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gastrointestinal tumours, non-colorectal

682P Nab-paclitaxel in substitution of oxaliplatin and irinotecan in folfirinox schedule as first-line therapy in patients with metastatic pancreatic cancer: results of phase I dose finding of NabucCO study by GOIRC

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Background: FOLFIRINOX and nab-paclitaxel (nab-p) plus gemcitabine are effective regimens in first line treatment for metastatic pancreatic cancer (mPC). NabucCO study is designed to define dose limiting toxicities (DLTs) and maximum tolerated dose (MTD) of nab-p added to FOLFIRI or FOLFOX in first line for mPC.We report final results of dose-finding for both schedules.

Methods: Patients with mPC, untreated for metastatic disease and PS ECOG 0-1 received leucovorin 400 mg/m^2, 5FU bolus 400 mg/m^2, 5FU 48h ci 2400 mg/m^2, and irinotecan 180 mg/m^2 (Arm A) or oxaliplatin 85 mg/m^2 (Arm B) plus nab-p iv per cohort escalation assignment every 2 weeks for up to 12 cycles.The design was the standard 3 + 3 phase I dose escalation, with a nab-p dose increased by 10 mg/m^2 for each cohort starting with 90 mg/m^2.The MTD was established by DLTs according with Common Toxicity Criteria for Adverse Events (CTCAE) v. 4.03 during the first cycle of therapy. Recommended dose for phase II evaluation was defined as the highest dose level at which less than 2 of 6 pts experienced a DLT during cycle I, with a confirmatory cohort expansion of at least additional 3 pts.

Results: From February 2014 to October 2015, a total of 63 pts were enrolled, 27 pts received nab-FOLFIRI while 36 pts were treated with nab-FOLFOX. For Arm A median age was 62 years (range 38-75) and in Arm B was 60 years (range 43-74). DLTs during first cycle at corresponding dose level are listed in the table below.

Table: 682P

LEVEL	Nab-p mg/m^2	DLTs with FOLFIRI	DLTs with FOLFOX
1	**90**	None	None
2	**100**	None	None
3	**110**	Liver toxicity G3 (1/6)	None
4	**120**	None **(MTD)**	None
5	**130**	Neutropenia G4 and leucopenia G3 (1/6) Thrombocytopenia G3 (1/6)	Nausea G3 diarrhea G3 and anorexia G3 (1/3)
6	**140**	Neutropenia G4 and thrombocytopenia G3 (1/3) Fever G3 and asthenia G3 with hospitalization (1/3)	None
7	**150**	NA	None
8	**160**	NA	Nausea G3 (1/6) **(MTD)**
9	**170**	NA	Febrile neutropenia and leucopenia G3 (1/3) Sepsis (1/3)

Conclusions: According to the study plan, the MTD of nab-p with FOLFIRI is 120 mg/m^2, and with FOLFOX is 160 mg/m^2. The phase II study to assess efficacy of these regimen in term of overall response rate (ORR) is currently ongoing.

Clinical trial identification: EudraCT 2013-002275-18

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