**441P** A study of vemurafenib and cetuximab in combination with FOLFIRI for patients with BRAF V600E-mutated advanced colorectal cancer (NCT03727763): Preliminary results


Department of Medical Oncology, Second Military Medical University, Shanghai, China

**Background:** The prevalence of BRAF V600E in colorectal cancer (CRC) was about 10%. Despite recent advances, BRAF V600E mutant CRC is still a challenge with a low response rate and suboptimal survival. Here we reported the safety and preliminary anti-tumor activity of vemurafenib and cetuximab in combination with FOLFIRI for BRAF V600E-mutated advanced CRC patients.

**Methods:** In this single-arm, single-center trial, we are currently in enrollment of patients with BRAF V600E-mutated, RAS-wild type advanced CRC. Patients received vemurafenib 960mg orally every 12 hours, cetuximab 500mg/m² in combination with FOLFIRI, consisting of irinotecan 180mg/m² 2-hour intravenous infusion, leucovorin 400mg/m², 5-fluorouracil (5-FU) 400mg/m² intravenous injection on day 1, followed by a 46-hour continuous infusion of 5-FU (2400 mg/m²). The primary objective was to measure the objective response rate (ORR). And the secondary objective included safety, progression-free survival and overall survival.

**Results:** 18 patients were enrolled in this study and 16 patients completed at least 3 sessions of treatment for efficacy assessment. The ORR was 81.3% with 2 complete response (CR) and 11 partial response (PR). The disease control rate (CR+PR+SD) was 100%. Four patients receiving the treatment at second or third line, 5 patients (1 CR, 4 PR) had an objective response (71.4%). 81.8% of the adverse events (AEs) were grade 1 or 2. Grade 3/4 AEs (>2 patients) included neutropenia (8 pts, 44.4%), rash (3 pts, 16.7%), anemia (3 pts, 16.7%), fatigue (2 pts, 11.1%), diarrhea (2 pts, 11.1%), and leukopenia (2 pts, 11.1%). 12 out of 18 patients (66.7%) reduced vemurafenib dose due to AEs, in which 4 patients reduced once from 960mg to 720mg and the remaining 8 patients reduced twice from 720mg to 480mg. Only one patient dropped out due to the intestinal obstruction.

**Conclusions:** A combination of vemurafenib, cetuximab and FOLFIRI was generally well-tolerated and the preliminary result indicated considerably increased response rate for advanced colorectal cancer patients with BRAF V600E mutation. The enrollment for the trial is still under way.

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**Legal entity responsible for the study:** The authors.

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**442P** A phase I-II multicenter trial with avelumab plus autologous dendritic cell vaccine in pre-treated mismatch repair-deficient (MMRD) colorectal cancer patients. GEMCAD 16-02 (AVEVAC trial)

M. Español-Rego1, C. Fernández-Martos2, M.E. Elez Fernandez3, C. Foguet1, L. Pedrosa1, N. Rodriguez1, A. Rui1, E. Pineda1, J. Cid1, R. Cabezon1, H. Oliveres1, M. Lozano1, A. Gines1, A. Garcia-Criado1, M. Cuatrecasas1, F. Torres1, M. Cascante1, D. Benitez-Ribas1, J. Maurel1

1Immunology, Hospital Clinic de Barcelona, Barcelona, Spain; 2Medical Oncology, Instituto Valenciano de Oncologia, Valencia, Spain; 3Medical Oncology Dept., Vall d’Hebron University Hospital Institut d’Oncologia, Barcelona, Spain; 4Department of Biochemistry and Molecular Medicine, Universitat de Barcelona, Barcelona, Spain; 5Medical Oncology, Hospital Clinic de Barcelona, Barcelona, Spain; 6Medical Oncology, Hospital Universitario Fundación Alcorcón, Madrid, Spain; 7Medical Oncology, Hospital Clínico de BarCELona, Barcelona, Spain; 8Radiology Department, Hospital Clinic de Barcelona, Barcelona, Spain; 9Pathology Department, Hospital Clinic de Barcelona, Barcelona, Spain; 10Biostatistics Unit, Faculty of Medicine, Autonomous University of Barcelona, Barcelona, Spain; 11Universitat de Barcelona, Universitat de Barcelona, Barcelona, Spain

**Background:** Colorectal cancer (CRC) is among the highest incidence and mortality cancer rates. Immune check-point blockade (ICB) showed clinical benefit in patients whom have experienced SD for at least 5.5 months.

**Methods:** Patients with advanced MMRD CRC who received at least one prior line of chemotherapy were treated at three escalating dose levels of domatinostat (OGA: 2; CRC 11) in a 3+3 design to evaluate the safety and tolerability of the combination and determine the recommended phase II dose (RPD). Tumor assessment was initially performed at 8 weeks. Once RPD was established, cohort expansion would include 29 CRC and 34 OGA patients at treated at RPD.

**Results:** At the time of data cut off, 27th April 2021, 13 patients (OGA 2; CRC 11) were enrolled in the study (domatinostat 100mg 4 patients, 200mg 3 patients, 400mg 6 patients). No dose limiting toxicities were reported. 12 patients (92.3%) experienced at least 1 related adverse event (TRA). 1 patient (7.7%) experienced a grade 3 TRAE (rise in alkaline phosphatase). No patients experienced a grade 4 or 5 TRAE. The most frequently occurring TRAEs (>5%) were fatigue (23%), anorexia (14%), anemia (8%), insomnia (8%), dry skin (6%) and nausea (6%). 3 patients (23.1%) experienced ≥ 1 serious adverse event (SAE); none were treatment related. 6 patients (46.2%) have so far achieved stable disease (SD) during treatment, 3 of whom have experienced SD for at least 5.5 months.

**Conclusions:** Domatinostat up to 200 mg BID (400mg TDD) in combination with avelumab 10mg/kg q2w was considered safe and 200 mg BID was determined as the RPD. Cohort expansion in phase IIb is now recruiting for OGA and CRC.

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**Disclosure:** E. Smyth: Financial Interests, Personal, Other: Aptitude Health; AstraZeneca; BMS; Celgene; Eli Lilly; Evergreen Clinical Research; First Word Group; Five Prime Therapeutics; Gritstone Oncology; Immedex; Merck; My Personal Therapeutics; Roche; Sai-Med; Servier; Zymeworks. S. Rao: Financial Interests, Personal, Other, DMC chairman: Five Prime Therapeutics; Financial Interests, Institutional, Other, DMC chairman: Five Prime Therapeutics; Financial Interests, Institutional, Other, DMC chairman: Five Prime Therapeutics; Financial Interests, Institutional, Other.

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