PD – 015 Optimizing the use of first-line chemotherapy in metastatic colorectal cancer patients with mucinous histology. A multicenter, retrospective, combined analysis on 897 patients

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Introduction: In metastatic colorectal cancer (MCRC), mucinous histology has been associated with poor response rate and prognosis. We have confirmed that mucinous colorectal cancer (MC) have an unfavourable prognosis to oxaliplatin/irinotecan-based first-line combination chemotherapy compared with nonmucinous (NMC) colorectal cancer patients (pts) (Catalano et al, BJC 2009, 100:881-887). Subgroup analysis showed a possible poor outcome of MCRC pts with mucinous histology treated with oxaliplatin-based regimens (Catalano et al, Ann Oncol 2017, 28 Supplement 6:A1). Therefore, we addressed this study to evaluate whether oxaliplatin-based chemotherapy regimens may affect survival of MCRC pts with mucinous histology.

Methods: We analyzed the population from two consecutive studies, consisting of 897 MCRC pts who were treated with first-line chemotherapy. Chemotherapy regimens consisted of OXA-based (FOLFOX, capecitabine and oxaliplatin, raltitrexed and oxaliplatin); IRI-based (FOLFIRI, capecitabine and irinotecan), FOLFOXIRI, or the same regimens plus bevacizumab (B). Pts were classified according to the histology in MC and NMC. The possible prognostic interaction between histology and different chemotherapy regimens was assessed by multivariate Cox proportional hazards analyses.

Results: One hundred thirty-nine (15.4%) pts had MC, male/female 528/369, median age 65 years (range, 25-89). More pts in the MC group had right-sided tumours (MC 47.5% vs NMC 30.9%, $p = 0.0002$) and peritoneal disease (MC 31.7% vs NMC 16.5%, $p < 0.0001$), whereas pts in the NMC group had more frequently liver metastasis (NMC 74.7% vs MC 58.3%, $p = 0.0001$). All other variables were comparable among the two groups. Pts received the following treatments: B+IRI-based, MC/NMC=43/263; B+OXA-based, MC/NMC=18/159; B+FOLFOXIRI, MC/NMC=29/130; IRI-based, MC/NMC 9/56; OXA-based, MC/NMC 34/135; FOLFOXIRI, MC/NMC 6/15. The overall response rates for MC and NMC were 33.8% (95% CI, 25.9-41.7) and 58.2% (95% CI, 54.7-61.7), respectively (chi-test, $p < 0.0001$). After a median follow-up of 50 months, median overall survival for the mucinous MCRC patients was 25.2 months compared with 26.4 months in the control group (univariate analysis, HR = 0.89; 95% C.I., 0.71-1.12; $p = 0.333$).The analysis of interaction between chemotherapy regimens and histology has given a highly significant result ($p < 0.0001$). In particular, in mucinous MCRC, by assuming as reference treatment OXA-based regimens, pts having a better outcome were those who were treated with IRI-based (HR = 0.47; 95% C.I., 0.29-0.75; $p = 0.002$) or FOLFOXIRI (HR = 0.40; 95% C.I., 0.23-0.70; $p = 0.001$). As expected, patients with non-mucinous histology treated with IRI-based ($p = 0.0001$), OXA-based ($p = 0.005$) and FOLFOXIRI ($p = 0.001$) achieved better survival than MC treated with OXA-based chemotherapy.

Conclusion: Pts with mucinous histology have poor survival and responsiveness to chemotherapy as compared with non-mucinous MCRC. However, OXA-based regimens may not represent the optimal chemotherapy treatment options in MCRC with mucinous histology. In this subgroup of pts, regimens containing irinotecan should be considered.