P — 159   **Analysis of early tumor shrinkage and depth of response in metastatic pancreatic cancer patients treated with first-line modified FOLFIRINOX or gemcitabine + nab-paclitaxel**

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Introduction: Early Tumor Shrinkage (ETS) and Depth of Response (DoR) can help in predicting favourable outcome in metastatic colorectal cancer. Combination chemotherapy such as FOLFIRINOX or gemcitabine+nab-paclitaxel (GemNab) represents the main options for fit metastatic pancreatic cancer (PC) patients (pts). Data about the role of ETS and DoR in PC are lacking. The aim of the present analysis is to investigate the putative prognostic role of these parameters in PC.

Methods: One hundred thirty nine metastatic PC pts treated in a single center with modified FOLFIRINOX (mFOLFIRINOX) or GemNab (81 and 57, respectively) and evaluable for response were enrolled. Best response according to RECIST criteria, ETS and DoR were analyzed. ETS was defined as a $\geq$ 20% reduction in the sum of longest diameters of RECIST target lesions after 8 weeks of treatment compared to baseline. DoR was defined as the percentage of shrinkage in the sum of longest diameters of RECIST target lesions observed at the nadir compared to baseline; pts with appearance of new lesions were excluded from the analysis regarding DoR. Association of ETS and DoR with progression-free survival (PFS) and overall survival (OS) was assessed by univariate and multivariate Cox models.

Results: Main pts characteristics were: male/female, 51.4%/48.6%; median age, 64 years (range 41-76); PS 0/1, 60.8%/39.2%; previous resection of primary tumor, 26.8%, median number of metastatic sites, 2 (range 1-5), median Ca19.9 value, 471 U/mL (range 0.6-100000). In the whole population median OS was 10.9 months (11.5 in mFOLFIRINOX and 10.6 in GemNab) and median PFS was 6.2 months (6.4 in mFOLFIRINOX and 6.2 in GemNab). Fourty-seven (34%) pts achieved partial response, of whom 35.8% in mFOLFIRINOX group and 32.2% in GemNab group. ETS was achieved in 49 pts (35.5%), 39.5% of mFOLFIRINOX and 29.8% of GemNab group, respectively (p = 0.280). Median ETS was 23% with mFOLFIRINOX and 13% with GemNab (p = 0.029). Considering the entire population, ETS was significantly associated with better PFS (8.0 vs. 4.8 months, p < 0.001) as well as OS (13.2 vs. 9.7 months, p = 0.001). Median DoR was 27.5% (29.4% with mFOLFIRINOX and 21.4% with GemNab, p = 0.016). DoR was significantly associated with better PFS (9.0 vs 6.7 months, p < 0.001) and OS (14.3 vs 11.1 months, p = 0.031). Multivariate analysis didn't confirm the association of ETS with PFS and OS (p > 0.05). The association of DoR with PFS was confirmed in multivariate analysis stratified for other prognostic variables (p = 0.005), while a trend toward association with OS was observed (p = 0.079).

Conclusion: In our retrospective cohort, ETS and DoR can help in predicting favorable outcome in PC treated with first-line combination chemotherapy; these parameters should be integrated as secondary endpoints in future prospective clinical trials.