ANNUAL MEETING ON WOMEN'S CANCER

TAMPA, FL • 2023

PATIENTS • PURPOSE • PROGRESS

Overall Survival in NRG Oncology GOG258, a Randomized Phase III Trial of Chemo-Radiation vs. Chemotherapy Alone for Locally Advanced Endometrial Carcinoma

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Unlabeled/Investigational Uses

I will not be discussing any unlabeled or investigational uses of any pharmaceutical products or medical devices.

Locally Advanced Endometrial Cancer (III/IVA)

- Endometrial cancer statistics:
  - 61,380 cases
  - 10,920 deaths
- Stage III/IVA EC -heterogeneous group -10-15% of all cases, account for >50% of deaths
- Five-year survival ranges from 50-70%
- High risk of local (~ 20-30%) and systemic recurrence (~40%)

Siegel R et al. CA Cancer J Clin 2013;63:11-3;
Behbakht K et al. Gynecol Oncol 1994; 55:363-7;
Cook AM et al. Br J Radiol 1999;72:485-8;
Greven KM et al. Cancer 1993;71:3697-702;
ACS Statistics, 2017
Grigsby PW et al. Gynecol Oncol 1987;27:44-57.

Chemo-Radiation for Endometrial Cancer

Clinical trial	Stage	Treatment arms	Local recurrence	Distant recurrence	5 yr Survival
GOG 122	III/IVA	WAI vs. AP	WAI 13% AP 18%	WAI 38% AP 32%	WAI 42% AP 53%
GOG 184	III/IVA	EBRT followed by AP vs. TAP	10%	30%	(5 yr RFS) AP 56% TAP 59%
Maggi	IC/II/III	EBRT vs. CAP	EBRT 12% CAP 15%	EBRT 26% CAP 20%	EBRT 69% CAP 66%
Portec III	High risk stg I + stg II/III	Cis-RT+ CTX4 vs. EBRT		CRT 75.5% RT 68.6%	CRT 81.8% RT 76.7%

WAI = whole abdominal irradiation
EBRT=external beam radiotherapy
AP=doxorubicin + cisplatin

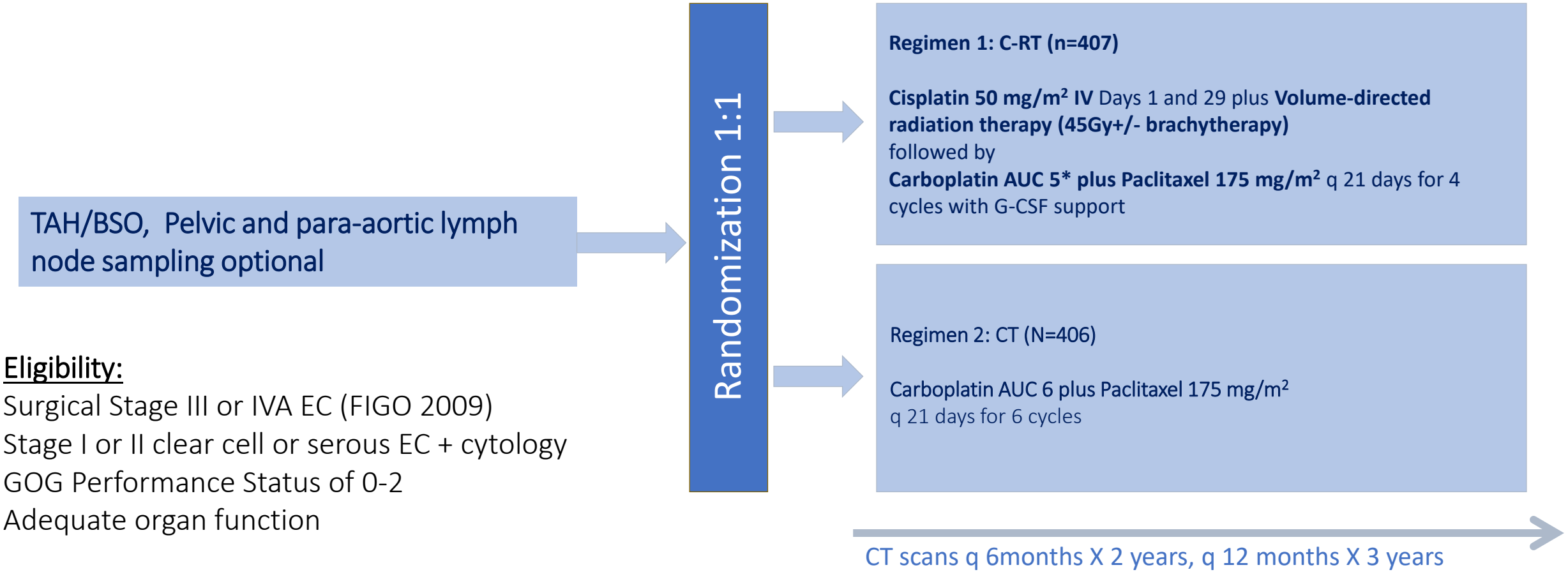
TAP=paclitaxel + doxorubicin + cisplatin
CAP=cyclophosphamide+ doxorubicin + cisplatin,
RFS=Recurrence-Free Survival

Randall, JCO, 2006;24:36-44
Homesley, Gynecology Oncology, 112 (3), 543-552, 2009
Maggi R et al. Br J Cancer 2006; 95:266-71
SM de Boer, Lancet Oncology 2018
SM de Boer, Lancet Oncology 2019

Research Hypothesis

Combined systemic chemotherapy and tumor volume directed radiotherapy (C-RT) improves recurrence- free survival and overall survival compared to systemic chemotherapy alone (CT) in patients with surgically staged III/IVA uterine cancer.

Study Schema



Eligibility:

Surgical Stage III or IVA EC (FIGO 2009)
Stage I or II clear cell or serous EC + cytology
GOG Performance Status of 0-2
Adequate organ function

Ineligible Patients

Carcinosarcoma
Recurrent EC
Residual tumor after surgery > 2 cm

Open: 6/29/2009
Closed: 7/28/2014

Study Objectives

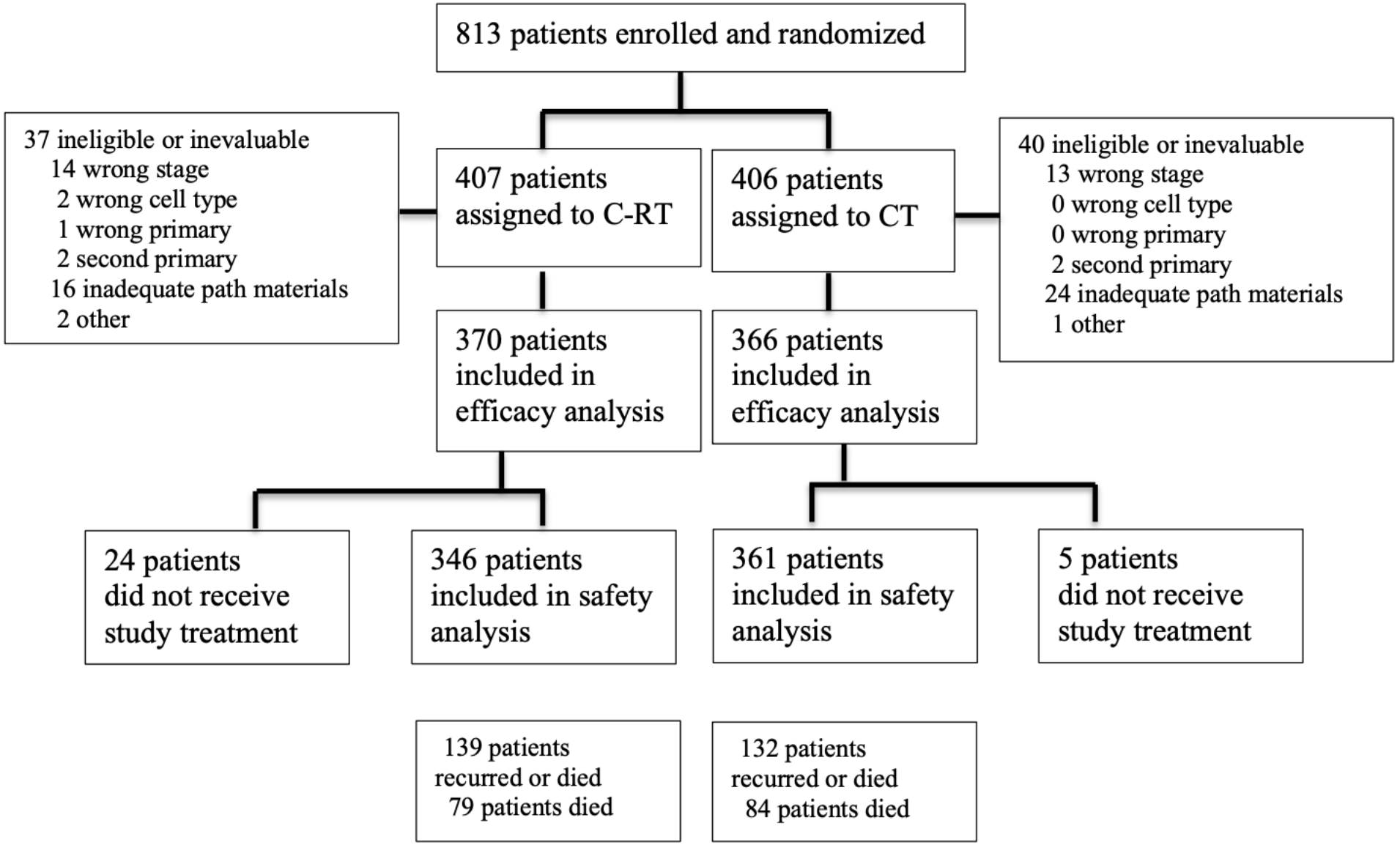
Primary Objective:

- To determine if C-RT increases recurrence-free survival (RFS) vs. CT.

Secondary Objectives:

- **To determine if C-RT reduces the rate of death (i.e., increases survival) when compared to CT.**
- To compare acute and late adverse effects of C-RT and CT.
- To determine patient-reported quality of life during and following treatment.

Patient Enrollment & Randomization



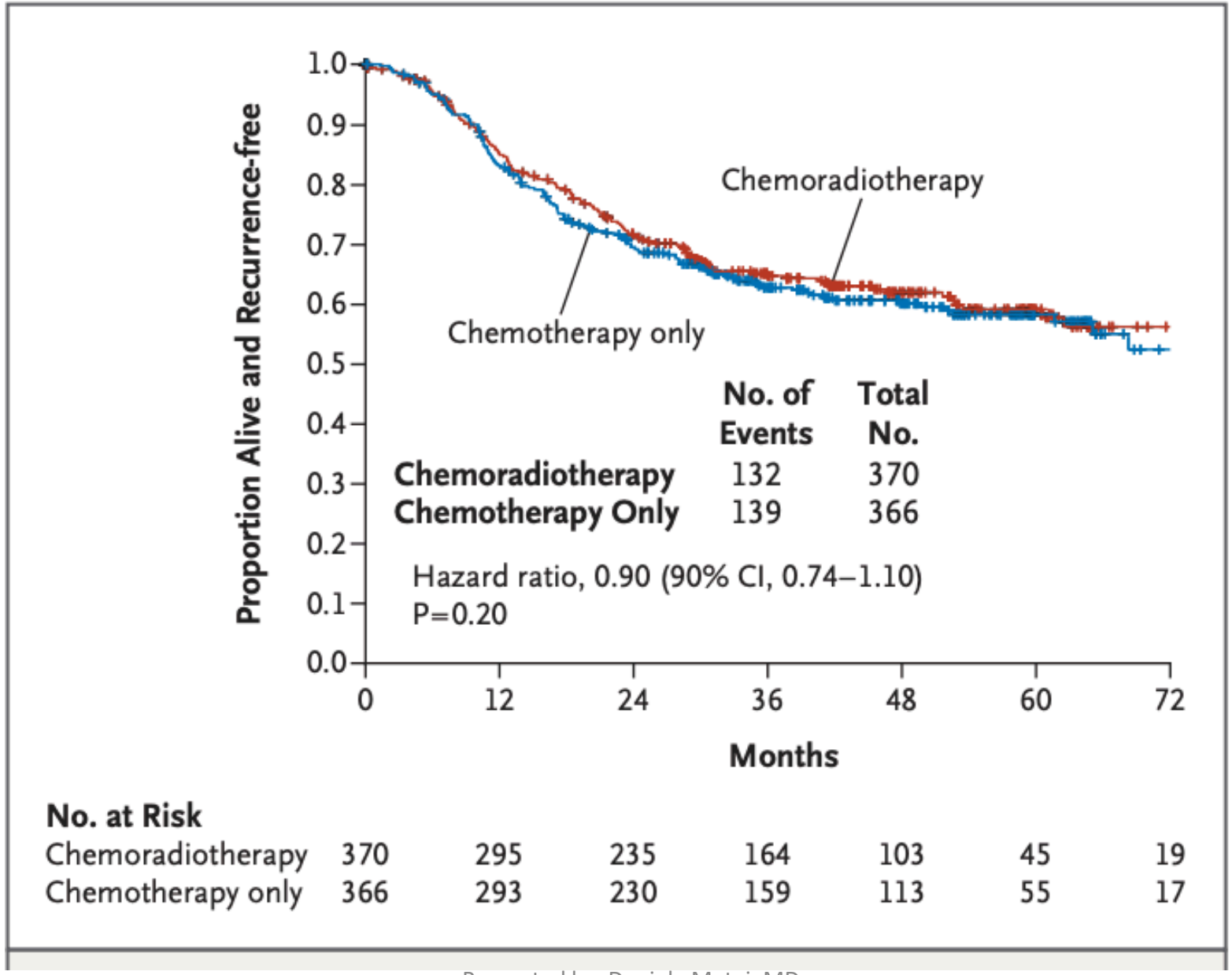
Presented by: Daniela Matei

Matei et al, NEJM, 2019

Patient Characteristics

Characteristic	Chemoradiotherapy (N = 370)	Chemotherapy Only (N = 366)
Mean age (range) — yr	60.5 (31–88)	60 (31–85)
Race — no. (%)†		
White	291 (78.6)	279 (76.2)
Black	37 (10.0)	42 (11.5)
Asian, other, or not specified	42 (11.4)	45 (12.3)
GOG performance status score — no. (%)‡		
0	278 (75.1)	268 (73.2)
1	88 (23.8)	96 (26.2)
2	4 (1.1)	2 (0.5)
FIGO stage — no. (%)§		
I or II	6 (1.6)	10 (2.7)
IIIA	70 (18.9)	81 (22.1)
IIIB	12 (3.2)	13 (3.6)
IIIC1	189 (51.1)	166 (45.4)
IIIC2	90 (24.3)	93 (25.4)
IVA	3 (0.8)	3 (0.8)
Histology and grade — no. (%)		
Endometrioid, grade 1	87 (23.5)	79 (21.6)
Endometrioid, grade 2	103 (27.8)	118 (32.2)
Endometrioid, grade 3	64 (17.3)	61 (16.7)
Serous	66 (17.8)	65 (17.8)
Clear cell	10 (2.7)	12 (3.3)
Mixed epithelial or other	40 (10.8)	31 (8.5)
Gross residual disease — no. (%)		
Absent	360 (97.3)	359 (98.1)
Present	10 (2.7)	7 (1.9)
Median BMI (range)¶	32.0 (11.2–65.3)	32.9 (18–60.2)

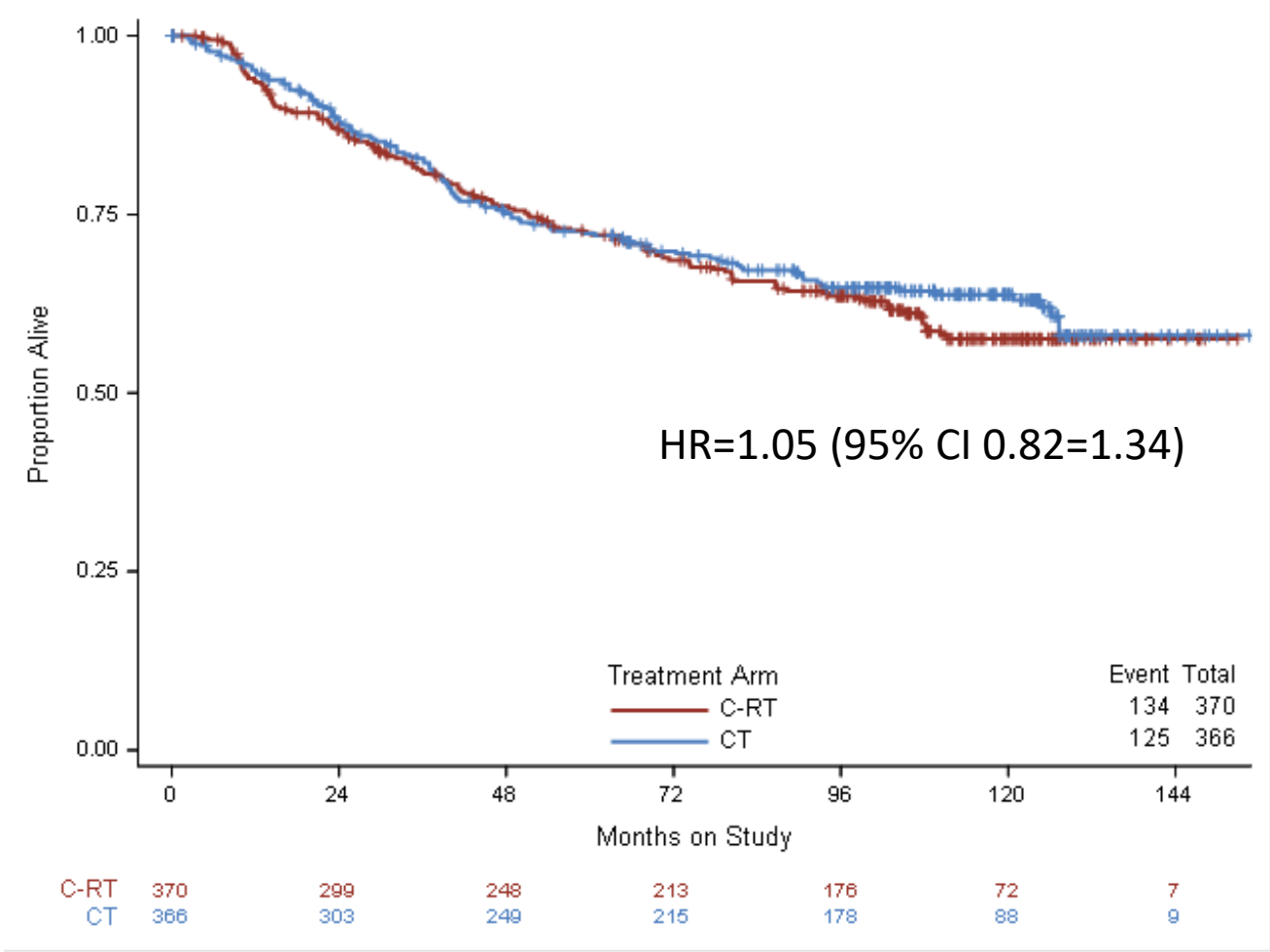
Recurrence-Free Survival



Matei et al, NEJM, 2019

Overall Survival

Kaplan Meyer OS Distribution Estimates



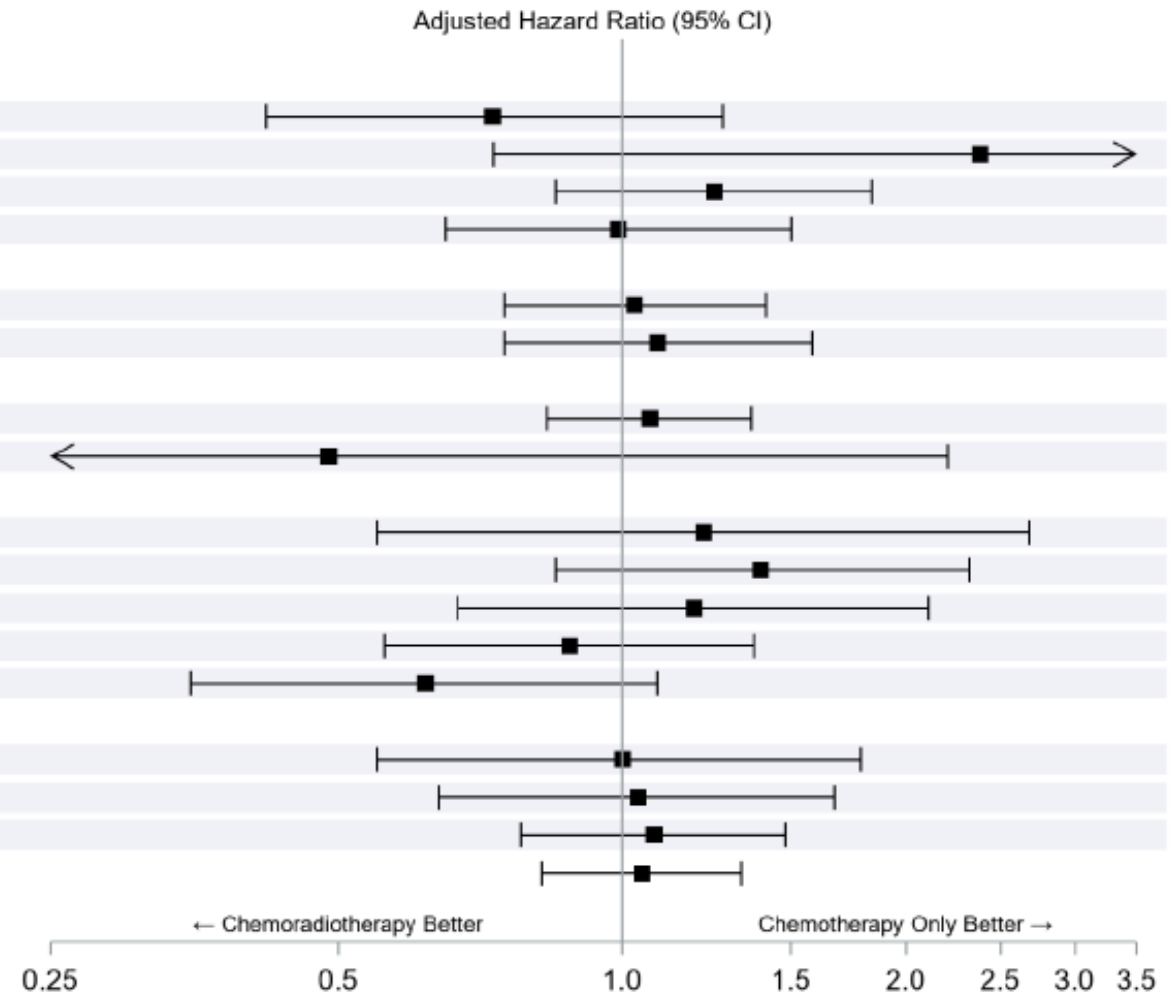
Total number of deaths: 259
CT: 125
C-RT: 134

Median follow up 112 months (max 155 months)

Presented by: Daniela Matei, MD

Overall Survival: Potential Predictive Factors

Subgroup	No. of Events	Total No.	Adj-HR	95% CI
FIGO stage				
I, II, or IIIA	52	167	0.73	(0.42-1.28)
IIIB	13	25	2.39	(0.73-7.79)
IIIC or IIIC1	107	355	1.25	(0.85-1.84)
IIIC2 or IVA	87	189	0.99	(0.65-1.51)
Age at entry				
65 years or younger	150	532	1.03	(0.75-1.42)
Older than 65 years	109	204	1.09	(0.75-1.59)
Gross residual disease				
Absent	252	719	1.07	(0.83-1.37)
Present	7	17	0.49	(0.11-2.21)
Histology				
Endometrioid, grade 1	25	166	1.22	(0.55-2.69)
Endometrioid, grade 2	62	221	1.40	(0.85-2.33)
Endometrioid, grade 3	48	125	1.19	(0.67-2.11)
Serous	77	131	0.88	(0.56-1.38)
Other	47	93	0.62	(0.35-1.09)
BMI category				
Normal or underweight	45	143	1.00	(0.55-1.79)
Overweight	67	165	1.04	(0.64-1.68)
Obesity class I, II, or III	147	428	1.08	(0.78-1.49)
Analysis population	259	736	1.05	(0.82-1.34)



Models adjusted for age at entry and gross residual disease.

Conclusions

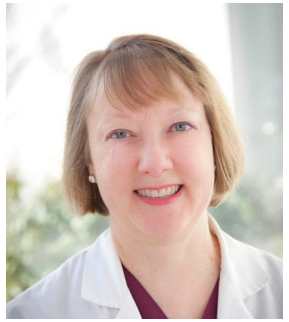
- Chemo-RT did not improve OS compared to chemotherapy (HR=1.05; 95% CI 0.82-1.34).
- Chemo-RT did not improve OS in any subgroup (stage, histology, BMI, residual disease, age)
- Chemo-RT did not improve PFS compared to chemotherapy (HR=0.9, CI 0.74-1.1—previously reported).
- Chemo-RT reduced the incidence of vaginal, pelvic, and para-aortic recurrences vs. CT, but distant recurrences were more common with C-RT

(previously reported).

- Molecular predictors of PFS or OS: not yet studied.

Acknowledgements

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NATIONAL CANCER INSTITUTE

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