

Title:

SCALOP-2: A multi-centre randomised trial of induction chemotherapy followed by capecitabine +/- nelfinavir with high or standard dose radiotherapy for locally advanced pancreatic cancer (LAPC): results of Stage 1 - the non-randomised dose-finding component

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Background:

The anti-retroviral agent, nelfinavir, demonstrates radiosensitising effects in pre-clinical models of pancreatic cancer. The primary objective of Stage 1 was to establish the maximum tolerated dose (MTD) of nelfinavir combined with capecitabine-chemoradiation (CRT) after gemcitabine+nab-paclitaxel (GEMABX) induction chemotherapy.

Methods:

Patients with inoperable, histologically/cytologically proven LAPC and WHO performance status 0-1 were eligible for this rolling-six dose-escalation stage. After 3 cycles of induction GEMABX (28-day cycle of nab-paclitaxel 125mg/m² and gemcitabine 1000mg/m² on days 1, 8, and 15), patients with non-progressive disease had 1 further cycle followed by CRT (50.4Gy/28 fractions, capecitabine 830mg/m² bd on radiotherapy days) and 1000mg or 1250mg nelfinavir bd continuously during CRT. Other outcomes included overall survival and progression-free survival.

Results:

27 patients were recruited from 8 UK centres (March 2016-June 2017). Median age was 62 years, 30% were male, 78% had head tumours, and 30% had biliary stents. Baseline median tumour diameter was 36mm.

67% commenced CRT. 11 patients received 1000mg and there was one dose-limiting toxicity (DLT) in this group: grade 3 acute coronary syndrome. The nelfinavir dose was escalated as per the rolling-six design. 7 patients received 1250mg nelfinavir and no DLTs were observed.

During GEMABX, common grade ≥ 3 toxicities among participants were neutropenia (30%), fatigue (22%), and diarrhoea (15%). During CRT, grade ≥ 3 toxicities included fatigue (6%) and anorexia (6%). No grade 5 adverse events were reported in Stage 1.

Survival analysis will be presented.

Conclusions:

1250mg nelfinavir was recommended for combining with capecitabine-CRT in the ongoing randomised component of the trial (Stage 2).

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