Tolerability and efficacy of modified FOLFIRINOX versus standard FOLFIRINOX in patients with advanced pancreatic cancer

S Gray[1], S Wardell[1], A Lamarca[2], R A Hubner[1,3], J W Valle[3,1], M G McNamara[3,1]

[1]Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK. [2]Department of Oncology – OncoHealth Institute, Fundación Jiménez Díaz University Hospital, Madrid, Spain. [3]Division of Cancer Sciences, University of Manchester, UK.

Background

- At the onset of the Covid-19 pandemic in April 2020, our centre's chemotherapy regimens were reviewed to minimise infection risk
- First-line treatment for advanced (locally advanced – LA, or metastatic – M) pancreatic ductal adenocarcinoma (PDAC) was changed from standard (s)FOLFIRINOX to modified (m)FOLFIRINOX
- mFOLFIRINOX features a reduced dose of irinotecan (150mg/m^2 from 180) and omission of the 5-fluorouracil (5-FU) bolus. There is retrospective evidence of reduced toxicity with maintained efficacy of the mFOLFIRINOX regimen, versus sFOLFIRINOX[1]

Tolerability

Table 2. Planned outcome measures of tolerability

Planned outcome measure	sFOLFIRINOX	mFOLFIRINOX
1. Patients requiring dose reduction	90.3% (28/31)	67.7% (21/31)
2. Total relative dose intensity (RDI) received	59.7%	74.0%
2a. RDI of infused 5-fluorouracil	67.3%	75.0%
2b. RDI of bolus 5-fluorouracil	43%	N/A
2c. RDI of irinotecan	63.6%	72.5%
2c. RDI of oxaliplatin	64.9%	74.3%
3. Proportion of patients who experienced Grade 3 toxicity during treatment	44.1%	33.3%
4. DPYD mutation	0 tested	8% (of 25 tested)
5. Neutropenic sepsis on treatment	8.8%	6.1%

Relative dose intensity (RDI) was calculated as an average of 4 drugs for FOLFIRINOX (oxaliplatin, irinotecan, bolus 5-FU and infused 5-FU), and 3 drugs for mFOLFIRINOX. Each drug was given equal weighting in the total RDI calculation. DPYD = dihydropyrimidine dehydrogenase.

- 53% of FOLFIRINOX patients completed 12 cycles (18/34), versus 61% of mFOLFIRINOX patients (20/33)
  - Rationale for stopping early (respectively; n=): Progression (4 vs 1), Toxicity (6 vs 6), Operable disease before completion (0 vs 1), Patient choice (0 vs 1), Other* (6 vs 4)

*reduced performance status or death not clearly attributable to toxicity or progression

Methods and patient demographics

- This was a retrospective single-centre analysis of consecutive patients treated with ≥1 cycle of m/sFOLFIRINOX for LA/M PDAC
- Electronic case records were reviewed, including electronic prescribing software
- 34 patients were treated with sFOLFIRINOX between November 2018 and March 2020. 33 patients were treated with mFOLFIRINOX between May 2020 and August 2021

Table 1. Patient demographics

	sFOLFIRINOX	mFOLFIRINOX
Male N (%)	23 (67.6)	23 (70.0)
Age - mean (IQR)	60.3 (56.6-64.3)	60.7 (55.5-67.3)
Prior surgery (%)	2 (5.9)	0
Metastatic disease (%)	20 (58.8)	16 (48.5)
Locally advanced (%)	14 (41.2)	17 (51.5)
ECOG PS 0 (%)	14 (41.2)	5 (15.2)
ECOG PS 1 (%)	20 (58.8)	22 (84.6)

s/mFOLFIRINOX = standard/modified 5-fluorouracil, irinotecan, oxaliplatin. IQR = interquartile range.
ECOG PS = Eastern co-operative oncology group performance status.

Second-line treatment offered

Consolidation chemo-radiotherapy (CRT) was received by 28.6% of LA sFOLFIRINOX patients and 41.2% of LA mFOLFIRINOX patients*

Table 3. Second-line treatment offered

	sFOLFIRINOX		mFOLFIRINOX	
	LA	M	LA	M
Curative-intent surgery	14.3%	-	29.4%	-
Combination chemotherapy	50%	30%	23.5%	37.5%
Single-agent chemotherapy	21.4%	25%	17.6%	6.3%
Irreversible electroporation	7.1%	-	5.8%	-
Other treatment	-	10%	-	-
No other treatment, no progression	0	0	17.6%	18.8%
Best supportive care only	14.3%	35%	11.8%	37.5%

*Table includes next treatment subsequent to consolidation CRT.

Progression-free survival (PFS)

- sFOLFIRINOX: median PFS 7.1 months (95% CI 5.2-9.1) after 33/34 events
- mFOLFIRINOX: median PFS 11.1 months (95% CI 6.8-15.5) after 25/33 events
- PFS was significantly increased in patients who received mFOLFIRINOX (p<0.01, log rank test)
- Overall survival data was not mature at the time of analysis

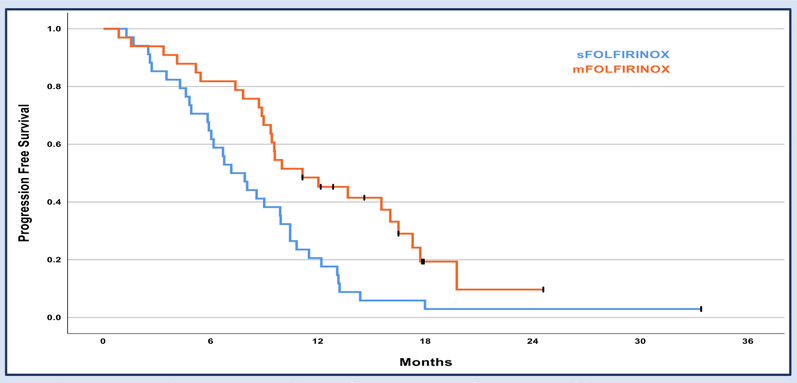

Figure 1. Kaplan-Meier analysis of progression-free survival by treatment type

Conclusions:

- Modified FOLFIRINOX was associated with increased tolerability versus sFOLFIRINOX in this single-institution cohort
  - Fewer dose reductions
  - Lower rates of ≥Grade 3 toxicity
- Greater relative dose intensity was given with mFOLFIRINOX
- Progression-free survival was significantly increased with mFOLFIRINOX versus sFOLFIRINOX
- Rates of curative-intent resection and consolidation chemo-radiotherapy were higher for LA-PDAC treated with mFOLFIRINOX
- Our centre will continue to utilise mFOLFIRINOX in this setting

References

1. Mahaseth et al. Modified FOLFIRINOX regimen with improved safety and maintained efficacy in pancreatic adenocarcinoma. Pancreas 2013; 42(8):1311-5

Corresponding Author: Dr Simon Gray (Simon.gray6@nhs.net)