

Pro: Neoadjuvant Chemoradiation for Pancreas Cancer

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Disclosures

- Employed by Duke University
- Varian: Research funding
- Merck: Research funding
- UptoDate: section editor author

3 Reasons in Favor of Neoadjuvant Chemoradiation

- Local recurrence is common in pancreas cancer
- Neoadjuvant radiation therapy facilitates a margin negative resection
- Higher rates of compliance and less toxicity with neoadjuvant radiation therapy

Respecting Disease Biology

Patterns of Recurrence

Study	# Pts.	Local (%)	Peritoneal (%)	Liver (%)
Tepper	26	50	-	-
Griffin	36	53	31	44
Whittington	29	85	23	23
Ozaki	14	86	36	79
Westerdahl	74	86	-	92

Even in the modern era.....

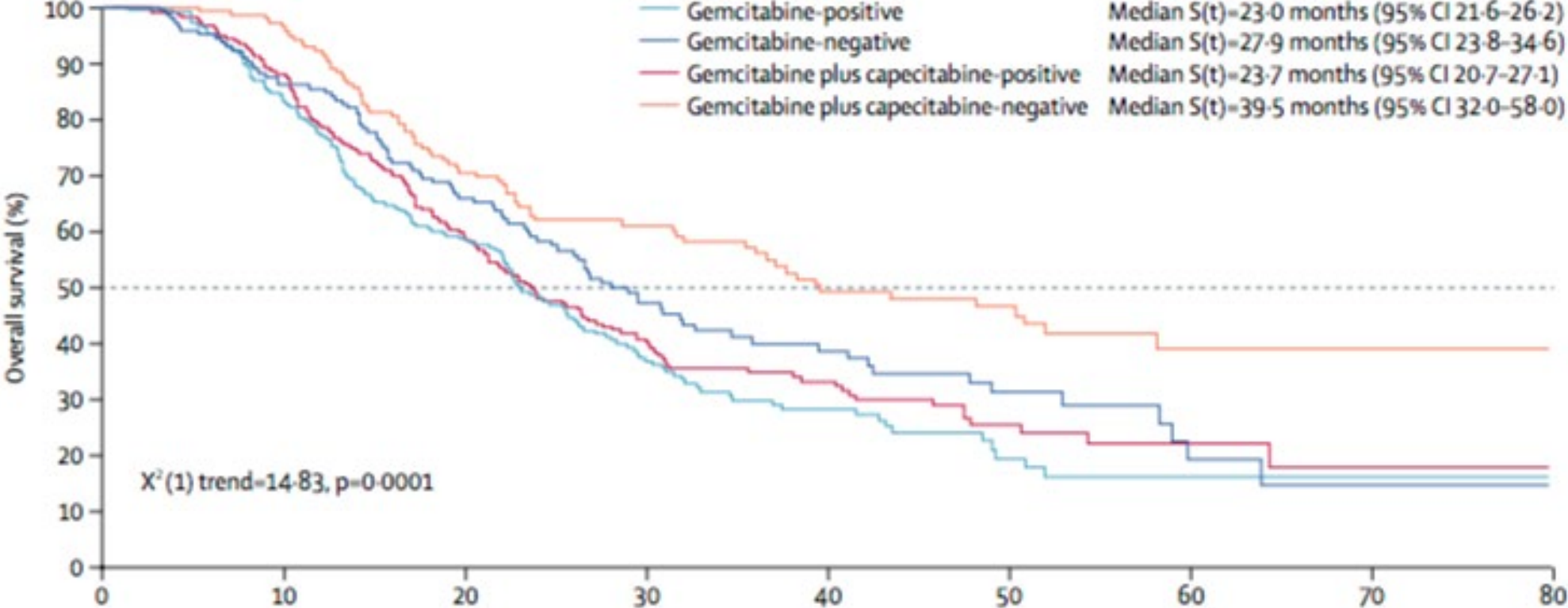
	Gemcitabine (n=366)	Gemcitabine plus capecitabine (n=364)	Total (n=730)	p value*
Disease relapse	243 (66%)	236 (65%)	479 (66%)	0.715
Site of relapse				
Local	129 (53%)	109 (46%)	238 (50%)	0.156
Liver	106 (44%)	92 (39%)	198 (41%)	0.348
Other intra-abdominal	46 (19%)	63 (27%)	109 (23%)	0.055
Lung	23 (9%)	29 (12%)	52 (11%)	0.398
Bone	7 (3%)	6 (3%)	13 (3%)	1.000
Unknown	4 (2%)	5 (2%)	9 (2%)	0.965
Death without recurrence	43 (12%)	35 (10%)	78 (11%)	0.416

Table 4: Pattern of disease relapse

Higher rates of R0 resection

Trial	N	Treatment Arms	R0 resection rate	Median Survival	OS
CONKO (98-04)	368	Obs Gem	83%	20.2 mo 22.8 mo	5 yr 10% 21%
RTOG 9704 (98-02)	451 388 head	5FU, CRT, 5FU Gem, CRT, Gem	42%	17.1 mo 20.5 mo	5 yr 18% 22%
ESPAC-3 (07-09)	1088	5FU Gem	84%	23 23.6	2 yr 48% 49%
ESPAC-4 (08-14)	732	Gem Gem/Cap	60%	25.5 mo 28 mo	2 yr 52.1% 53.8%
PRODIGE (12-16)	493	Gem FOLFIRINOX	60%	35 mo 54.4 mo	3 yr 48.6% 63.4%

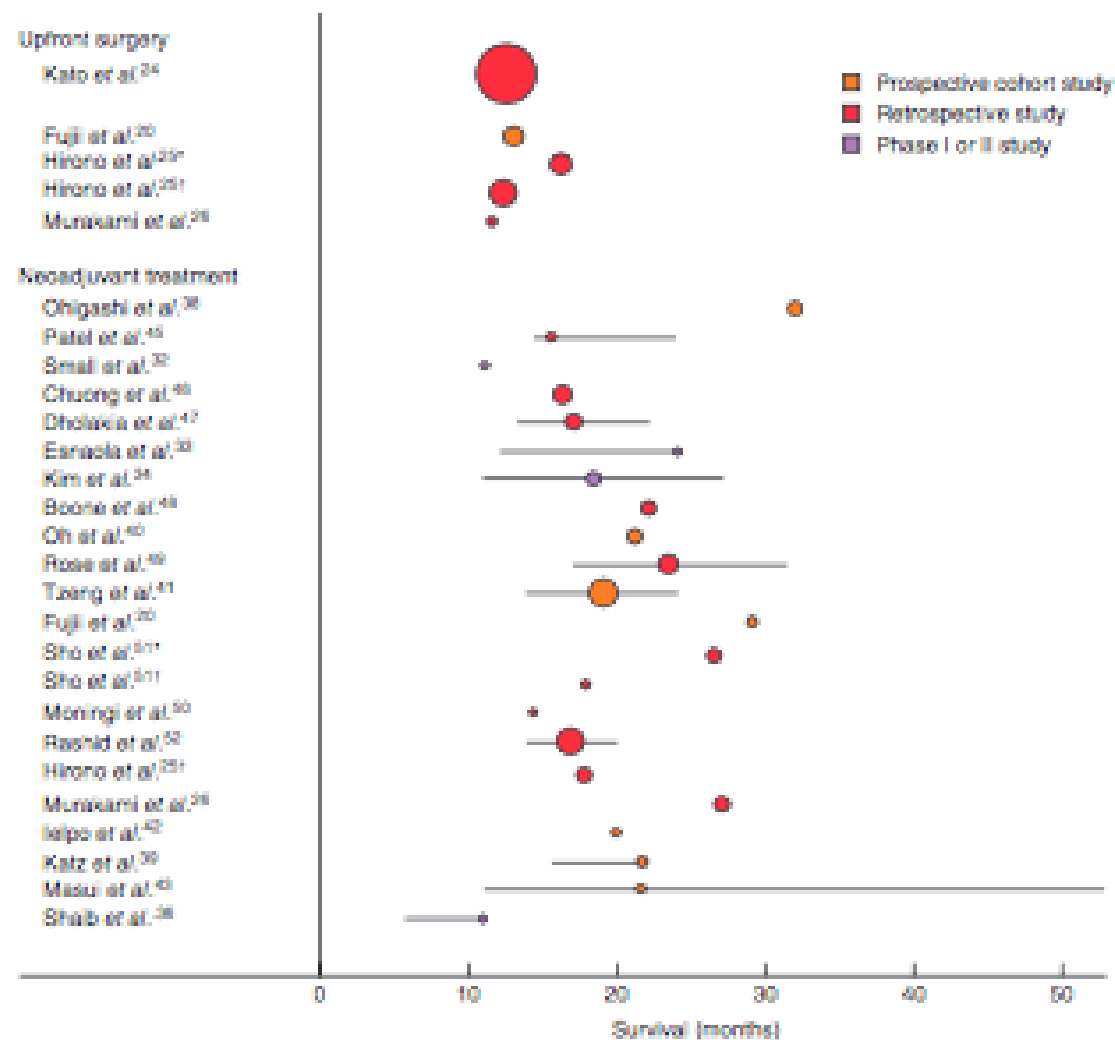
R0 Resection is Important



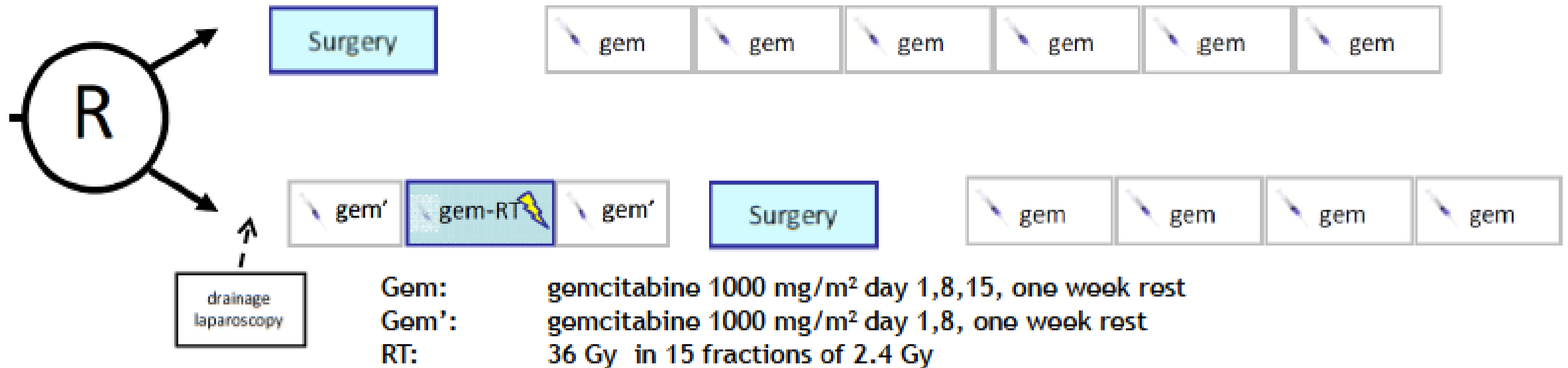
	0	10	20	30	40	50	60	70	80
Number at risk									
Gemcitabine-positive	219	178	118	58	31	12	3	1	0
Gemcitabine-negative	147	124	89	51	30	15	6	2	0
Gemcitabine plus capecitabine-positive	221	193	124	71	42	20	6	3	1
Gemcitabine plus capecitabine-negative	143	135	95	68	41	30	13	7	0

R0 resection with Neoadjuvant Therapy

- Meta-Analysis
 - 38 studies
 - 3484 patients
 - 1738 neoadjuvant therapy
- R0: 66.9% (surgery 1st) vs. 86.8% (NAT)
- Median OS: 14.8mo (surgery 1st) vs. 18.8mo (NAT)



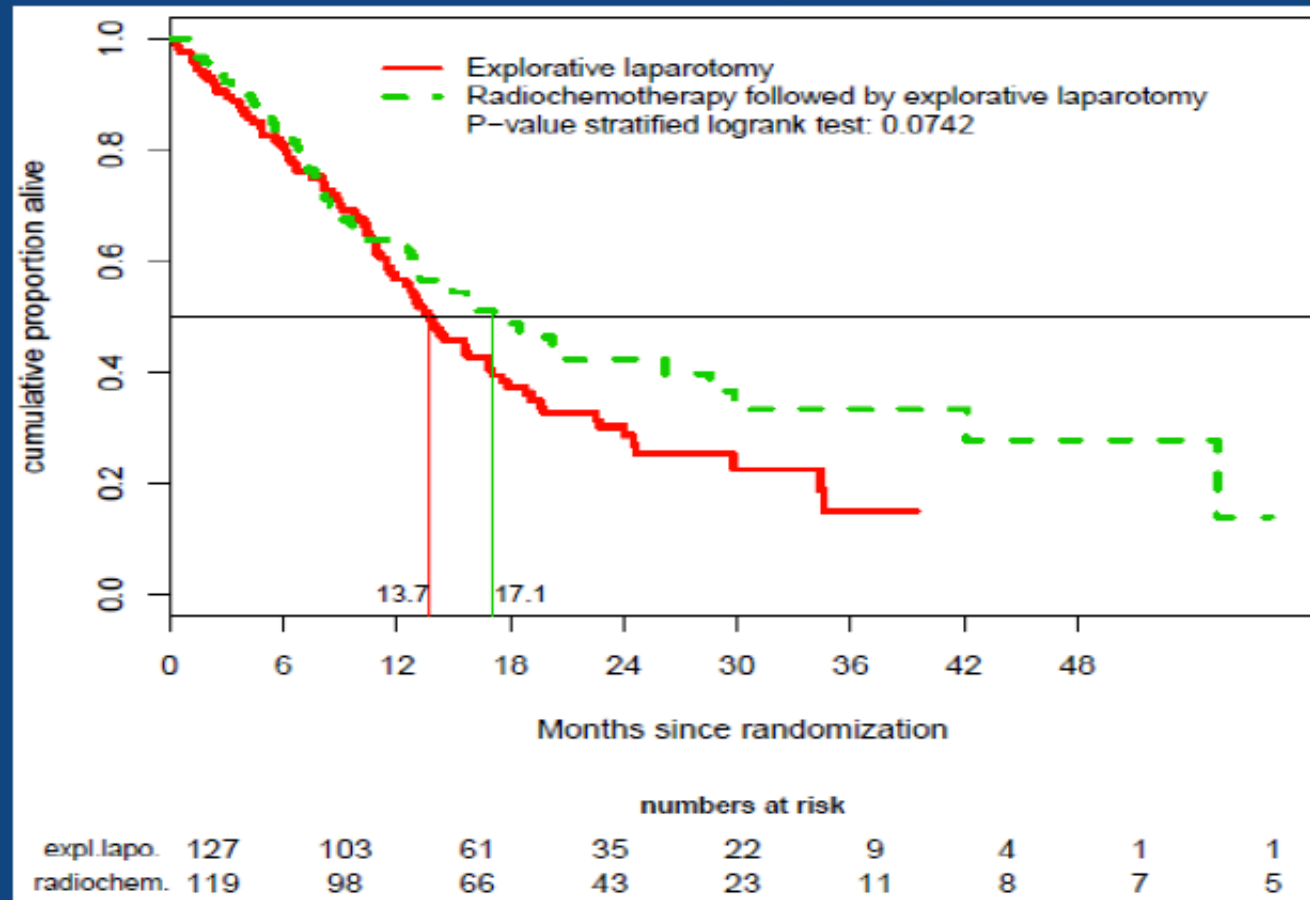
Preopanc RCT



R0 resection: 31% (surgery 1st) and 63% (CRT)

Preopanc Trial

Overall survival (ITT)



Preliminary: 149/176 events

Median survival:

13.7 vs 17.1 months

HR 0.74

p=0.074

Phase II/III RCT Borderline Resectable Pancreas Cancer

Borderline Resectable
Pancreas
Adenocarcinoma
(NCCN)

58/110 pts
(planned interim
analysis)

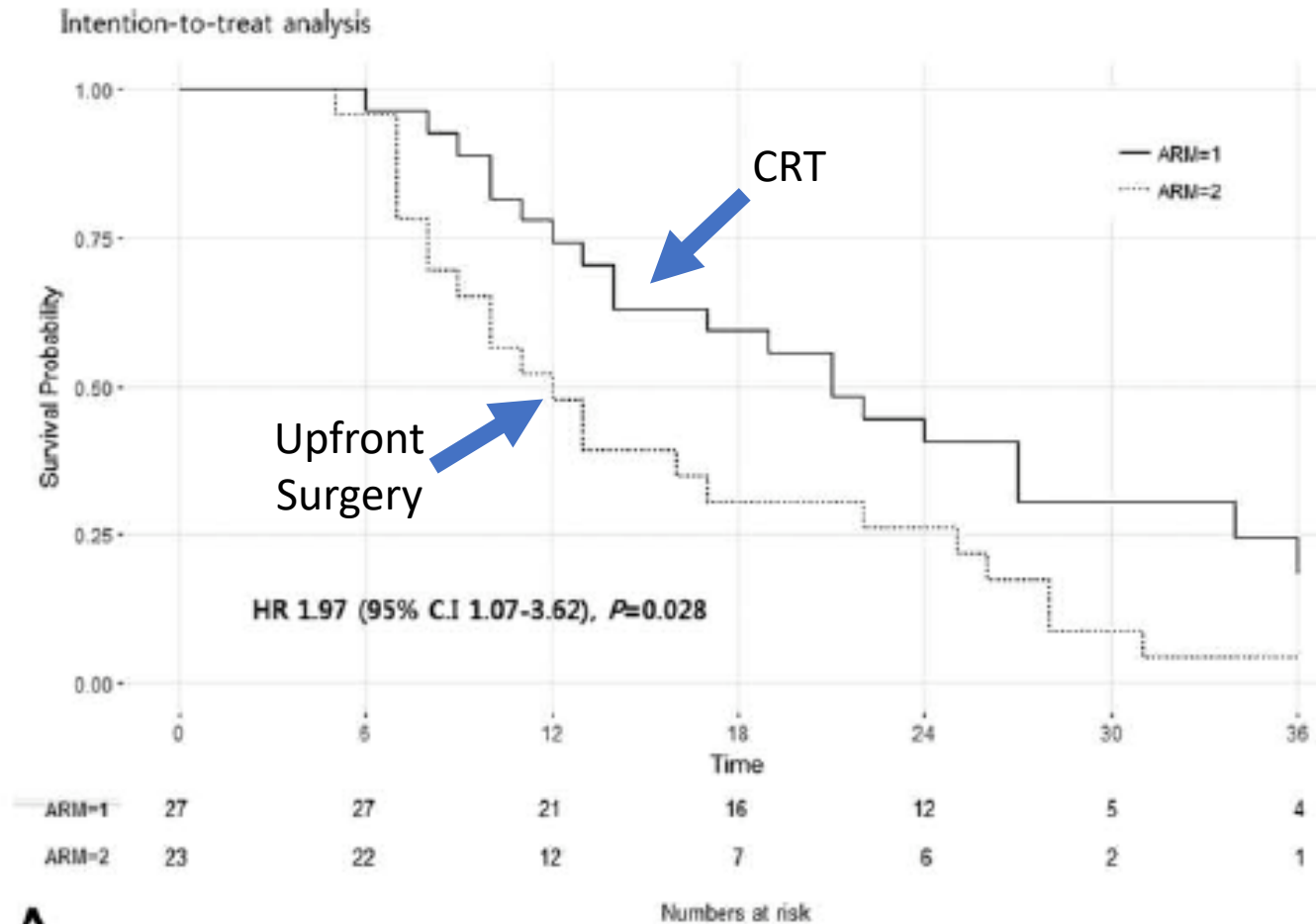
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Upfront Surgery

Neoadjuvant CRT

54Gy
Gem: 400mg/m², Weekly

Phase II/III RCT Borderline Resectable Pancreas Cancer



- R0: 26% (surgery 1st) vs. 52% (CRT)
- Median OS: 12mo (surgery 1st) vs. 24mo (CRT)

A

Higher rates of
compliance/Less toxicity

Trial	N	Treatment Arms	Completion Adjuvant Tx	Median Survival	OS
CONKO (98-04)	368	Obs Gem	62%	20.2 mo 22.8 mo	5 yr 10% 21%
RTOG 9704 (98-02)	451 388 head	5FU, CRT, 5FU Gem, CRT, Gem	87%/86% 90%/88%	17.1 mo 20.5 mo	5 yr 18% 22%
ESPAC-3 (07-09)	1088	5FU Gem	55% 60%	23 23.6	2 yr 48% 49%
ESPAC-4 (08-14)	732	Gem Gem/Cap	65% 54%	25.5 mo 28 mo	2 yr 52.1% 53.8%
PRODIGE (12-16)	493	Gem FOLFIRINOX	79% 66%	35 mo 54.4 mo	3 yr 48.6% 63.4%

Compliance with Neoadjuvant CRT

Trial	N	Treatment Arms	Completion Neoadjuvant Tx	Median Survival
Preopanc	248	Upfront Surgery CRT->Surgery	89%	13.7 mo 17.1 mo
Korea RCT	58/110	Upfront Surgery CRT->Surgery	96%	12 mo 24 mo

Toxicity: Neoadjuvant vs. Adjuvant CRT

Trial	N	Treatment Arms	Toxicity	Median Survival
Preopanc	248	Upfront Surgery CRT->Surgery	46%	13.7 mo 17.1 mo
RTOG 97-04	451 388 head	5FU, CRT, 5FU Gem, CRT, Gem	62% 79%	5 yr 18% 22%

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