Early onset metastatic colorectal cancer: Clinical-prognostic characteristics and correlation to molecular profile.

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Background: Despite a reduction of both incidence and mortality of CRC in the elderly population, several studies published in the last decade have shown an increase in the incidence of early-onset CRC (EO-CRC). Clinical and prognostic data on this setting are limited and conflicting. The aim of our study was to evaluate the clinical, prognostic, and molecular differences in a large group of patients (pts) with early onset mCRC. **Methods:** We collected data from 589 metastatic EO-CRC from 4 different Italian Institutions. A historical control group of 316 pts > 50 year old was also included in the analysis. All pts had one or more metastatic sites, molecular profiling available (including RAS, BRAF, and MSI status), and underwent at least one line of treatment. The main objective of the study was to evaluate clinical outcome in terms of median overall survival for the global population of EO-CRC pts and in different molecular subgroups according to RAS and BRAF status. **Results:** In the EO-CRC group median age was 44 (±6) and 67 (±11) in the historical control group. M/F ratios were 2:1 and 1:1, respectively. In the overall population mOS was 34,1 in EO-CRC pts vs 42,0 months (mo) (p = 0,0006) in the control group. In the RAS/BRAF mutated subgroup mOS in EO-CRC pts was 28,6 vs 36,0 mo in the control group (p = 0,0065). In RAS/BRAF wild type subgroup mOS in EO-CRC pts was 44,1 vs 49 mo (p = 0,13). Finally, in the BRAF V600E mutated subgroup EO-CRC pts showed a 16 mo mOS vs 26 mo (p = 0,04). In the overall population mPFS was 12,0 in EO-CRC pts vs 10,0 mo (p = 0,02) in the control group. Furthermore, the overall response rate (ORR) was 53% in EO-CRC and 69% in LO-CRC. **Conclusions:** Our work including a large population of EO-CRC pts indicates a general worse prognosis for pts with early onset colorectal cancer compared to late onsets. Interestingly this seems to occur regardless of the molecular status. On the other hand findings in the RAS/BRAF wild type population might also suggest a less unfavourable impact of EO-CRC on prognosis possibly related to anti-EGFR therapy. Subsequent investigations will be needed to further understand the specific clinical and molecular characteristics of this growing group of pts to better define the more appropriate treatment strategy. Research Sponsor: None.