

## Clinical Trials In Progress

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**A PHASE 1 STUDY TO CHARACTERIZE THE SAFETY AND TOLERABILITY OF MP0317, A TUMOR TARGETING FAP DEPENDENT CD40 AGONIST DARPIN, IN PATIENTS WITH RELAPSED/REFRACTORY SOLID TUMORS**

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**Background** The development of CD40 agonists in immunoncology has been hampered by dose-limiting toxicity (DLT) mainly caused by systemic CD40 activation and peripheral target-mediated drug disposition. By targeting fibroblast activating protein (FAP), our FAP/CD40 directed DARPIn, MP0317, selectively activates CD40 within the tumor microenvironment, while precluding CD40 activation in the periphery. Here we present emerging data from the first-in-human trial (NCT05098405).

**Methods** This is a Phase 1, first-in-human, multicenter, open label, dose escalation study followed by a safety expansion part, evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and preliminary antitumor activity of MP0317 in adult patients with advanced solid tumors. The dose escalation scheme uses an adaptive Bayesian logistic regression model guided by the escalation with overdose control principle to determine the recommended dose. Up to 6 cohorts receive intravenous MP0317 3-weekly until disease progression, unacceptable toxicity, or other discontinuation criteria are met. Dose selection was guided by a translational PK/PD model that accounted for baseline FAP and CD40 expression levels and turnover rates.

Primary endpoints are incidence of DLTs and adverse events. Secondary and exploratory endpoints include PK/PD parameters, response rate (per RECIST and iRECIST), progression free and overall survival.

**Results** At time of submission, cohort 4 was enrolled, and cohorts 1-3 had completed the study, with no DLT observed. The most frequent AE were grade 2 infusion related reactions in 3/12 dosed patients.

The 7 patients in cohorts 1-3 received  $\geq 2$  (range 2-8) doses (range 0.03–0.3 mg/kg) of MP0317 and completed the 28-day DLT period. Preliminary PK data show sustained MP0317 serum levels across the dosing interval with evidence of target-mediated drug disposition.

Exposure in the tumor was confirmed with MP0317 co-localizing with FAP and CD40 in 3 out of 5 evaluable paired biopsies. No systemic toxicities were observed and there were no signs of systemic CD40 activation based on circulating PD markers and immunophenotyping data. A PD signal consistent with a tumor-localized myeloid cell activation was observed in cohort 3. Although limited clinical efficacy is expected in monotherapy setting, one heavily pre-treated patient maintained stable disease for 8 cycles.

**Conclusions** The preliminary clinical and biomarker data provide early evidence of the tumor-targeted CD40 activation mechanism of action of MP0317. As of submission, no DLTs had been observed. Enrollment in dose cohorts covering the projected therapeutic dose range is ongoing to further characterize MP0317 mechanisms of action and safety profile.

**Trial Registration** NCT05098405 and EudraCT : 2020-005516-22

**Ethics Approval** This study received ethics approval in France from ETHICS COMMITTEE SUD-OUEST ET OUTRE-MER II initially on 23 July 2021 (and most recently on 27 June 2022) (Dossier: 21.00452.000006) and in The Netherlands from NedMec Medisch-Ethische Toestingscommissie initially on 1 September 2021 (METC21.0653/M21MPA) and most recently on June 10, 2022, (PE/mk/22/500340). All Patients gave written informed consent before taking part in the study. **Consent** N/A at this point

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