immunotherapy of cancer

IMPACT STUDY: A SUBGROUP OF METASTATIC COLORECTAL CANCER PATIENTS WITH VERY PROLONGED DISEASE CONTROL UNDER MAINTENANCE THERAPY WITH THE TLR-9 AGONIST MGN1703


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Aim: The IMPACT trial was conducted to assess the clinical efficacy, safety, and immunological effects of the immunomodulator MGN1703, a potent TLR9 agonist, at the dose of 60 mg subcutaneously twice weekly as switch maintenance after first-line induction therapy in mCRC.

Methods: In the double-blind placebo-controlled phase 2 IMPACT trial patients with mCRC and disease control after induction with 1st-line chemotherapy +/- bevacizumab were included. The trial was prematurely closed after randomization of 59 patients. The final analysis conducted in 2013 showed a superior effect of MGN1703 compared to placebo; the hazard ratio (HR) for the primary endpoint PFS on maintenance was 0.55 (p = 0.041) by local investigator assessment and 0.56 (p = 0.070) by independent radiological review. Three responses were observed in the MGN1703 arm during the study, two of them appearing as late as 9 months after the start of treatment. At time of study closure 4 patients (3 responders to MGN1703 and one patient in CR after induction chemotherapy) were still free of progression and continued MGN1703 treatment.

Results: As of April 2014, 3 patients are still receiving MGN1703 monotherapy being on treatment for more than 32, 36, and 40 months. One of the patients with a response to MGN1703 eventually progressed after 17 months on treatment. No SAE were reported during the compassionate use programs. Exploratory analyses of pretreatment characteristics identified patients with normal CEA (HR of 0.07; p < 0.0001) and objective response (HR of 0.39; p = 0.005) at the end of induction chemotherapy to benefit the most from maintenance with MGN1703. Interestingly, the presence of activated NKT-cells (CD3+/CD56+/CD69+) also appears to predict a benefit, possibly linked to the activation status of the immune system before receiving MGN1703.

Conclusions: We provide preliminary evidence that MGN1703 achieved very prolonged disease control in some patients without causing relevant toxicity. IMPALA, a large international phase 3 study, aims to confirm the role of MGN1703 as first-line switch maintenance in mCRC patients with an objective response to induction chemotherapy.

Disclosure: M. Schmidt: M.S. is an employee of Mologen AG. All other authors have declared no conflicts of interest.