Memorial Sloan Kettering Cancer Center

Updates in Esophageal and Pancreatic Cancer in 2024: Practice-changing or –informing studies

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2024 ASCO ANNUAL MEETING

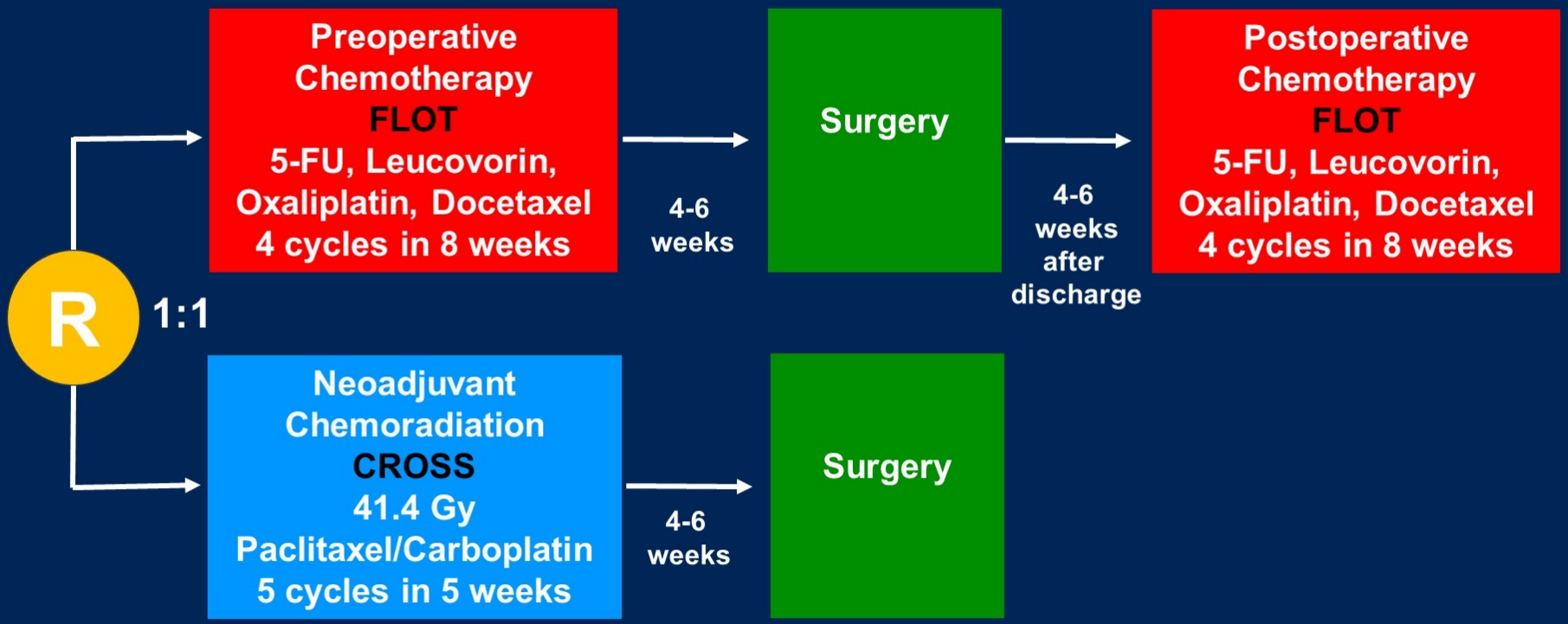
Perioperative Chemotherapy (FLOT) versus Neoadjuvant Chemoradiotherapy (CROSS) for Resectable Esophageal Adenocarcinoma

The ESOPEC Trial (NCT02509286)

J Hoeppner, F Lordick, T Brunner, C Schmoor, B Kulemann, UP Neumann, G Folprecht, T Keck, F Benedix, M Schmeding, E Reitsamer, CJ Bruns, JF Lock, B Reichert, M Ghadimi, K Wille, I Gockel, JR Izbicki, S Utzolino, P Grimminger

PRESENTED BY: Jens Hoeppner MD FACS FEBS

ESOPEC Trial Scheme



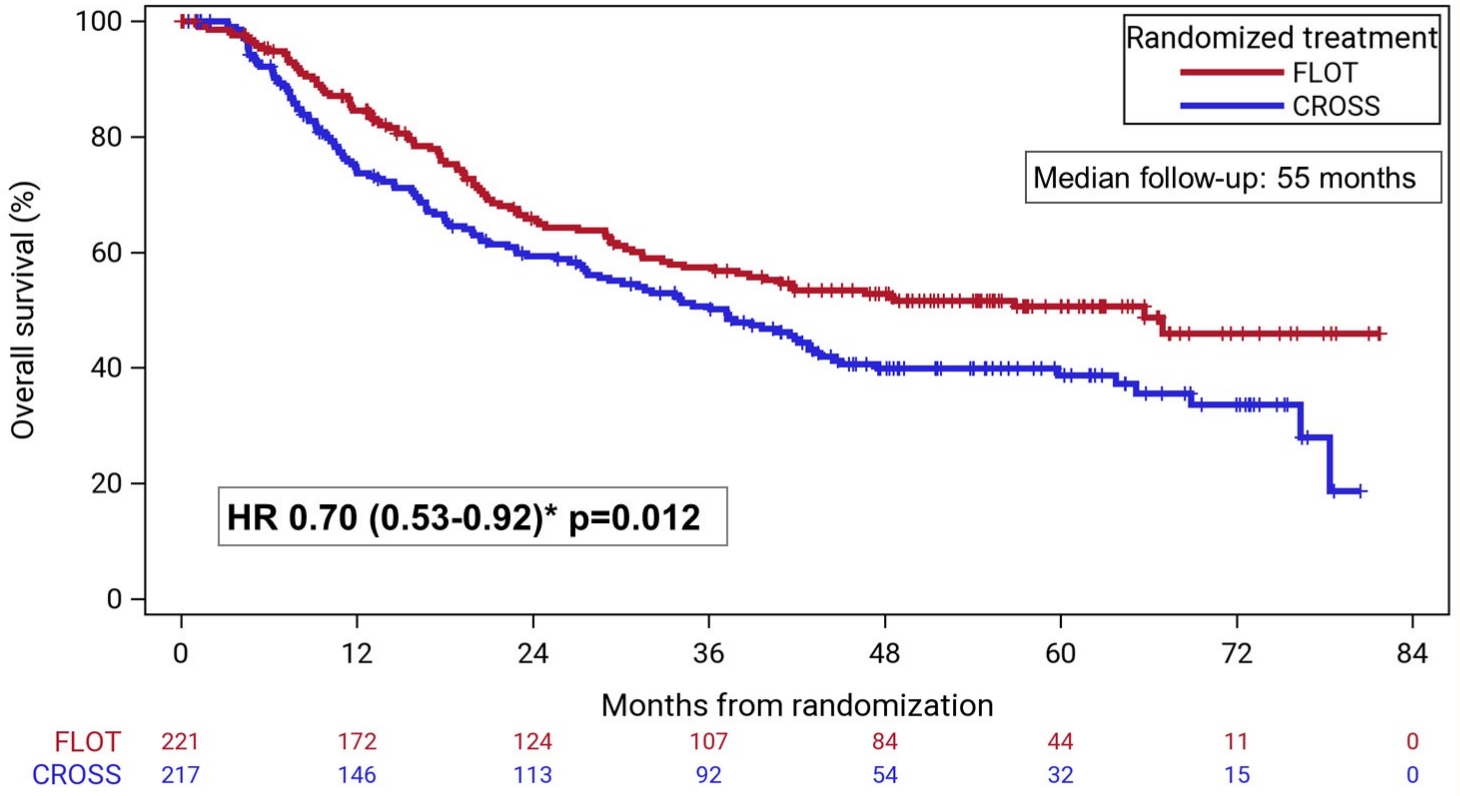
Treatment Exposure

	FLOT Group	CROSS Group
N	221	217
Started neoadjuvant treatment (PP population*)	93.7 %	90.3 %
Completed neoadjuvant treatment	87.3 %	67.7 %#
Received neoadjuvant treatment plus surgery	86.0 %	82.9 %
Received adjuvant treatment	63.3 %	
Completed adjuvant treatment	52.5 %	

*Per protocol population according to Clinical Trial Protocol and Statistical Analysis Plan

#Completion rate (41.4Gy) of radiotherapy **98%**

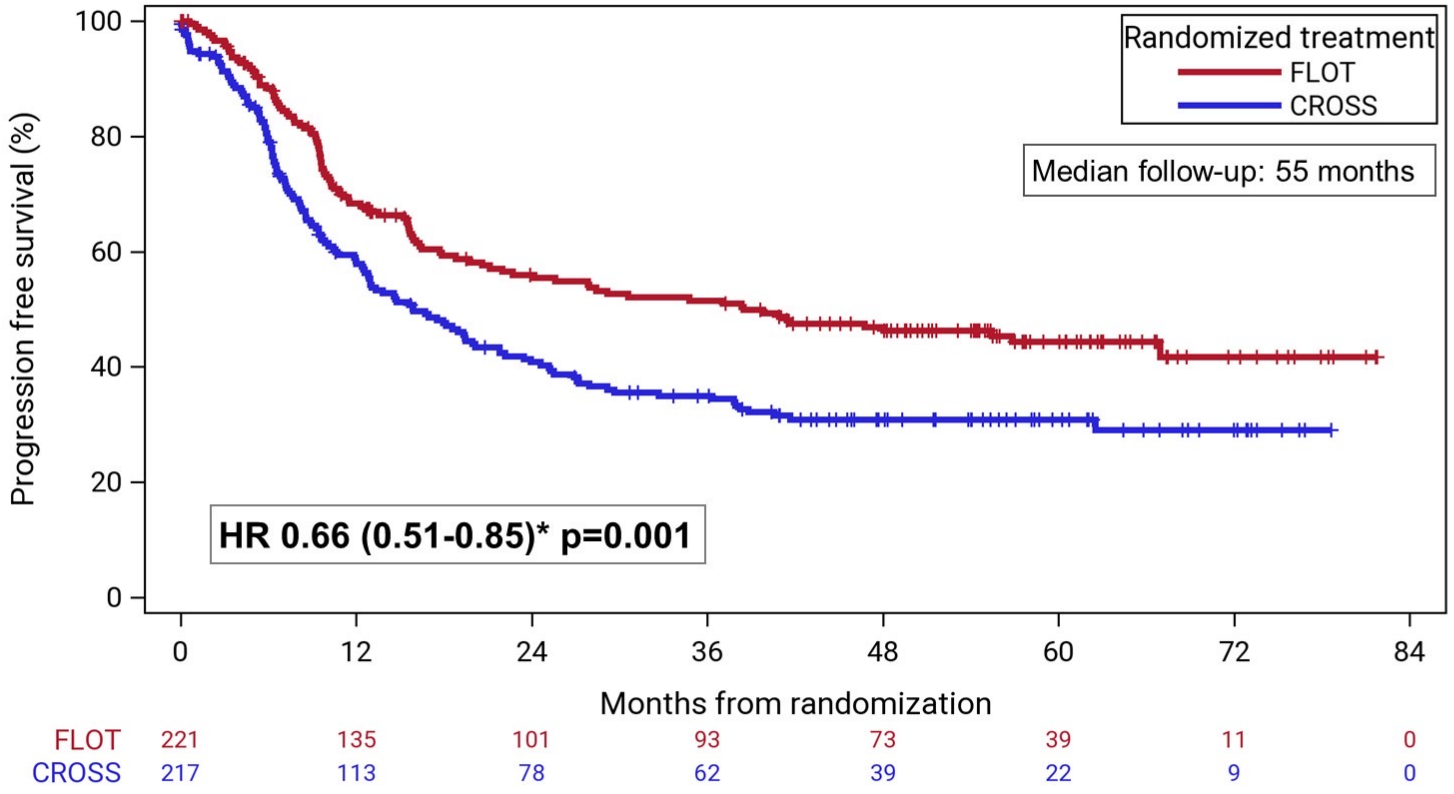
Overall Survival - ITT Population



	FLOT	CROSS
Events	97	121
Median OS time (months)	66 95% CI 36 – n.e	37 95% CI 28 – 43
3-year OS rate	57.4%	50.7%
5-year OS rate	50.6%	38.7%

*Two-sided 95% confidence interval; Cox regression adjusted for N stage and age, stratified for trial site

Progression Free Survival – ITT Population



	FLOT	CROSS
Events	107	137
Median PFS time (months)	38 95% CI 21 – n.e.	16 95% CI 12 – 22
3-year PFS rate	51.6%	35.0%
5-year PFS rate	44.4%	30.9%

*Two-sided 95% confidence interval; Cox regression adjusted for N stage and age, stratified for trial site

PRESENTED BY: Jens Hoeppner MD FACS FEBS

Postoperative Complications – Surgery Population

	FLOT Group	CROSS Group
N	191	180
Postoperative morbidity		
Clavien Dindo I	20.9%	20.0%
Clavien Dindo II	13.6%	15.0%
Clavien Dindo III	23.0%	23.3%
Clavien Dindo IV	6.8%	4.4%
Postoperative mortality		
30-days	1.0%	1.7%
90-days	3.2%	5.6%

Summary of Trial Results

	ESOPEC Trial				
	FLOT Group	CROSS Group	CROSS Trial (CRT Group - AC)	Neo-AEGIS Trial (CRT Group)	FLOT-4 (FLOT Group)
Completed **pre-op** treatment	87.3%	**67.7%**	92%	87% (RT - 99%)	90%
Completed **post-op** treatment	52.5%				46%
pCR	16.8%	**10%**	23%	12%	16%
Median OS	66 mos	**39 mos**	43 mos	49 mos	50 mos
3-year OS	57.4%	50.7%	54%	57%	57%

PRESENTED BY: Karyn A. Goodman, MD, MS

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ESOPEC study

- Lack of benefit for RT has now been definitively established by ESOPEC
- NeoAEGIS – where 85% of Pts received MAGIC-type regimen – showed no PFS/OS difference between chemoRT and peri-op chemo
- Unanswered questions:
  - Is adjuvant nivolumab after chemoRT and surgery superior to peri-op chemo? [Checkmate 577]
  - Is durvalumab + peri-op chemo superior to peri-op chemo? [MATTERHORN]
  - What if a Pt isn't a candidate for FLOT?
  - How does PET-directed therapy compare? [CALGB 80803]

Best of Both Worlds: FLOT + CROSS

TNT-OES-2 Trial: Phase II

- N+ EAC/EJC
- N = 216

FLOT → CROSS → Surgery

TOPGEAR: Phase III

- Locally Advanced Gastric/EJC

R 1:1

- EC(O)F(X) or FLOT x 3 → Surgery → EC(O)F(X) or FLOT x 3
- EC(O)F(X) or FLOT x 2 → 45Gy + 5-FU → Surgery → EC(O)F(X) or FLOT x 3

NCT06161818; Leong T, Annals of Surgery, 2017

PRESENTED BY: Karyn A. Goodman, MD, MS

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2024 ASCO ANNUAL MEETING

Effect of chemotherapy/targeted therapy alone vs. chemotherapy/targeted therapy followed by radical surgical resection on survival and quality of life in patients with limited-metastatic adenocarcinoma of the stomach or esophagogastric junction – The IKF-575 / RENAISSANCE phase III trial

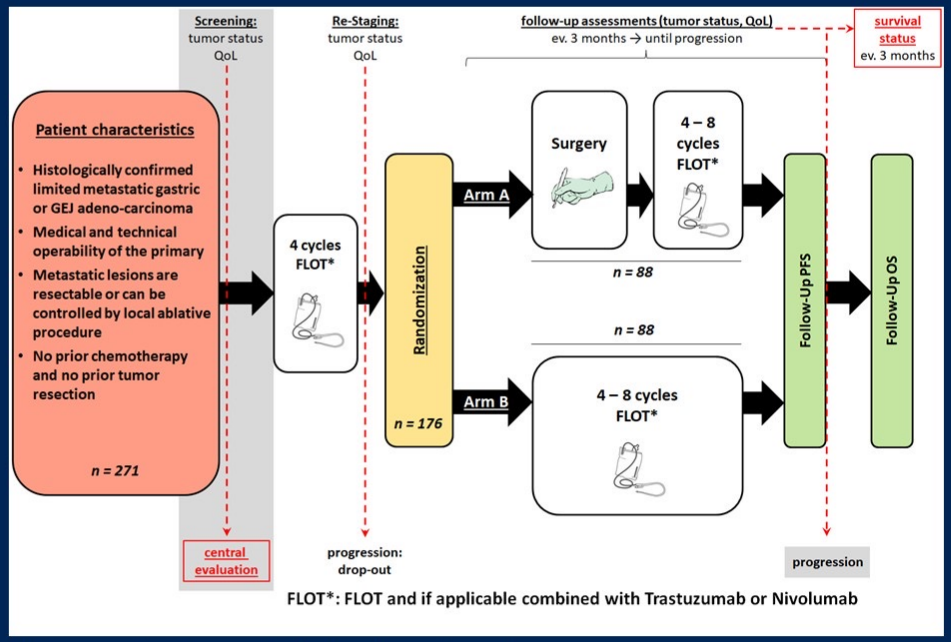
Salah-Eddin Al-Batran, Sylvie Lorenzen, Jorge Riera Knorrenschild, Karel Caca, Christian Mueller, Daniel E Stange, Thomas Zander, Claus Bolling, Nils Homann, Jochen Gaedcke, Peter C. Thuss-Patience, Patrick Michl, Wolfgang Blau, Kai Wille, Christine Koch, Claudia Pauligk, Daniel W. Mueller, Ulli Simone Bankstahl, Stefan Paul Mönig, Thorsten Oliver Goetze

On behalf of the FLOT-AIO German Gastric Study Group

Presented by
Salah-Eddin Al-Batran, MD
Northwest Hospital Frankfurt, University Cancer Center (UCT) Frankfurt and
The Frankfurt Institute for Clinical Cancer Research IKF

Study Flow Chart

RENAISSANCE is an investigator-initiated phase III trial



Stratification criteria:

- tumor location:
  GC vs. GEJ adenocarcinoma
- response to preoperative FLOT: CR/PR vs. SD
- distant lymph node metastases (RPLN) only vs. additional organ involvement

Note: sample sizes are initially planned numbers
Actually enrolled: 182; actually randomized: 141 (69 Arm A; 72 Arm B)

Definition of the limited metastatic status

Pre-defined subgroups

1. Retroperitoneal lymph node (RPLN) metastases
   e.g. para-aortal, intra-aorto-caval, parapancreatic or mesenterial lymph nodes
   Note: in duodenum invading gastric cancer or retropancreatic nodes were not regarded M1

   or/and

2. at maximum one organ involved with or without RPLN metastases according to the following schema:
   - I. Localized potentially operable peritoneal carcinomatosis: stage P1 according to classification of the „Japanese Research Society for Gastric Cancer“ (Clinically visible carcinomatosis of the peritoneum or of the pleura and >P1 peritoneal carcinomatosis were not allowed!) or
   - II. Liver: maximum of 5 metastatic lesions that are potentially resectable or
   - III. Lung: unilateral involvement, potentially resectable or
   - IV. Uni- or bilateral Krukenberg tumors (ovarian met.) in the absence of macroscopic peritoneal carcinomatosis or
   - V. Uni- or bilateral adrenal gland metastases or
   - VI. Extra-abdominal lymph node metastases such as supraclavicular or cervical lymph node involvement or
   - VII. Localized bone involvement (defined as being within one radiation field) or
   - VIII. Other metastatic disease location that is considered limited by the investigator and is confirmed by the review committee

Treatment

Treatment cycle completed (ITT)	Arm A (N= 67)	Arm B (N= 72)	Total (N= 139)
Mean	6.4	8.9	7.7
Range	4-12	4-12	4-12
Pre-randomization cycle 1	67 (100%)	72 (100%)	139 (100%)
Pre-randomization cycle 2	67 (100%)	72 (100%)	139 (100%)
Pre-randomization cycle 3	67 (100%)	72 (100%)	139 (100%)
Pre-randomization cycle 4	67 (100%)	72 (100%)	139 (100%)
Cycle 5 (Post-randomization cycle 1)	44 (66%)	60 (83%)	104 (75%)
Cycle 6 (Post-randomization cycle 2)	42 (63%)	58 (81%)	100 (72%)
Cycle 7 (Post-randomization cycle 3)	35 (52%)	55 (76%)	90 (65%)
Cycle 8 (Post-randomization cycle 4)	29 (43%)	53 (74%)	82 (59%)
Cycle 9 (Post-randomization cycle 5)	10 (15%)	41 (57%)	51 (37%)
Cycle 10 (Post-randomization cycle 6)	6 (9%)	37 (51%)	43 (31%)
Cycle 11 (Post-randomization cycle 7)	4 (6%)	30 (42%)	34 (24%)
Cycle 12 (Post-randomization cycle 8)	3 (4%)	28 (39%)	31 (22%)

End of study treatment and further therapy

	Arm A (N= 67)	Arm B (N= 72)	Total (N= 139)
Reason for end of therapy			
Per protocol	22 (33%)	37 (51%)	59 (42%)
Patient wish or toxicity	20 (30%)	22 (31%)	42 (30%)
Progression/recurrence	16 (24%)	11 (15%)	27 (19%)
Other	5 (7%)	2 (3%)	7 (5%)
Death	4 (6%)	-	4 (3%)
At least one further anticancer therapy	35 (52%)	59 (82%)	94 (68%)

Surgery (ITT)

	Arm A (N= 67)	Arm B (N= 72)	Total (N= 139)
Surgery executed	61 (91%)	15 (21%)	76 (55%)
Timing of surgery			
After cycle 4 (after rando)	61 (100%)	12 (80%)	73 (96%)
Later time point[1]	-	2 (13%)	2 (3%)
If surgery was not executed, reasons:			
Patient wish	4 (6%)	n.a.	
Progression	2 (3%)	n.a.	
Resection executed	59 (97%)	15 (100%)	74 (97%)

[1]both after cycle 6

Surgery (Surgery Population)

	Arm A (N= 61)	Arm B (N= 15)	Total (N= 76)
Complication due to surgery	36 (59%)	6 (40%)	42 (55%)
Type of complication			
Surgical	5 (8%)	1 (7%)	6 (8%)
Medical	9 (15%)	3 (20%)	12 (16%)
Surgical and medical	22 (36%)	2 (13%)	24 (32%)
Re-Surgery	12 (20%)	-	12 (16%)
30-day mortality	1 (2%)	1 (7%)	2 (3%)
90-day mortality	5 (8%)	1 (7%)	6 (8%)

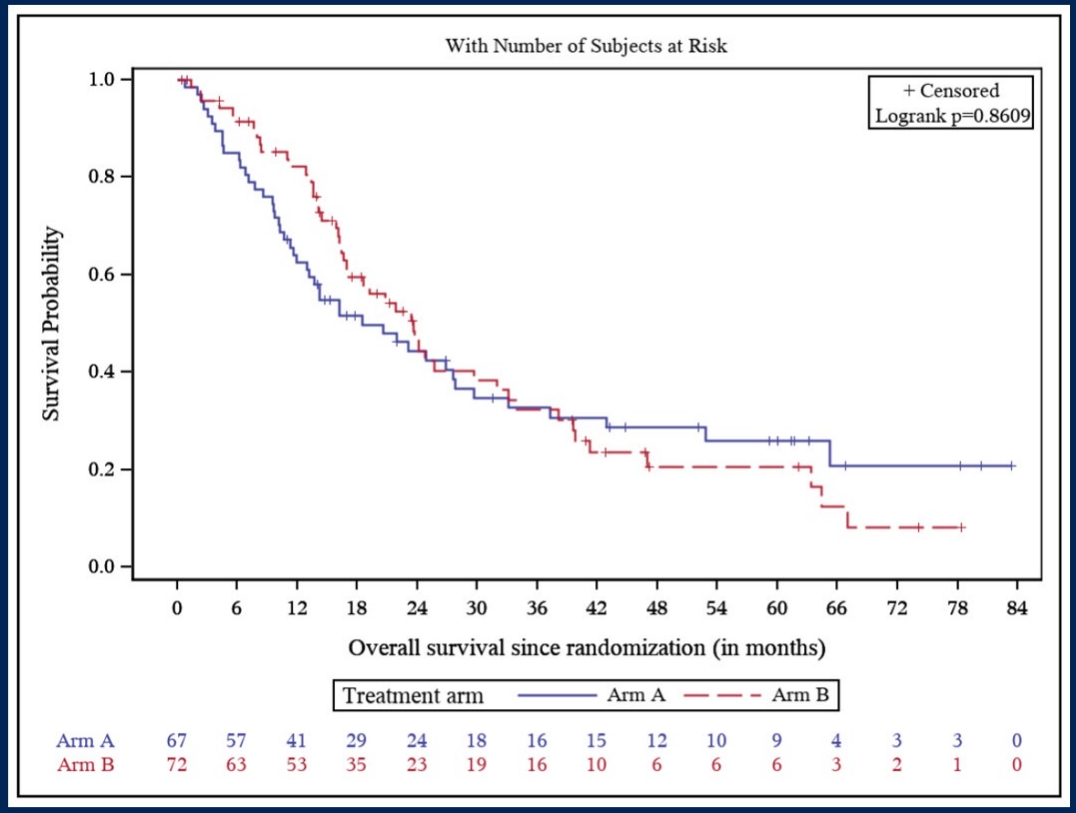
Overall Survival

Primary Endpoint: Overall survival (since randomization)

	Arm A (N= 67)	Arm B (N= 72)
Time until event, months [95% CI]		
25% Quantile	**9.5** [4.6, 11.6]	**14.0** [8.3, 16.4]
Median	**18.5** [11.9, 27.7]	**23.6** [16.6, 31.9]
75% Quantile	**65.2** [27.7, -]	**41.2** [31.9, 67.0]

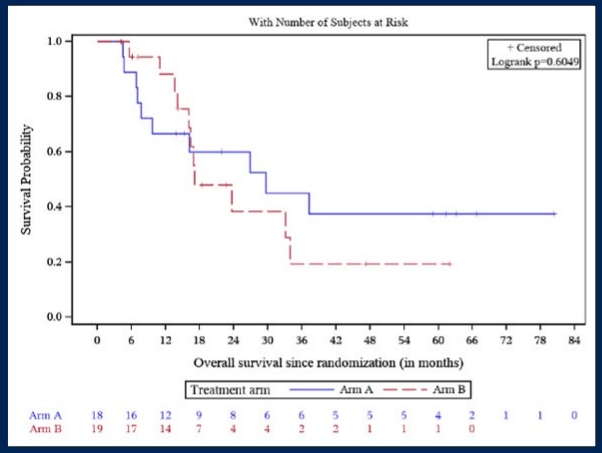
Log Rank Test: p = 0.8609

Cox Proportional Hazard Model:
Hazard Ratio (95% CI), 1.037 (0.691 - 1.556), p = 0.8610



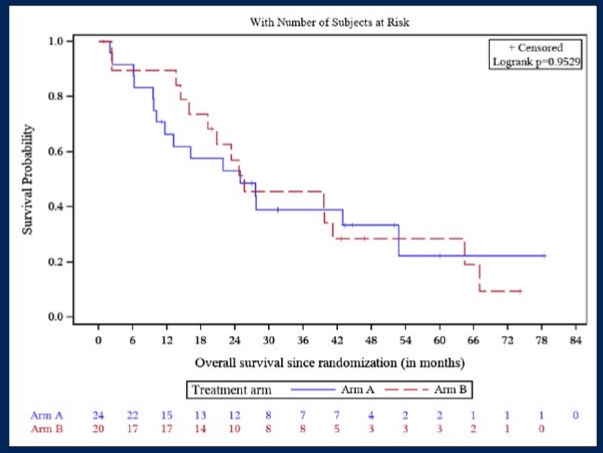
Overall Survival: Subgroup analyses

RPLN only (subgroup 1)



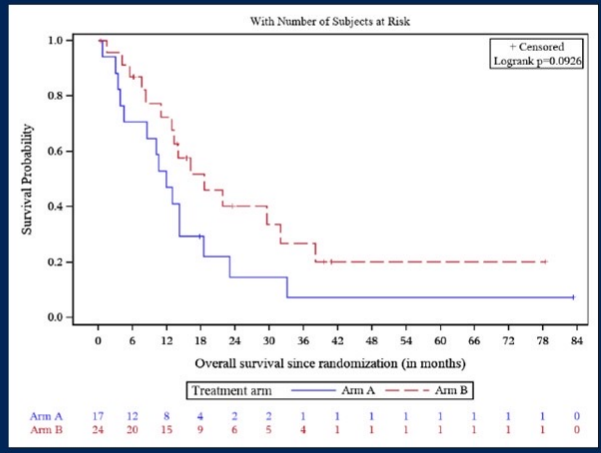
Median OS 29.6 vs. 17.1 months
36-mon OS 45% vs. 19%

Liver metastases (subgroup 2.II)



Median OS 24.9 vs. 25.7 months
36-mon OS 39% vs. 46%

Peritoneal metastases (subgroup 2.I)



Median OS 11.9 vs.18.6 months
36-mon OS 7% vs. 27%

Data for Arms A vs. B, respectively

RENAISSANCE study

- Resecting oligometastatic dz should NOT be standard
- Considerations for this population:
  - Should ideally be treated on a study, e. EA2183
  - Should exclude Pts with peritoneal carcinomatosis
  - Should treat Pts with visceral metastases with great caution
  - Should administer ≥6 mos of best systemic therapy and have ongoing dz control
  - Should be decided by an experienced MDT
  - Should include surgery, definitive chemoRT and ablation

2024 ASCO ANNUAL MEETING

ECOG-ACRIN cancer research group

A randomized phase II study of gemcitabine and nab-paclitaxel compared with 5-fluorouracil, leucovorin, and liposomal irinotecan in older patients with treatment-naive metastatic pancreatic cancer (**GIANT**) ECOG-ACRIN EA2186

Efrat Dotan[1], Paul J. Catalano[2], Leon Lenchik[3], Robert Boutin[4], Xin Yao[5], James P. Ohr[6], Kian-Huat Lim[7], Namrata Vijayvergia[1], Sreenivasa R. Chandana[8], Aparna Kalyan[9], Richard F. Dunne[10], David B. Zhen[11], Daneng Li[12], Melissa A. Simon[9], Jordan Berlin[13], Lynne I. Wagner[3], Peter J. O'Dwyer[14].

[1]Fox Chase cancer Center, [2]Dana Farber Cancer Institute – ECOG ACRIN Biostatistics Center, [3]Wake Forest University Health Sciences, [4] Stanford University, [5]ThedaCare Regional Cancer Center, [6]UPMC Hillman Cancer Center, [7]Washington University School of Medicine, [8]Trinity Health Muskegon Hospital, [9]Northwestern University, [10]University of Rochester, [11]Fred Hutchinson Cancer Center, [12]City of Hope Comprehensive Cancer Center, [13]Vanderbilt University/Ingram Cancer Center, [14]University of Pennsylvania Abramson Cancer Center.

PRESENTED BY: Efrat Dotan, MD

EA2186 (GIANT) - Study Design

Study Patients

- Untreated metastatic pancreatic cancer
- Age ≥70
- ECOG PS: 0-2

Stratification

- ECOG 0-1 vs 2
- Age 70-74 vs ≥75

Screening Geriatric Assessment (GA)

Fit
No GA abnormalities
→ *Standard of care treatment off study*

Vulnerable
Mild-moderate GA abnormalities
→ Complete Geriatric & Quality of Life (QOL) Assessment

Frail
Severe GA abnormalities
→ *Supportive care off study*

1:1 Randomization

Arm A (control): Modified Gemcitabine + Nab-Paclitaxel every 2 weeks

Arm B (experimental) : Dose-reduced 5FU + Liposomal Irinotecan every 2 weeks

Disease evaluation + repeat modified GA + QOL assessment every 8 weeks

Treatment until disease progression or intolerance

Primary Endpoint: Overall Survival (OS)

Key Secondary Endpoints: Progression Free Survival (PFS), Objective Response Rate (ORR)

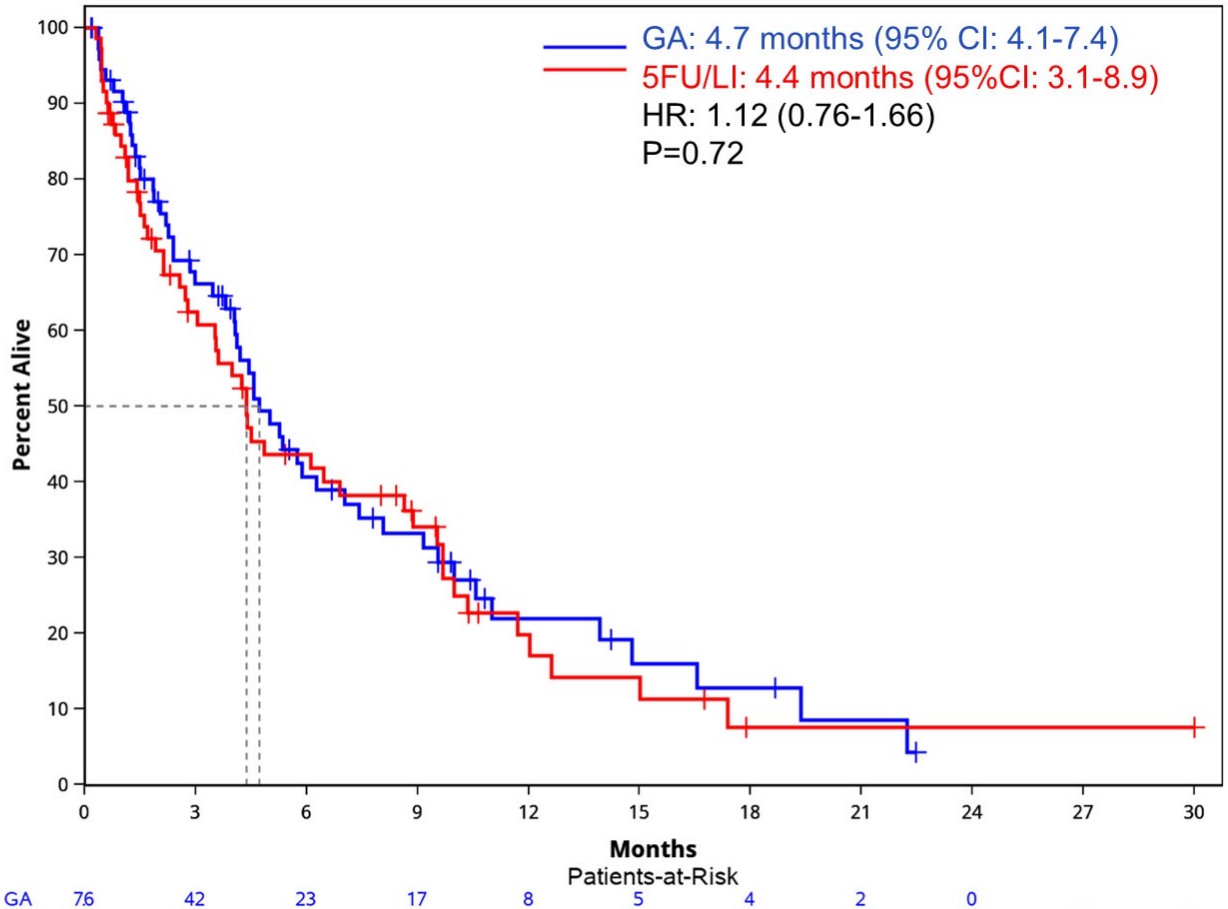
Additional Secondary Endpoints: QOL, Toxicities of Interest to Older Adults

EA2186 (GIANT) - Screening Geriatric Assessment

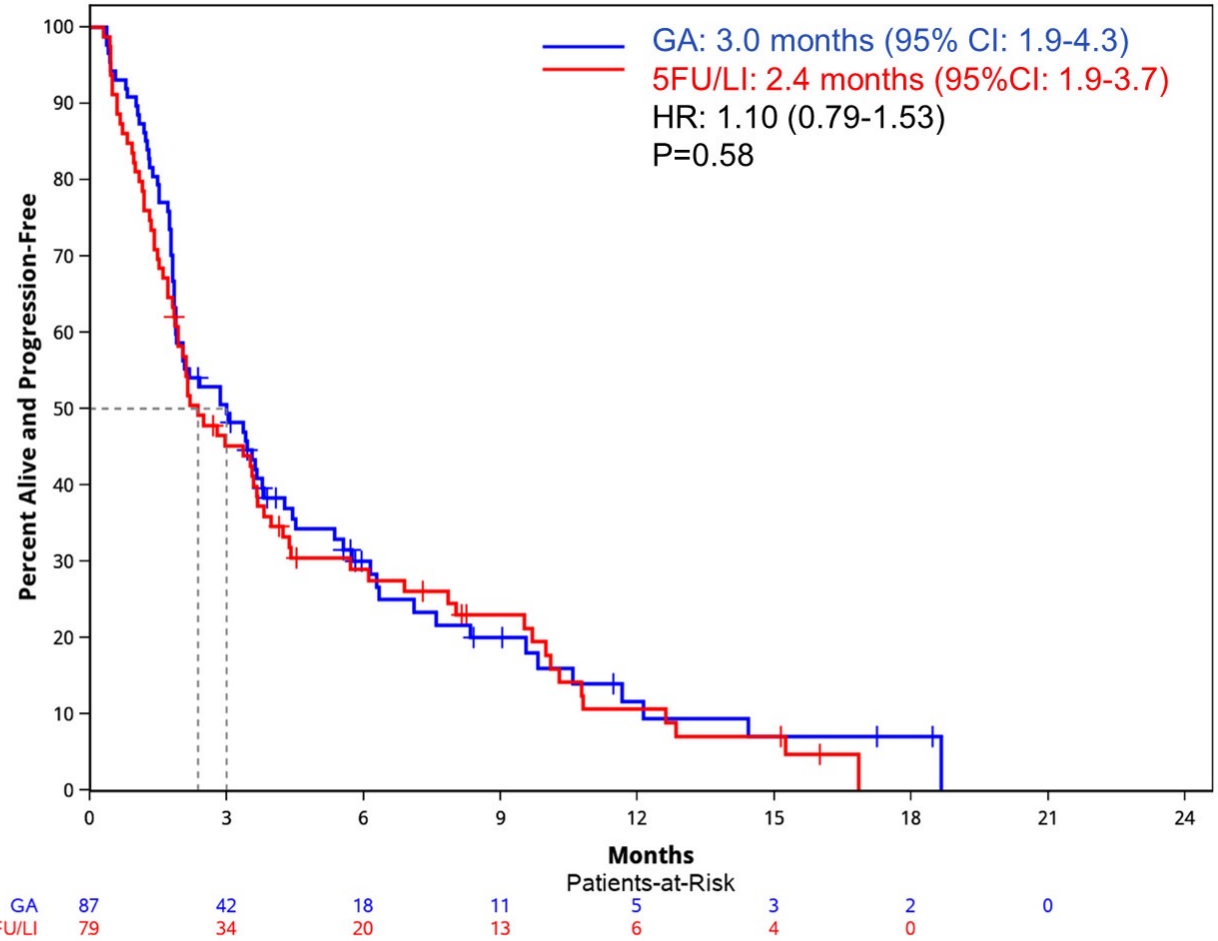
Domain	Assessment Tool	Fit - no abnormalities	Vulnerable- any mild-moderate abnormalities	Frail- any severe abnormalities
Function[1]	ADL IADL (Female/Male)	6 8 /5	5 6-7/4	≤4 ≤5/≤3
Co-morbidities[2]	CIRS-G	No score 3-4 AND <5 comorbidities with a score of 2	No score 3-4 AND 5-8 comorbidities with a score of 2	≥1 score 3-4 OR >8 comorbidities with a score of 2
Cognition[3]	Blessed Orientation Memory Concentration Test	0-4	5-10	≥11
Age[2]*			≥80	
Geriatric Syndromes[4]	• Falls (>3 in 6m) • Urinary/Fecal incontinence	None	None	Presence of any of these would exclude patients

[1]Corre et al. JCO 2016 [2]Tucci et al; Leukemia and Lymphoma 2015. [3] Mohile et al; JCO 2018. [4]GrantPax study - Betge et al. BMC 2018

Primary end point OS - ITT



Secondary end point PFS - ITT



GIANT study

- Investigators, Pts and their families are to be congratulated and thanked for participating in this important study
- It was designed to show superiority of 5-FU/Nal-IRI, which was not proven
- While outcomes were comparable in both arms, they were very poor; study was closed for futility!
- Palliative care is a critical component for these Pts
- Is BSC alone appropriate?
- Is there a subset of Pts we can identify with standard clinical factors who might benefit from tx?

NRG ONCOLOGY

Advancing Research. Improving Lives.™

NRG Oncology/RTOG 0848 Trial: Adjuvant Chemotherapy +/- Chemoradiation For Patients With Resected Head of Pancreas Adenocarcinoma -

Results of the RT + 5FU/Capecitabine Randomization Step

Ross A Abrams, MD, Kathryn A Winter, MS, Karyn A Goodman, MD, William F Regine, MD, Howard P Safran, MD, Adam C Berger, MD, Chandan S Guha, MD, PhD, Lisa A Kachnic, MD, Michael T Gillin, PhD, Samantha A Seaward, MD, Abraham J Wu, MD, Jennifer J Wu, MD, Raid M Aljumaily, MD, Thomas A Dipetrillo, MD, Ravit Geva, MD, Pramila Rani Anne, MD, Jennifer Yannucci, MD, Darla K Liles, MD, Jennifer Moughan, MS, Christopher H Crane, MD

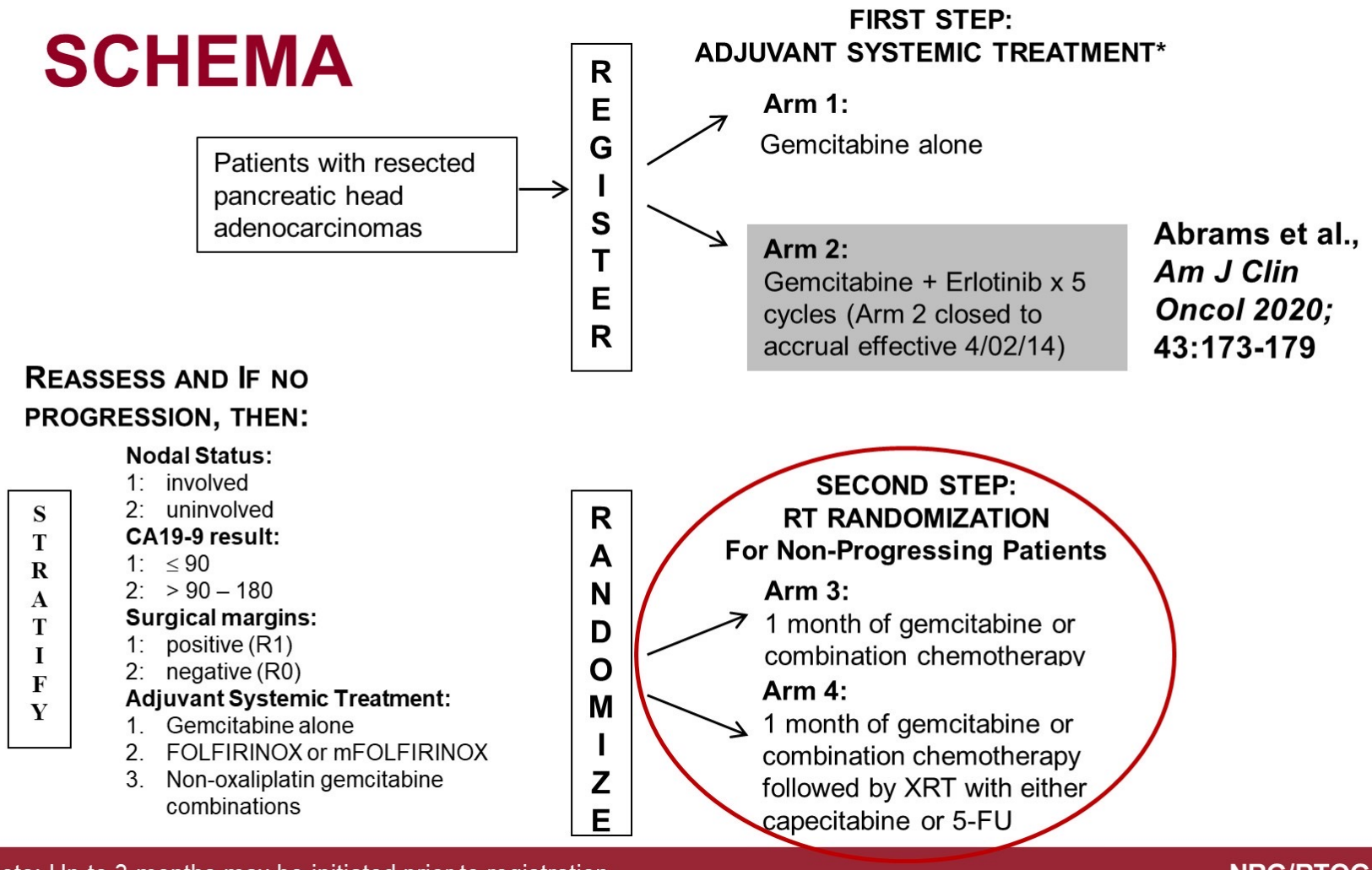
ASCO 2024

6/4/2024

NCI National Clinical Trials Network — a National Cancer Institute program

NCI Community Oncology Research Program — A program of the National Cancer Institute of the National Institutes of Health

SCHEMA



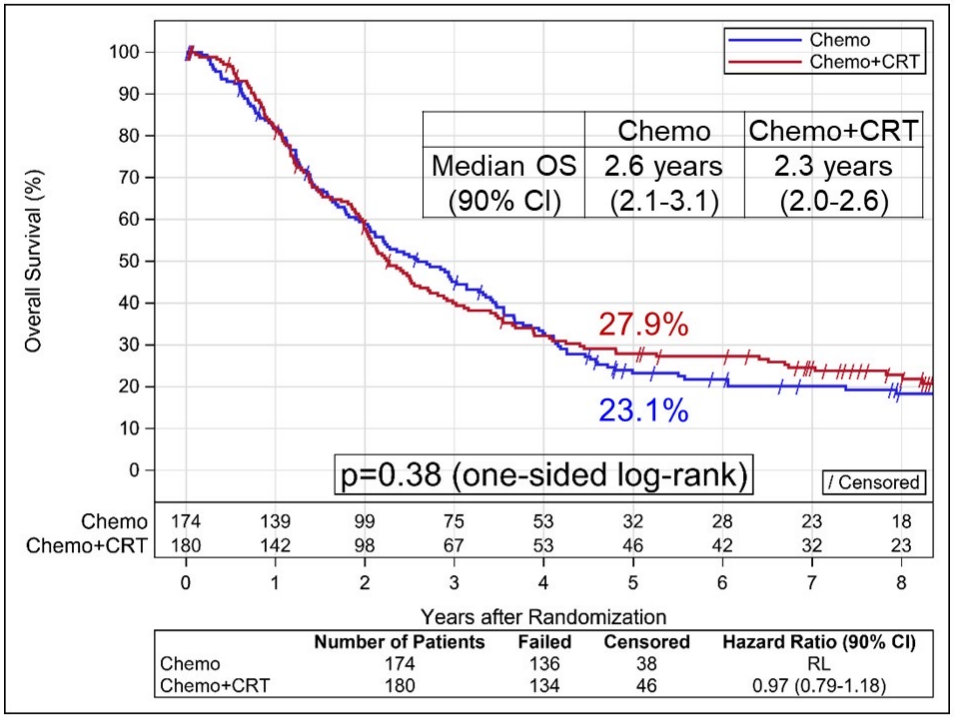
*Note: Up to 3 months may be initiated prior to registration.

NRG/RTOG 0848

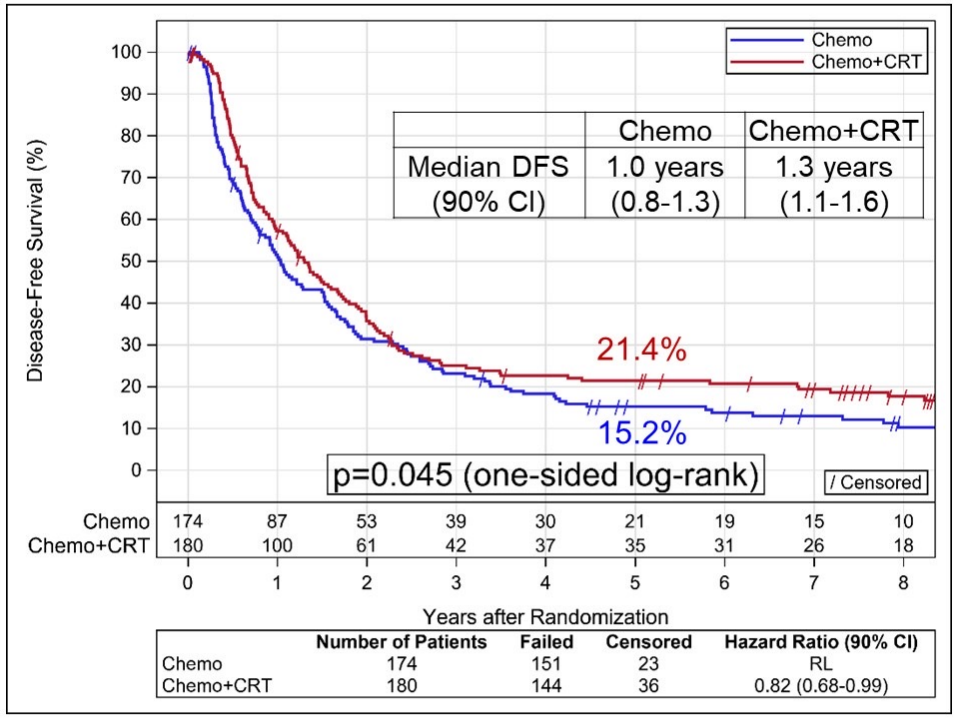
Results: Adjuvant Systemic Treatment Received

	Chemo	Chemo+CRT	Total
Enrollment Timing	174	180	354
Before June 28, 2016	148	161	309
After June 28, 2016	26	19	45
Regimen Received			
Gemcitabine	116	120	236 (67%)
Gemcitabine+Erlotinib	50	50	100 (28%)
Non Oxaliplatin Gem Combo	8	10	18 (5%)
FOLFIRINOX / mFOLFIRINOX	0	0	0 (0%)

Results: OS and DFS for All Patients

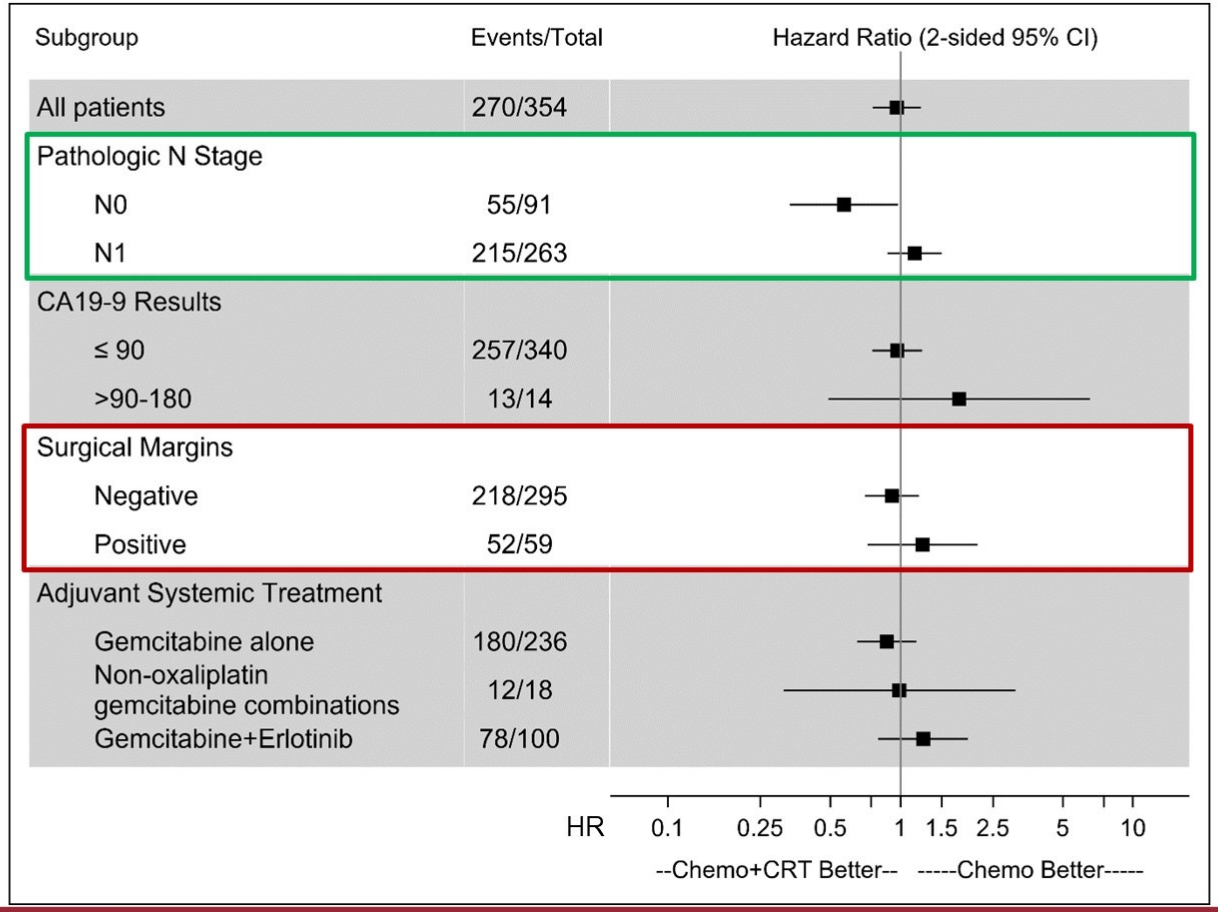


Overall Survival

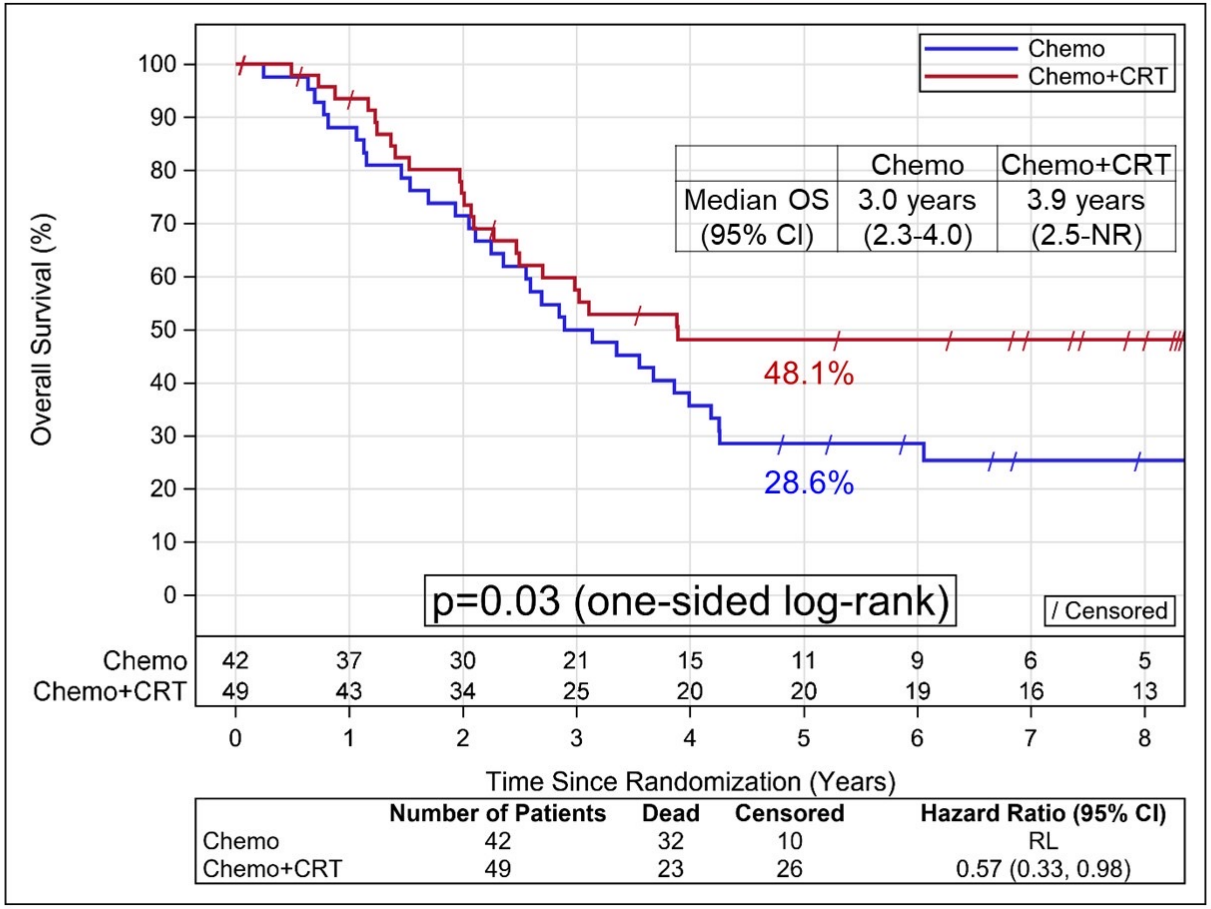


Disease-Free Survival

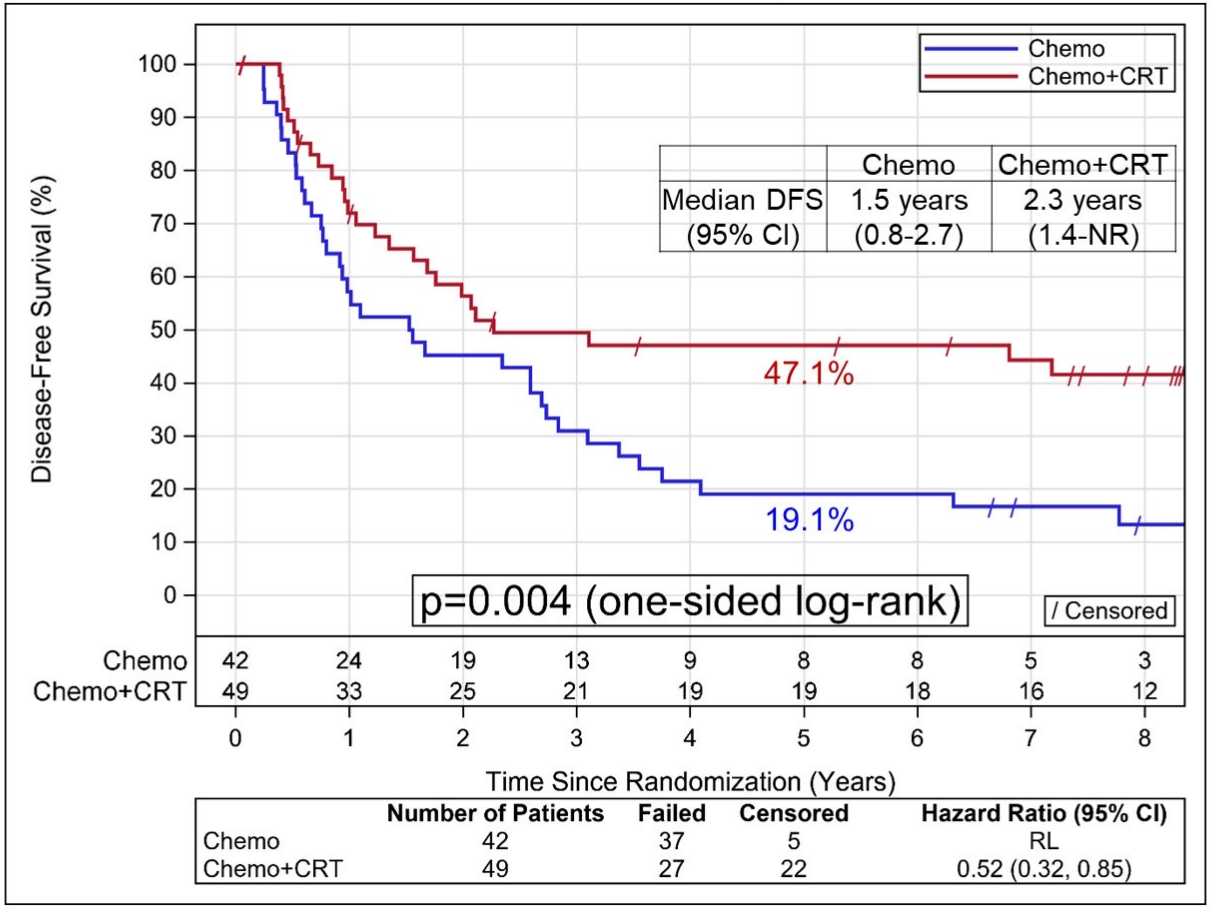
Results: Forest Plot for OS Treatment Effect



Results: OS for Node Negative Patients



Results: DFS for Node Negative Patients



RTOG 0848 study

- Long accrual time and changing practice patterns, e.g. adjuvant FOLFIRINOX, make this study difficult to interpret
- DFS/OS benefit for chemoRT in LN –ve Pts is hypothesis-generating:
  - Is there decreased local +/- distant recurrence in these Pts?
- Is there a role for standard chemoRT s/p FOLFIRINOX in this subgroup?
- Given lack of benefit in Pts with +ve margins, should we stop offering chemoRT to them?

Memorial Sloan Kettering Cancer Center

Thank you!

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