
ASTRO
ANNUAL MEETING
2020
NEWS BRIEFING
The briefing will begin shortly.

ASTRO ANNUAL MEETING 2020

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October 26, 2020

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Initial report of a randomized trial comparing conventional- vs conventional plus fluciclovine (^{18}F) PET/CT imaging-guided post-prostatectomy radiotherapy for prostate cancer (LBA-1)

Dr. Ashesh Jani, Winship Cancer Institute of Emory University

CCTG SC.24/TROG 17.06: A randomized phase II/III study comparing 24Gy in 2 stereotactic body radiotherapy (SBRT) fractions versus 20Gy in 5 conventional palliative radiotherapy (CRT) fractions for patients with painful spinal metastases (LBA-2)

Dr. Arjun Sahgal, Sunnybrook Cancer Center of University of Toronto

Phase III randomized trial of postoperative adjuvant conventional radiation (3DCRT) versus image guided intensity modulated radiotherapy (IG-IMRT) in cervical cancer (PARCER): Final analysis (Abstract 2)

Dr. Supriya Chopra, Tata Memorial Centre

Stereotactic ablative fractionated radiotherapy versus radiosurgery for oligometastatic neoplasia to the lung: A randomized phase II trial (Abstract 5)

Dr. Shankar Siva, Peter MacCallum Cancer Centre

Stereotactic radiosurgery versus whole-brain radiation therapy for patients with 4-15 brain metastases: A phase III randomized controlled trial (Abstract 41)

Dr. Jing Li, The University of Texas MD Anderson Cancer Center

Initial Report of a Randomized Trial Comparing Conventional- vs Conventional plus Fluciclovine (^{18}F) PET/CT Imaging-Guided Post-Prostatectomy Radiotherapy for Prostate Cancer

Ashesh B. Jani, MD, FASTRO

Winship Cancer Institute of Emory University

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Disclosures

Funding Source: NIH – RO1 CA169188 (PI's: Dr. Ashesh B. Jani / Dr. David Schuster)

- Dr. Ashesh B. Jani:
  - Employee: Emory University / The Emory Clinic
  - Advisory Board: Blue Earth Diagnostics, Ltd. (last in 3/2018)
- Dr. Mark Goodman:
  - Royalties: Nihon MediPhysics Co, Ltd.
- Dr. David Schuster:
  - Consultant: Syncona; AIM Specialty Health; Global Medical Solutions Taiwan; Progenics Pharmaceuticals, Inc.
  - Research Grants: Blue Earth Diagnostics, Ltd; Nihon MediPhysics Co, Ltd.; Telix Pharmaceuticals (US) Inc.; Advanced Accelerator Applications; FUJIFILM Pharmaceuticals U.S.A., Inc; Amgen
- Emory University:
  - Blue Earth Diagnostics, Ltd. (Cassette Arrangement)

Background

- The decision to offer radiation after prostatectomy for patients with recurrent prostate cancer is complex
  - High failure rates
  - More accurate radiation therapy decisions and treatment planning needed
  - Limitations of conventional imaging

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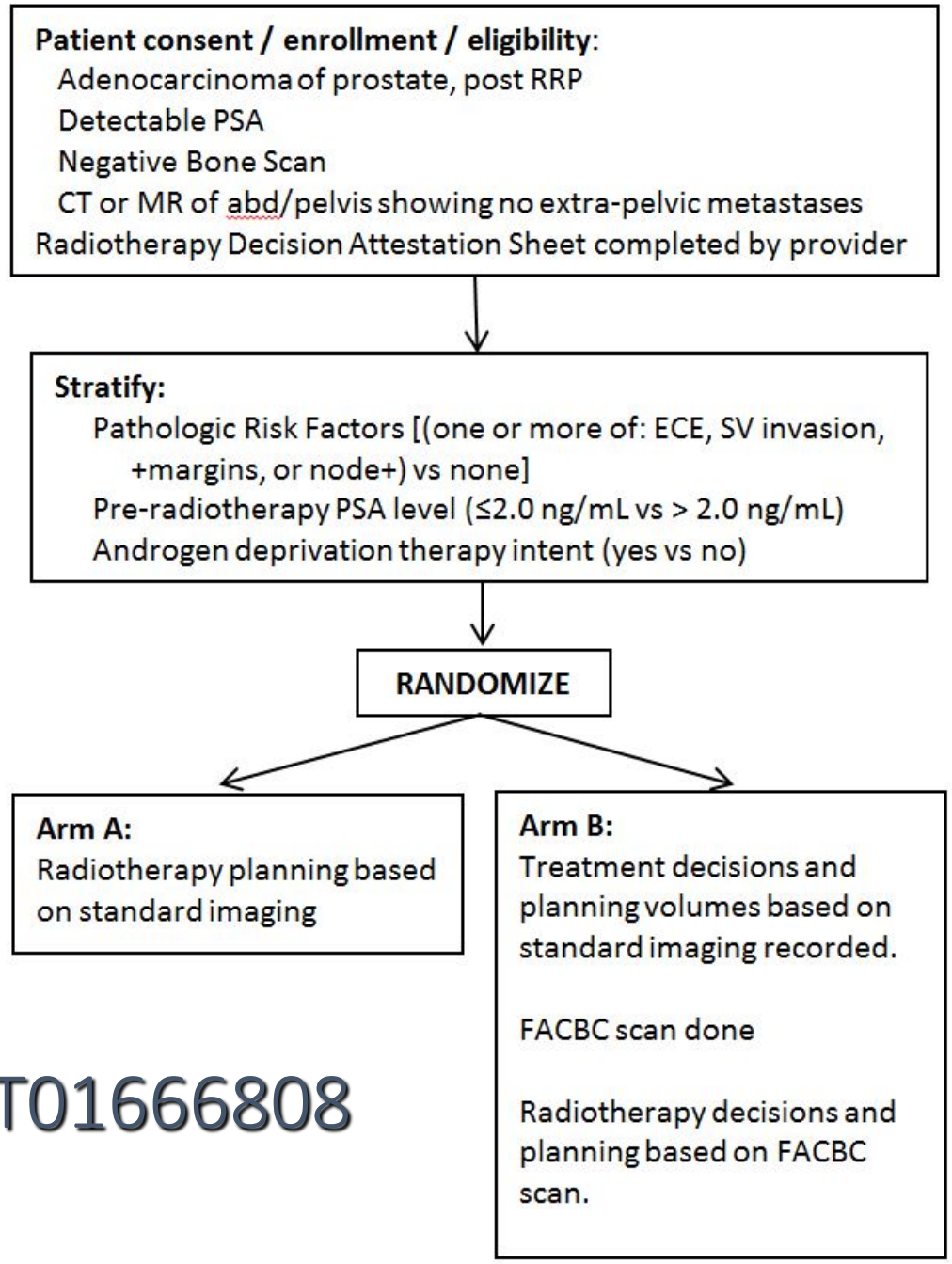
  - Limitations of conventional imaging

EMPIRE-1 Trial

Emory Molecular Prostate Imaging for Radiotherapy Enhancement



NIH RO1 CA169188

Jani & Schuster

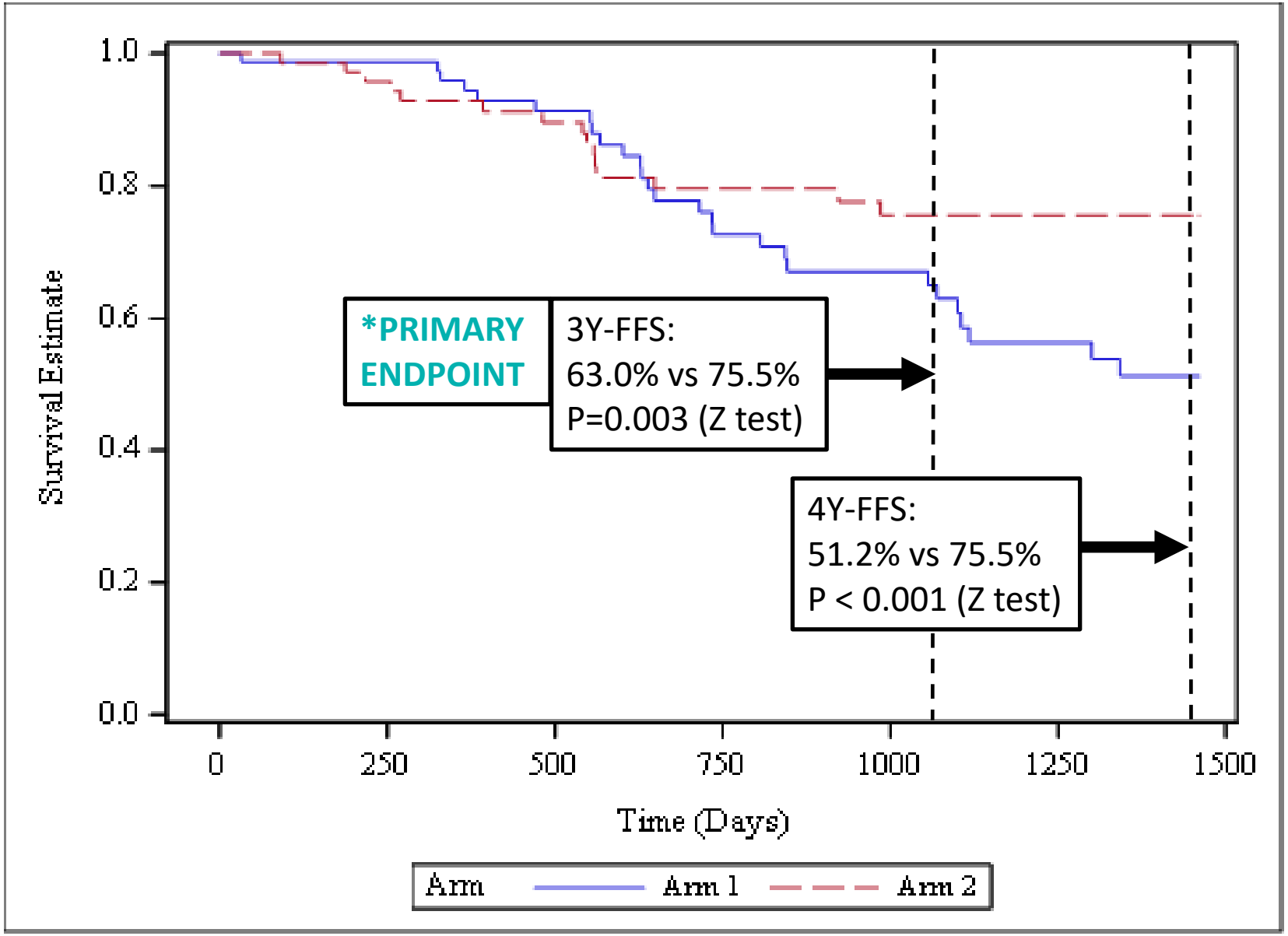
ClinicalTrials.gov: NCT01666808

Fluciclovine (^{18}F) Findings/ Treatment decision:

1. Extra-pelvic uptake:
   - Abort XRT
2. Pelvic nodal uptake:
   - Prostate bed (64.8-70.2/1.8Gy)
   - \+
   - Pelvis (40.5-50.4/1.8Gy)
3. Prostate-bed only uptake:
   - Prostate bed (64.8-70.2/1.8Gy)
4. No uptake:
   - Prostate bed (64.8-70.2/1.8Gy)

Failure-Free Survival

- Three years after treatment, failure-free survival rates were higher in the PET arm
- FFS benefit remained four years after treatment
- Median follow-up
  - Overall: 2.48 Y
  - Failure-free pts: 3.06 Y



Provider-Reported Toxicity
(CTCAE v.5.0)

No significant differences in maximum:

- Acute GU
- Acute GI
- Late GU
- Late GI

Suggests treatment to PET-directed volumes was tolerable.

Patient-reported toxicity (AUA & EPIC-CP) analysis pending

Acute GU (max)	Grade 0	Grade 1	Grade 2	Grade 3	P-value
Arm A/1 (no PET)	7 (8.64%)	53 (65.43%)	18 (22.22%)	3 (3.70%)	0.255
Arm B/2 (PET)	3 (3.95%)	55 (72.37%)	18 (23.68%)	0 (0.00%)	

Acute GI (max)	Grade 0	Grade 1	Grade 2	Grade 3	P-value
Arm A/1 (no PET)	23 (28.40%)	47 (58.02%)	11 (13.58%)	0 (0.00%)	0.436
Arm B/2 (PET)	18 (23.68%)	42 (55.26%)	16 (21.05%)	0 (0.00%)	

Late GU (max)	Grade 0	Grade 1	Grade 2	Grade 3	P-value
Arm A/1 (no PET)	6 (7.50%)	32 (40.00%)	37 (46.25%)	5 (6.25%)	0.678
Arm B/2 (PET)	10 (13.33%)	29 (38.67%)	31 (41.33%)	5 (6.67%)	

Late GI (max)	Grade 0	Grade 1	Grade 2	Grade 3	P-value
Arm A/1 (no PET)	47 (58.75%)	23 (28.75%)	10 (12.50%)	0 (0.00%)	0.580
Arm B/2 (PET)	49 (65.33%)	20 (26.67%)	6 (8.00%)	0 (0.00%)	

Conclusions/Summary

- Randomized trial of imaging tests with primary cancer control endpoint are important but uncommon
- First trial of PET over conventional imaging alone for post-prostatectomy radiation therapy (Note: single institution study where radiotracer was invented)
- **Inclusion of fluciclovine (^{18}F) resulted in significant improvement in failure rate at 3Y**

- Integration of novel PET radiotracers into XRT decisions and planning warrant further study

EMPIRE-2 Trial

Emory Molecular Prostate Imaging for Radiotherapy Enhancement

NIH RO1 CA226992

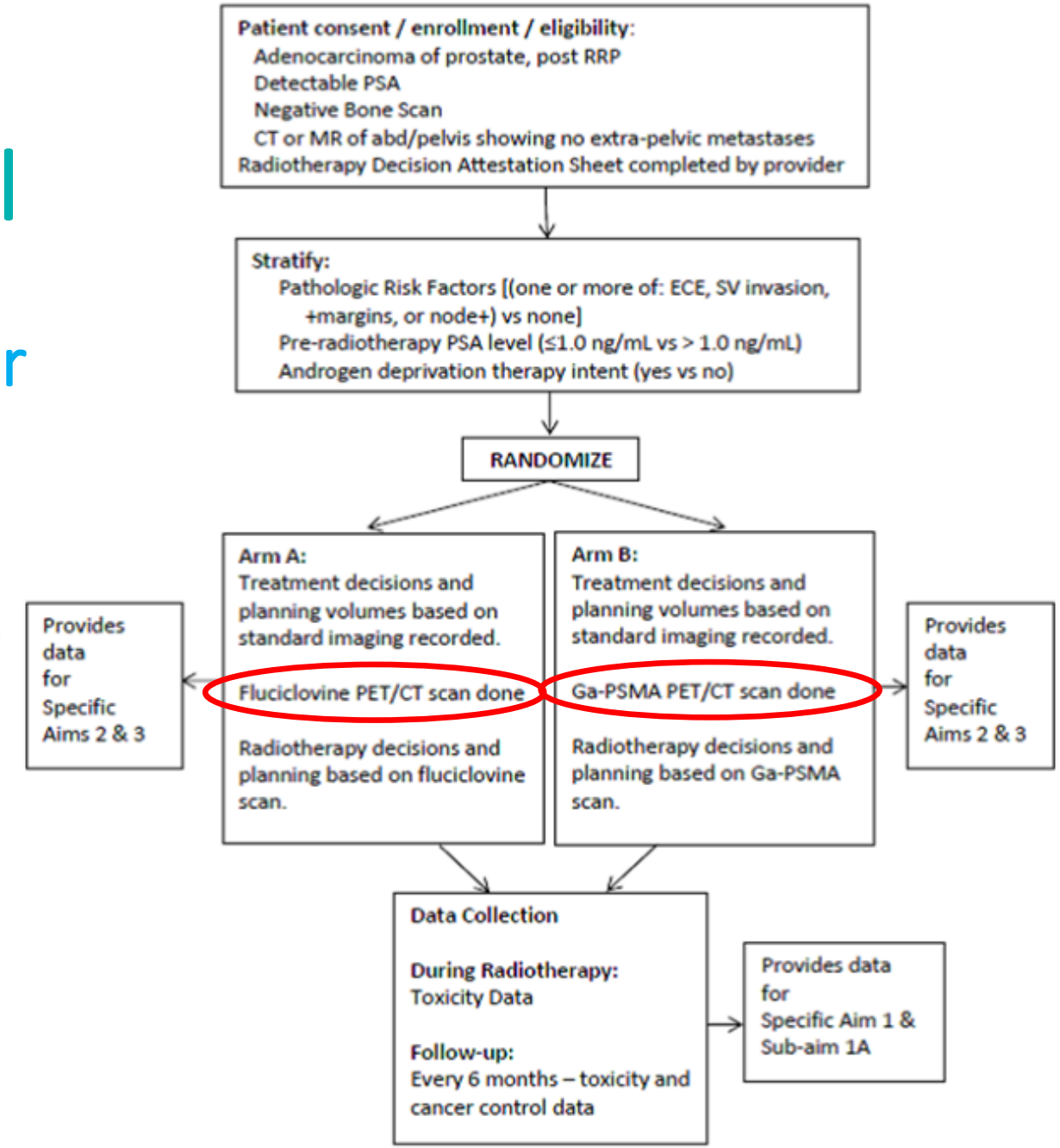
Jani & Schuster

ClinicalTrials.gov:

NCT03762759

2019-2024

n=140 (enrolled ~50)



PET Findings / Treatment decision:

1.
Extra-pelvic uptake:
Abort XRT

2.
Pelvic nodal uptake:
Prostate bed + Pelvis XRT
(Boost sites of uptake)

3.
Prostate-bed only uptake:
Prostate bed XRT
(Boost sites of uptake)

4.
No uptake:
Prostate bed XRT (no boost)

Boost:
Pelvic nodes: 54-56 Gy
Prostate bed: 70-76 Gy

CCTG SC.24/TROG 17.06: A Randomized Phase II/III Study Comparing 24gy in 2 Stereotactic Body Radiotherapy (SBRT) Fractions Versus 20gy In 5 Conventional Palliative Radiotherapy (CRT) Fractions for Patients with Painful Spinal Metastases

Arjun Sahgal, MD

Sunnybrook Odette Cancer Centre, University of Toronto

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- Employer: University of Toronto
- Research grants: Elekta, BrainLAB, Varian
- Consulting services: Elekta, Merck, Abbvie, Roche
- Honoraria and Travel Support: Elekta, Medtronic, BrainLAB, Varian, Accuray
- Advisory Board: Varian, VieCURE, ISRS, AOSPINE Tumour Knowledge forum co-chair

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Sunnybrook
ODETTE CANCER CENTRE
A Cancer Care Ontario Partner

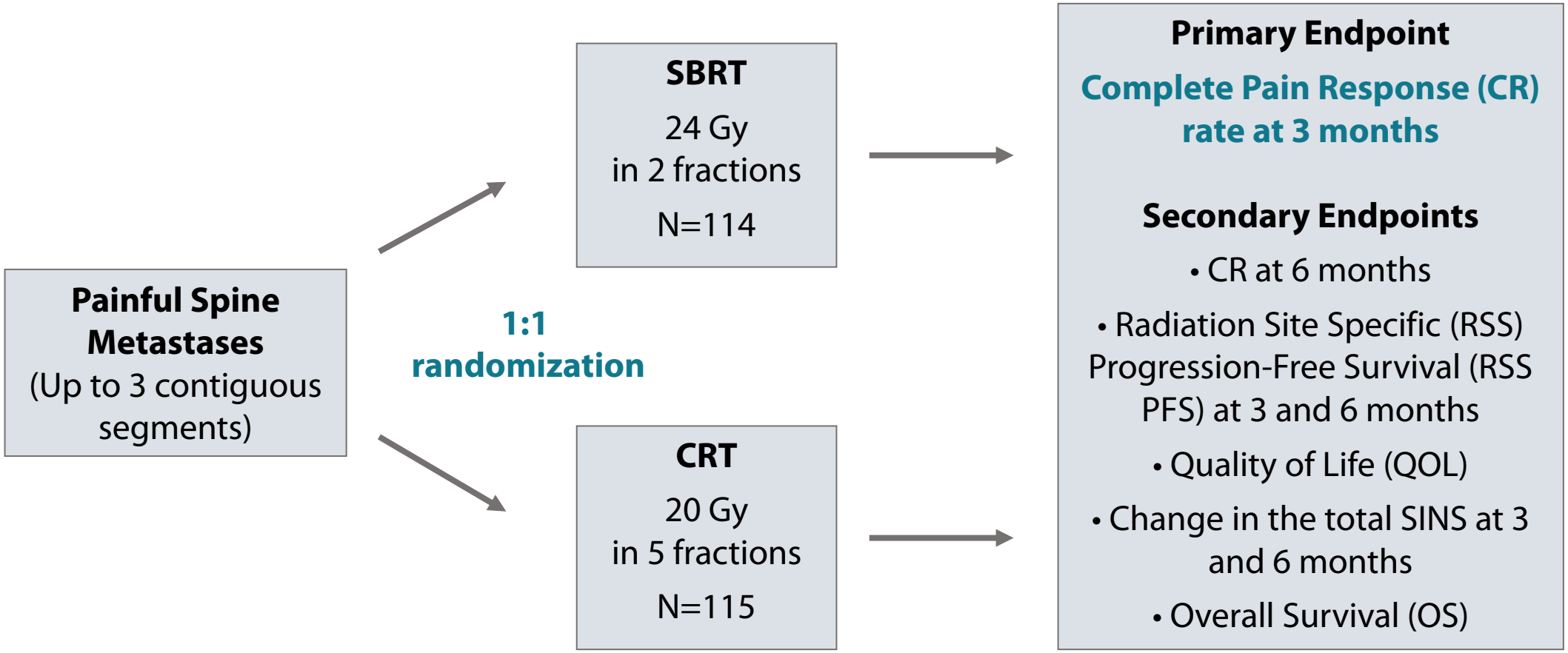
Radiation Oncology
UNIVERSITY OF TORONTO

Canadian Cancer Trials Group
Groupe canadien des essais sur le cancer

Overview

- **Purpose**: For patients with painful spinal metastases, determine if complete pain response rate can be improved with spine SBRT vs. CRT
- SBRT fractionation scheme of 24 Gy in 2 fractions* compared with standard of care CRT regimen of 20 Gy in 5 fractions
- Phase 2/3 randomized controlled trial

Trial Design



Trial Participants

- Initial Phase 2 RCT converted to a Phase 3 RCT without interruption of accrual
- Accrual period: January 2016 – September 2019

	SBRT	CRT	Total
Total patients randomized	114	115	229
Did not receive study treatment	4	0	14
Not evaluable at 3 months	16	22	38
Intent to treat (ITT) analyses	114	115	229
Safety/QA Analyses (as-treated)	110	115	225

Results: Pain Response Rates

	3 Month Assessment		6 Month Assessment	
	SBRT (N=114)	**CRT** (N=115)	**SBRT** (N=114)	**CRT** (N=115)
Complete response	**35%**	**14%**	**16%**	**32%**
Partial response	18%	25%	16%	9%
Stable disease	24%	30%	27%	23%
Progressive disease	6%	12%	7%	4%
Indeterminant	18%	19%	34%	32%
Mean change in total SINS (SD)	**-0.94 (1.69)**	**-0.49 (1.61)**	**-0.74 (1.99)**	**-0.73 (1.86)**

Multivariable Analyses for CR at 3 and 6 months

	3 Month Assessment			6 Month Assessment		
Variable	**Odds Ratio**	**95%CI**	**P Value**	**Odds Ratio**	**95%CI**	**P Value**
SBRT	**3.47**	**1.77-6.80**	**0.0003**	**2.45**	**1.28-4.71**	**0.007**
CRT	**1**			**1**		
Age ≥ 65	1.58	0.82-3.06	0.17	0.65	0.34-1.25	0.20
Age < 65	1			1		
Male	1.33	0.54-3.26	0.54	1.39	0.56-3.45	0.48
Female	1			1		
ECOG 2	0.74	0.19-2.89	0.67	0.39	0.08-1.86	0.24
ECOG 0 or 1	1			1		
Pain Score at Baseline						
8 to 10	0.92	0.39-2.20	0.85	1.39	0.60-3.21	0.44
5 to 7	0.74	0.36-1.54	0.43	0.94	1.45-1.96	0.86
2 to 4	1			1		
Primary Cancer:						
GU (excluding RCC)	1.22	0.32-4.65	0.77	0.99	0.26-3.79	0.99
Lung	1.49	0.54-4.08	0.44	0.96	0.36-2.63	0.95
Other	0.58	0.09-3.77	0.57	0.74	0.14-3.86	0.72
Breast	1			1		
Total baseline SINS						
7 to 12	1.12	0.58-2.15	0.57	0.91	0.48-1.71	0.78
≤ 6	1			1		

Conclusions

- This is the first Phase 3 randomized trial to show that dose escalation with modern radiation therapy techniques improves pain outcomes for patients with spinal bone metastases
- Spine SBRT is superior to CRT and achieved a 21% absolute increase in the CR to pain at 3 months, which was durable at 6 months and statistically significant
- A regimen of 24 Gy in 2 SBRT fractions was safe, non-destabilizing and associated with better patient financial perception

Phase III Randomized Trial of **P**ostoperative **A**djuvant Conventional Radiation (3DCRT) versus Image Guided Intensity Modulated Radiotherapy (IG-IMRT) in **C**ervical Cancer (PARCER): Final Analysis

Supriya Chopra, MD

Tata Memorial Centre

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Disclosures

Research Funding PARCER Trial

- Department of Science and Technology, India
- Department of Atomic Energy, Clinical Trials Centre, India.

- Other Research Funding: Varian International, Terry Fox Foundation, Terry Fox International, Department of Atomic Energy Clinical Trials Centre, India

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Background

- Postoperative Radiation indicated for Cervix and Endometrial Cancers.
- Increase in GI symptom burden and toxicity in long term survivors after adjuvant radiation
- Phase II Studies
  - RTOG 0418/ RTCMIENDOMETRE demonstrated 27-28% acute GI toxicity with IMRT
  - No comparator arm
- Phase III Trial
  - NRG 1203: Improvement in patient reported outcomes at wk 5 and year 1 with IMRT as compared to 3DCRT.
  - No difference at 3 years with IMRT.
- Lack of Clarity on Long Term Impact of Postoperative IMRT

Hypothesis

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

Conducted across 3 clinical sites of Tata Memorial Centre

NCT01279135/CTRI2012/120349

Study Eligibility

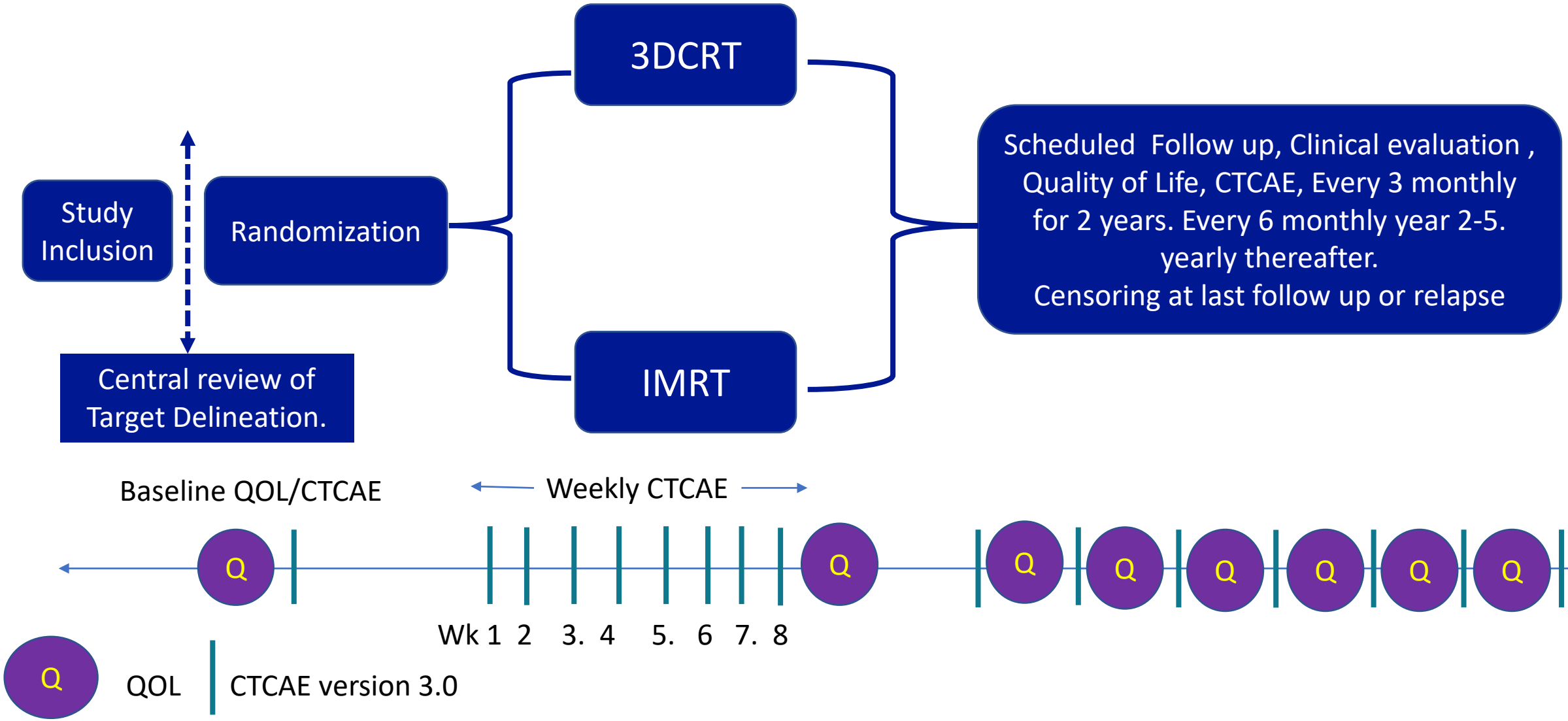
Inclusion Criteria

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

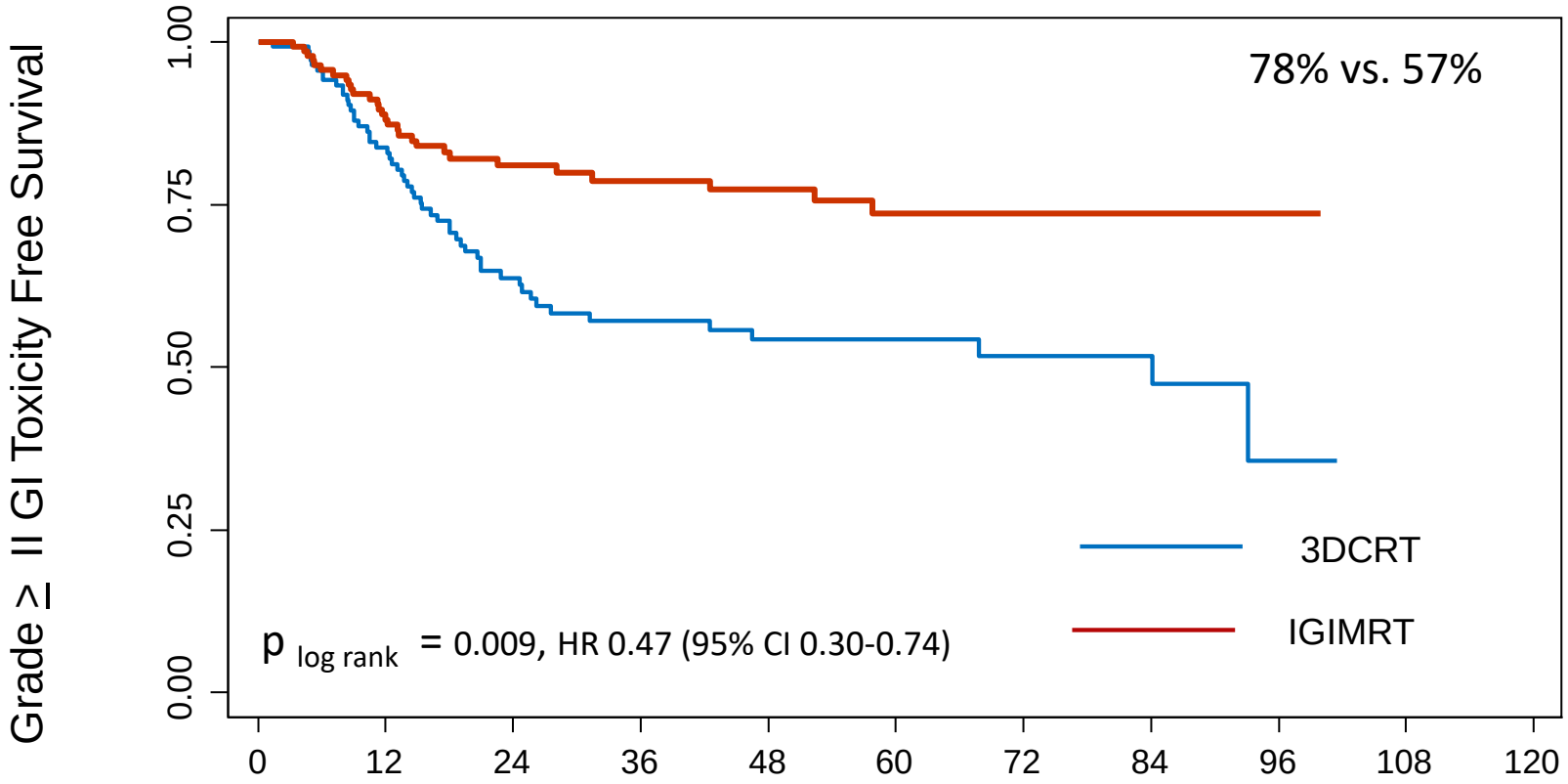
Exclusion Criteria

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

Trial Schema: PARCER



Primary Endpoint

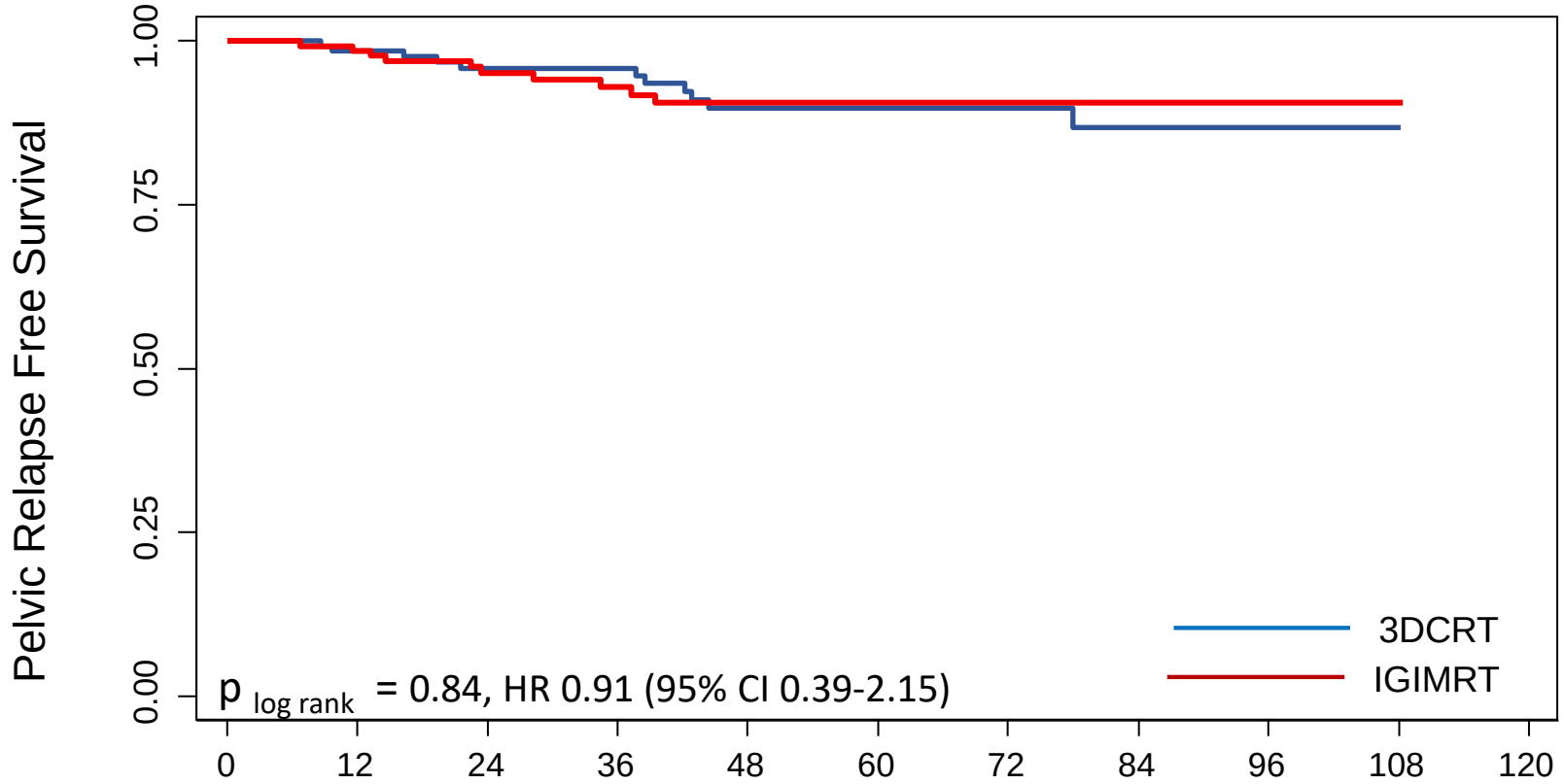


Number at risk (number censored)

3DCRT	141	(19)	101	(19)	60	(10)	44	(3)	39	(12)	27	(9)	17	(5)	12	(8)	2	(2)	0	(0)	0
IGIMRT	142	(14)	112	(28)	76	(13)	61	(11)	49	(12)	35	(12)	23	(12)	11	(9)	2	(2)	0	(0)	0

Adjusted for stratification factors- RT type and Sx type

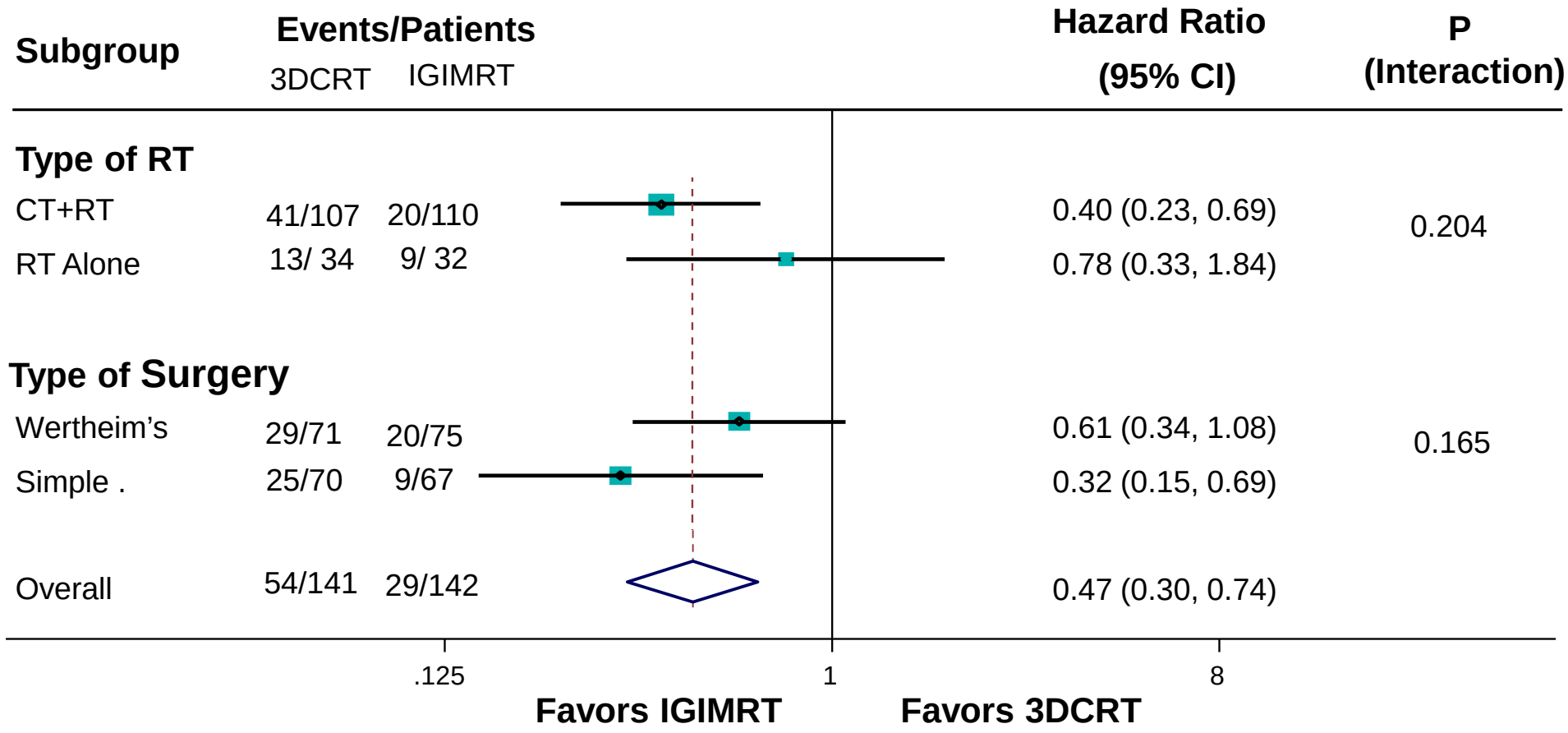
Pelvic Relapse Free Survival



Number at risk (No. censored)

3DCRT	141	(13)	124	(21)	100	(17)	80	(17)	63	(20)	43	(11)	32	(9)	23	(15)	8	(7)	1	(0)	0
IGIMRT	142	(11)	127	(24)	99	(17)	80	(18)	62	(15)	47	(17)	30	(10)	20	(11)	9	(7)	2	(2)	0

Planned Subgroup Analysis



Conclusions

- 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 radio-sensitizing concurrent chemotherapy.
- No difference in tumour control rates in the pelvis with use of IG-IMRT
- IG-IMRT should represent the new standard of care for postoperative pelvic RT in women with gynecological cancers.

Stereotactic **A**blative **F**ractionated **R**adiotherapy versus Radiosurgery for **O**ligometastatic **N**eoplasia to the Lung: A Randomized Phase II Trial

Shankar Siva, MD

Peter MacCallum Cancer Centre

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Disclosures

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- Speaker Honoraria: Astra Zeneca, Bristol Meyer Squibb, Reflexion
- Travel support: Astra Zeneca

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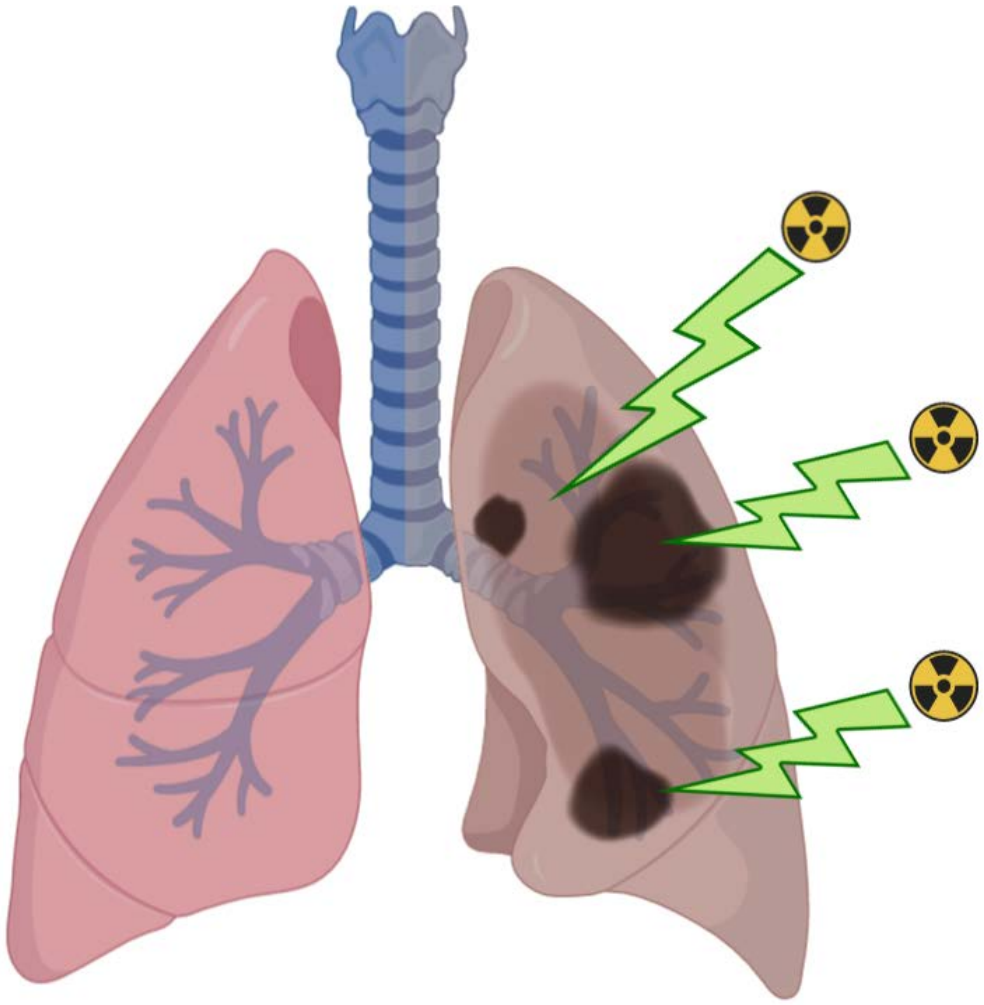
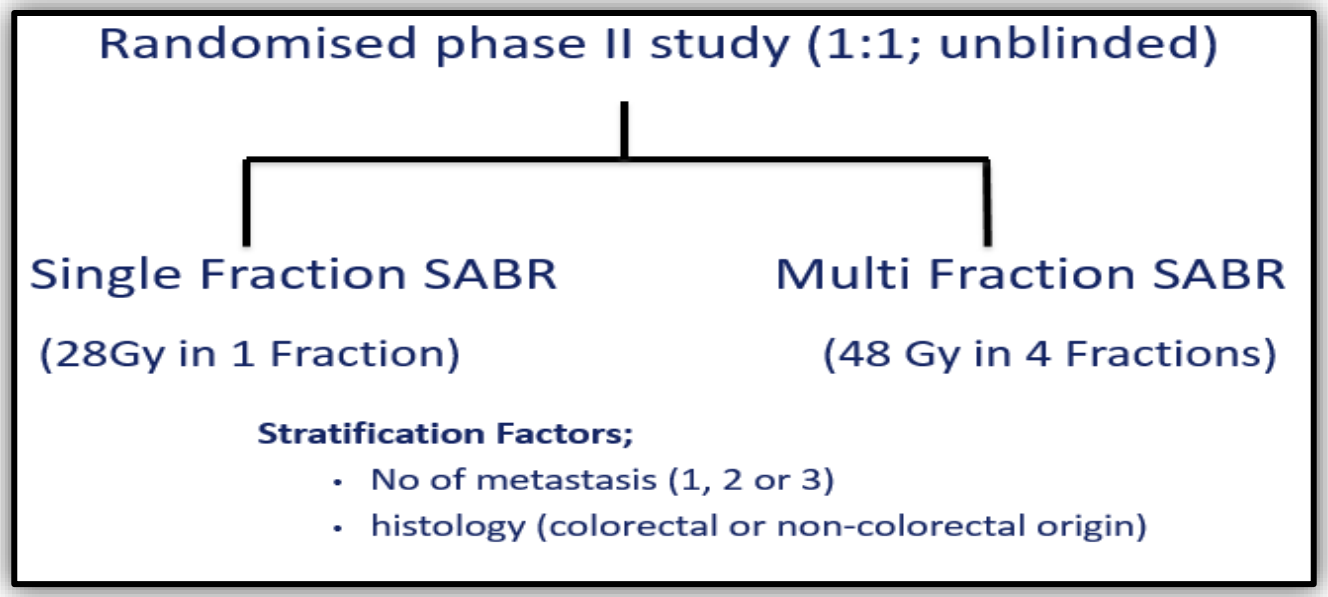
Background: Why this Trial?

- The lung is the second most common place for cancer to spread
- Most patients are treated with lifelong anti-cancer drug therapy only, with little prospect for long term cancer control
- Some patients have limited spread to the lungs, and may be suitable for surgery (invasive) or Stereotactic body radiotherapy (SBRT, non-invasive)
- In this study, we evaluated two schedules of SBRT, single session and multi-session, for patients with limited secondary spread to the lung



TROG 13.01 SAFRON II: Trial Summary

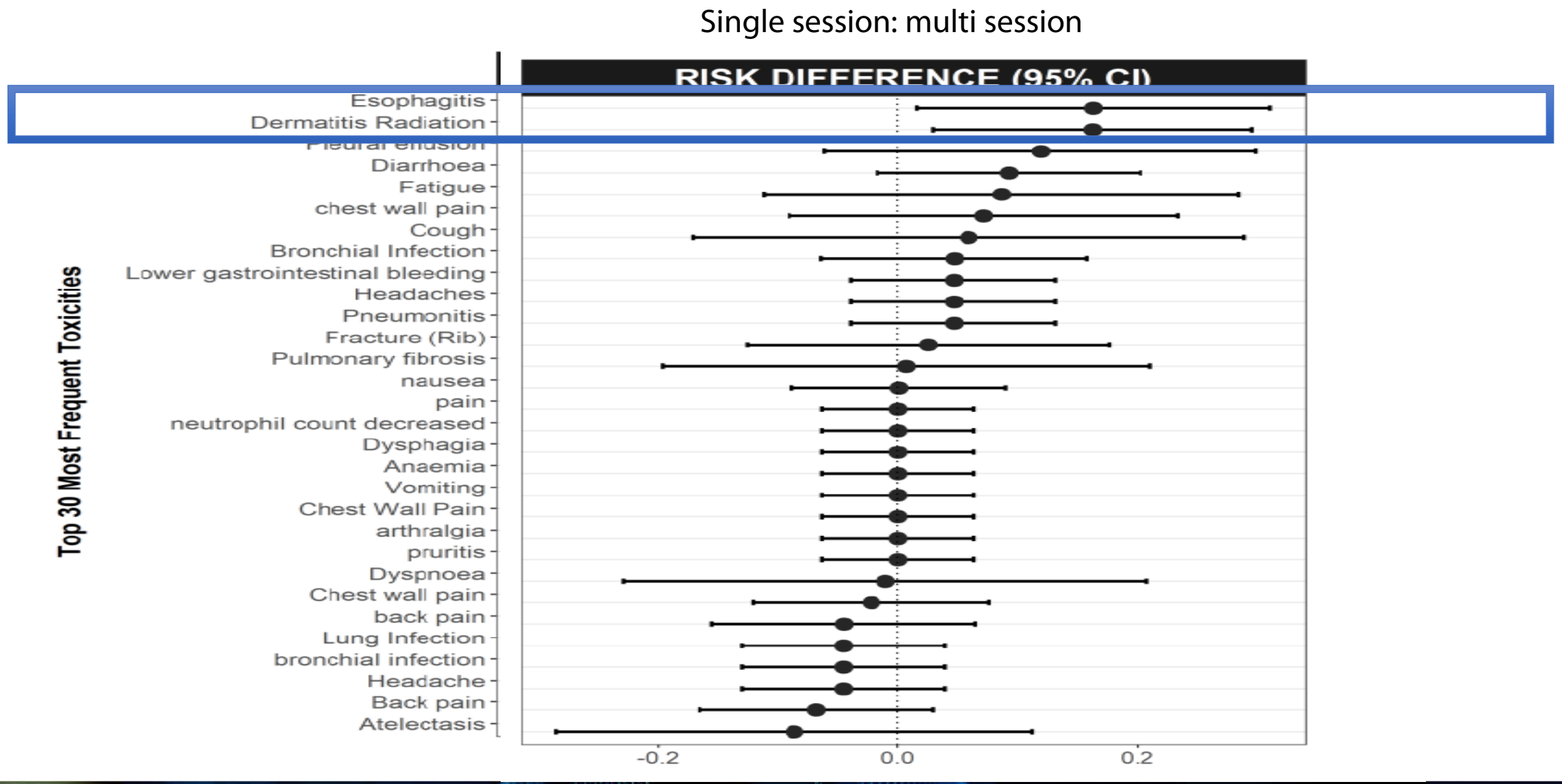


Key Inclusion: ≤3 secondaries to the lung from any non-blood malignancy, tumor size ≤ 5cm, peripheral lung location, all primary and extrathoracic disease treated

- Primary Endpoint: Severe side effects at 1 year
- Total sample size = 90 patients over 3 years (13 centers Australia and NZ), recruited 2015-2018

Side effects (any grade) and difference between arms

Higher swallowing symptoms and skin rash with multi-session SBRT



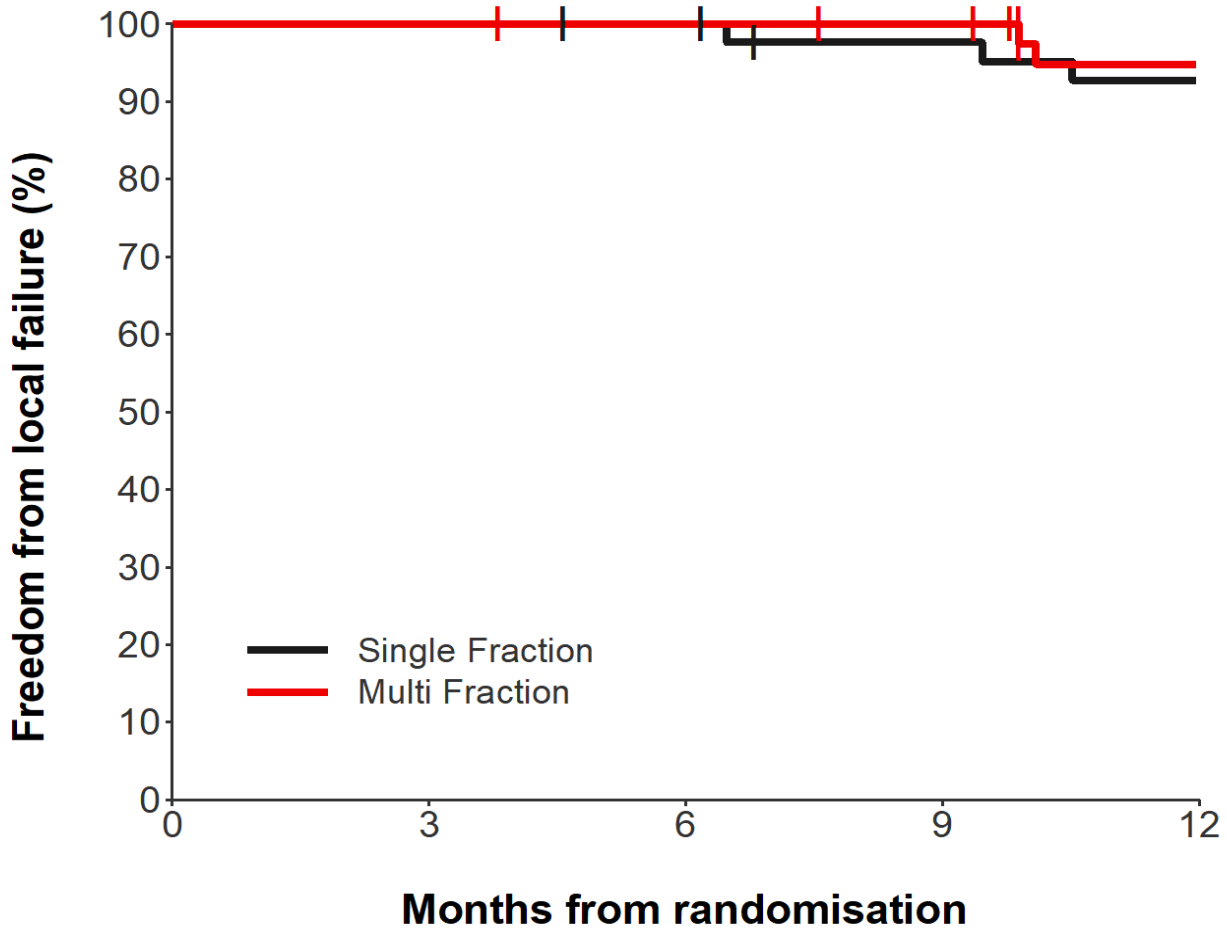
Primary Endpoint – high grade side effects within 1 year

- ARM 1 (single fraction) - There were two patients with grade 3 (*medical intervention*) events, both lasted < 3 months in duration, with no grade 4 (*life threatening*) or 5 (*fatal*) events.

- ARM 2 (four fraction) – There was one patient with a grade 5 event (pneumonitis within 3 months of SBRT, underlying ILD), with no grade 3 or 4 events.

- Grade 3+ toxicities related to treatment within 1 year
  - ARM 1 = 5% [80% CI: 1-14]
  - ARM 2 = 3% [80% CI: 0.3% - 10%]

Oncological Outcomes – Local Control



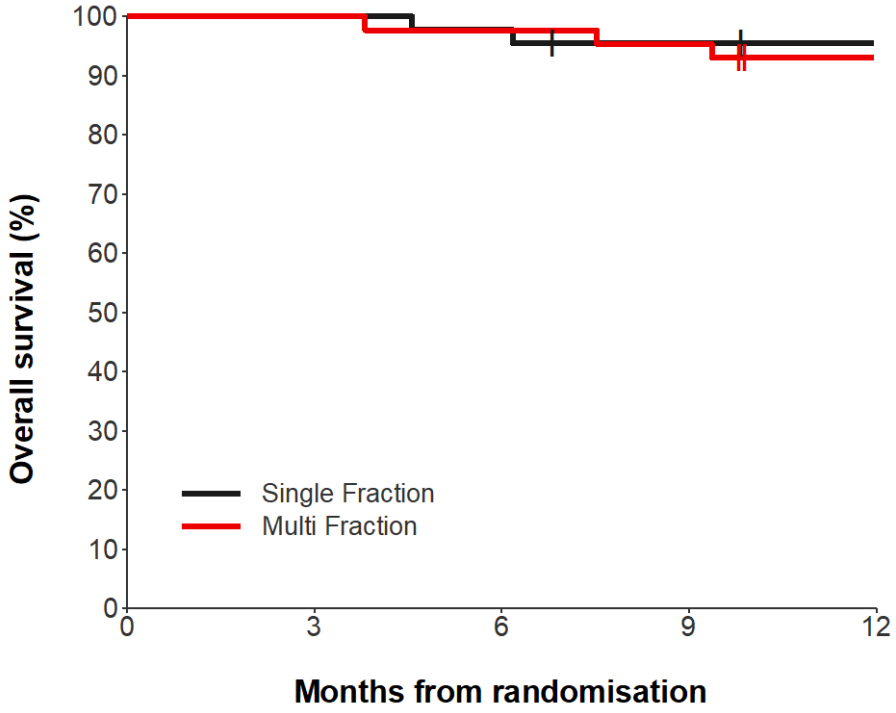
No. at risk

Single Fraction	44	44	43	40	38
Multi Fraction	43	43	42	41	36

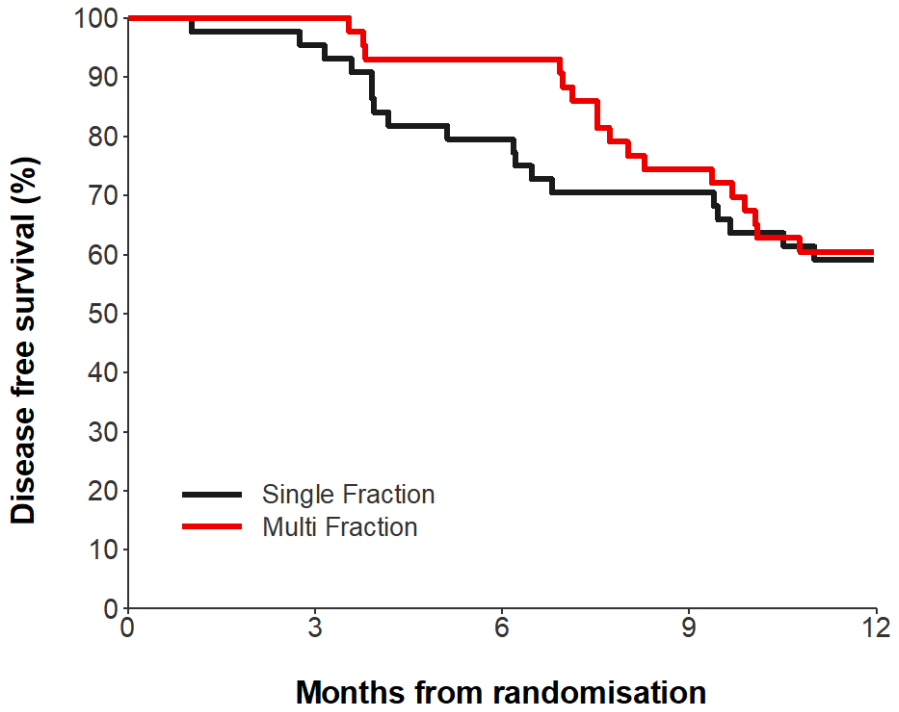
Freedom from local failure % (95% CI) at 12 months by arm

Single Fraction = 93% (79, 98)
Multi Fraction = 95% (81, 99)

Oncological Outcomes – Recurrence, Survival



No. at risk					
Single Fraction	44	44	43	41	40
Multi Fraction	43	43	42	41	38



No. at risk					
Single Fraction	44	42	35	31	26
Multi Fraction	43	43	40	32	26

Kaplan-Meier estimates % (95% CI) at 12 months by arm

Endpoint	Single Fraction	Multi Fraction
Overall survival	95 (83, 99)	93 (80, 98)
Disease free survival	59 (43, 72)	60 (44, 73)

Conclusions

- Both single fraction (28Gy) and four fraction (48Gy) SBRT have acceptable toxicity for patients with 1-3 secondary cancer deposits in the lung

- Oncological outcomes from both approaches appear similar to 1-year

IMPACT - WHAT DOES THIS MEAN?

- Single session SBRT is convenient, non-invasive safe and appears effective to date for lung secondaries
- Maybe considered a one-stop, 'knockout punch'
- These findings may have implications for treatment selection in resource-constrained environments (such as the pandemic)

Stereotactic Radiosurgery Versus Whole-brain Radiation Therapy For Patients With 4-15 Brain Metastases: A Phase III Randomized Controlled Trial

Jing Li, MD, PhD

University of Texas MD Anderson Cancer Center

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Disclosures

- Employer: University of Texas – MD Anderson Cancer Center
- Research funding from BMS
- Reearch funding from Medtronic
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- MD Anderson internal research grants

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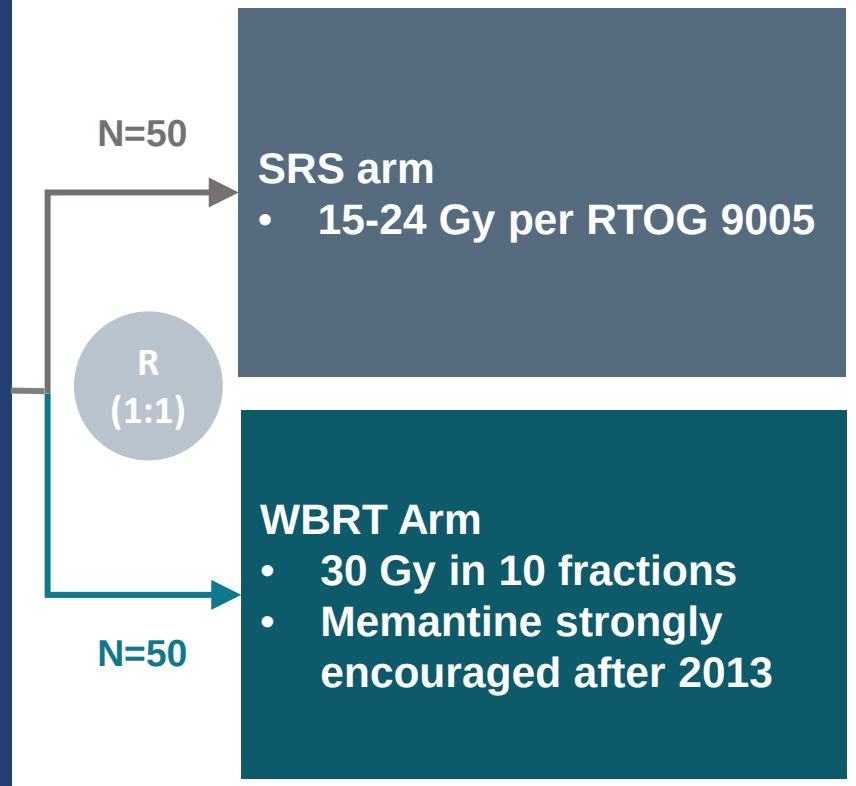
Background

- Up to 30% of cancer patients develop brain metastases
  - Rising incidence due to prolonged survival and better imaging surveillance
  - Historically poor overall survival (~1-4 months)
    - Main treatment modalities: radiation and surgery
    - Whole brain radiation (WBRT) associated with significant cognitive side effects
- In patients with 1-3 (or 4) brain metastases
  - Two Phase III randomized trials established stereotactic radiosurgery (SRS) as the standard care, replacing WBRT, due to better preservation of patients' cognitive function, without compromising overall survival *(Chang EL, Lancet Onc 2009; Brown PD, JAMA 2016)*
- Purpose of the current study
  - To investigate if SRS could replace WBRT in patients with 4-15 brain metastases in a phase III randomized trial

Trial Design (Schema)

Key Eligibility Criteria:

- Adult patient with 4-15 untreated brain mets confirmed by neuroradiology (up to 20 lesions allowed at the time of treatment)
- All lesions amenable to SRS treatment
- KPS >/=70
- No LMD (radiographic or cytological)
- No prior WBRT
- Prior SRS to 1-3 brain mets with > 6 weeks intervals allowed
- Excluded prior surgical resection of brain mets
- Excluded histology: melanoma, small cell carcinoma, lymphoma/leukemia, or germ cell histology
- Systemic therapy allowed at the discretion of treating oncologist

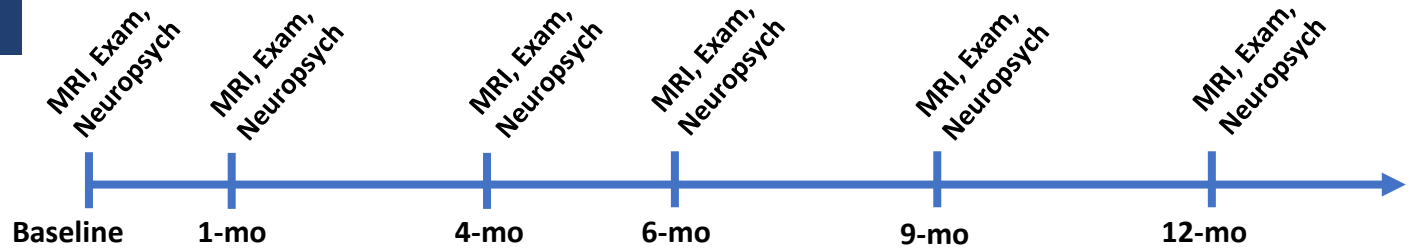


Stratification factors:

- **Histology** (breast vs. other)
- **Age** (18-59 vs. 60 and over)
- **Number of lesions** (4-7 vs. 8-15)
- **KPS** (70-80 vs. 90-100)
- **Extra-cranial disease status** (progressive disease prior to enrollment vs. no progression)
- **Baseline HVLT** (</= 17 vs. >/=28
- **Radiotherapy** (Prior SRS vs. no prior SRS)

Neurocognitive function tests:

- **Memory:** HVLT_R_TR, HVLT_R_DR, HVLT_R Recognition
- **Executive function:** COWA, and Trail Making test Part B (TMTB)
- **Attention Span:** WAIS-III Digit Span
- **Psychomotor Speed:** WAIS-III Digit Symbol, Trail Making test Part A (TMTA)
- **Motor dexterity:** Grooved Pegboard



Primary Endpoints

- **Memory function at 4 mo (HVLT_R_TR)**
- **Local control at 4 mo**

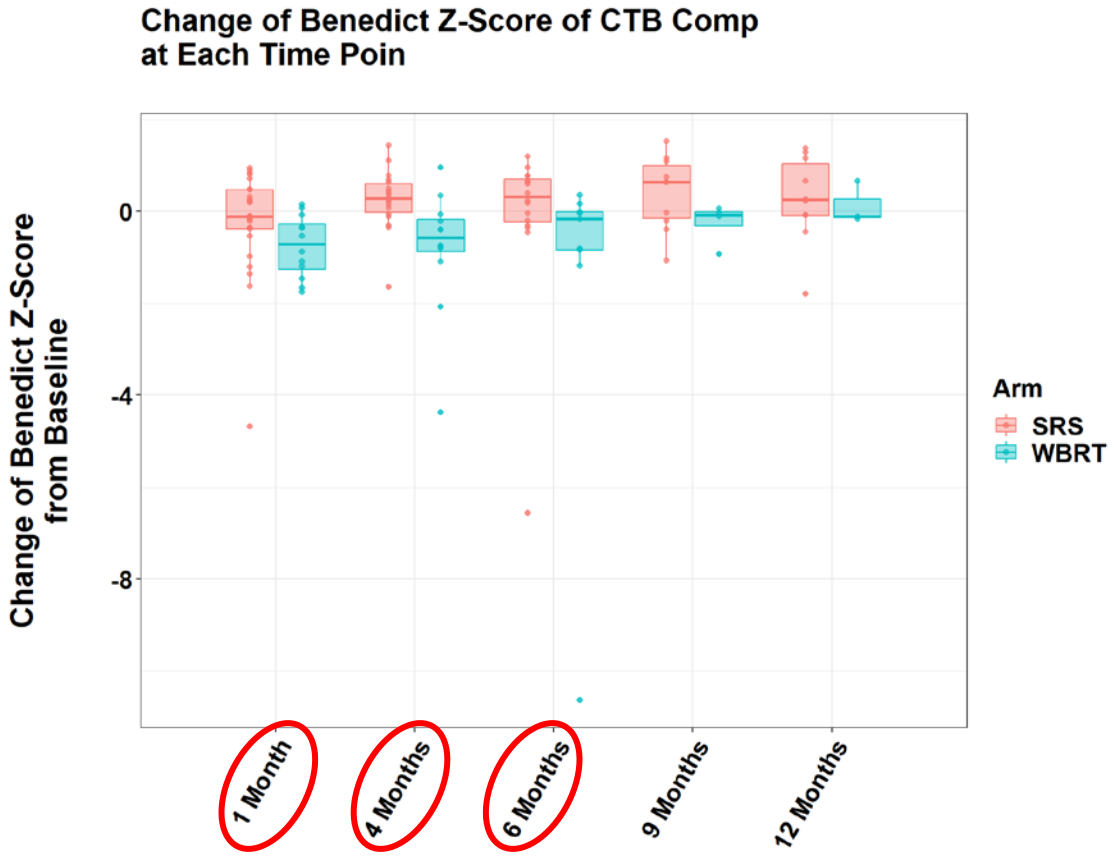
Memory Function at 4 Months
-- Primary Endpoint

- HVLT_R_TR: change of Z-score from baseline
- **At 4 months**
  - o **SRS:** Increased by 0.21 (SD 1.15) (n=18)
  - o **WBRT:** Decreased by 0.74 (SD 1.31) (n=13)
  - o ***p*=0.041**
- **At 1 month and 6 months**
  - o Clinically meaningful and statistically significant benefit with SRS was also observed at **1 month (*p*= 0.033)** and **6 months (*p*=0.012)**

Global Cognitive Function Measure
(Clinical Trial Battery Composite Score)

- Composite score
  - Mean Z-score from HVLT_R_TR, HVLT_R_DR, and HVLT_R Rec, COWA, TMTA, and TMTB
  - Change from baseline
- **Better cognitive composite scores in SRS arm**
  - **Statistically significant at months 1, 4 and 6**

Follow up Time Point	SRS	WBRT	p
1-mo (median [IQR])	-0.12 [-0.38, 0.47]	-0.71 [-1.26, -0.28]	0.024
4-mo (median [IQR])	0.28 [-0.03, 0.60]	-0.57 [-0.88, -0.17]	0.004
6-mo (median [IQR])	0.31 [-0.23, 0.70]	-0.16 [-0.84, -0.01]	0.027
9-mo (median [IQR])	0.64 [-0.16, 1.00]	-0.08 [-0.32, -0.01]	0.153
12-mo (median [IQR])	0.25 [-0.09, 1.03]	-0.12 [-0.14, 0.27]	0.823

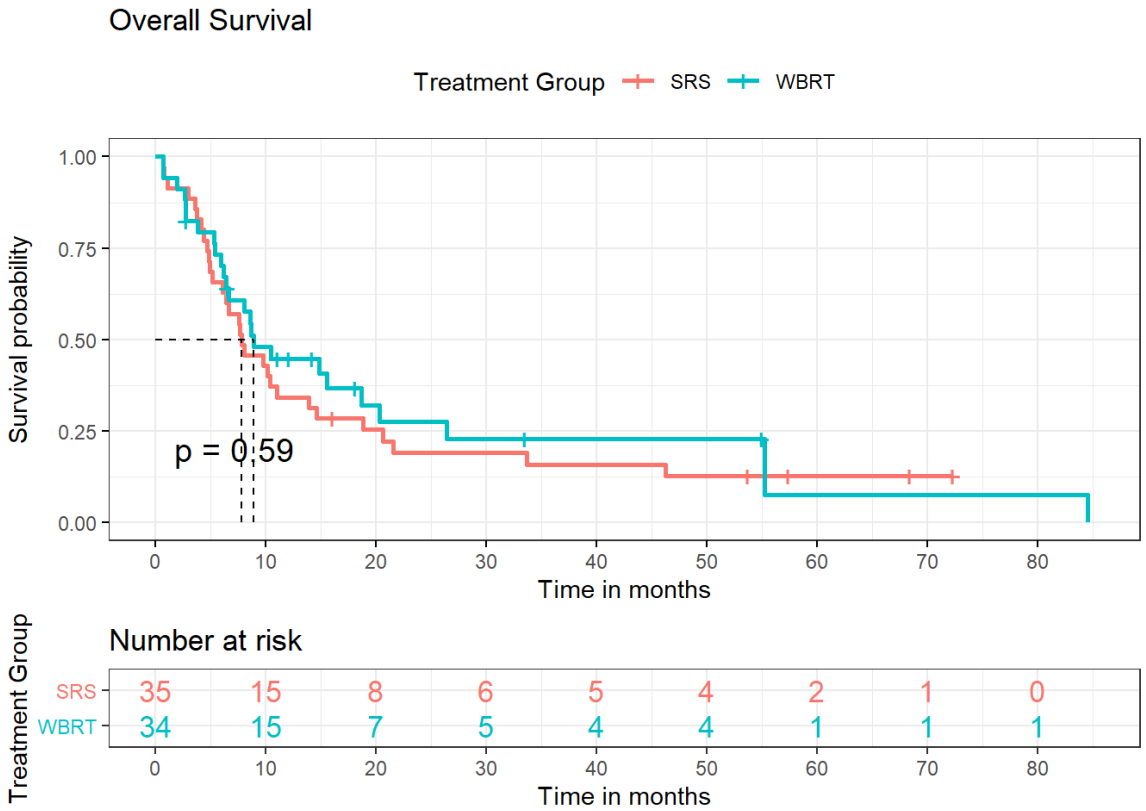


Overall Survival

- **Overall survival by intention-to-treat**
  - o 69 out of 72 pts evaluable for OS
    - o 35 for SRS and 34 for WBRT
  - o Estimate median OS

	N	Events (death)	Median (month)	95% CI (month)
SRS	**35***	**30**	**7.8**	**6.1 – 14.6**
WBRT	**34****	**26**	**8.9**	**6.4 – 26.4**

*Include 6 patients who had more than 20 lesions at time of SRS planning and received WBRT off protocol
** Include 4 patients received SRS and 2 patients received HA-WBRT off protocol



Estimating Overall Survival Curves with the Kaplan-Meier Method by intention-to-treat: *P*= 0.59

Other Results

- Local Control at 4 mo
  - 95% (SRS) vs 87% (WBRT), p-value 0.79
- Distant brain control
  - 60% (SRS) vs 80% (WBRT), p-value 0.37
- **Time to systemic therapy**
  - 1.7 weeks (SRS) vs 4.1 weeks (WBRT), **p-value 0.001**
- Toxicities
  - $\geq$ Grade 3 toxicities 8% (SRS) vs 15% (WBRT)
  - Radiation necrosis: 17% at patient level and 4% at lesion level

Summary

Despite early termination of the trial due to NRG CC001 and use of memantine in 2/3 WBRT patients, in patients with 4-15 brain mets:

- SRS was associated with reduced risk of neurocognitive deterioration compared to WBRT, as demonstrated by a constellation of neurocognitive tests, individually or by composite scores
  - The differences between the two arms were large and clinically meaningful
- No difference in overall survival rates
- SRS was associated with shorter time to systemic therapy

Conclusion

The results from this phase III randomized trial strongly supports the use of SRS in patients with 4-15 brain metastases to better preserve cognitive function and to minimize interruption of systemic therapy, without compromising overall survival.

Expert Perspective

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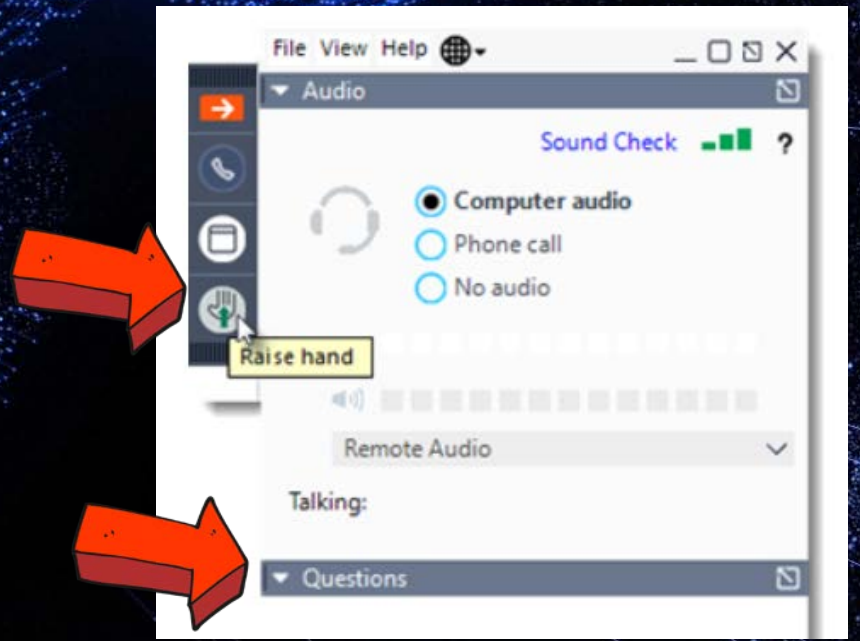
Q&A

You can submit questions to via the “Questions” pane,

or use the "Raise hand" option if you would like to ask your question directly (we will unmute your microphone).



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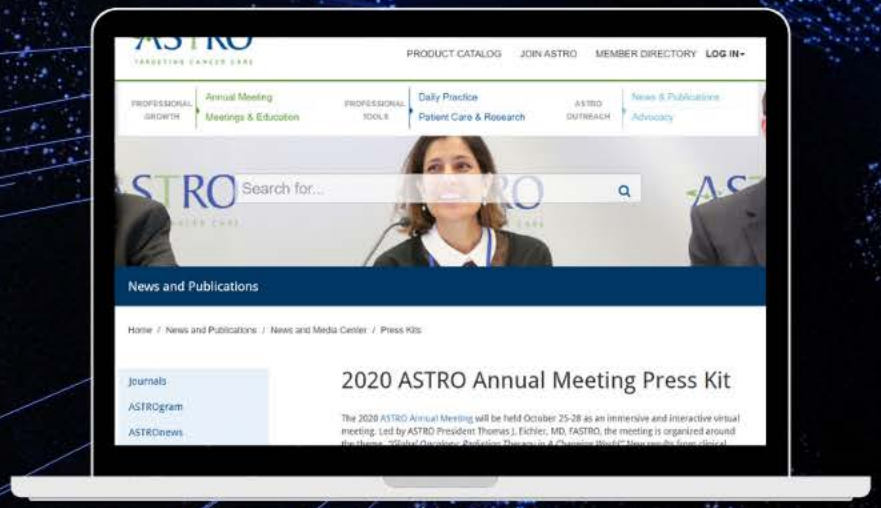

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