

The GOFURTGO Study

an AGITG multicentre phase II study of fixed dose rate gemcitabine-oxaliplatin integrated with concomitant 5FU and 3-D conformal radiotherapy for the treatment of locally advanced pancreatic cancer

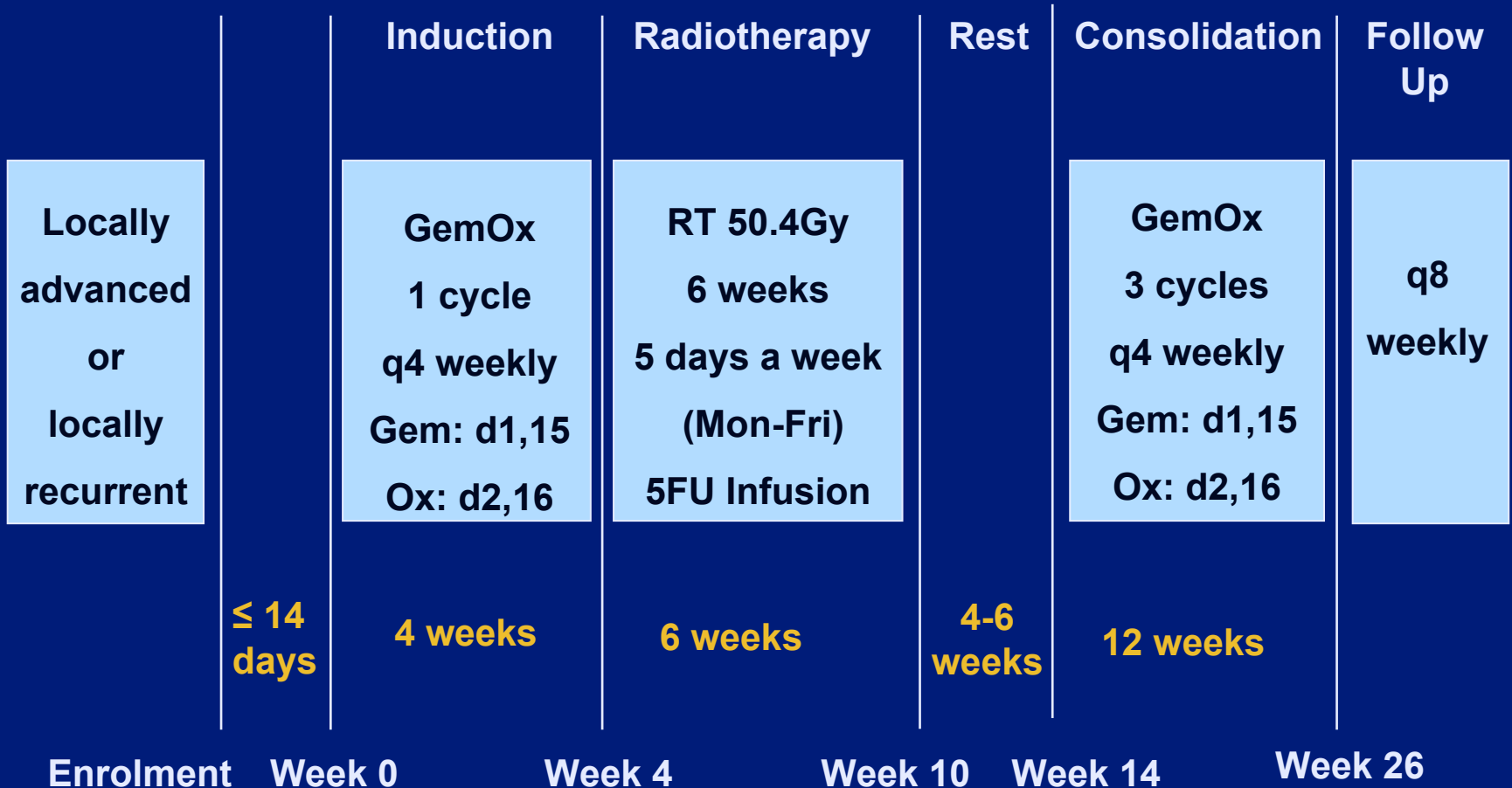
Authors: D. Goldstein, G. van Hazel, S. Selva-Nayagam, S. Ackland, J. Shapiro, S. Carroll, M. Cummins, C. Brown, R. J. Simes, N. Spry: on behalf of the Australasian Gastro-Intestinal Trials Group (AGITG)

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Background

- Our previous study of Gemcitabine (Gem) with sandwich 5- fluorouracil and 3-D conformal radiotherapy (5FU-3DRT) for locally advanced pancreatic cancer was encouraging (BJC 2007: 97, 464-471).
- Gemcitabine-Oxaliplatin (Gem-Ox) has a higher response rate than Gem alone, and improved progression free survival, but not overall survival.
- The use of a Gem-Ox regimen in locally advanced pancreatic cancer may improve local control and delay systemic spread.

Schema



Eligibility/Endpoints

- Histologically/cytologically proven adenocarcinoma of the pancreas head or body
- Locoregional disease confirmed by CT without distant metastases
- Measurable disease according to RECIST
- ECOG PS 0-2
- Adequate organ function
- Informed consent
- Feasibility, specifically the proportion of patients completing >80% of each treatment component
- Safety/toxicity (according to CTCAE v3.0 and the RTOG/EORTC late radiation morbidity scoring schema)
- Activity (objective tumour response according to RECIST, local control, PFS and OS)
- Quality of Life (assessed using EORTC QLQ C30 and pancreatic PAN 26 questionnaires)



Baseline characteristics

	n = 48 pts
Median age (years, range)	61 (44-81)
Male (%)	67
PS 0-1 (%)	96
Primary site in head of pancreas (%)	75
Regional lymph nodes involved (%)	44
Locally advanced disease (%)	94
T1 / T2 / T3 / T4 (%)	6 / 31 / 17 / 46
Inoperable due to extension of tumour (%)	42
Inoperable due to vascular compromise (%)	38
Median CA19-9 (ku/L, range)	202 (0.3-11,430)

Feasibility/Treatment discontinuation

	Induction	Chemoradiation 37/48	Consolidation 1 31/48	Consolidation 2 27/48	Consolidation 3 24/48	Overall 24/48
Toxicity	0	4	2	1	1	8
PD	1	3	4	1	1	10
Dr pref	1	0	0	0	1	2
Pt pref	0	1	0	0	0	1
Other	1	0	0	2	0	3

Toxicities causing discontinuation:

- Fatigue
- Allergic reaction/hypersensitivity, nausea, vomiting, fatigue
- Raised γ GT, nausea, vomiting, flu-like symptoms
- Raised γ GT, ALT, AST, ALP
- Raised γ GT
- Weight loss, low protein, low albumin, hypocalcaemia
- Weight loss, nausea, anorexia
- Anorexia, epigastric pain

Toxicity

n = 48 pts	% all grades	% grade 3, 4
Liver function (γ GT)	65	23 , 6
Anaemia	60	10 , 0
Nausea	87	8 , 0
Fatigue	81	8 , 0
Diarrhoea	52	4 , 0
Vomiting	46	4 , 0
Neutropenia without infection	21	4 , 0
Infection without neutropenia	8	4 , 0
Thrombocytopenia	54	2 , 2
Late radiation toxicity* (n=45 pts)^	20	2 , 2
Anorexia	58	2 , 0
Stomatitis/mucositis	19	2 , 0

* Grade 3 and 4 late radiation toxicity was gastric bleeding ; ^ 45 pts commenced chemoradiation
60 day all cause mortality: 0%; Treatment related deaths: 0%

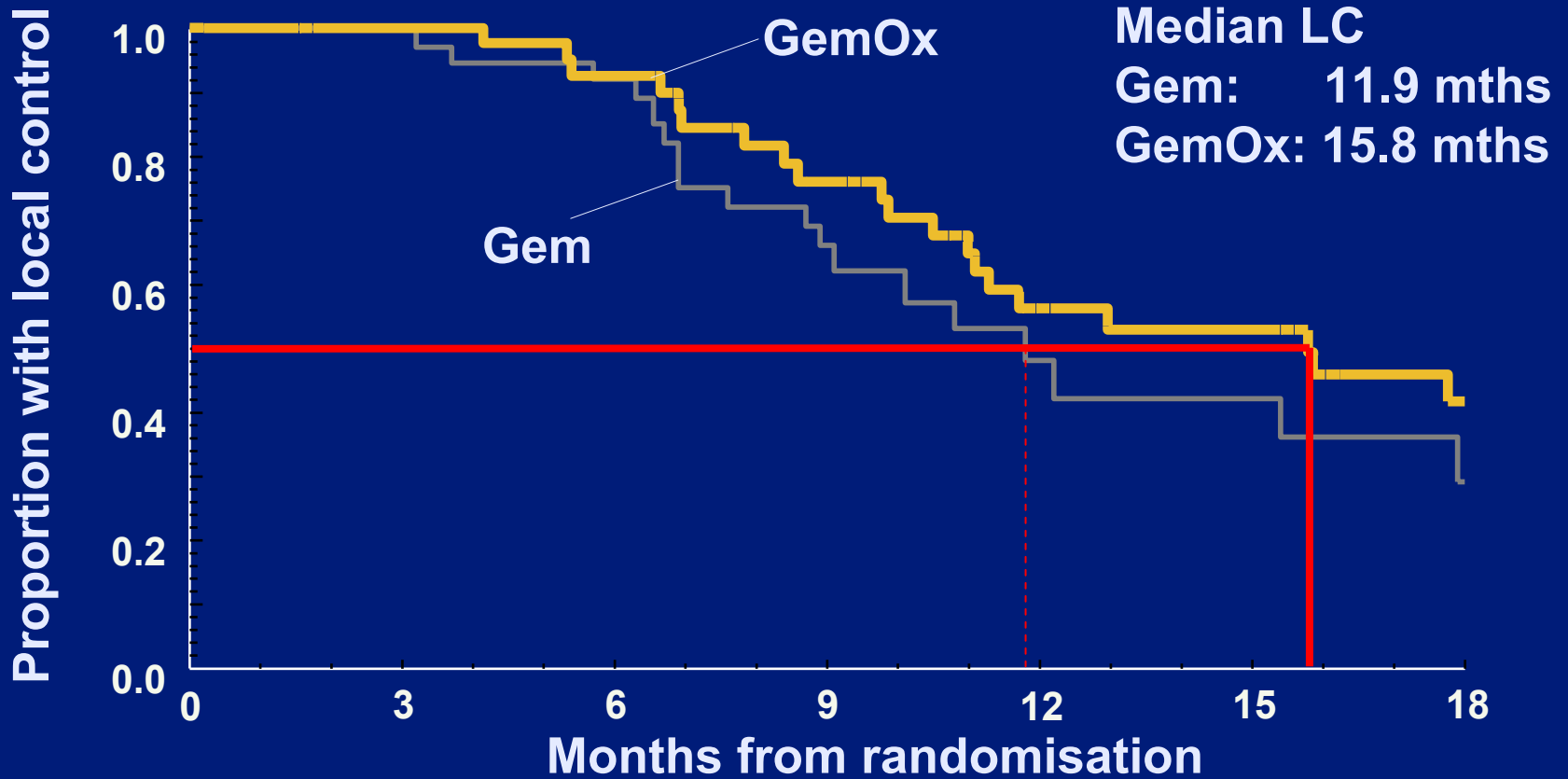
Response rate

n = 46 evaluable pts	(%) (95% CI)
Confirmed complete response (CR)	0 (0-7)
Confirmed partial response (PR)	35 (23-49)
Stable disease (SD)	54 (40-68)
Progressive disease (PD)	11 (5-23)
Clinical benefit (CR + PR + SD)	89 (77-95)

Comparison to previous study

Component	Confounder	Gem	GemOx	Favours
Inclusion criteria	Liver function tests	No limit	<3xULN or stented	GemOx
	Operability	Inoperable only	Included pts strongly declining surgery	Gem
Baseline character – istics	Male (%)	37	67	unknown
	T4 (%)	20	46	Gem
	N0 (%)	61	42	Gem
	Age (minimum)	30	44	Gem
Treatment	Schedule	Gem d1 d8 d15	GemOx d1 d16	N/A
Assessment	Tumour assessment	WHO	RECIST	unknown
	CT scans during Rx	>4 weeks apart	Weeks 4, 14, 26	unknown
Analysis	Censor non-PD pts	Last alive date	Last CT scan date	Gem

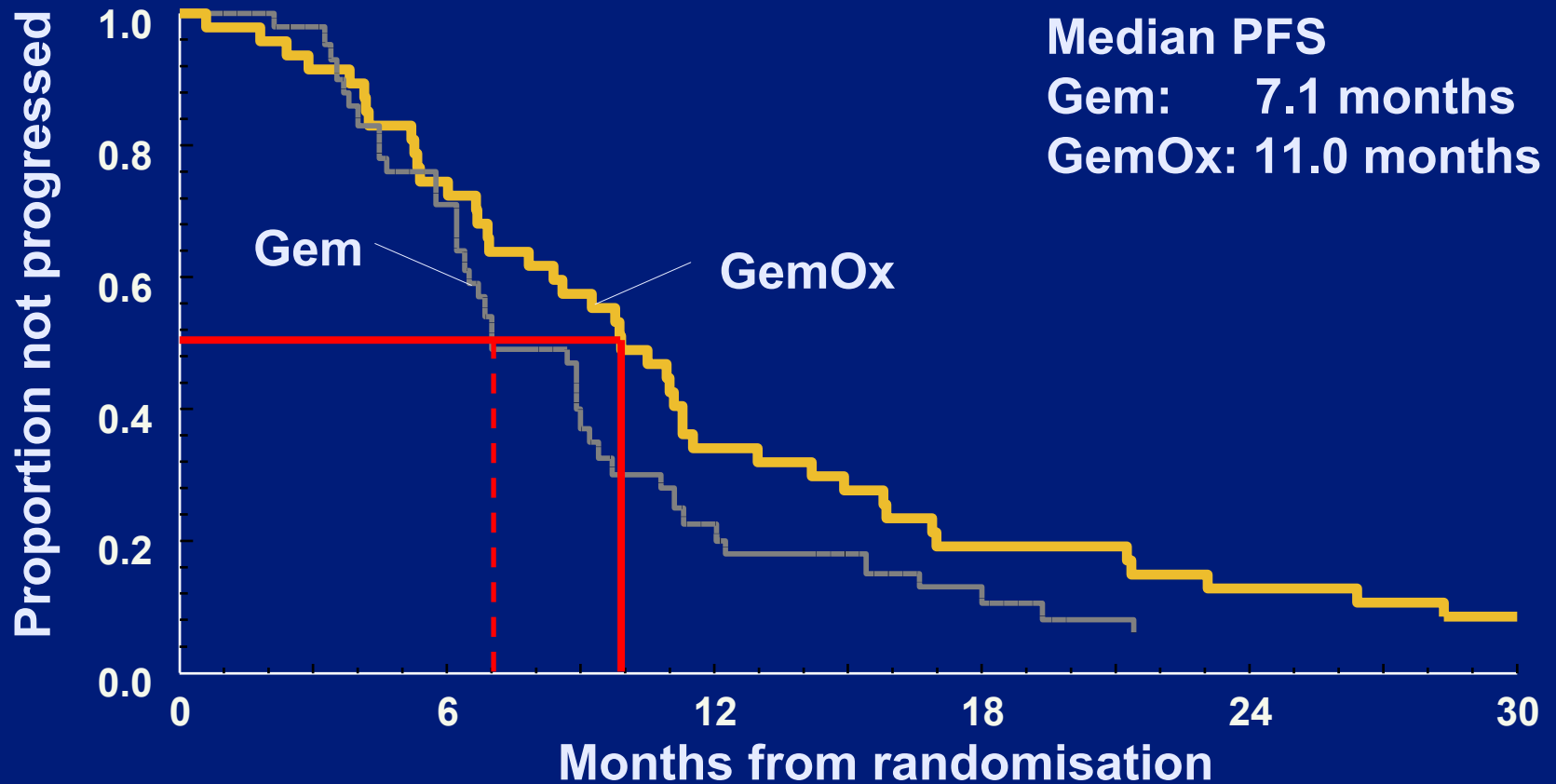
Local control



Number at Risk

GemOx: 48 44 37 28 19 17 11

Progression free survival



Number at Risk

GemOx: 48

36

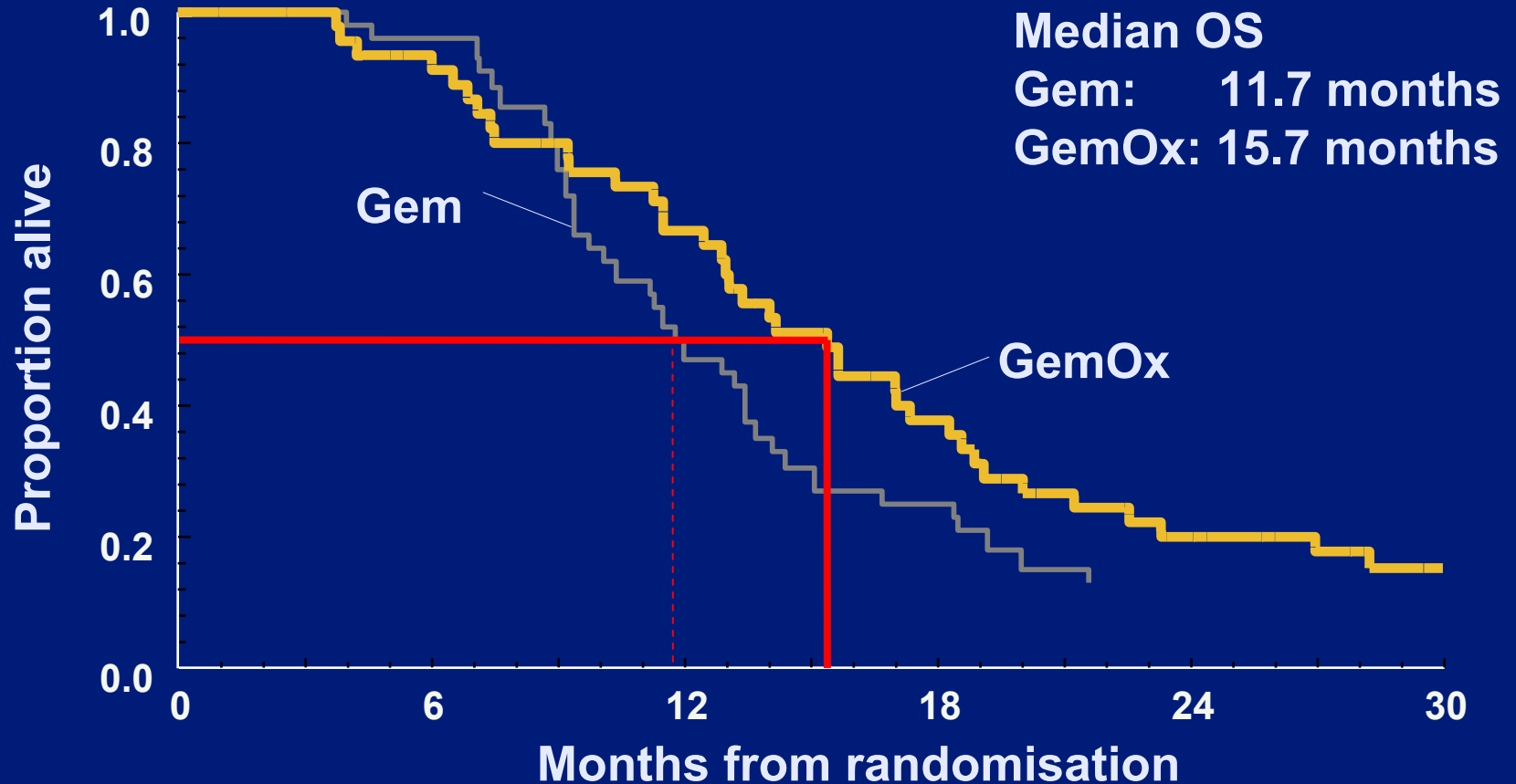
17

10

7

5

Overall survival



Number at Risk

GemOx: 48

43

32

18

10

7

CA19.9

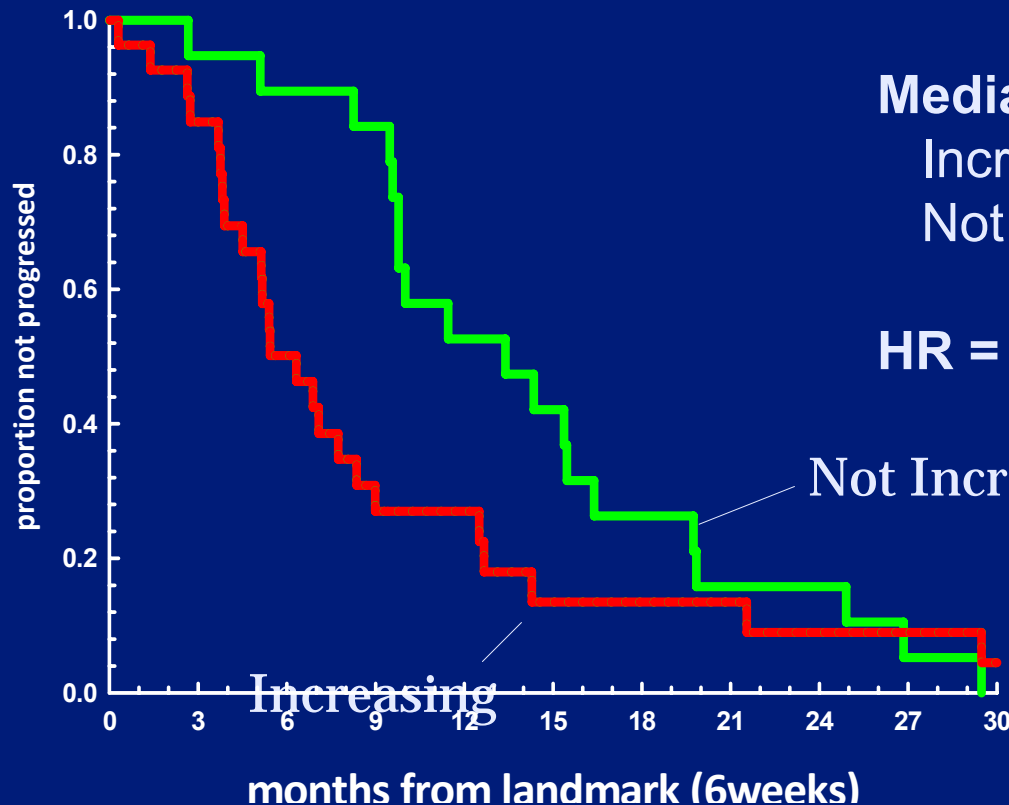
- Patients with CA19.9 reductions were 5 times as likely to also have a partial RECIST response. Odds Ratio = 5.2, 95% CI (1.3, 24), p=0.019

RECIST Response		Yes N (%)	No N (%)	Total N (%)
CA19.9 Smallest Observed (% Baseline)	Reduced 50%	13 (50)	13 (50)	26 (100)
	Not Reduced 50%	3 (15)	17 (85)	20 (100)
	Total	16 (35)	30 (65)	46 (100)

Sensitivity = 81%, Specificity = 57%

Landmark Analysis

- Change in CA19.9 over 6 weeks observed and classified:



Median PFS (after 6 weeks)
 Increasing : 6m months
 Not Increasing : 13 months

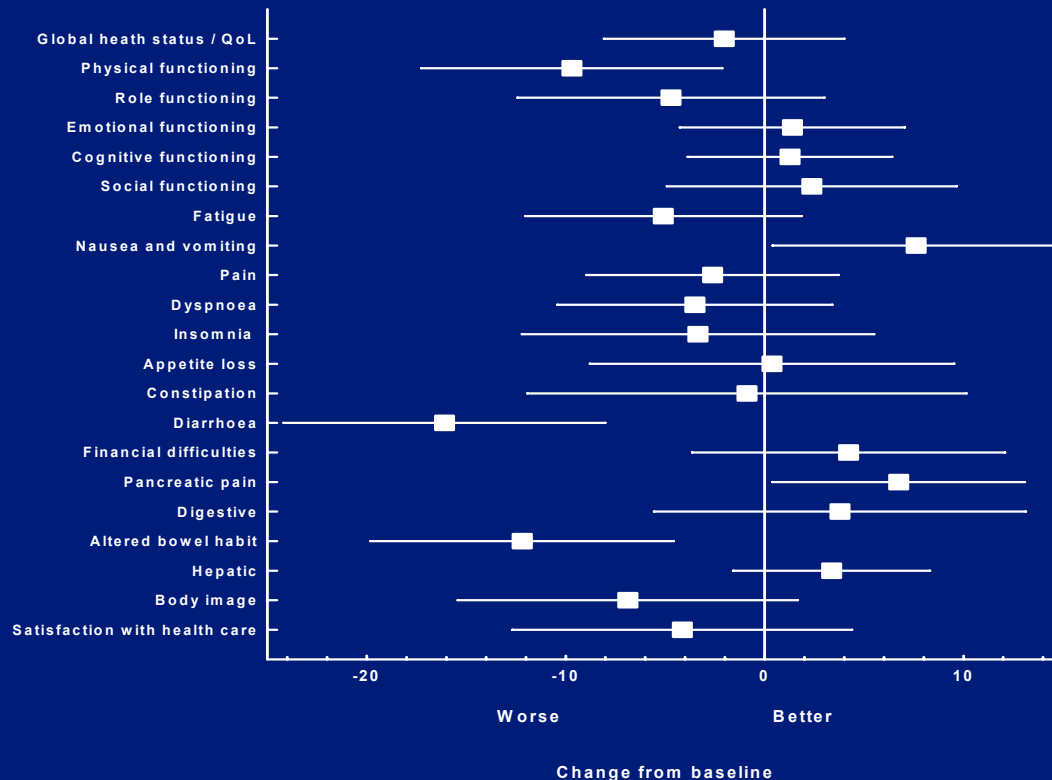
HR = 1.75 95% CI (0.94, 3.4)

Number at Risk

Increase:	27	14	7	4	3	1
Not Inc:	20	18	11	6	4	0



Quality of Life



Mean patient rating throughout treatment for global health status and a range of physical and social items did not significantly change when compared with baseline levels.

Physical items : fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea, indigestion, altered bowel habit.

Social items : financial difficulties, body image, satisfaction with health care, sexuality.

Conclusions

- Compared to our previous study using the same radiation schedule, addition of oxaliplatin was associated with improved local control, PFS & OS without significant offset by toxicity.
- The apparent longer duration of local control and survival may be due to patient selection or other factors but also may be due to an incremental benefit from more intensive systemic therapy and warrant further study in controlled trials.