Background
PolyPEPI1018 is an off-the-shelf, multi-epitope peptide vaccine against CRC, containing 12 immune epitopes encoded by 7 conserved cancer antigen epitopes frequencly expressed in CRC, as well as a set of additional epitopes. Here we report the results of the phase I study of PolyPEPI1018 vaccine as an addition to standard of care treatment in patients with advanced colorectal cancer.

Methods
Patients were assigned to regimens of Msi2-Msi3 in the first-line setting were vaccinated with PolyPEPI1018 just after the transition to maintenance therapy with a fluoro-uracil-based and a targeted agent (bevacizumab). (Part A: n= 8, 4 doses, GOG). Primary endpoints were safety and immuno-activity. Multiple analyses of vaccine-induced immune responses in blood and tumor were conducted. Both immune response and clinical benefit were assessed using the analogous IHC-prognostic determined from patients' salves sample.

The vaccine was well tolerated, most common side effects were transient skin reactions and flu-like symptoms. No vaccine-related SAE occurred. 60% of patients had vaccine-specific CD8+ T-cell responses, 90% of patients showed a CD4+ T-cell response against at least 2 of the 7 vaccine antigens, 30% of vaccine-specific CD8+ T-cell responses were measured in patients. 0.5+ CD4+ T-cell responses were measured in 60% of patients, as well as increased frequencies of CRC-reactive, polyfunctional, circulating CD8+ and CD4+ T-cell responses. Among the 11 patients, 3 patients had objective tumor responses according to RECIST v1.1, one of them a radiological single and 2 of them 3 radiological responses. For the Part of the study, the Objective Response Rate (ORR) was 26.3% (10/38), with 7 patients having a novel antigen-specific CD8+ T-cell responses against multiple antigens. Notably, one patient had emergency complete tumor shrinkage of 3 out of 3 target lesions and partial tumor shrinkage in 1 lesion after 20 weeks of treatment, qualifying for curative surgery. Median duration of disease control was 67% (4/6). Notably, one patient experienced complete tumor shrinkage on 2 of 3 target lesions and partial shrinkage on the third lesion. Median tumor shrinkage was observed at 3 months. All patients were followed up to 38 weeks. Median PFS (m) 9 (95%CI 6.3-11.5) (Not reached during the study). The 10 month PFS was 50% (9/18). Predicated vaccine antigen-specific CD8+ T cell responses were confirmed in vitro with a PPV of 79% (95% CI 59-95). The trial is being amended to enroll additional patients.

Conclusions
Vaccination was safe and well-tolerated and demonstrated evidence of immunological and clinical activity in Msi2-Msi3 mCRC. In addition puzzle predictive immune responses induced treatment benefit, which supports further development of a companion diagnostic together with the vaccine.