Primary tumor site (pTS) as a key factor in influencing differential outcome in resected colorectal cancer patients treated with adjuvant XELOX/FOLFOX

Gampieri Riccardo1, Lanese Andrea2, Del Prete Michela3, Carinci Luca4, Maccaroni Elena5, Bittoni Alessandro6, Delprete Stefano7, Caramanti Miniam8, Pellei Chiara9, Meletani Tania2, Baleani Maria Giuditta2, Di Pietro Paolo Marzia3, Berardi Rossana1

1Clinica Oncologica, AOU Ospedali Riuniti, Ancona, Italy, 2Università Politecnica delle Marche, Ancona, Italy, 3Clinica Oncologica AOU Ospedali Riuniti, Ancona, Italy, 4Università Politecnica delle Marche, Ancona, Italy, 5Ospedale Riuniti, Ancona, Italy, 6Università Politecnica delle Marche, Ancona, Italy

Introduction: Colon cancer is one of the most commonly diagnosed malignancies, and, although the prognosis has been improved, remains one of the most lethal tumours worldwide. Several studies highlighted primitive tumor site (pTS) in metastatic colorectal cancer (mCRC) as prognostic factor, with a worse outcome for right-sided (RSCC) compared to left-sided tumours (LSCC) and, in RAS wild type tumours, a differential profile of outcome in patients submitted to anti-EGFR therapies. Finally, for rectal cancers there are some data pointing out a significantly worse outcome in RSCC vs LSCC. Nevertheless, no prior study has been analyzed the outcomes for patients treated with FOLFROX or XELOX in adjuvant setting.

Aim of this retrospective study is to describe the different outcomes for resected stage III colon cancer patients, submitted to adjuvant chemotherapy, stratified by pTS and treatment received.

Methods: Patients with resected pN+ colon cancer and who received XELOX or FOLFOX adjuvant treatment, stratified by pTS, have been enrolled. We defined right side as cancers arising from caecum, ascendant colon, hepatic flexure and transverse colon whereas left side tumors as those from splenic flexure, descendent and sigmoid colon. Patients with rectal cancer were excluded. Another exclusion criterion was withdrawal or change of treatment within 3 month time.

Relapse free survival (RFS) and overall survival (OS) were calculated accordingly to Kaplan-Meier method. Survival analysis was conducted by log-rank test based on pre-specified stratification factors.

Results: 133 patients have been enrolled, 72 (54%) with LSCC and 61(46%) with RSCC. 43(60%) LSCC patients relapsed with a mRFS of 29 months, whereas 28(46%) RSCC patients with a mRFS of 45 months (p = 0.36, HR:1.1512, 95%CI:0.7181 to 1.8410).

Stratifying by chemotherapy regimen, 48(36%) patients received XELOX and 85(64%) FOLFOX. mRFS were respectively not reached vs 29 months (p = 0.048, HR:0.59, 95%CI:0.38 to 0.99) (Figure 1). According to pTS, 33(54%) RSCC patients received FOLFOX and 28(46%) XELOX, with a mRFS of 15 months and not reached respectively (p = 0.0094, HR:0.36, 95%CI:0.17 to 0.78). No statistically significant differences were seen in LSCC patients receiving XELOX or FOLFOX (mRFS 22.4 vs 35 months respectively).

Conclusion: Our analysis shows that RSCC patients had lower recurrence rate and better RFS compared with LSCC, although not in a statistically significant fashion. However, this is the first time that a significantly better RFS was observed by using XELOX rather than FOLFOX as adjuvant treatment in pN+ CRC patients. This difference was only observed in RSCC, but not in LSCC. We hypothesize that this might be due to different dose of oxaliplatin used in each cycle (130 mg/mq in XELOX vs 85mg/mq)

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in FOLFOX) accordingly to the increased activity of ERCC1 enzyme in RSCC vs LSCC previously described. Even if prospective trials are needed to confirm this initial report, we suggest that due to the noticeable difference in terms of activity, tumor sidedness will gain a potential role as factor influencing the best choice of treatment to offer to our patients.