P — 209   **P 53 abnormal expression might influence global outcome through EGFR modulation in RAS/BRAF wild type metastatic colorectal cancer patients receiving later-line irinotecan cetuximab**

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Introduction: Preclinical data suggest that loss of p53 might influence epidermal growth factor receptor (EGFR) promoter activity in different tumour types. The clinical role of p53 status in colorectal tumours, however, is still controversial. In the present study we assessed the role of p53 abnormal expression in patients with colorectal tumours treated with anti-EGFR therapy.

Methods: Tumour samples from RAS/BRAF WT patients with colorectal tumours treated with second-third line irinotecan-cetuximab were analysed for the immunohistochemical expression of p53. Aim of the present study was to evaluate the correlation of p53 abnormal expression with clinical outcome in terms of OS, PFS, ORR. Tumour sidedness, EGFR promoter methylation and EGFR GCN were evaluated as covariates. The association between categorical variables has been estimated with the chi-squared test. Statistical analysis has been performed with the MedCalc package. Survival distribution has been estimated by the Kaplan–Meier method. Comparison of survival curves has been performed with log-rank test. Logistic regression analysis has been used to assess the independent role of variables resulted significant at univariate analysis.

Results: Eighty-eight patients were included in the study, 36/88 (40.9%) had abnormal expression of p53 (abnormal p53), 52/88 (59.1%) had normal expression of p53 (normal p53). Abnormal p53 status was more frequent in left sided tumours (88.9% vs 16.7% of abnormal p53 for left sided and right sided tumours respectively) whereas it was less frequent in EGFR promoter methylated tumours (19.4% vs 71.2% of abnormal p53 for methylated and unmethylated respectively) and in EGFR GCN<2.12 tumours (5.6% vs 57.7% of abnormal p53 for EGFR GCN$\geq$2.12 and EGFR GCN<2.12 respectively). Median PFS was 8,00 (95% CI: 6,98 to 8,10) vs 3,00 (95% CI: 2.90 to 3,63) months in patients with abnormal p53 tumours and in patients with normal p53 tumours respectively (HR 0.36; p < 0.0001). Median OS was 18 (95% CI:) vs 8 (95% CI: 6.98 to 8.10) months in patients with abnormal p53 tumours and in patients with normal p53 tumours respectively; HR: 0.21; p < 0.0001). ORR was 61.1%VS 3.8% in patients with abnormal p53 tumours and in patients with normal p53 tumours respectively (p < 0.0001). In multivariate analysis, EGFR promoter methylation and p53 expression maintained their independent role for OS (p:0.0003, Exp(b):0.21 and

p:0.01, Exp(b):2.82 respectively) whereas only EGFR promoter methylation resulted independently correlated with PFS (p:0.025, Exp(b):3.03 and p:0.056, Exp(b):0.51 for EGFR promoter methylation and p53 expression respectively).

Conclusion: The crosstalk between p53 and EGFR represents a poorly understood issue which could be significant in clinical practice. Our findings suggest a potential prognostic/predictive role of p53 status in patients with colorectal cancer treated with anti EGFR therapy. Further studies are needed to better understand the clinical role of p53 status in this setting.