A phase I/II trial of live biotherapeutic MRx0518 in combination with pembrolizumab in patients refractory to immune checkpoint inhibitors

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MRx0518 is single strain Live Biotherapeutic product (LBP), a highly purified, single-strain bacterium of the Enterococcus genus, selected for development in the treatment of solid tumours for its strong immunostimulatory activity.

RATIONAL

• Clinical responses to immunotherapies such as anti-PD-1 antibodies can be profound, however responses vary, and many patients experience a decline in efficacy over time - secondary resistance may develop.
• Oral LBP MRx0518 may re-engage the antitumor effect of anti-PD-1 therapy after resistance has developed.

STUDY DESIGN

A phase I/II, open-label, safety and preliminary efficacy study of MRx0518 in combination with pembrolizumab in patients with advanced malignancies who have progressed on PD-1/PD-L1 inhibitors.

ELIGIBILITY CRITERIA

• Eligible patients will have advanced and/or metastatic or recurrent solid tumors including renal cell carcinoma (RCC), non-small cell lung cancer (NSCLC), bladder cancer, triple-negative breast cancer, head and neck squamous cell carcinoma or microsatellite instability-high/mismatch repair deficient tumours.
• Eligible patients are refractory to immune checkpoint inhibitors (ICIs). This is defined as having an initial benefit from PD-1 pathway targeting ICIs but developing disease progression confirmed by two radiological scans ≥4 weeks apart, in the absence of rapid clinical progression, and within 12 weeks of last dose of ICI.
• Eligible patients have failed to respond to standard therapy or have no appropriate therapy options known to provide clinical benefit.

STUDY EVALUATIONS

Tumour response is assessed every 9 weeks per RECIST v1.1. After first evidence of progression, patients may continue with treatment and are assessed by iRECIST.

Safety and tolerability will be evaluated through the collection of adverse events, ECOG performance status, physical examinations, vital signs, blood chemistry and hematology and function tests.

STUDY STATUS

• Part A of the study is complete. 9 RCC and 3 NSCLC patients were evaluated for safety of the combination therapy.
• The Cycle 1 data was assessed by the Safety Review Committee and it was determined appropriate to proceed to Part B as no dose-limiting toxicities were reported.
• Part B is now recruiting up to 120 additional patients at 5 US centers.
• Ongoing study read-outs will determine future clinical development of the combination.

For additional information on the completed phase I see poster 283

The study is sponsored by 4D pharma plc. For more information, contact clinicaltrials@4dpharmaplc.com

Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA provided pembrolizumab for the study

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