref. 2018-0290