FOLFOXIRI as primary treatment for locally advanced unresectable pancreatic cancer (LAPC): a prospective study

C. Vivaldi1, E. Vasile1, C. Caparello1, V. Perrone1, F. Caniglia1, N. De Lio1, C. Groce1, L. Fornaro2, G. Musetti1, G. Pasquini2, I. Pecora1, M. Lencioni1, C. Cappelli1, D. Caramella1, A. Falcone1, U. Boggi1

1Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
2U.O. Oncologia Medica 2, Azienda Ospedaliero-Universitaria Pisana, Istituto Toscana Tumori, Pisa, Italy
3Department of Oncology, University Hospital, Pisa, Italy

Introduction: Chemotherapy and chemoradiation are the main options in LAPC while surgery becomes feasible only in a small proportion of patients after neoadjuvant therapy. FOLFIRINOX is an active treatment in advanced pancreatic cancer. FOLFOXIRI is a similar regimen, with lower dose of irinotecan and no 5-fluorouracil bolus, that has shown good activity in advanced colorectal cancer. We prospectively evaluated the activity of FOLFOXIRI in LAPC.

Methods: This is a prospective single-arm trial. Patients with LAPC (cT4, cN0-1, cM0, considered unresectable according to definition of the American Hepato-Pancreato-Biliary Association consensus conference), ECOG PS 0-1, age 18-75y, were treated with modified FOLFOXIRI (irinotecan 150 mg/sqm, oxaliplatin 85 mg/sqm, folinate 200 mg/sqm, 5-fluorouracil 2800 mg/sqm in 48h) every 2 weeks. Tumor assessment was performed by CT scan every 8 weeks and multidisciplinary team evaluated patients after every CT scan. If tumor was judged resectable, patients underwent surgery after 4-6 weeks from last chemotherapy cycle, otherwise after 8 cycles radiotherapy was evaluated. Primary endpoint is rate of secondary radical surgery; treatment will be considered of interest if it shows an increase in surgical procedures from an expected 30% to at least 45% and in particular if 27 patients will be resected over 67 enrolled (alpha and beta errors: 0.05 and 0.10, respectively). Progression-free survival (PFS), overall survival (OS), response rate (RR) and safety were secondary objectives.

Results: From 2008 to 2015, we enrolled a total of 59 patients. Main characteristics were: male/female, 44%/56%; median age, 61y (range 34-74); PS 0/1, 68%/32%; head/body-tail, 63%/37%; cN0/N+, 38%/62%; 51 tumors involved both arteries and veins, while in 8 cases only arterial or venal encasement was present; the involved vessels were: superior mesenteric artery (SMA) in 38 cases, celiac axis (CA) in 21, hepatic artery (HA) in 20, portal vein (PV) in 16, superior mesenteric vein (SMV) in 39. Median number of FOLFOXIRI cycles was 8 (2-14). After the first 34 patients, considering good tolerability, protocol was amended and we started to use classic schedule of FOLFOXIRI (irinotecan 165 mg/sqm and 5FU 3200 mg/sqm). Main grade 3-4 toxicities were: neutropenia (46%), asthenia (15%), diarrhea (8%). There were no significant differences in toxicities between the two schedules. RR was 34%, disease control rate 88%. After chemotherapy 28 patients (47%) underwent radical surgery; 17 patients received total pancreatectomy, 8 pancreaticoduodenectomy and 3 left pancreatectomy; SMA, CA and HA were resected in 12, 1 and 6 cases respectively, while PV or SMV were resected in 25 cases. Early post-operative mortality rate was 8%. Accrual was stopped after the number of planned resections was reached. With a median follow up of 26.9 months, median PFS was 11.9 months in global population and 14.9 in resected patients. Median OS was 15.3 months in the whole population and 19.8 in resected patients. Two-year OS rate was 22.5% in the whole population and 35% in resected patients.

Conclusion: Chemotherapy with FOLFOXIRI seems feasible and active in LAPC and may allow achieving resectability in some patients. Results in terms of PFS and OS are encouraging.