Differential prognosis of MCRC patients post-progression to first line triplet chemotherapy/bevacizumab, FIr-B/FOX, according to second line treatment and KRAS genotype

Gemma Bruera1, Katia Cannita2, Aldo Victor Giordano3, Roberto Vicentini4, Corrado Ficorella5, Enrico Ricevuto5
1Medical Oncology, S. Salvatore Hospital, University of L’Aquila, L’Aquila, Italy; Department of Biotechnological and Applied Clinical Sciences, University of L’Aquila, L’Aquila, Italy, 2Medical Oncology, S. Salvatore Hospital, University of L’Aquila, L’Aquila, Italy, 3Radiology, S. Salvatore Hospital, L’Aquila, Italy, 4Hepatobiliary-pancreatic Surgery, S. Salvatore Hospital, L’Aquila, Italy, 5Medical Oncology, S. Salvatore Hospital, University of L’Aquila, L’Aquila, Italy; Department of Biotechnological and Applied Clinical Sciences, University of L’Aquila, L’Aquila, Italy

Background: First-line triplet chemotherapy (CT) plus targeted agent can increase efficacy of fit metastatic colorectal cancer (MCRC) patients (pts). Clinical outcome post-progression to previously reported FIr-B/FOX regimen was evaluated and retrospectively compared according to second line treatments and KRAS genotype.

Methods: Method: Second-line treatment was selected among available medical and/or surgical options in clinical practice by a multidisciplinary team, according to fitness (age, comorbidities), KRAS genotype, efficacy and safety of first line FIr-B/FOX. Activity and efficacy were evaluated and compared according to treatment or KRAS genotype, using log-rank test.

Results: Results: Fifty-four pts were evaluated after progression to FIr-B/FOX: 40 (74.1%) underwent second line treatment; 14 (25.9%) died without further treatment. Median overall survival (OS) post-progression was 12 months, significantly better in treated compared to untreated pts. Surgical treatment was selected in 4 pts (7.4%). Second line medical treatment was administered in 36 pts (66.7%): triplet CT plus targeted agent, 10 (18.5%); triplet regimens, 19 (35.2%); doublet and monotherapy, 7 (13%). At median follow-up 14 months, objective response rate (ORR) was 38%, secondary metastasectomies 12.5%, median progression-free survival (PFS) 10 months, median OS 14 months, not significantly different in KRAS wild-type compared to mutant pts. According to treatment, ORR, secondary metastasectomies, PFS, and OS were: triplet CT plus targeted agent, 80%, 40%, 13 months, not reached at median follow-up of 31.5 months; triplet regimens, 28%, 6%, 8 months, 11 months. PFS and OS were significantly favourable in triplet CT plus targeted agent compared to triplet regimens, and significantly worse in c.35 G > A mutant compared to wild-type and/or other KRAS mutant pts.

Conclusion: Conclusion: After progression to first line FIr-B/FOX regimen, prognosis may be significantly favourable in MCRC pts re-challenged with intensive regimens, and unfavourable in c.35 G > A KRAS mutant pts.