gastrointestinal tumours, colorectal

**ANGIOGENIC SWITCH AS PREDICTOR OF RESPONSE TO CHEMOTHERAPY + BEVACIZUMAB IN PATIENTS WITH METASTATIC COLORECTAL CANCER**

A. Cubillo 1, R. Álvarez 1, J. Rodríguez-Pascual 1, M. Muñoz 2, G. Pond 3, S. Perea 1, G. Sanchez 1, M. Martin 1, E. Garralda 1, E. De Vicente 1, Y. Quijano 4, M. Hidalgo 2

1 Medical Oncology, CIOLCC, Madrid, SPAIN
2 Clinical Program, CNIO, Madrid, SPAIN
3 Oncology, McMaster University, Toronto, ON, CANADA
4 Surgery, CIOLCC, Madrid, SPAIN

**Aim:** There is a need to develop biomarkers to predict the outcome of patients with metastatic colorectal cancer (CRC) treated with chemotherapy (Ch) plus Bevacizumab (B). It has been reported that during exposure to B there is a switch in the plasma levels of angiogenesis growth factors and related cytokines called angiogenic switch (AS). It is not known if changes in these circulating factors affect the response of patients with CRC to Ch + B. The aim of this study is to determine the influence of AS in the PFS in pts with metastatic CRC treated with Ch + B.

**Methods:** Treatment naive, ECOG 0-1, metastatic CRC pts were eligible. Patients received induction treatment with XELOX-B or XELIRI-B at standard doses x 6 cycles followed by maintenance treatment with B plus Capecitabine until progression. Angiogenic related cytokines (HGF, PIGF, MCP-3, MM-9, Eotaxin, bFGF and IL-18) were prospectively analyzed at baseline and at the time of each CT evaluation (every eight weeks). AS + was defined by A) doubling of PIGF compared to baseline or B) PIGF elevation with a simultaneous elevation of any two of bFGF, HGF, MCP-3, IL-18 or MMP-9 compared to baseline.

**Results:** Of 62 patients enrolled, 24 (36.7%) have progressed. Median PFS is 15.6 (95% CI: 8.3 to 16.4) months for the entire population. Twenty-five pts (40.3%) were AS + , out of which 23 were detected at first on-study evaluation (week 8). 18 were classified as AS+ based on both criteria, 4 based on criteria A) and 3 based on criteria B). One year (95% CI) PFS for AS+ pts was 82.6% (53.0% to 94.4%) versus 32.9% (13.9% to 53.5%) for AS- pts (p = 0.001). A landmark analysis was performed using only those patients alive and progression-free at 6-months. Additional 6-month (95% CI) PFS was 90.9% (50.8% to 98.7%) among 17 AS+ patients (2 of whom progressed) versus 47.6% (19.6% to 71.3%) among 16 AS- patients (12 progressions), p = 0.002.

**Conclusions:** There is a statistically significant improved PFS amongst metastatic CRC AS+ pts treated with first line Ch + B combination compared with AS- pts.

**Disclosure:** All authors have declared no conflicts of interest.