PARCER Trial: An opportunity to reduce toxicity in early cervical cancer

Final Analysis

NCT01279135/CTRI2012/120349

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Disclosures

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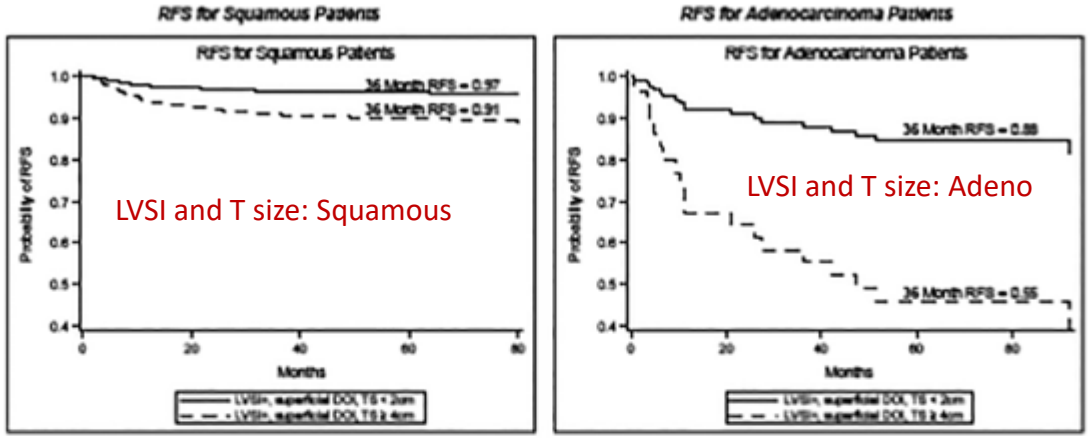
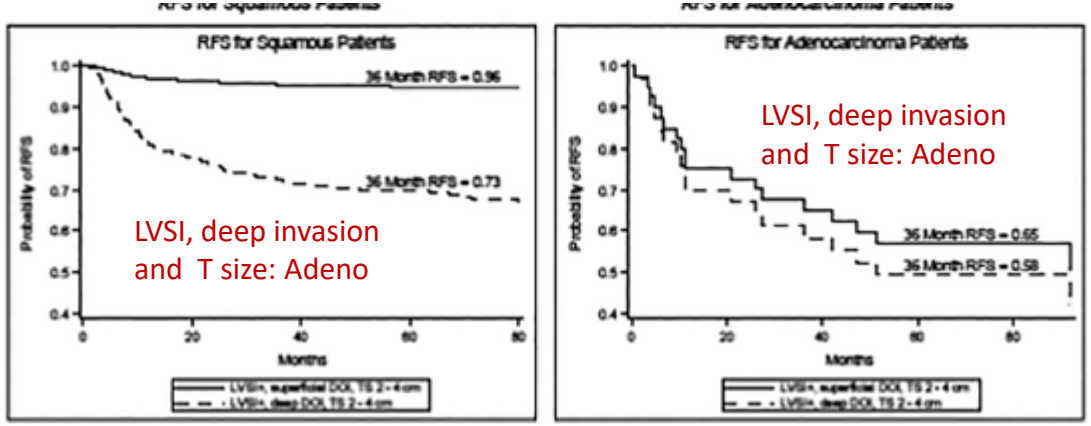
GOG 49,92,141 (Surgery Alone Arms)

Surgery Alone is an Ineffective Treatment for Women with Cervix Cancer IB1-IIA1



Tumours even less than 4 cm have poor outcomes with Surgery Alone

For Tumours < 2 cm and no other risk factors RFS approx. 95%



Levinson, Gynec Oncology 2020

Beyond Sedlis—A novel histology-specific nomogram for predicting cervical cancer recurrence risk: An NRG/GOG ancillary analysis

Comparison of 3 yr RFS, nomogram recurrence risk, and Sedlis criteria for predictor variable combinations.

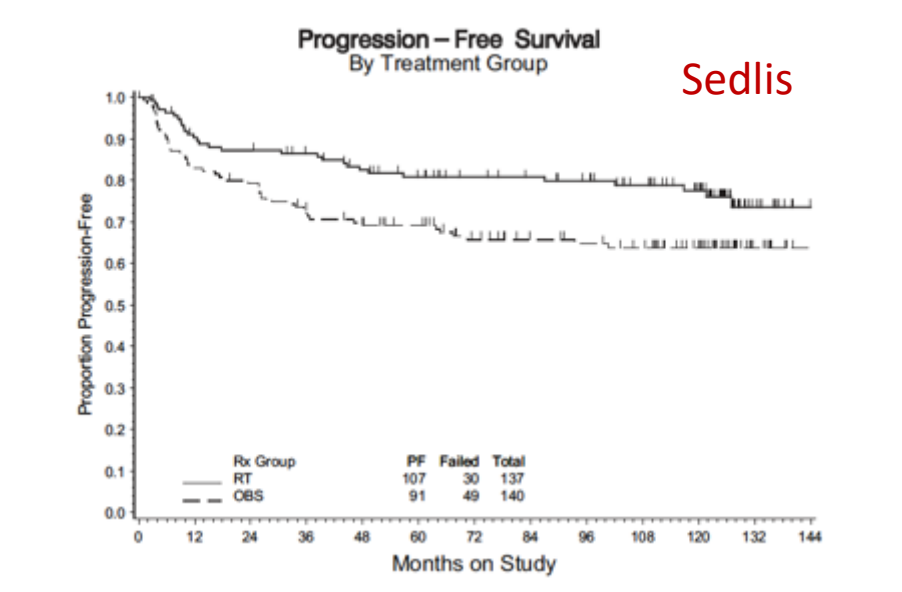
Vascular Invasion	Invasion Depth	Tumor Size	SCC			AC		
			RFS (3 yr, CI)	Sedlis Criteria (+/−)	nomogram recurrence risk	RFS (3 yr, CI)	Sedlis Criteria (+/−)	nomogram recurrence risk
N	Superficial	(<2 cm)	0.98 (0.96,1)	−	<5%	0.96 (0.90, 1.00]	−	<5%
N	Middle	(<2 cm)	0.91 (0.87,0.95)	−	18%	0.97 (0.92, 1.00]	−	<5%
N	Deep	(<2 cm)	0.86 (0.79,0.93)	−	32%	0.95 (0.87, 1.00]	−	6%
N	Superficial	(2–4 cm)	0.97 (0.95,1)	−	<5%	0.86 (0.70, 1.00]	−	24%
N	Middle	(2–4 cm)	0.88 (0.84,0.93)	−	22%	0.89 (0.77, 1.00]	−	20%
N	Deep	(2–4 cm)	0.82 (0.75,0.89)	−	38%	0.83 (0.66, 1.00]	−	26%
N	Superficial	(≥4 cm)	0.94 (0.9,0.99)	−	10%	0.81 (0.59, 1.00]	−	34%
N	Middle	(≥4 cm)	0.78 (0.7,0.86)	+	28%	0.85 (0.70, 1.00]	+	30%
N	Deep	(≥4 cm)	0.66 (0.58,0.75)	+	42%	0.77 (0.56, 1.00]	+	36%
Y	Superficial	(<2 cm)	0.97 (0.94,0.99)	−	<5%	0.88 (0.71, 1.00]	−	20%
Y	Middle	(<2 cm)	0.86 (0.8,0.92)	−	22%	0.91 (0.78, 1.00]	−	18%
Y	Deep	(<2 cm)	0.78 (0.7,0.88)	+	38%	0.85 (0.70, 1.00]	+	22%
Y	Superficial	(2–4 cm)	0.96 (0.92,1)	−	8%	0.65 (0.32, 1.00]	−	40%
Y	Middle	(2–4 cm)	0.82 (0.76,0.89)	+	26%	0.71 (0.48, 1.00]	+	38%
Y	Deep	(2–4 cm)	0.73 (0.65,0.81)	+	40%	0.58 (0.36, 0.96]	+	42%
Y	Superficial	(≥4 cm)	0.91 (0.84,0.99)	+	14%	0.55 (0.19, 1.00]	+	50%
Y	Middle	(≥4 cm)	0.67 (0.57,0.79)	+	32%	0.63 (0.37, 1.00]	+	46%
Y	Deep	(≥4 cm)	0.52 (0.43,0.64)	+	46%	0.47 (0.24, 0.95]	+	52%

Sedlis Criteria Designed to Select Patients with >30% risk of local relapse for Adjuvant Treatment

Patients with even single risk factor may have elevated risk mandating adjuvant Treatment

Levinson, Gynec Oncology 2020

Outcomes following postoperative adjuvant RT+/- chemo

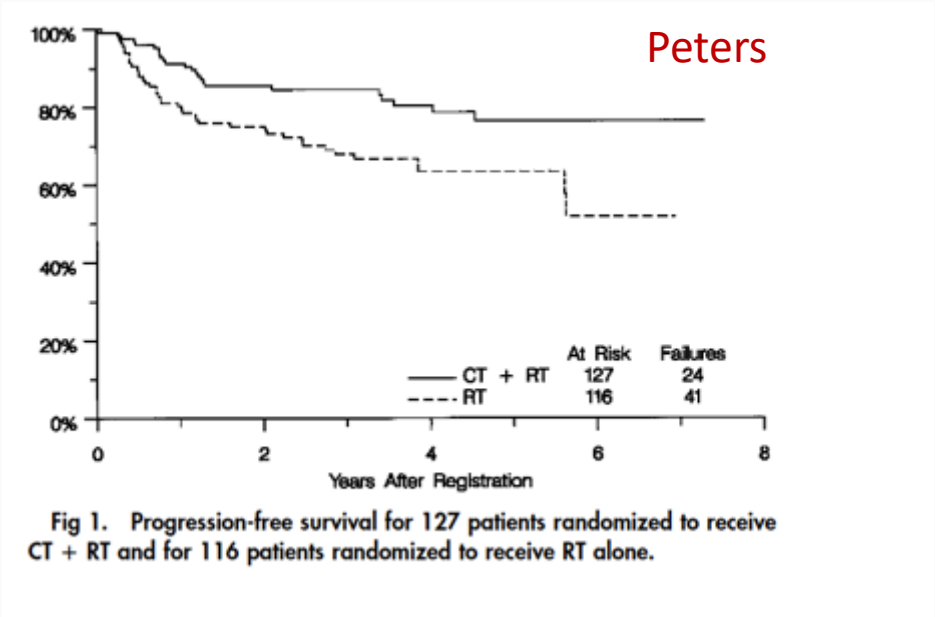


Sedlis

(Gyn Oncol 1999, Rotman IJROBP 2006)

RT vs Observation

14% vs 20% Local Relapse



Peters

(Peters, JCO, 2000)

CTRT vs RT

5.5% vs 17% Local Relapse

20 year follow up of Landoni's Trial

Type of complication	Surgery	Surgery+RT	RT
No. of patients	61	108	158
Urologic			
Hydroureteronephrosis*	2 (3.3)	11 (10.1)	9 (5.6)
Ureteral fistula	1 (1.6)	-	-
Urinary incontinence	2 (3.3)	4 (3.7)	-
Atonic bladder	8 (13.1)	5 (4.6)	1 (0.6)
Actinic cystitis	-	7 (6.4)	9 (5.6)
Vascular			
Pulmonary embolism	2 (3.3)	1 (0.9)	-
Legs edema	-	12 (11.1)	1 (0.6)
Lymphocyst	5 (8.2)	5 (4.6)	1 (0.6)
Vascular lesion	1 (1.6)	-	-
Intestinal			
Rectal fistula	-	-	1 (0.6)
Bowel obstruction	-	6 (5.5)	2 (1.2)
Proctitis	-	-	14 (8.8)
Others			
Wound abscess	-	-	-
Abdominal hernia	4 (6.6)	4 (3.7)	2 (1.2)
Bone necrosis	-	1 (0.9)	-
Vaginal necrosis	-	-	1 (0.6)
Vaginal stenosis	-	1 (0.9)	2 (1.2)
Pelvic fibrosis	-	4 (3.7)	3 (1.8)
Uterine perforation	-	-	1 (0.6)
Peritonitis	-	1 (0.9)	-
Total	25 (40.7)	62 (56.4)	47 (29.0)

Overall Higher Adverse Events with Surgery than RT at 20 yr follow up or Surgery+RT. RT alone most favourable

Adverse Events with Adjuvant RT

- Postoperative Radiation indicated for Cervix and Endometrial Cancers
- Increase in GI symptom burden and toxicity in long term survivors after adjuvant radiation
- Associated with further increase in GI toxicity due to radiosensitizing impact of concurrent chemotherapy.
- Until 2010: RTOG 0418/ RTCMIENDOMETRE demonstrated 27-28% acute GI toxicity with IMRT: No comparator arm. No robust data on late toxicity

Late Gastrointestinal Toxicity

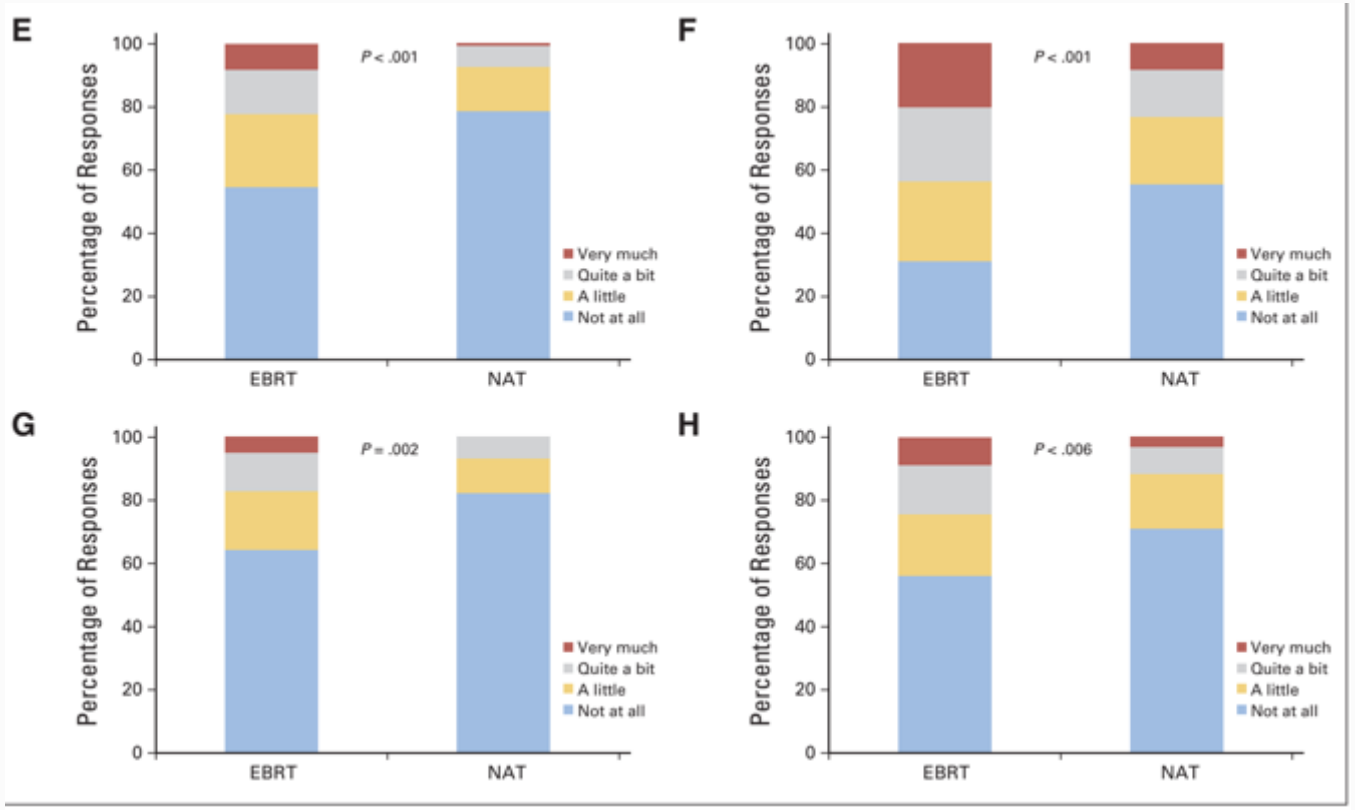
Postoperative Pelvic Radiation: CTCAE/RTOG Physician Reported Toxicity

RCT	Treatment	Late Grade III-IV Gastrointestinal Toxicity (GI)
Rotman	Sx Sx+RT (No BT)	2.1% vs 6.6%
Keys	Sx Sx+RT (No BT)	0.4% vs 8%
Peters	Sx+ RT CT/RT+ Adj chemo	5% vs 10%
Chen	Sx+ RT+ BT	Grade I-IV:19.2% (nonrectal GI)

Peters JCO 2000. Keys. Gynec Oncol 2004, Rotman IJROBP 2006,Chen SW Eu J Go 2004

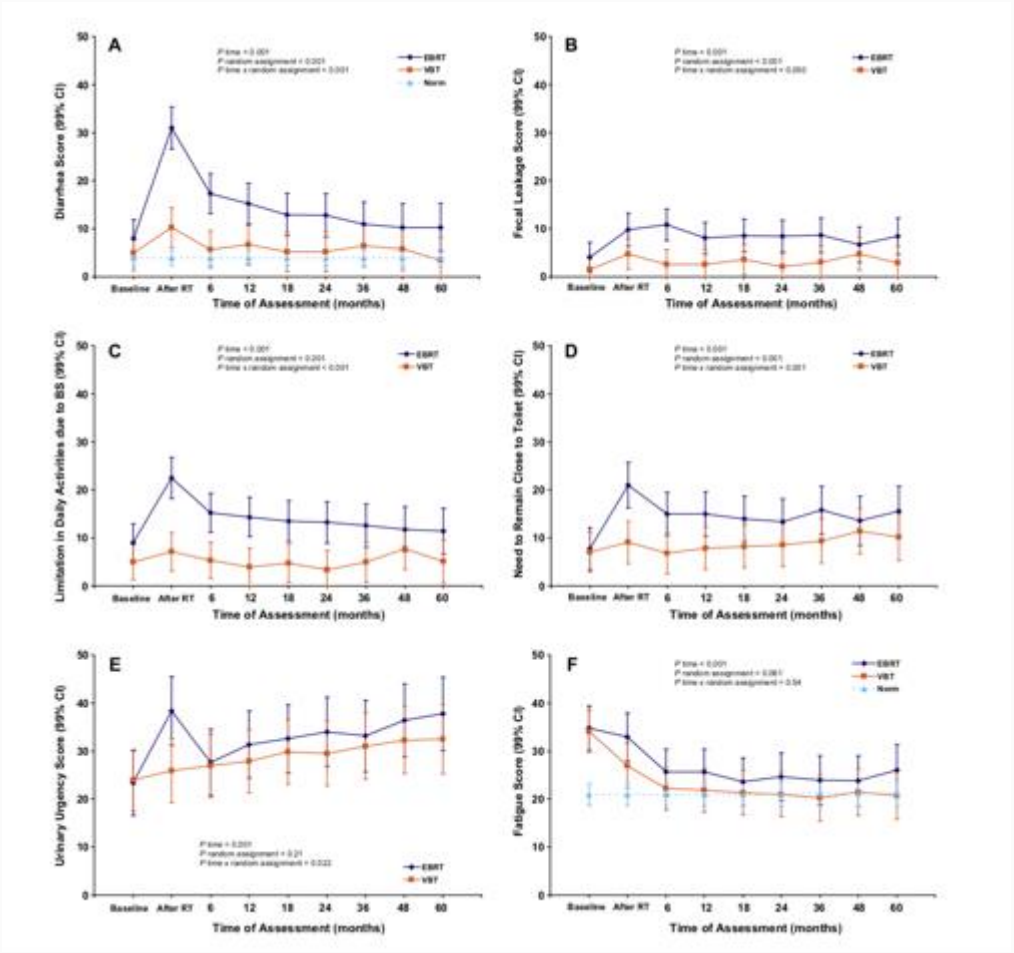
Impact on Patient Reported QOL (GI)

PORTEC I and II Endometrial Trial : EBRT (3DCRT) vs. Vaginal BT



Diarrhoea, Fecal Urgency, Fecal Leakage, Limitation of ADL

Nout RA, JCO 2011



Nout RA, Eur J Cancer 2012

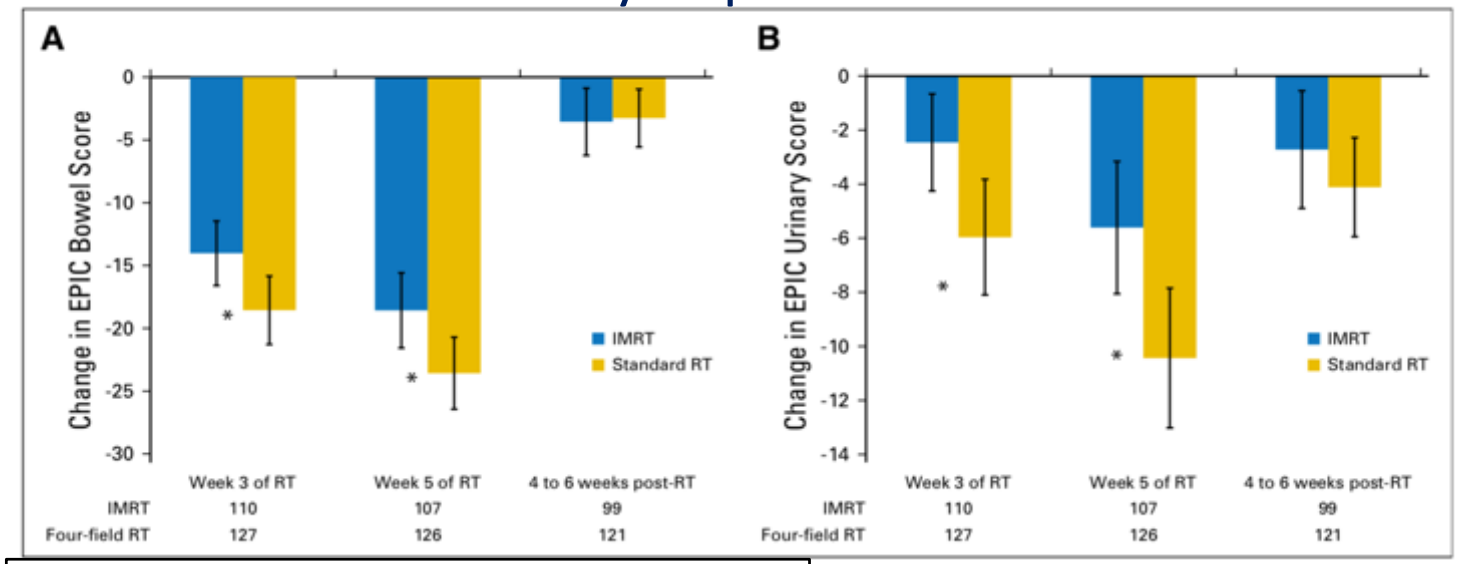
Phase II Trials IG-IMRT: Acute and Late GI Toxicity (Until 2011)

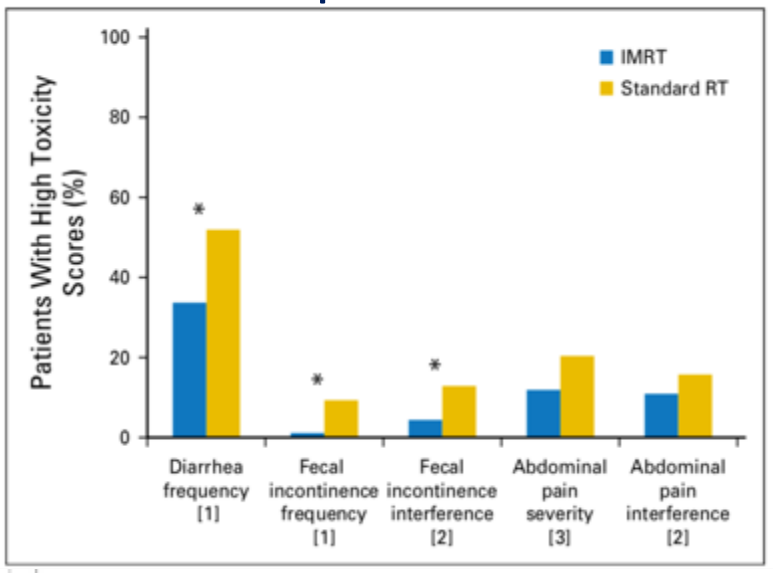
Study	Number	Follow Up	Grade II-IV Toxicity
Grigsby (2009)	20 EBRT	19 mths	35% (Acute)
Kabarriti (2009)	26 EBRT Only	18 mths	15.4% (Acute)
Barrilott (2013)	49	Wk15	<30%
RTOG 0418 (2009)	98 (EBRT+BT)	30 mths	3.2%
Folker MR (2013)	34 (EBRT+ Chemo)	44 mths	Late: 3%

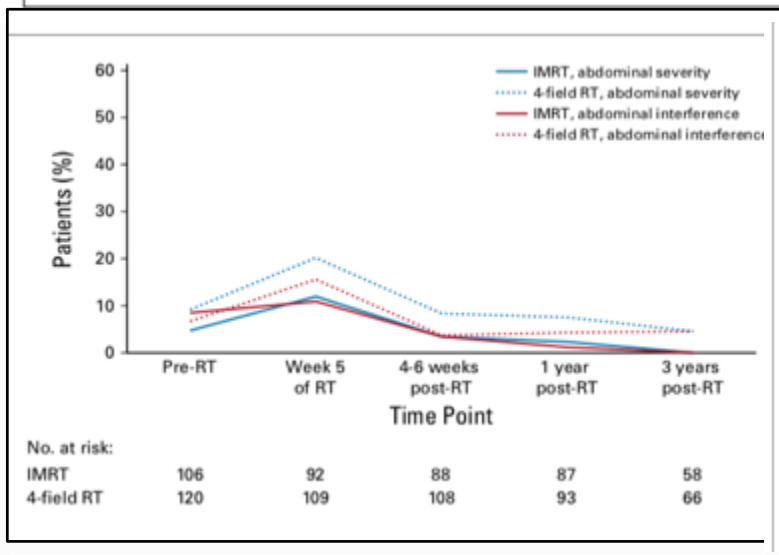
Long Term Benefit for IG-IMRT was not Clear

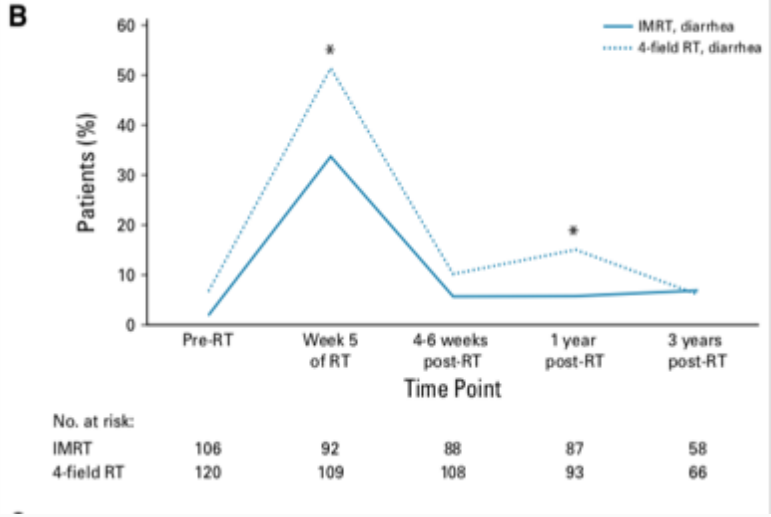
TIME -C NRG Study

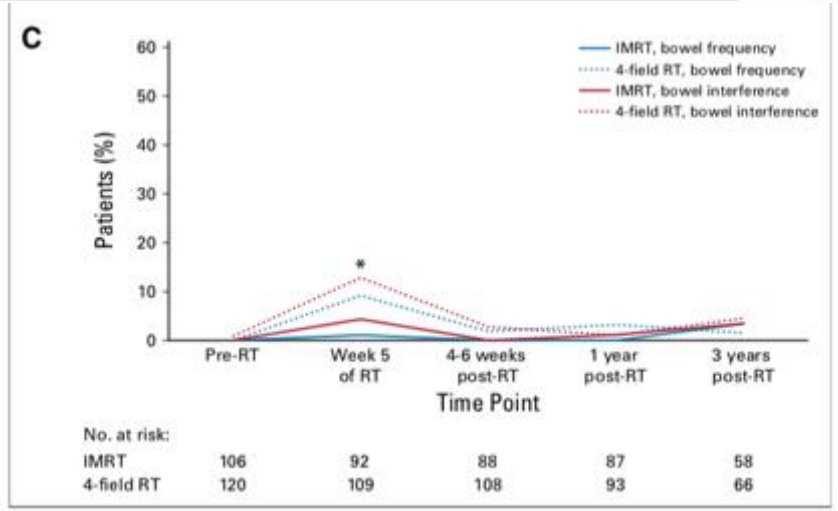
Early Impact on RT. No benefit at long term follow up











Klopp JCO 2018

Yeung, JCO 2020

Hypothesis

IG-IMRT will improve late GI toxicity free survival in patients undergoing adjuvant RT for cervix cancer.

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Study Eligibility

Inclusion Criteria

- Cervical Cancer
- Age >18 years
- Type III Hysterectomy with intermediate or high risk features
- Type I/II hysterectomy necessitating adjuvant CRT

Exclusion Criteria

- Positive Para aortic nodes or indication for extended field RT.
- History of multiple previous abdominal surgeries/radiation
- Any medical condition predisposing to bowel toxicity

Endpoints

Primary

•To demonstrate difference if any in GI late toxicity free survival with use of IG-IMRT (CTCAE version 3.0)

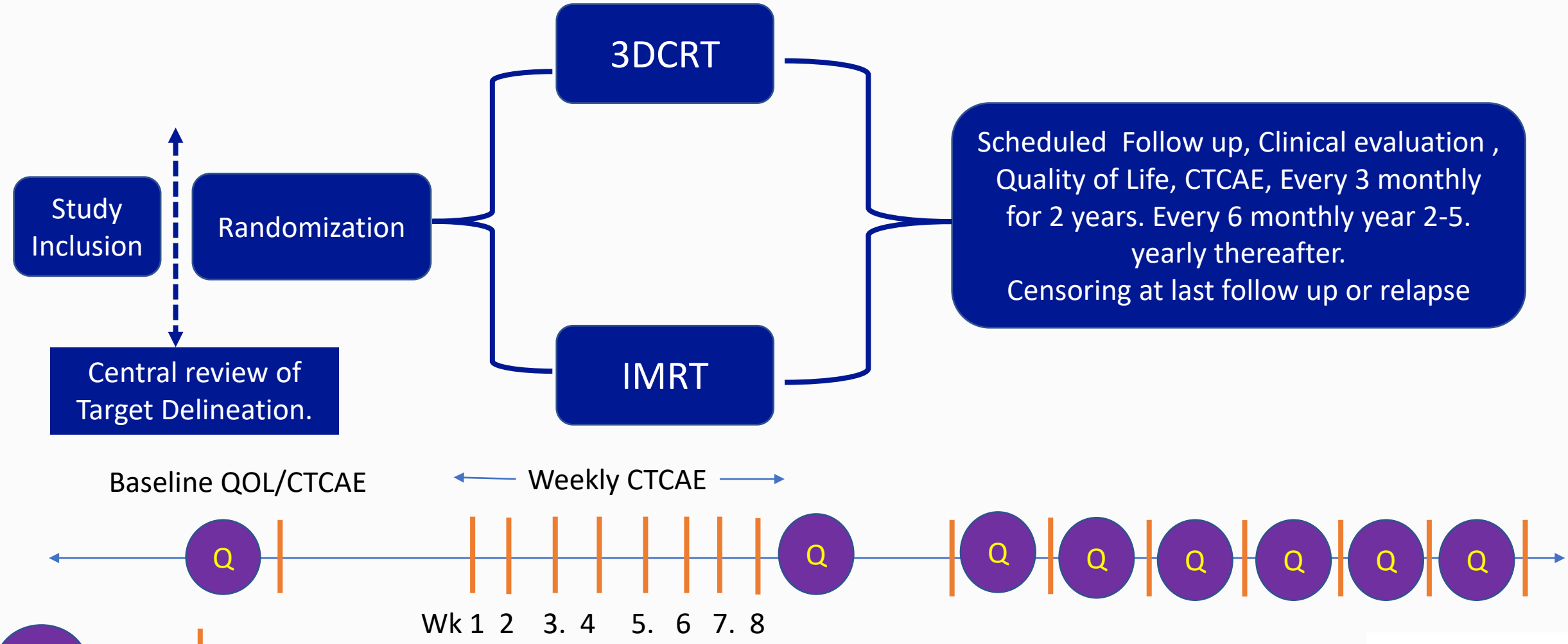
Secondary

• To compare acute toxicity between 3DCRT and IG-IMRT arm

•To compare QOL between the 3DCRT and IMRT

•To identify DVH characteristics that predict for late GI toxicity

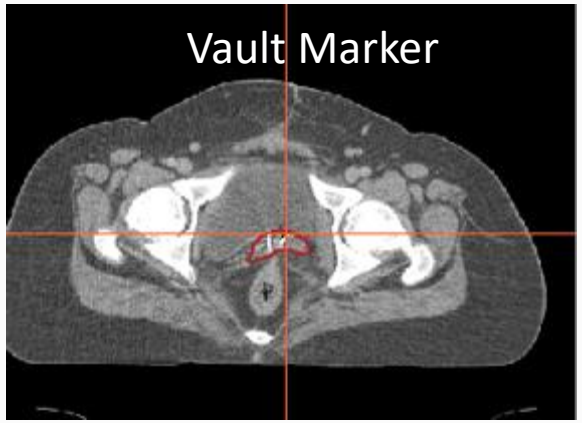
Trial Schema

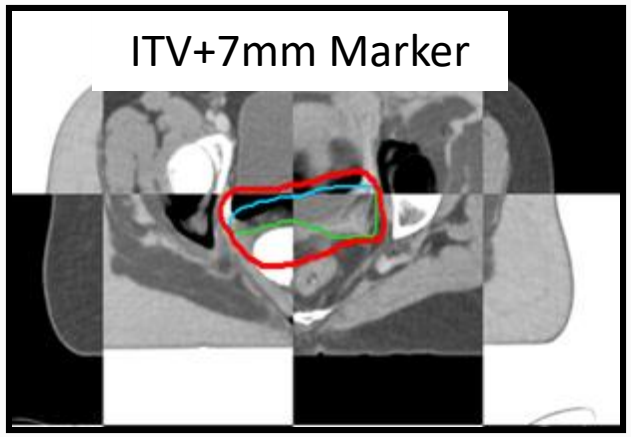


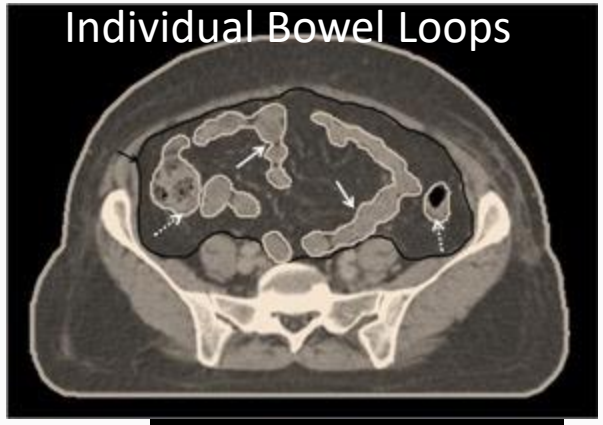
Sample Size

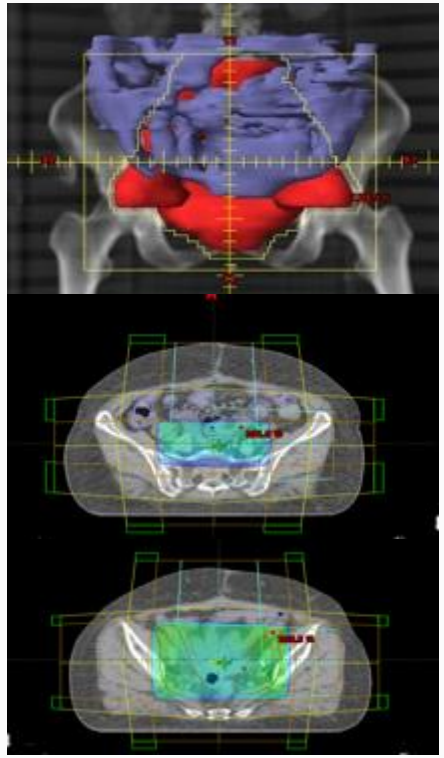
- To demonstrate 13% reduction (18% to 5%) in Late Grade ≥ II GI Toxicity at a median f/up of 36 months.
- Preplanned strata: Type of Hysterectomy and Use of concurrent chemotherapy
- One planned interim analysis when 50% patients reach median follow up of 18 months.
- 218 patients needed (240 with attrition accounted)

Treatment









50 Gy/ 25#/5 weeks +/- Cisplatin

CT Based Brachytherapy
(HDR 6 Gy x 2#)

Strict Bowel Constraints in IG-IMRT (V15,V40)

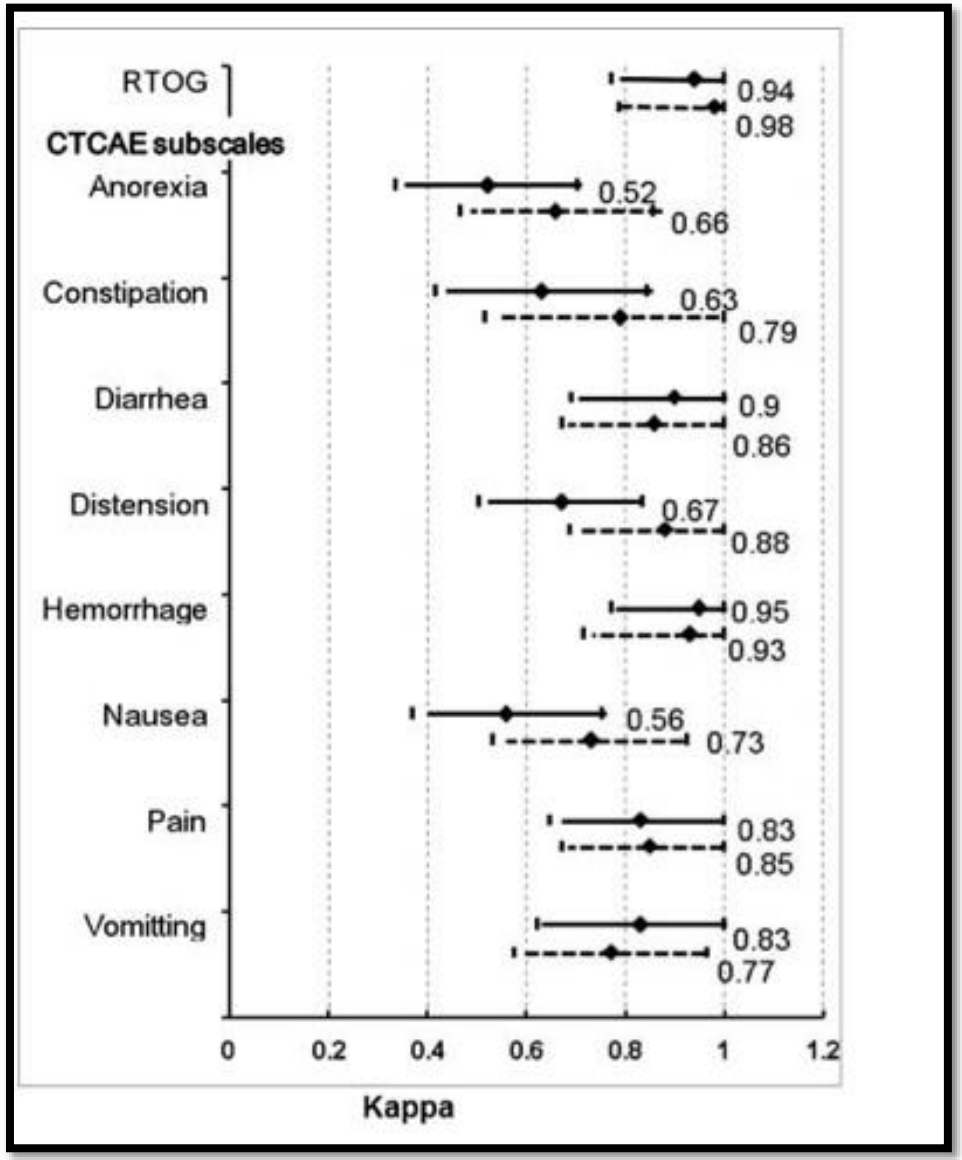
Image guidance in both arms

CTCAE v 3.0 baseline and F/U

3DCRT

IG-IMRT

Late Toxicity Assessment



- *11 GI Items of CTCAE version 3.0*
- *Additional GU, Lymphedema, Vaginal, Constitutional scales used*
- *Inter-rater agreement of GI subscales validated prior to study initiation.*
- *PI led study team performed all the toxicity scoring*
- *Patients censored for primary endpoint assessment at relapse.*

Chinachammy, Chopra, JJCO 2013

Longitudinal Capture of Treatment Related Toxicity and QOL Parameters (CTCAE and EORTC QLQC30 and Cx 24)

R.NO.	TFU	6	12	18	24	36	48	60	72	84	96
51 (QOL)	48	1	2		1	2	1				
51 (CTCAE)		**0**	**3**		**0**	**1**	**0**				
219(QOL)	24	1	3		3						
219(CTCAE)		**3**	**3**		**2**						
18(QOL)	60	1	1	3	2	1		1			
18(CTCAE)		**1**	**1**	**2**	**0**	**0**		**0**			
170(QOL)	30	3	2		3						
170(CTCAE)		**2**	**1**		**1**						
6(QOL)	96	2	2	1	1	1		1		1	2
6(CTCAE)		**1**	**0**	**1**	**1**	**0**		**0**		**0**	**0**
35(QOL)	84	1	3	1	1	1	2		2	1	
35(CTCAE)		**0**	**1**	**0**	**0**	**0**	**0**		**0**	**0**	
56(QOL)	72	1	1	1	1	1	2	1	1		
56(CTCAE)		**0**	**0**	**0**	**1**	**0**	**0**	**0**	**0**		
42(QOL)	72	1	1	2	1	2	1	2	2		
42(CTCAE)		**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**		

Not at All – 1

A little – 2

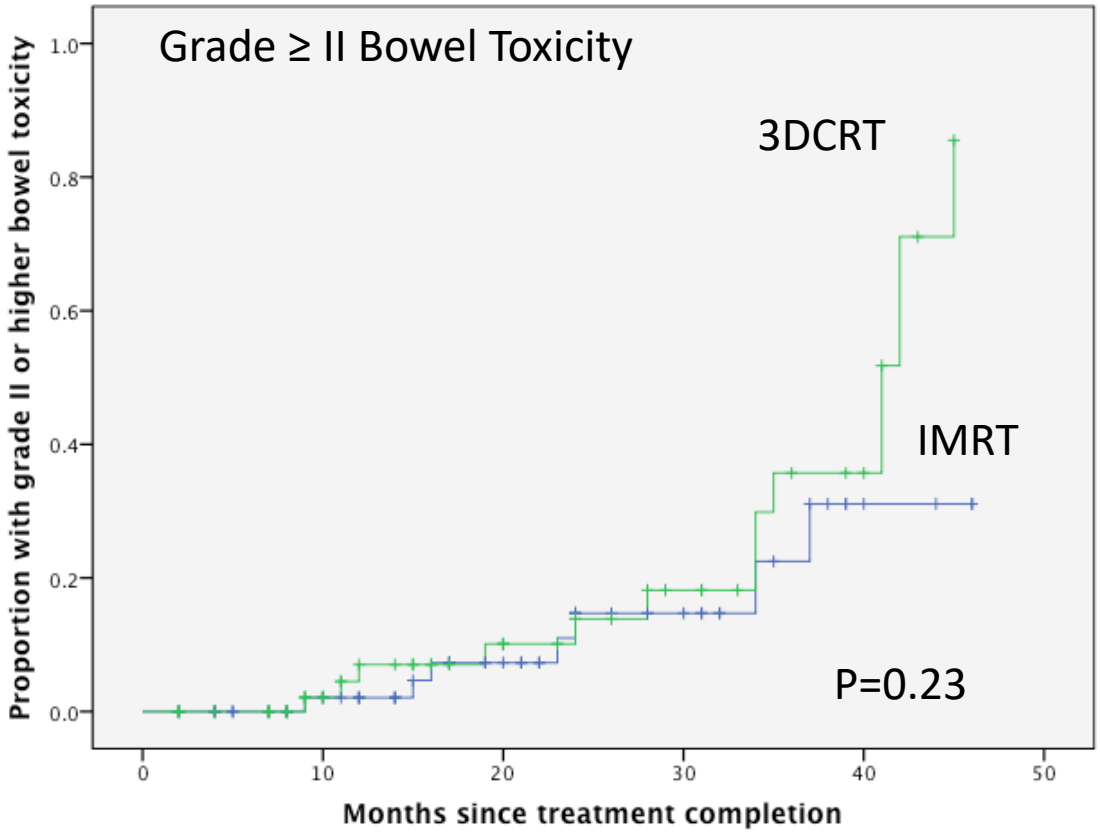
Quite a bit- 3

Very much- 4

Toxicities captured across multiple scales : 11 GI/5 GU and others

Planned Interim Analysis: 2015

- Primary endpoint 24% vs 11%, p=0.12).
- Alpha spending 0.03.
- Final Sample Size amended
- A total of 43 events needed (N=300).
- p=0.047 reserved for final analysis



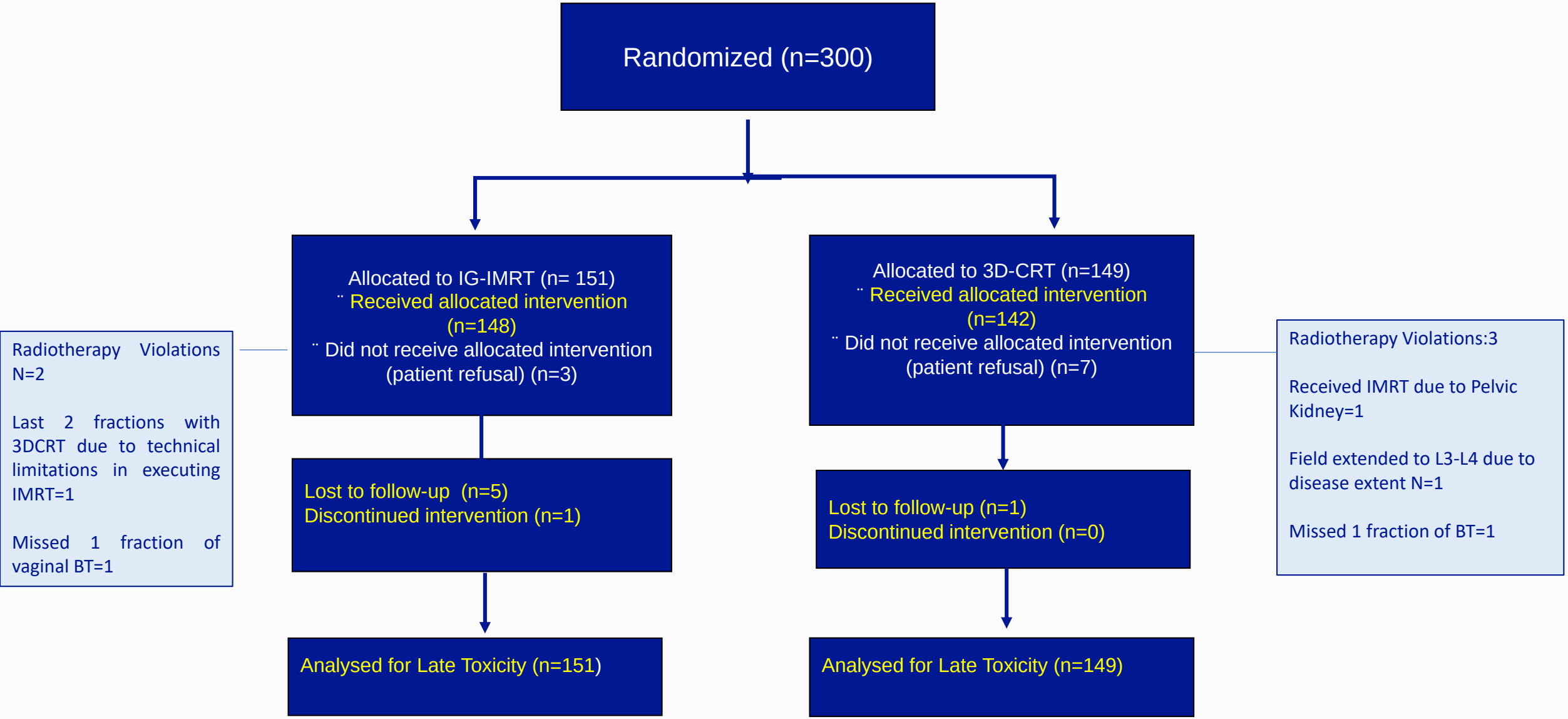
Number at Risk (Number of Events)					
3DCRT (n=56)	42(1)	28 (3)	17(2)	8(2)	7(3)
IMRT (n=61)	46 (1)	29 (2)	15(2)	3(2)	3(0)

Presented at ASTRO Plenary Session 2015

Planned Accrual completed in October,2019.

Median Follow up of 48 months was reached.

Study Closed for Final Analysis 31st January,2020.



Study closed 31st January 2020 for primary analysis

Baseline Patient Characteristics

	IG-IMRT (n=151)	3D-CRT (n=149)
Age ≥ 48	83 (55%)	85 (57%)
<48	68 (45%)	64 (43%)
BMI		
≥ 24	69 (45.7%)	77 (51.7%)
<24	82 (54.3%)	72 (48.3%)
Hypertension		
Yes	13 (8.6%)	22 (14.8%)
No	138 (91.4%)	127 (85.2%)
Diabetes	6 (4.0%)	12 (8.1%)
Yes		
No	145 (96%)	137 (91.9%)
Tobacco use	6 (4.2%)	7 (4.7%)
Yes		
No	145 (96%)	142 (95.3%)
Previous Abdominal surgery		
>1	6 (4%)	7 (4.7%)
≤ 1	145 (96%)	142 (95.3%)
Type of Surgery		
Laparoscopic	11 (7.3%)	10 (6.7%)
Open	140 (92.7%)	139 (93.3%)
Type of surgery		
WH	80 (53%)	74 (49.7%)
TAH-BSO	71 (47%)	75 (50.3%)
Histology		
Squamous	113 (74.8%)	127 (85.2%)
Adenocarcinoma	38 (25.2%)	22 (14.8%)
Concurrent chemotherapy		
Yes	117 (77.5%)	114 (76.5%)
No	34 (22.5%)	35 (23.5%)
Treatment completion as intended External Radiotherapy	146 (96.7%)	138 (92.6%)
Recommended Chemotherapy* (n=231)		
Chemotherapy dose reduction (overall)	17 (11.8%)	13 (9.1%)
Chemotherapy 4 or more cycles	103(88%)	100 (87.7%)
Chemotherapy 3 cycles	3 (2.1%)	3 (2.1%)
Chemotherapy 2 cycles	4 (2.8%)	2 (1.4%)
Chemotherapy 1 cycle	3 (2.1%)	1 (0.7%)
Chemotherapy 0 cycle	0 (0.0%)	2(1.7%)

*=Data specified for patients only who were recommended concurrent chemotherapy and stratified in chemo-radiotherapy subgroup.

Balance between Test and Standard Arm

96% compliance to IG-IMRT

92% to 3DCRT

Balance in Concurrent chemotherapy recd and type of Surgery in both arms.

Acute Toxicity

	3DCRT (N=149)	IG-IMRT(N=151)	P value
	Grade ≥ II Toxicity	Grade ≥ II Toxicity	
Diarrhea	**27.7%**	**17.8%**	**0.04**
Any Gastrointestinal Toxicity	52.5%	53.5%	0.93
Any Genitourinary Toxicity	5.7%	9.9%	0.19
Any Hematological Toxicity	33.7%	41%	0.14
Fatigue	22.7%	19.1%	0.54

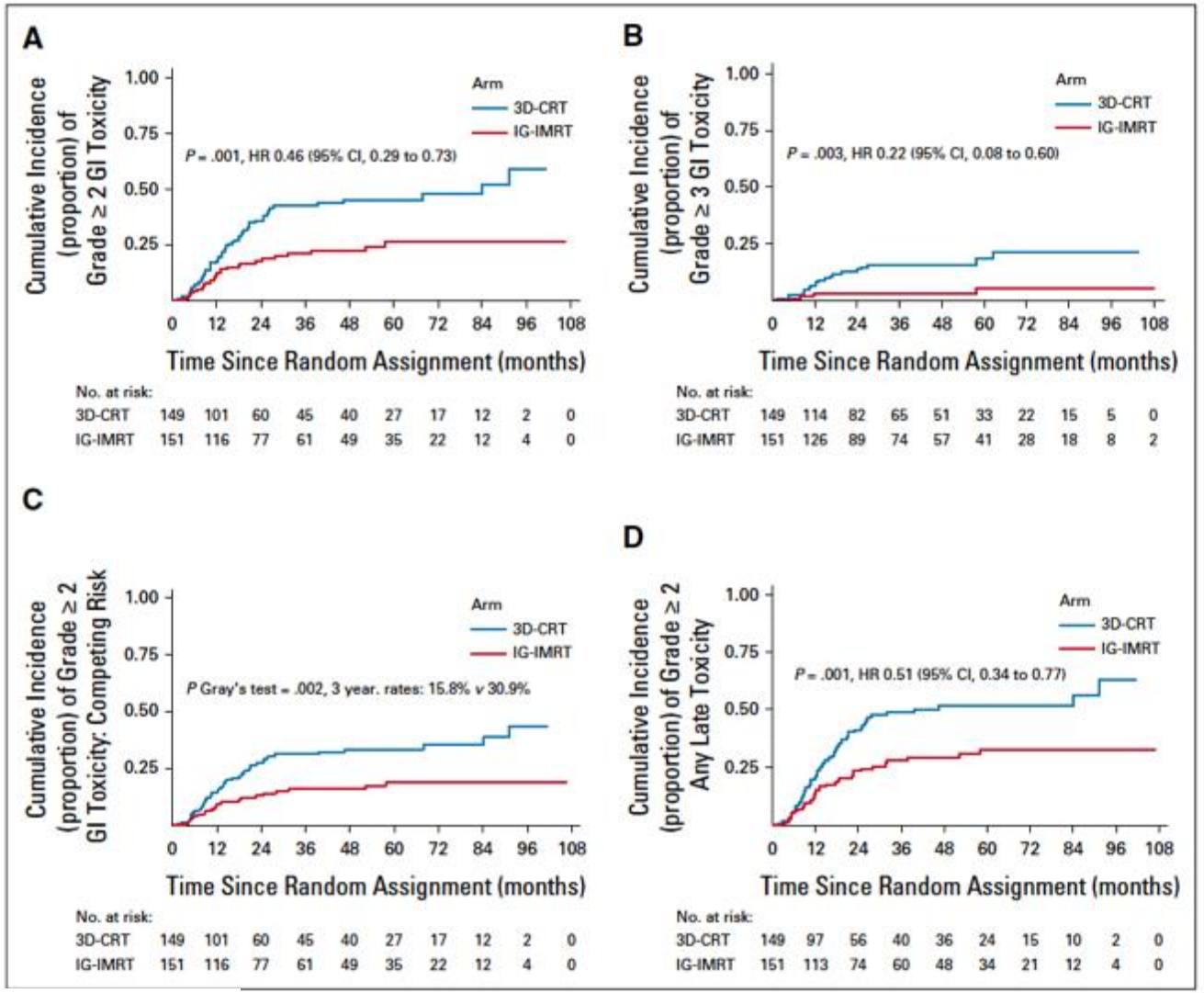
Results: Late Gastrointestinal Toxicity

	Grade ≥ II Toxicity 3DCRT	Grade ≥ II Toxicity IG-IMRT	P value
Diarrhea	8%	4.3%	0.21
Anorexia	**7.3%**	**1.4%**	**0.02**
Nausea	1.5%	0.7%	0.62
Vomiting	4.4%	1.4%	0.17
Abdominal Bloating	**27.7%**	**14.4%**	**0.01**
Abdominal Pain	15.3%	10.9%	0.27
Bowel Perforation	1.5%	0.7%	0.62
Bowel Obstruction	**7.3%**	**0.7%**	**0.01**
Gastrointestinal Stricture	0.7%	0.7%	0.25
Rectal Bleeding	3.6%	1.4%	0.17
Malabsorption	1.5%	1.4%	0.62

Results: Non Gastro-Intestinal Late Toxicity

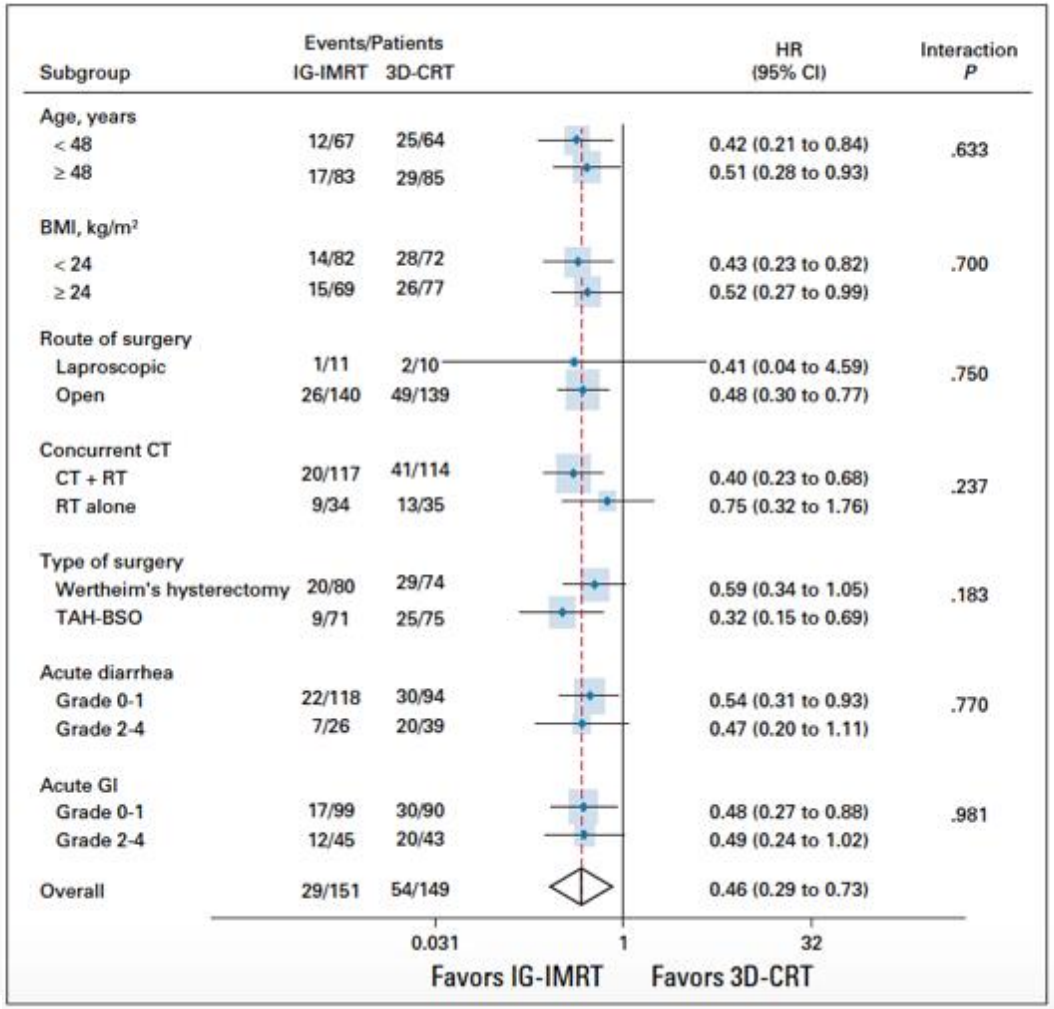
	3DCRT Grade ≥ II Toxicity	IG-IMRT Grade ≥ II Toxicity	P value
Cystitis	7.5%	5%	0.60
Urinary Frequency	4.4%	1.4%	0.33
Urinary Incontinence	2.2%	0.7%	0.37
Bladder Spasms	1.5%	0%	0.25
Any Genitourinary Toxicity	11.8%	6.5%	0.21
Lymphedema	1.5%	1.4%	1.0
Fatigue	**13.9%**	**5.1%**	**0.01**
Constitutional Symptoms	**8.1%**	**2.2%**	**0.03**
Vaginal Stenosis	**5.9%**	**1.4%**	**0.06**
Second Cancers	1.5%	0%	0.25
Toxicity Related Death	2.1%	0.7%	0.31

Physician Reported Adverse Effects: PARCER Phase III Trial



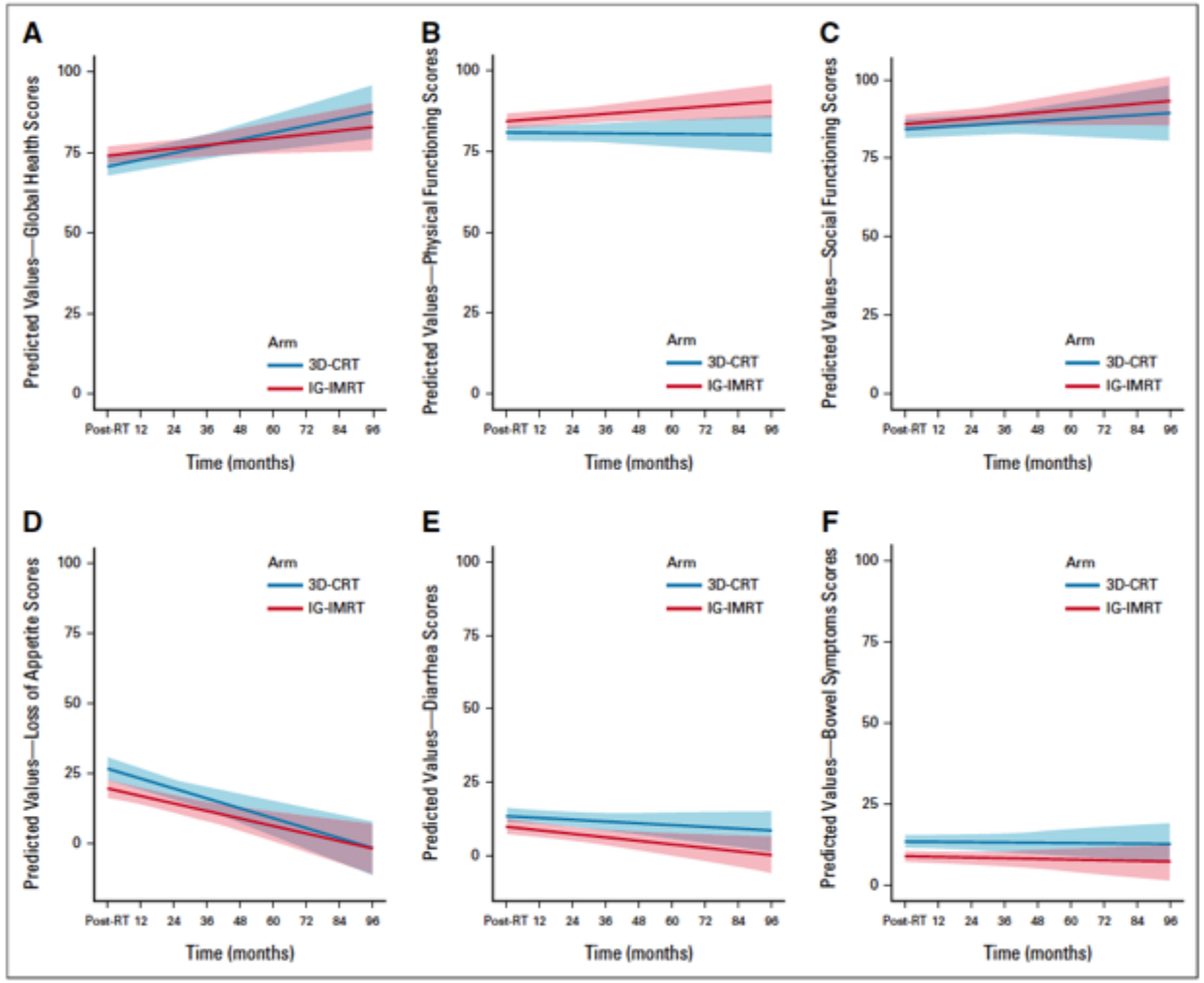
Chopra, JCO,20121

Subgroup Analysis



Chopra, JCO,2021

Quality of Life



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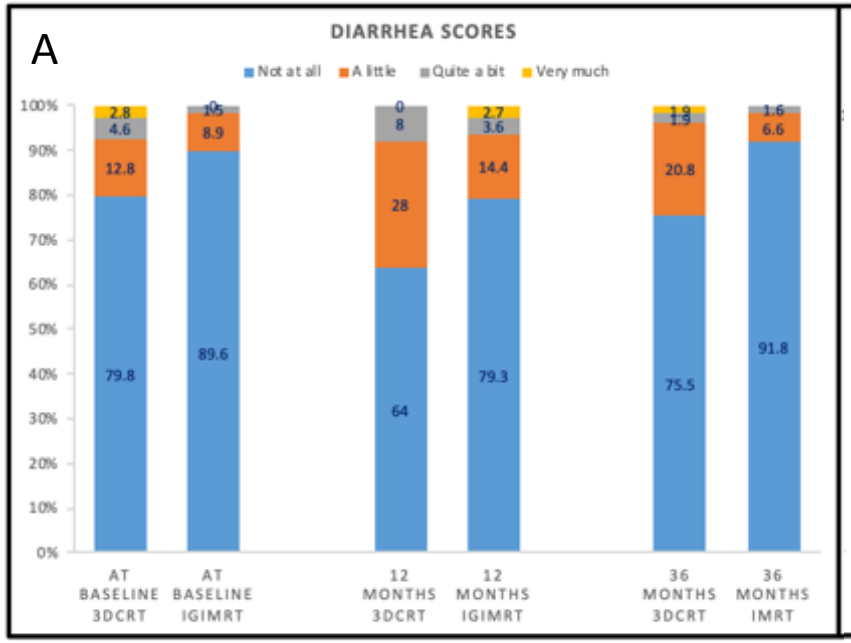
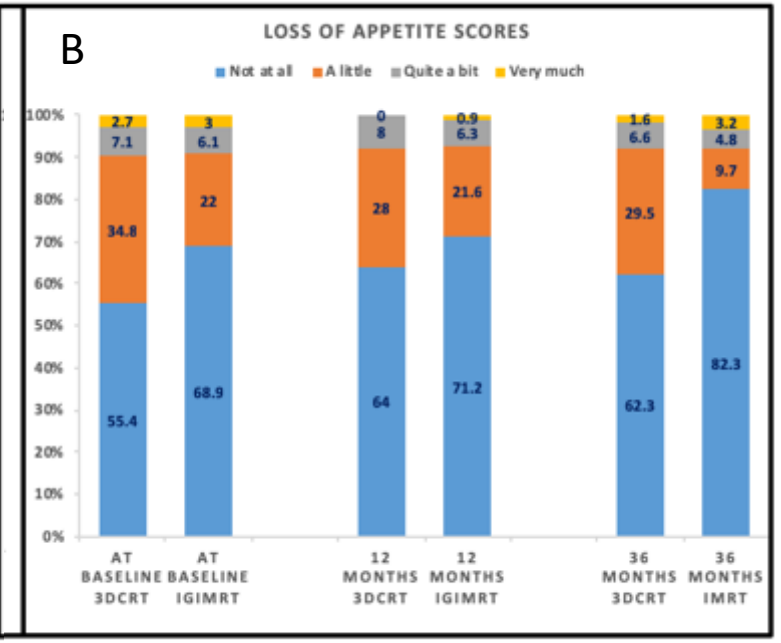
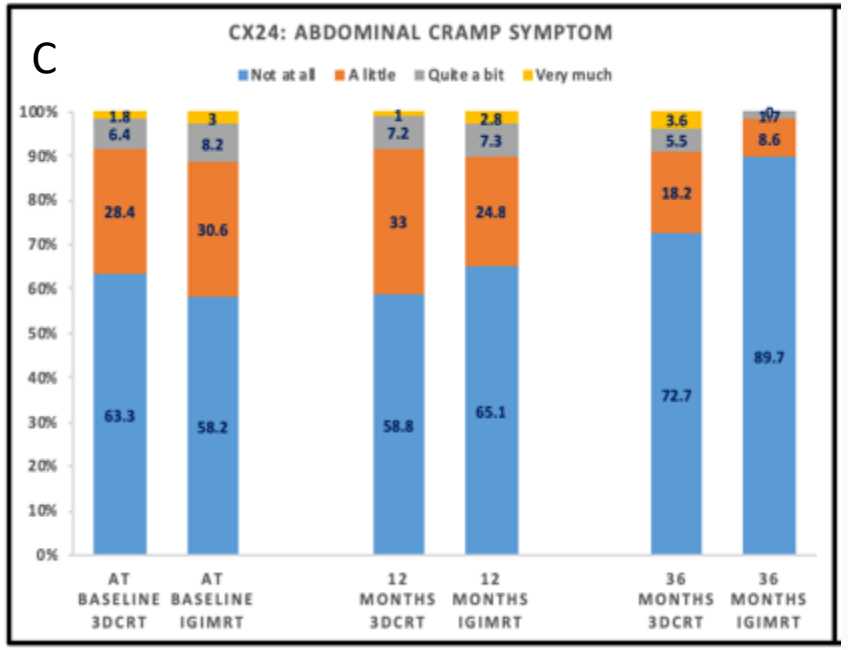
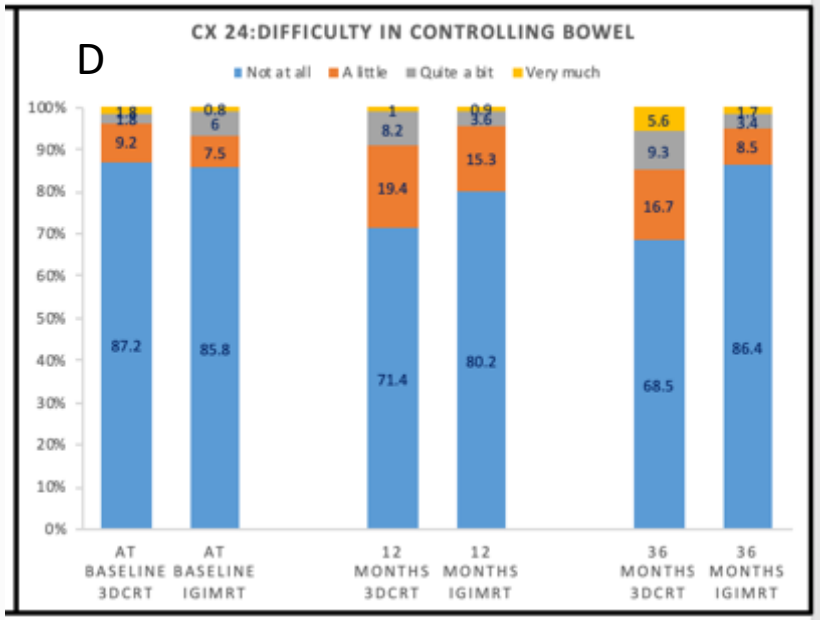
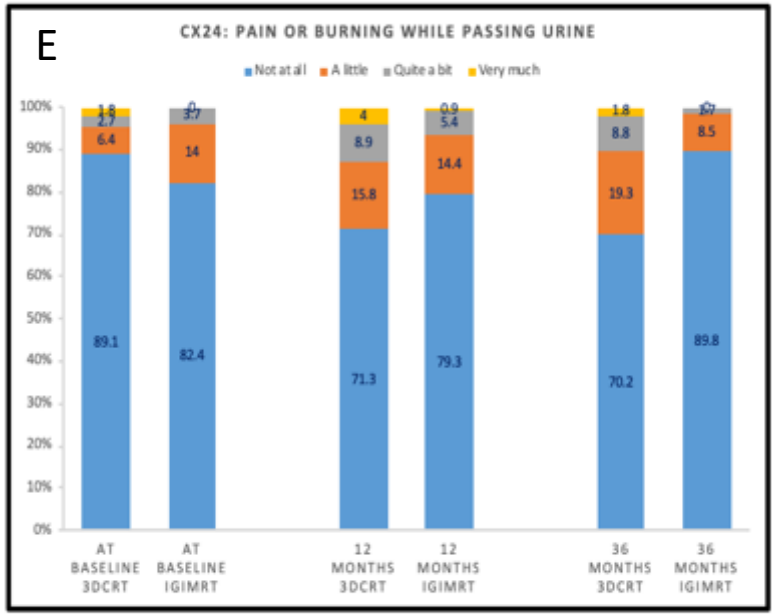

A
DIARRHEA SCORES
Not at all
A little
Quite a bit
Very much
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2.8
4.6
12.8
79.8
0
8.9
89.6
0
8
28
64
2.7
3.6
14.4
79.3
1.9
1.9
20.8
75.5
1.6
6.6
91.8
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IMRT


B
LOSS OF APPETITE SCORES
Not at all
A little
Quite a bit
Very much
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2.7
7.1
34.8
55.4
3
6.1
22
68.9
0
8
28
64
0.9
6.3
21.6
71.2
1.6
6.6
29.5
62.3
3.2
4.8
9.7
82.3
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IMRT


C
CX24: ABDOMINAL CRAMP SYMPTOM
Not at all
A little
Quite a bit
Very much
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1.8
6.4
28.4
63.3
3
8.2
30.6
58.2
1
7.2
33
58.8
2.8
7.3
24.8
65.1
3.6
5.5
18.2
72.7
1.7
8.6
89.7
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IGIMRT


D
CX 24:DIFFICULTY IN CONTROLLING BOWEL
Not at all
A little
Quite a bit
Very much
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1.8
9.2
87.2
0.8
6
7.5
85.8
1
8.2
19.4
71.4
0.9
3.6
15.3
80.2
5.6
9.3
16.7
68.5
1.7
3.4
8.5
86.4
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IGIMRT


E
CX24: PAIN OR BURNING WHILE PASSING URINE
Not at all
A little
Quite a bit
Very much
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1.8
2.7
6.4
89.1
3.7
14
82.4
4
8.9
15.8
71.3
0.9
5.4
14.4
79.3
1.8
8.8
19.3
70.2
1.7
8.5
89.8
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IGIMRT

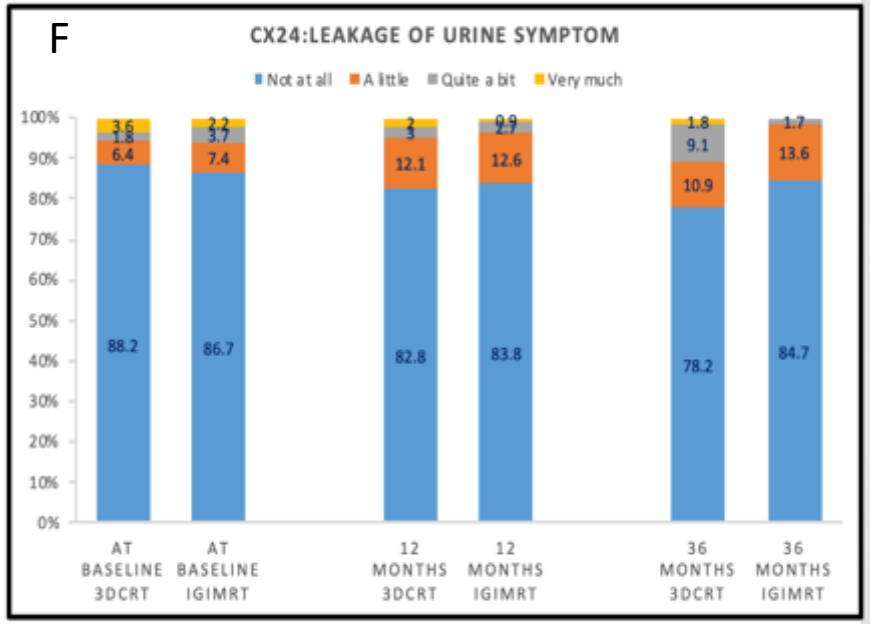
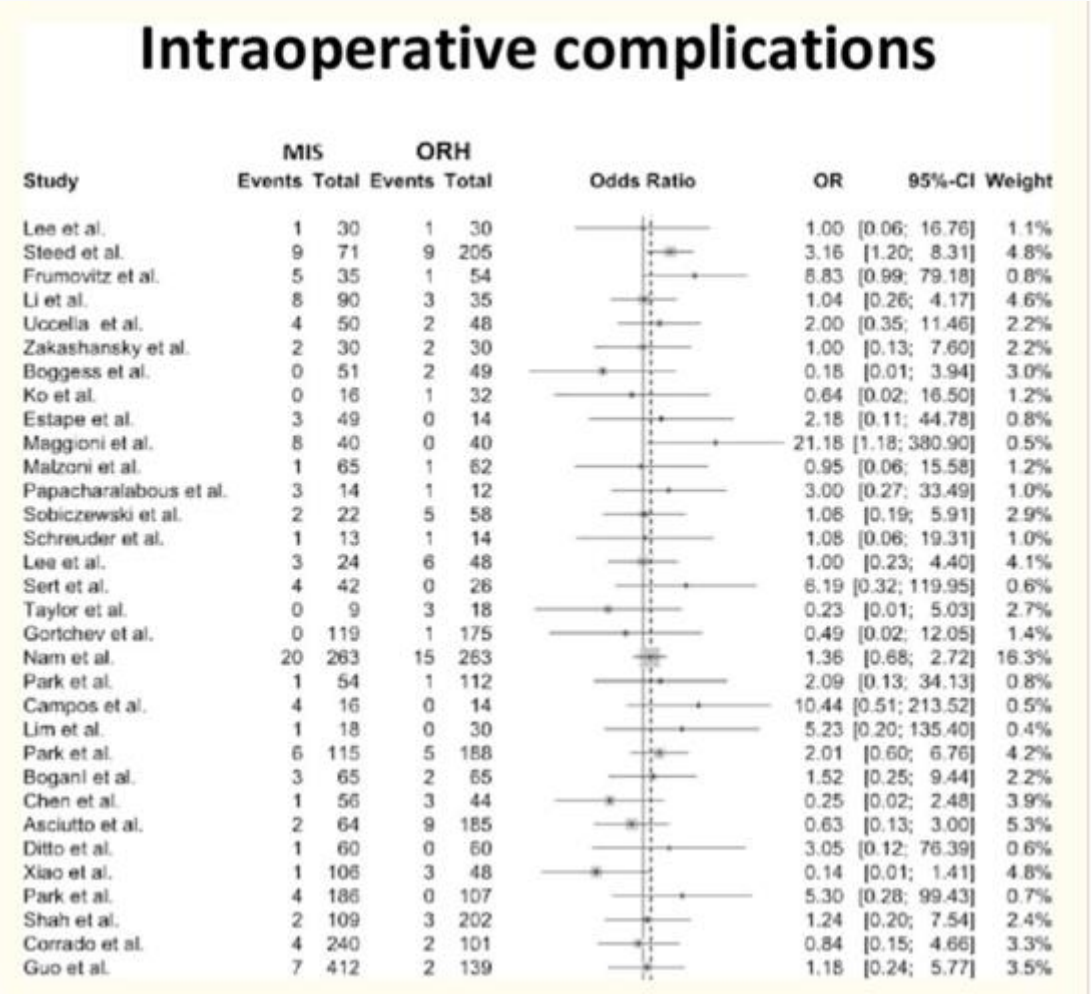

F
CX24:LEAKAGE OF URINE SYMPTOM
Not at all
A little
Quite a bit
Very much
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
3.6
1.8
6.4
88.2
2.2
3.7
7.4
86.7
2
3
12.1
82.8
0.9
2.7
12.6
83.8
1.8
9.1
10.9
78.2
1.7
13.6
84.7
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IGIMRT

Fig 4 A- F

Impact of Surgical Advances on Adverse Events



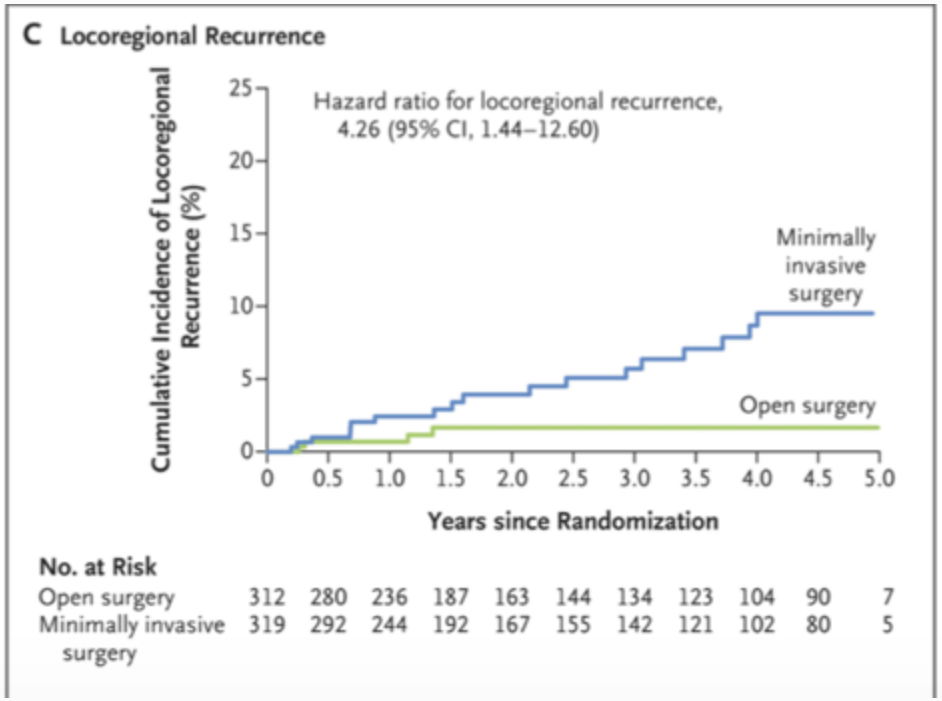
Category	MIS	ORH	OR (95% CI)	P value	I^2(%)
Transfusion	301/2490	494/4408	0.34[0.22,0.53]	**<0.001**	72.3
Intraoperative complications					
Bladder damage	25/2279	24/4009	1.28[0.75,2.19]	0.3	0
Cystotomy	32/586	14/677	2.27[1.23,4.20]	**0.002**	0
Bowel injury	12/1479	8/3449	2.15[0.95,4.89]	**0.041**	0
Subcutaneous emphysema	7/246	0/207	4.36[0.94,20.29]	**0.008**	0
Nerve injury	2/1181	5/802	0.51[0.14,1.93]	0.343	0
Ureteral injury	22/2519	24/4520	1.05[0.61,1.76]	0.959	0
Vessel injury	21/2328	27/4112	1.01[0.59,1.73]	0.753	0
Postoperative complications					
Wound infection	5/1380	104/3277	0.15[0.08,0.28]	**<0.001**	0
Incisional hernia	7/898	7/811	0.93[0.34,2.51]	0.803	0
Pelvic infection and abscess	30/1713	78/3396	0.40[0.26,0.63]	**<0.001**	39.9
Lymphedema	13/791	19/619	0.48[0.24,0.98]	**0.03**	0
Lymphocyst	40/1614	35/1194	0.73[0.46,1.15]	0.123	8.4
Intestinal obstruction	37/2490	281/4070	0.30[0.21,0.43]	**<0.001**	0
Pulmonary embolism	0/508	7/558	0.36[0.09,1.48]	**0.025**	0
Deep vein thrombosis	31/2289	78/3886	0.56[0.35,0.88]	**0.01**	0
Fistula	38/2203	17/1904	1.69[0.02,2.79]	**0.011**	0
Urinary tract infection	33/764	44/799	0.56[0.34,0.91]	**0.013**	3

MIS had a negative effect in increasing the complications of cystotomy, bowel injury, subcutaneous emphysema, and fistula.

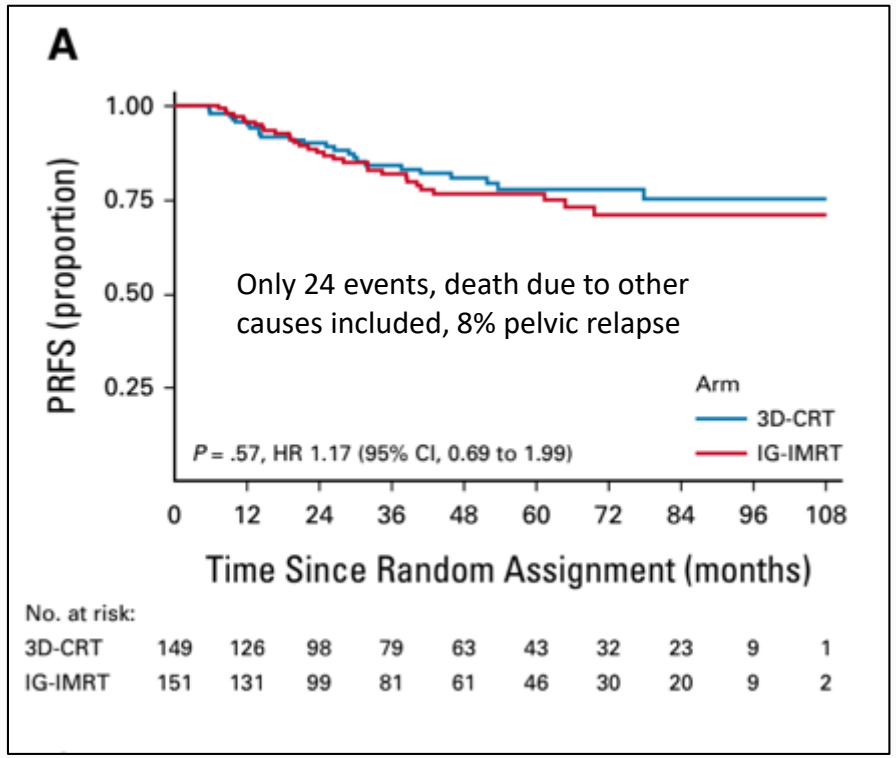
Yilin Li, PLOS One 2021

Advances in Surgical Techniques vs Advanced Radiation Techniques : Postoperative Setting Disease Control

Laparoscopic Surgery vs Open



IG-IMRT vs 3DCRT



Approx 30% use of adjuvant RT +/-chemo in both arms

100% use of adjuvant RT based on risk grouping

Detriment in Oncological Outcomes with Advances in Surgical Techniques

Ramirez, NEJM 2018

Chopra S, JCO, 2021

Summary

- IG-IMRT is superior to 3DCRT in reducing Late GI toxicity in women undergoing postoperative pelvic RT.
- Greater Benefit of IG-IMRT in those receiving concurrent chemotherapy though study underpowered to conclude on this subgroup.
- Statistically significant reduction in acute diarrhea.
- No difference in disease related outcomes or Genitourinary Toxicity.
- IG-IMRT should represent the new standard of care for postoperative pelvic RT.

Development of MOSES
Reanalysis of Phase III PARCER trial with MOSES.

Supriya Chopra, Nilesh Ranjan, Mayuri Charnalia

Background for Developing Time Weighted Toxicity Reporting System

- ✓ Classical CTCAE method of toxicity reporting relies on WORST Grade in an organ system.
- ✓ Cumulative effect of evolution of toxicity and multiplicity of events within an organ system not considered.
- ✓ Modest to Low Correlation between Physician and Patient reported outcomes in terms of QOL.
- ✓ Alternative methods of toxicity reporting in literature - LAPERS , Tox T, TAMES, Total toxicity burden.

Hypothesis

Time weighted CTCAE scores provide a better description of symptom burden.

This may better correlate with QOL.

Study Population for Prospective Cohort

- Patients included in Phase III RCT of 3DCRT vs IG-IMRT (postop RT in cervix cancer; PARCER)
- Symptomatic for toxicity either on physician or patient assessment
- Patients with at least 12 months of follow up
- At least 3 QOL scores available after baseline QOL (with 6 months post treatment representing the baseline QOL)

Steps in MOSES Calculation

- ✓ 6 symptoms selected (Most common and had corresponding QOL item).
- ✓ MOSES score calculated. ($\Sigma P \times S$): example to follow
- ✓ ROC performed against substantial symptom on QOL symptom item/ role functioning (50% adapted from LAPERS)
- ✓ MOSES score cut off in our population that provided good Sens/Spec for symptomatic on QOL : 0.20 (0.14-0.22).
- ✓ After sensitivity analysis for both cut off of MOSES and QOL MOSES = 0.20 retained as discriminator.
- ✓ For Multiple symptoms / patient C-MOSES score calculated
- ✓ C MOSES = (MOSES symptom1+ MOSES Symptom 2+…3+…4) . Cut off of 0.70 against QOL

MOSES Score Calculation

At month	6	9	12	15	18	21	24	27	30	33	36	42	48	54	60	72	84	TFU	MAX GRADE
Patient A	3	0	3	3	3	3	2											24	3
Patient B	0	3	No f/u	0	0	0	0	No f/u	0	1	No f/u	No f/u	0	No f/u	No f/u	0	0	84	3

10 fold difference in MOSES score

Patient A: Final score for diarrhoea = ΣP x S

=P(0) * S(0)+ P(I) * S(I)+ P(II) * S(II)+ P(III) * S(III)+ P(IV) * S(IV)+ P(V) * S(V)

=(3/24 * 0) + (0/24 * 1) +(3/24 * 2) + (15/24 * 3) + (0/24 * 4) + (0/24 * 5)

= 0+0+0.25+1.88+0+0

=2.13

@ Type in your Twitter handle here!

- Patient B– Final score for diarrhoea = ΣP x S

=P(0) * S(0)+ P(I) * S(I)+ P(II) * S(II)+ P(III) * S(III)+ P(IV) * S(IV)+ P(V) * S(V)

=(73.5/84 * 0) + (6/84 * 1) +(0/84 * 2) + (4.5/84 * 3) + (0/84 * 4) + (0/84 * 5)

= 0+0.07+0+0.16+0+0

=0.23

C-MOSES Score Calculation

R.No.	Diarrhoea	Anorexia	Pain	Urinary Incontinence	Urinary Frequency	Fatigue	Final Score	Max Grade
Patient A	2.13	0.52	0.52	0.41	0.52	0.21	4.30	3
Patient B	0.23	0.00	0.07	0.10	0.00	0.00	0.40	3

@ Type in your Twitter handle here!

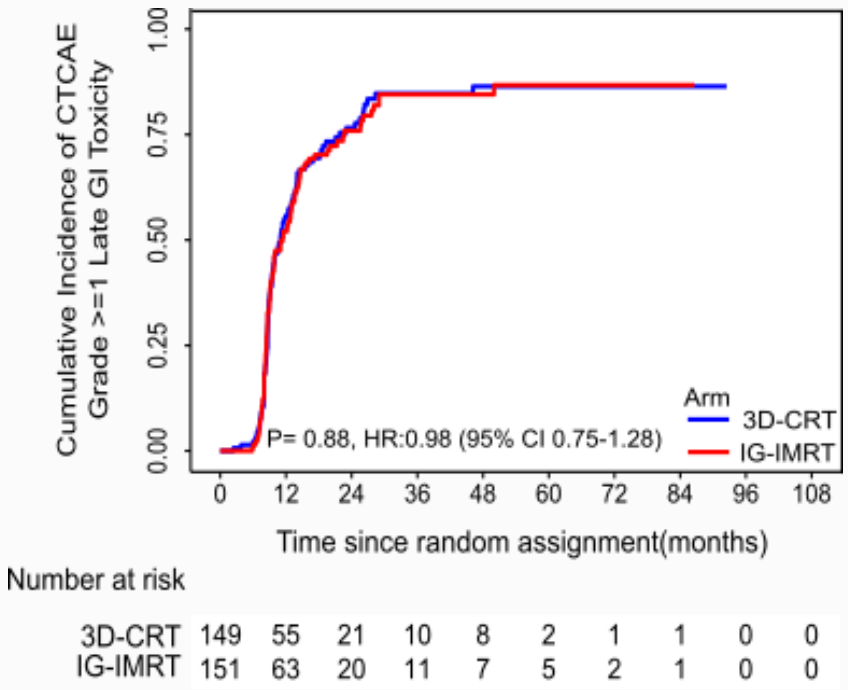
CTCAE vs. MOSES in predicting QOL Symptom

QOL Symptoms	CTCAE maximum grade method				MOSES Method				
	Sensitivity	Specificity	Accuracy	p-value	Sensitivity	Specificity	Accuracy	p-value (ϕ*)	AUC
Diarrhoea	50%	73%	69%	0.096	43%	94%	85 %	0·001	0.67
Anorexia	25%	63%	51%	0·24	9%	85%	61 %	0·40	0.45
Abdominal Pain	88%	24%	57%	0·046	58%	85%	71 %	0·001	0.76
Urinary incontinence	65%	59%	61%	0·04	30%	91%	72 %	0·01	0.65
Urinary frequency	63%	56%	59%	0·045	21%	91%	62 %	0·06	0.63
Fatigue	90%	24%	76%	0.03	63%	70%	64 %	0·001	0.71

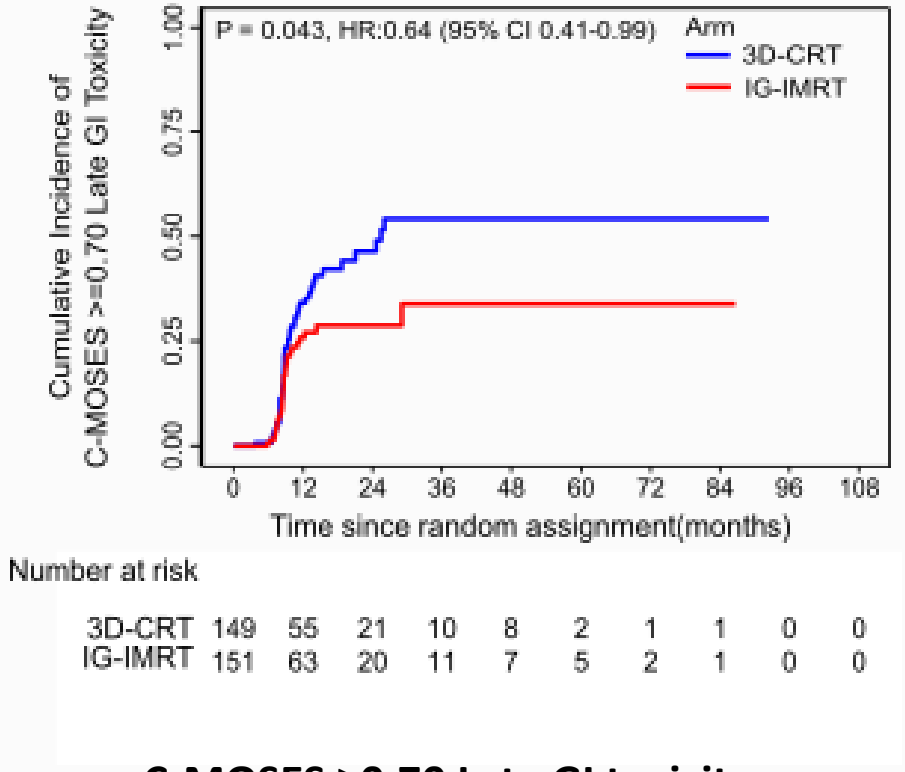
PARCER reanalysis using all CTCAE Grades

- ✓ 21 Symptoms selected(11 GI symptoms, 5 GU symptoms, 5 other symptoms)
- ✓ MOSES score calculated.
- ✓ C-MOSES score calculated
- ✓ Patients categorized above and below as C-MOSES>= 0.70 and C-MOSES<= 0.70
- ✓ CTCAE categorized as “Grade0” and “Grade 1-4”
- ✓ Time to event performed between IG-IMRT and 3D-CRT arm using CTCAE and MOSES.

CTCAE vs. MOSES: Late GI Toxicity



CTCAE grade ≥ 1 Late GI toxicity



C-MOSES ≥0.70 Late GI toxicity

Summary

- MOSES and C-MOSES are more accurate in predicting patient's symptoms burden(QOL).
- C-MOSES provides much more comprehensive discrimination of toxicity burden.
- As compared to CTCAE, MOSES reports higher bothersome symptom burden (25% vs 50% for any toxicity)
- MOSES allows better discrimination between treatment interventions.
- This method of toxicity reporting requires further testing and validation.
- Is a valuable complement to CTCAE reporting (Can miss isolated severe events)

Future Directions

- Compare MOSES with other AE scoring systems like LAPERS (EMBRACE)
- External Validation of MOSES initiated
- EMBRACE Adverse events planned to be analyzed using MOSES

  (Danish Research Grant , K Tanderup, K Kirchheiner, S Spampinato, S Chopra)


Conceive – Conduct – Communicate '*meaningful*'
Clinical, Translational & Epidemiological Cancer Research