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Randomised phase II study of mFOLFIRINOX ± SBRT in patients with high risk, borderline resectable or locally advanced pancreatic cancer: Results of the AGITG MASTERPLAN trial

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Background

Stereotactic body radiotherapy (SBRT) delivers high-dose, precision radiotherapy (RT). Despite advances in chemotherapy (CT) for pancreatic cancer (PC), locoregional recurrences (LRR) are frequent and contribute to morbidity/mortality.

Methods

Eligible pts had operable disease with ≥1 high risk feature (>4 cm, extrapancreatic extension, or node positive), or BRPC, or LAPC. High-risk operable and BRPC pts were classified as potentially operable PC (POPC), while LAPC/medically inoperable pts as inoperable PC (IPC). Staging followed AGITG guidelines with central radiology review. CT was clinician choice: mFOLFIRINOX or gem/nab-paclitaxel. Pts were randomised 2:1 to 3mths of CT+SBRT (I) or to 3mths CT alone (C). SBRT was 40Gy in 5 fractions with fiducial marker guidance and real time RT quality assurance. After CT±SBRT, pts were evaluated for surgery. Following resection pts received 3mths adjuvant CT. Pts unsuitable for resection, continued CT for further 3mths. The primary endpoint was 12mth LRR. Secondary endpoints included resection rate, margin status, toxicity per CTCAE (v5.0), progression-free survival (PFS), and overall survival (OS).

Results

Across 14 sites 75 pts were enrolled with 1 ineligible, including 48 POPC and 26 IPC. 12mth LRR rates were 20.2 % (95% CI: 9.9-33.2%) v 52.0% (95% CI: 30.3-69.9%) in I and C respectively (p=0.022). In POPC, 12mth LRR rates were 19.7% (95% CI: 7.8–35.6) (I) v 52.9% (95% CI: 25.9–74.1) (C) (p=0.031), and in IPC 21.4% (95% CI: 4.8–45.8) (I) v 50.0% (95% CI: 11.4-80.2) (C) (p=0.16). Overall Grade 3+ toxicity occurred in 70.2% (I) and 64.0% (C) (p=0.27). Median PFS was 11.9 v 6.3 mths (p=0.002) and median OS 22.0 v 14.0 mths (p=0.006) in I and C, respectively.Table: 3136R0

Clinicodemographics and outcomes

	C=Control (n=25) I=Investigational (n=49) P value		
Demographics			
Median age (IQR)	66 (55-70)	65 (58-70)	0.89
% Male	72%	51%	0.08
Baseline Ca19.9 (median, IQR)	340 (60-977)	180 (34-1152)	0.60
Staging	-	-	
Operable with ≥1 high-risk feature	3 (12%)	1 (2.0%)	-
BRPC	14 (56%)	30 (61%)	-
IPC	8 (32%)	18 (37%)	0.69
cNO	60%	71%	0.32

	C=Control (n=25)	I=Investigational (n=49)	P value
Treatment			
CT regimen	-	-	-
mFOLFIRINOX	23 (92%)	44 (90%)	-
Gemcitabine/nab-paclitaxel	2 (8%)	3 (6%)	1.0
Withdrawal prior to chemotherapy	0 (0%)	2 (4%)	
SBRT commenced	NA	39 (80%)	NA
Surgical Outcomes (POPC only; n=48)	C=Control (n=17) I=Investigational (n=31)		
Resection performed n (%)	10 (59%)	21 (68%)	0.54
R0 resection (>1mm)	4/10 (40%)	13/21 (62%)	0.44

Conclusions

SBRT improved LRR and PFS without additional toxicity. A significant OS signal was observed in this cohort. Further research to optimise the role of SBRT is required.

Clinical trial identification

ACTRN12619000409178 Registered 13/03/2019.

Legal entity responsible for the study

GI Cancer Trials.

Funding

Medical Research Future Fund.

Disclosure

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