Second-line treatment after disease progression following first-line chemotherapy with modified FOLFIRINOX in advanced pancreatic cancer patients: a single institution retrospective cohort study

C. Vivaldi1, C. Caparello1, G. Pasquini2, G. Musettini1, S. Catanese1, M. Lencioni3, A. Falcone4, E. Vasile1

1Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
2Oncologia Medica 2, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy
3Azienda Ospedaliero-Universitaria di Pisa, Pisa, Italy
4Department of Translational Research and New Technologies In Medicine, University of Pisa, Pisa, Italy

Introduction: FOLFIRINOX has been established as one of the standard first-line treatment options for advanced pancreatic cancer patients. However, the majority of patients develop disease progression within one year from the beginning of first-line chemotherapy. Recent studies showed the superiority of combination second-line regimens versus mono-chemotherapy after progression to gemcitabine but no standard second-line treatment has been yet identified for patients progressed after FOLFIRINOX. The aim of our analysis was to describe the second-line treatments used in this setting and their activity.

Methods: We collected data from patients with histological diagnosis of pancreatic adenocarcinoma treated with first-line modified FOLFIRINOX at our institution from 2011 to 2014. We identified patients who received a second-line treatment after radiologically documented disease progression to FOLFIRINOX. We considered eligible patients with metastatic disease or those with locally advanced disease who experienced progression within 6 months after the end of primary chemotherapy. We analyzed data on activity reporting response rate (RR), progression-free (PFS) and overall survival (OS) of second-line treatments, evaluated according to Kaplan-Meier method.

Results: From a total of 140 patients (50 stage III, 90 stage IV) treated with modified FOLFIRINOX, 100 patients experienced disease progressions; 73 patients received further treatments, 4 of them have been treated with radiotherapy for local recurrence. Therefore, 69 eligible patients (40 male, 29 female) have been included in this analysis. Median age was 60 years (range 41-75). Twenty-three patients (33.3%) had a partial response with FOLFIRINOX and 26 (37.7%) reported a stable disease. The median first-line PFS was 5.76 months. Second-line treatments were: gemcitabine in 31 patients (44.8%), gemcitabine plus nab-paclitaxel or plus capecitabine in 10 patients each (14.5%), FOLFIRI in 6 (8.7%), GEMOX in 5 (7.2%), retreatment with modified FOLFIRINOX in 3 cases (4.3%); XELOX, capecitabine, gemcitabine plus carboplatin, and paclitaxel have been used in 1 patient each (1.5%). Five partial responses (7.2%) and 24 stable diseases (34.8%) have been observed; 4 patients have not been revaluated yet. With a median follow up of 14.7 months, median PFS was 2.67 months (95% confidential interval, CI: 1.81-3.52) and median OS from the beginning of second-line treatment was 7.23 months (95% CI: 5.22-9.25). There were no major differences in RR, PFS and OS according to the number of drugs used in second-line (combination versus monotherapy) (RR: 11.1% vs 3%, p = 0.36; PFS: 3.13 vs 2.5 months, p = 0.688; OS: 8.33 vs 6.3 months, p = 0.154) even if a trend in favor of combination regimens could be observed. RR and OS were significantly better in patients treated with fluorour-based chemotherapy compared to those receiving gem-based treatment (RR: 37.5% vs 1.8%, p = 0.012, and median OS: not reached vs 6.63 months, p = 0.015); a trend towards better PFS was also observed (5.03 vs 2.36 months, p = 0.268).

Conclusion: Second-line chemotherapy after FOLFIRINOX has limited activity but survival data are encouraging. Waiting for new active drugs to be tested in this setting, prospective studies are needed to evaluate the best treatment and possible prognostic factors to guide clinical decisions.