ASTRO ANNUAL MEETING 2019

News Briefing
Highlights from ASTRO 2019

Sunday, September 15, 2019
1:30-2:30 p.m. CT

News Briefing: Highlights from ASTRO 2019 (Sunday)

Moderator: Anthony Zietman, MD, FASTRO, Massachusetts General Hospital

Two Years of Anti-Androgen Treatment Increases Other-Cause Mortality in Men Receiving Early Salvage Radiotherapy: A Secondary Analysis of the NRG Oncology/RTOG 9601 Randomized Phase III Trial (Abstract LBA-1)

Daniel Spratt, University of Michigan Rogel Cancer Center

Primary Outcomes of a Phase II Randomized Trial of Observation versus Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer (ORIOLE) (Abstract LBA-3)

Ryan Phillips, Johns Hopkins Kimmel Cancer Center

Cosmetic Outcome from Post Lumpectomy Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) on the NRG Oncology/NSABP B39-RTOG 0413 Phase III Clinical Trial (Abstract 5)

Julia White, The Ohio State University Comprehensive Cancer Center

Longer Term Results from a Phase I/II Study of EP-guided Noninvasive Cardiac Radioablation for Treatment of Ventricular Tachycardia (ENCORE-VT) (Abstract LBA-4)

Clifford Robinson, Washington University School of Medicine in St. Louis

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Two Years of Anti-Androgen Treatment Increases Other-Cause Mortality in Men Receiving Early Salvage Radiotherapy:

A Secondary Analysis of the NRG Oncology/ RTOG 9601 Randomized Phase III Trial

Daniel Spratt, MD

University of Michigan Rogel Cancer Center

Disclosures for Dr. Spratt

- Employee at the University of Michigan
- Advisory board: Janssen and Blue Earth
- Funding: Janssen

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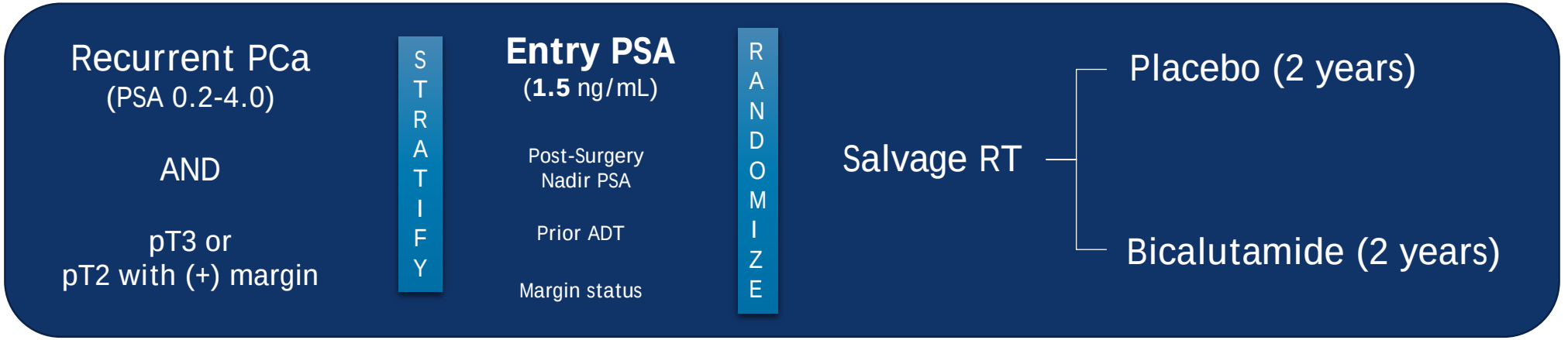
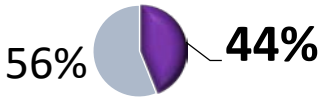
Background

NRG Oncology/RTOG 96-01



Sample size: 760 patients
Median follow up: 13 years
Primary endpoint: Overall Survival



Persistently elevated PSA post-RP of >0.1 ng/mL
Undetectable PSA

Late salvage RT (PSA >0.5 ng/mL)
Early salvage RT (PSA ≤0.5 ng/mL)

Methods

Secondary analysis of NRG Oncology/RTOG 9601 approval through the NCI

Developed ***a priori*** statistical plan to determine differential benefit and harm of antiandrogen treatment in men by entry PSA via statistical interaction tests

Early Salvage RT PSA subgroups:

Pre-specified protocol stratum:	**0.2-1.5 ng/mL**
Median PSA on RTOG 9601:	**0.2-0.6 ng/mL**
Median PSA of GETUG-16 & SPPORT:	**0.2-0.3 ng/mL**

Endpoints Assessed:

- Overall Survival
- Other-Cause Mortality
- Distant Metastasis

Toxicity Assessment:

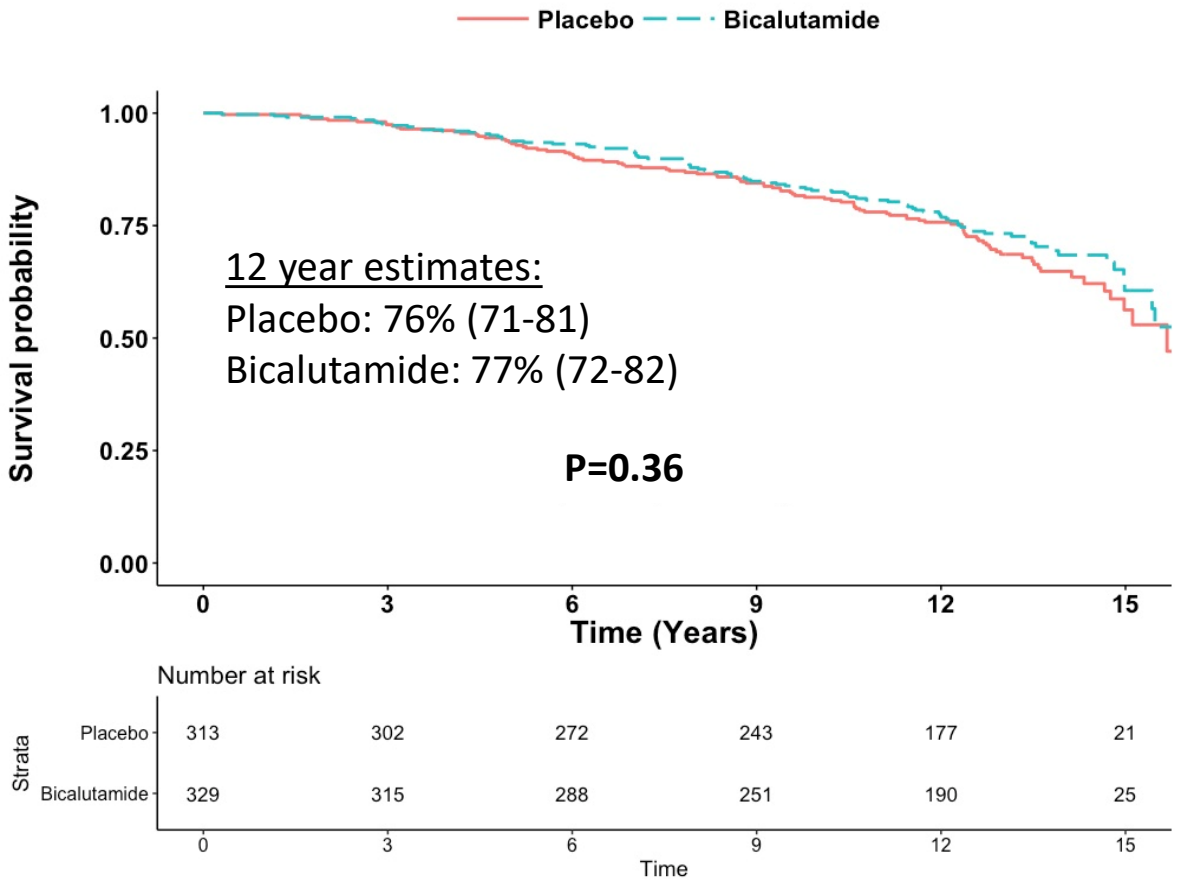
- Grade 3-5 Cardiac Events
- Grade 3-5 Neurologic Events

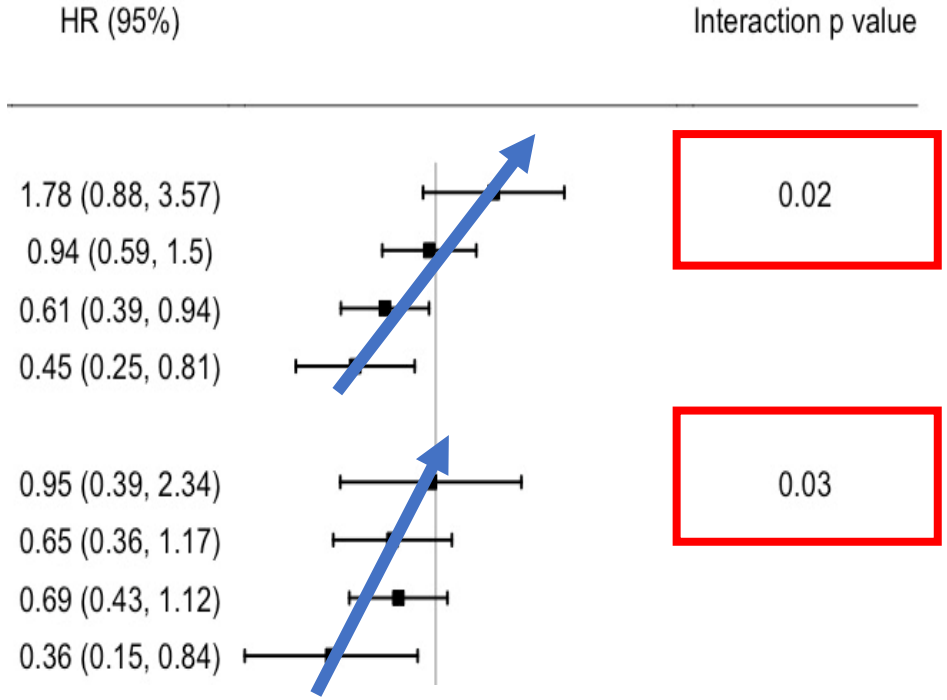
Nguyen P, et al, Euro Urol 2015

Results

85% of trial was in the PSA 0.2-1.5 stratum

PSA 0.2-1.5 ng/mL stratum

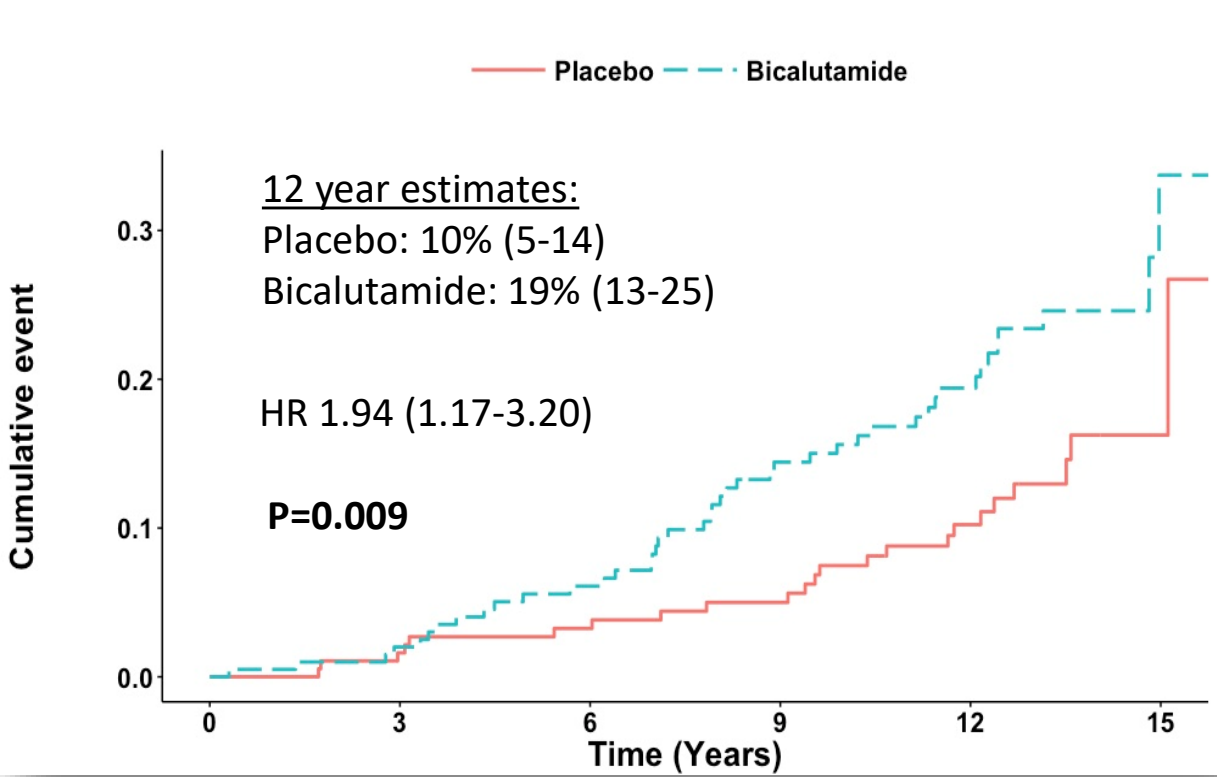




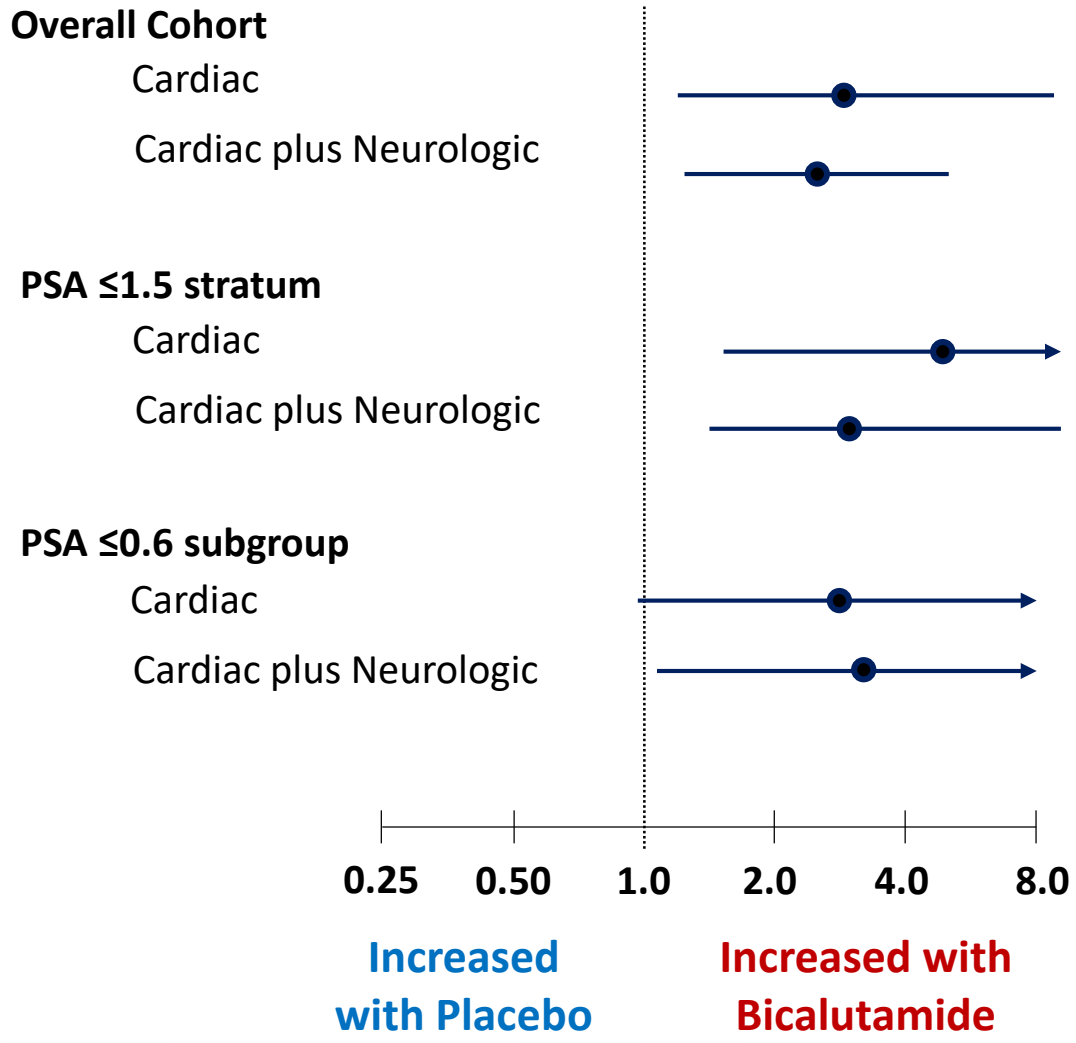
Results

Other-Cause Mortality

PSA 0.2-0.6 ng/mL



Odds Ratio for Grade 3-5 Event



Conclusions

- Current guidelines recommend all men be offered hormone therapy when receiving salvage radiotherapy.
- Our data demonstrate that men with lower PSAs are more harmed then helped by long-term hormone therapy.
- We have now 3 randomized trials with over 2400 men total that do not demonstrate that short or long-term hormone therapy improves overall survival in men receiving early salvage radiotherapy at low PSAs.
- PSA prior to salvage radiotherapy predicts who will benefit most from hormone therapy.
    - ***Guidelines should change to reflect this finding.***

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JOHNS HOPKINS MEDICINE
RADIATION ONCOLOGY & MOLECULAR RADIATION SCIENCES

Primary Outcomes of a Phase II Randomized Trial of Observation versus Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer (ORIOLE)

Ryan Phillips, MD, PhD

Johns Hopkins Sidney Kimmel Cancer Center

Disclosures for Dr. Phillips

- Resident physician at Johns Hopkins University School of Medicine
- Consultant for RefleXion Medical, Inc.

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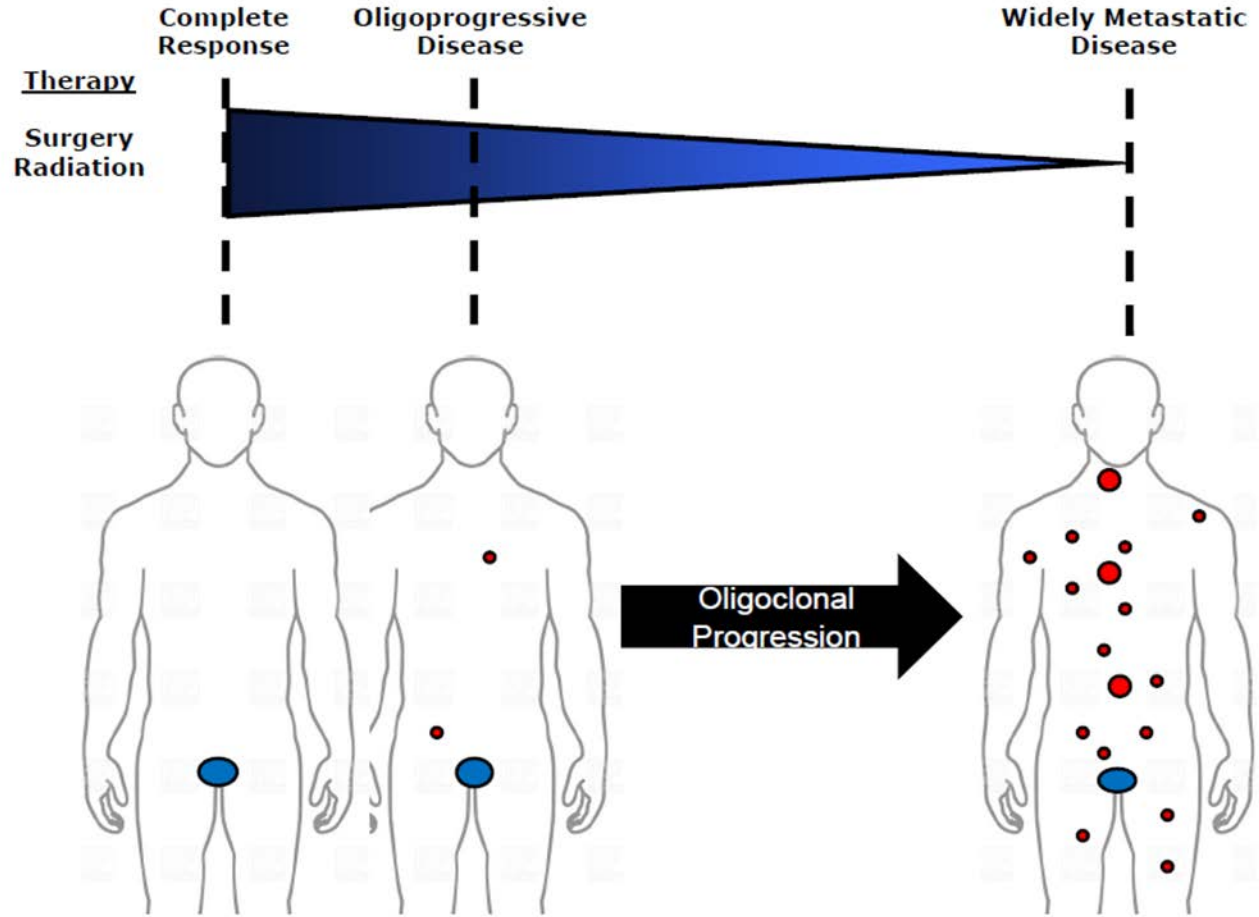
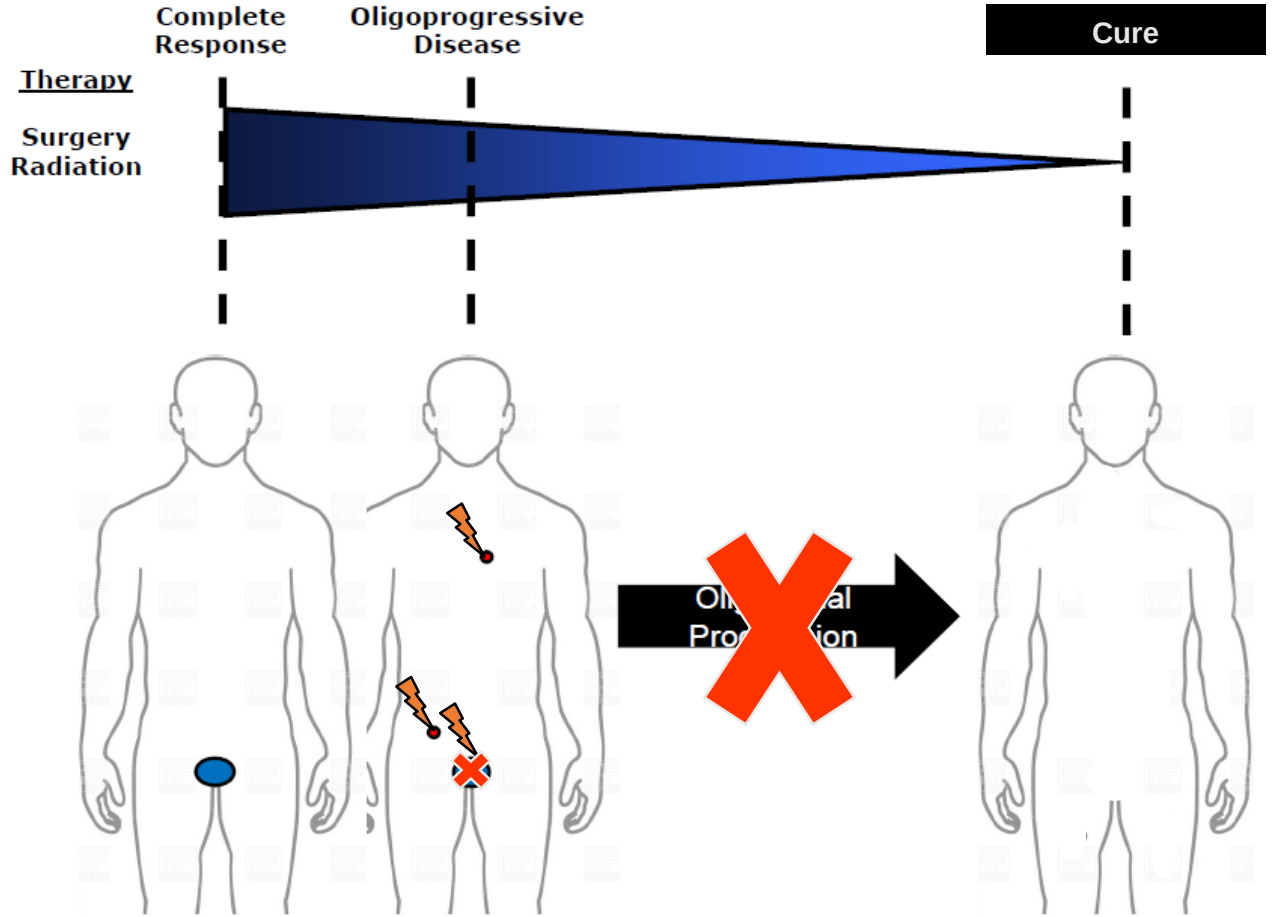
Background

- Prostate cancer may spread to a few initial sites before widespread metastasis.



Background

- Eliminating sites of initial spread may help control or cure metastatic prostate cancer.



Trial design

- Eligibility:
  - Recurrent hormone-sensitive prostate cancer
  - 1-3 metastatic lesions ≤ 5 cm by CT, MRI, or bone scan
  - PSA doubling time < 15 months
  - ECOG performance status ≤ 2

- 54 men were randomized 2:1 to stereotactic ablative radiation (SABR) or observation for 6 months

- Follow-up every 3 months including H&P and PSA, with CT and bone scan performed at 6 months

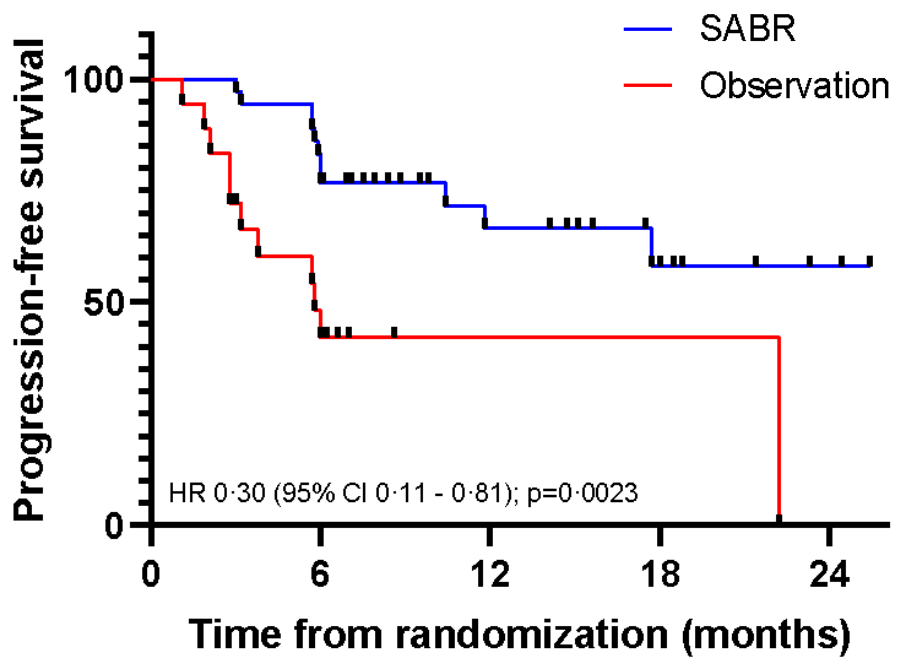
- Correlative studies included prostate-specific membrane antigen (PSMA)-PET scans as well as analysis of T-cell repertoires and circulating tumor DNA.

SABR improved progression at 6 months and progression-free survival

	Progression at 6 months	P-value
SABR (n = 36)	19%	0.005
Observation (n = 18)	61%	

Progression defined as:

- PSA increase ≥ 2 ng/mL AND ≥ 25% above nadir
- Evidence of new metastases by CT, MRI, or bone scan
- Symptomatic progression
- Initiation of ADT for any reason



Number at risk					
SABR	36	26	13	7	2
Observation	18	8	1	1	0

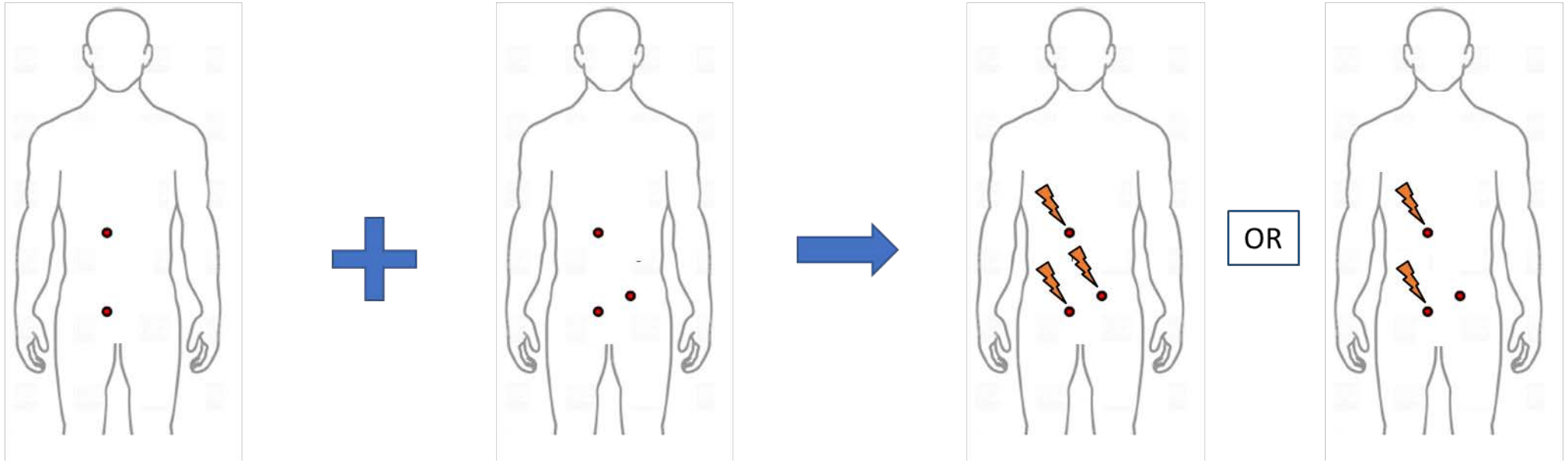
About half of men who received SABR had additional lesions detectable by PSMA-PET

Conventional imaging for eligibility and treatment planning (n = 36)

Blinded PSMA-PET obtained at baseline and Day 180 (n = 35)

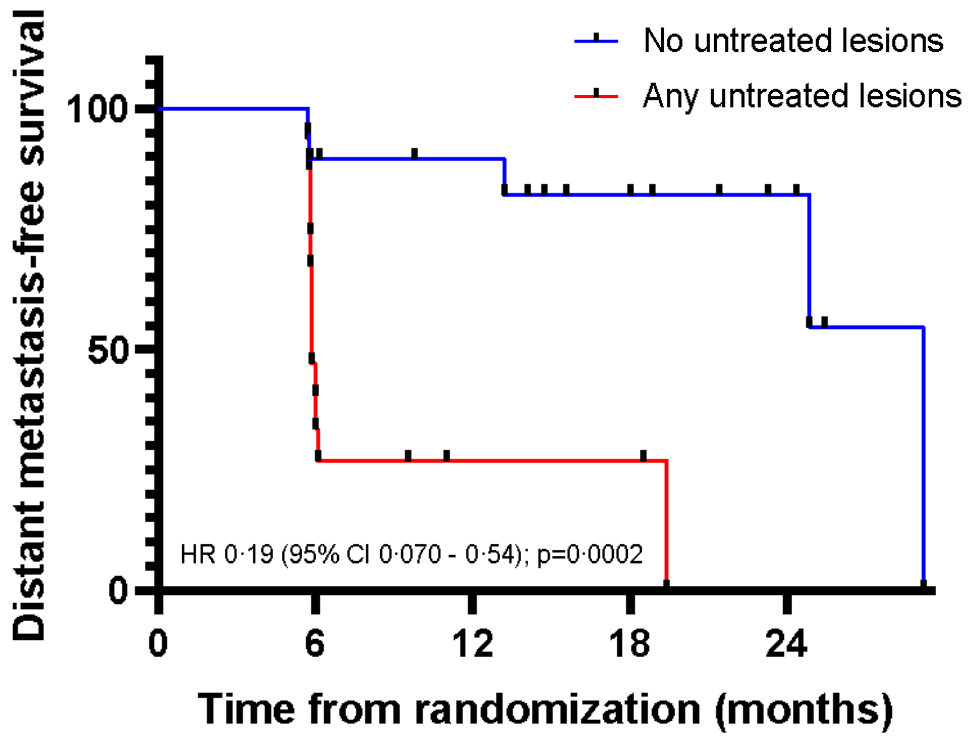
Total consolidation (n = 19)

Subtotal consolidation (n = 16)



Total consolidation of PSMA-PET detected lesions decreased risk of new metastasis formation

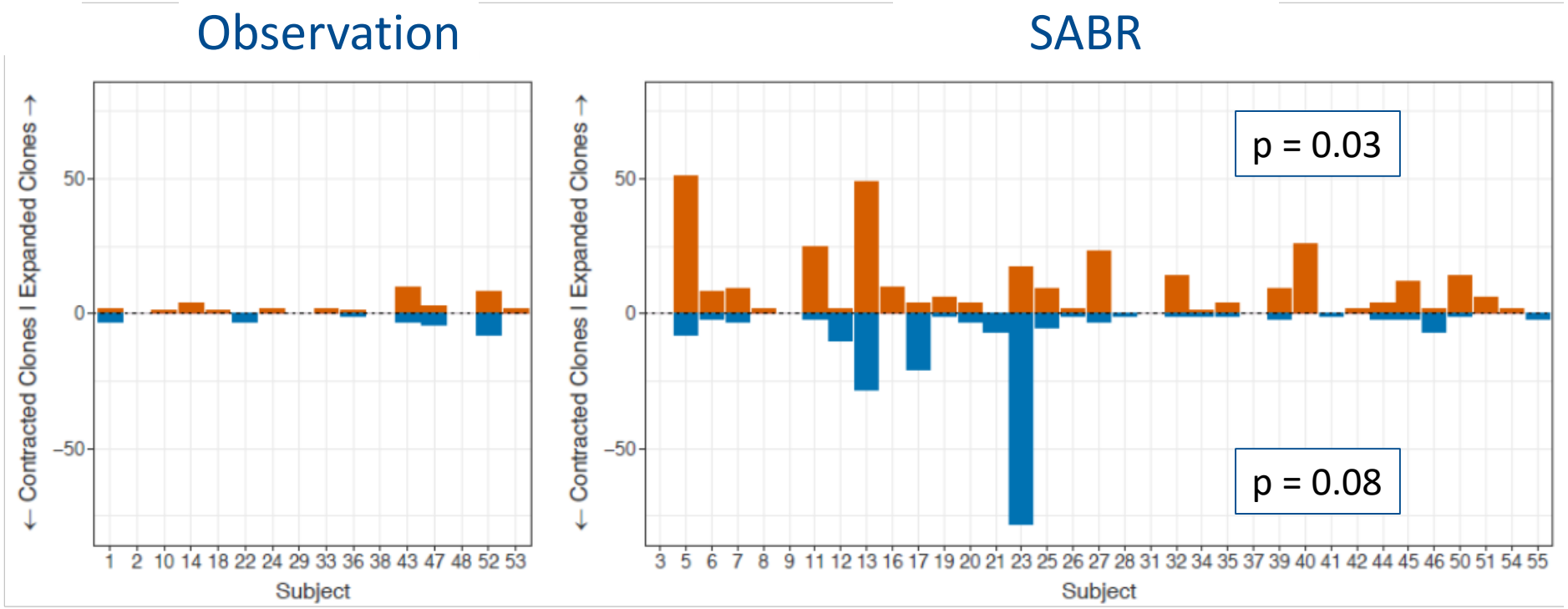
Consolidation	New metastases at 6 months	P-value
Total (n = 19)	16%	0.006
Subtotal (n = 16)	63%	



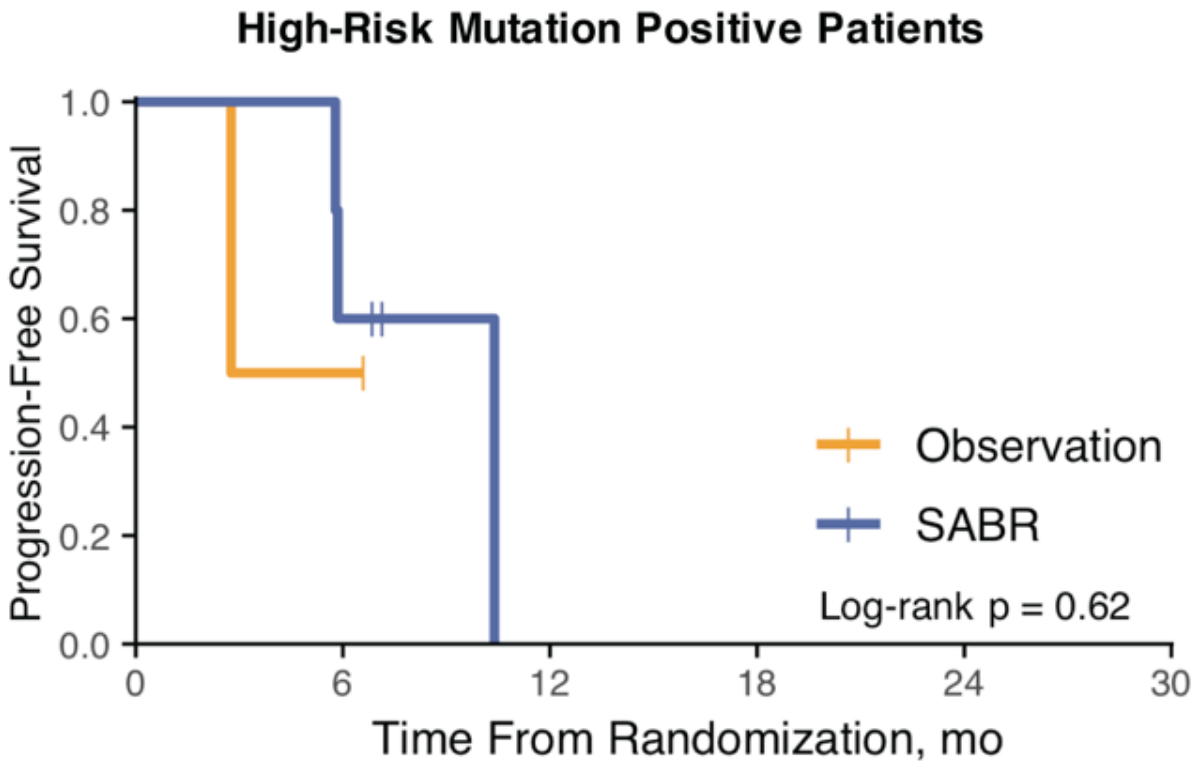
Number at risk

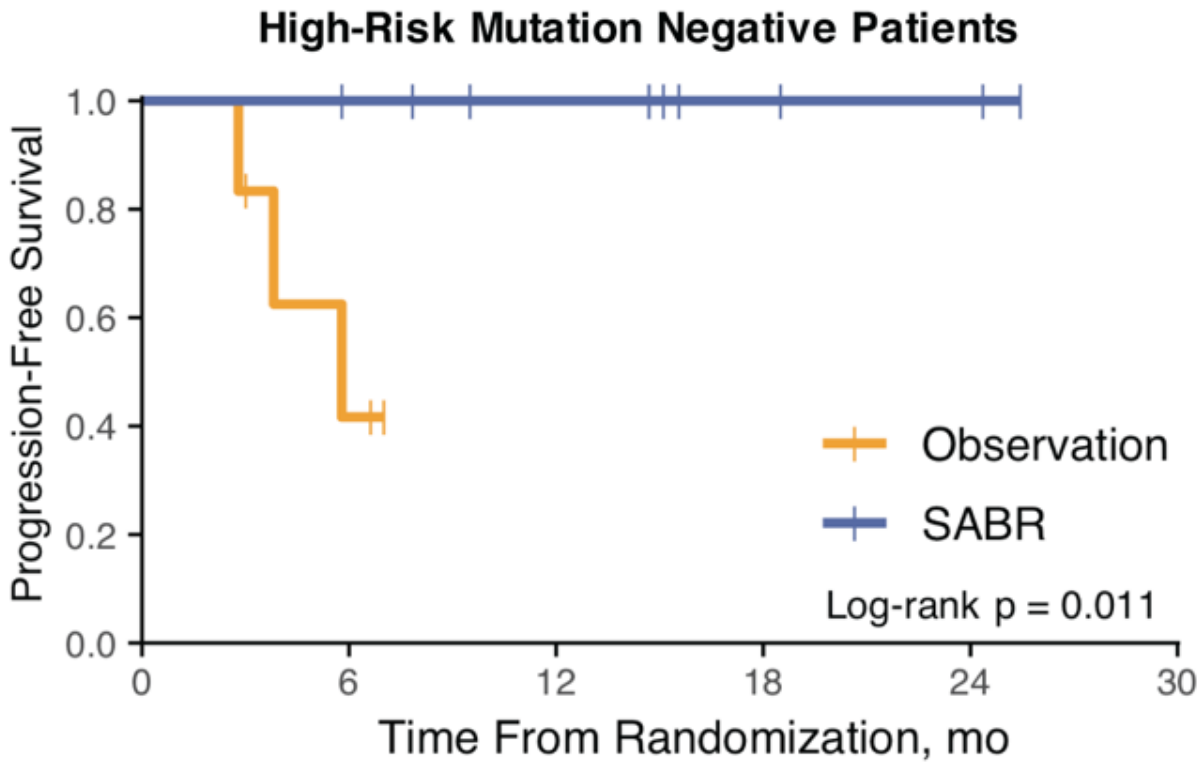
No untreated	19	14	12	8	4
Any untreated	16	6	2	2	0

SABR resulted in expansion of more T-cell clones, suggesting a systemic immune response



Presence of high-risk mutations by circulating tumor DNA was associated with progression after SABR





Conclusions

- SABR improves PFS in men with oligometastatic prostate cancer compared to observation alone.
- Total consolidation of PSMA radiotracer-avid lesions may decrease risk of new metastases and alter the natural history of this disease.
- SABR induced a systemic immune response in a prototypically "cold" tumor type.
- Continued biomarker development and validation may help us tailor individualized treatment approaches.

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Expert Perspective

Anthony Zietman, MD, FASTRO

Editor in Chief,
International Journal of Radiation Oncology•Biology•Physics

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Cosmetic Outcome from Post Lumpectomy Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) on the NRG Oncology/NSABP B39-RTOG 0413 Phase III Clinical Trial

Julia White, MD, FASTRO

The Ohio State University Comprehensive Cancer Center

Disclosures for Dr. White

- I have no conflicts of interest to disclose.

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NSABP B-39/RTOG 0413 Study Design

Selected Eligibility Criteria

- Lumpectomy
- Stage 0, I, II
- Tumor size ≤3.0 cm
- Negative margins (No ink on tumor)
- N0, N1 ≤3 positive nodes
- Age >18

RANDOMLY ASSIGNED

STRATIFICATION

- Disease Stage (DCIS; Invasive N0; Invasive N1)
- Menopausal Status (pre- and post-)
- Hormone Receptor Status (ER and/or PR+; ER− and PR−)
- Intention to Receive Chemotherapy

Whole Breast Irradiation (WBI)
50 Gy (2.0 Gy/fraction) or
50.4 Gy (1.8 Gy/fraction) to whole breast,
followed by optional boost to ≥ 60 Gy
5-6 weeks

Partial Breast Irradiation (PBI)
10 fractions/ BID / **5-8 days**
34 Gy in 3.4 Gy fractions Interstitial
Brachytherapy or Mammosite Balloon Catheter
Or 38.5 Gy in 3.85 Gy fractions 3DCRT

QOL SubStudy: **Cosmetic Outcome Assessments**

- 975 enrolled from March 2005 to May 2009
- 900 (420 CT and 480 no-CT) had baseline forms and at least one PT/Site MD/DP Review at 12 or 36 months
- **Global Cosmetic Score (GCS):** Patient (PT) and MD (Site)
  - 4 Point Scale NRG-RTOG
  - 1-Excellent, 2-Good, 3-Fair, 4-Poor
- Digital Photos (DP):
  - Both breasts and close-up of treated breast
  - Submitted separate database
- Time points:
  - PT – baseline; last day of treatment; 4 weeks, 6,12, 24, and 36 months after treatment
  - MD – baseline; 12 and 36 months after treatment
  - DP – baseline; 12 and 36 months after treatment

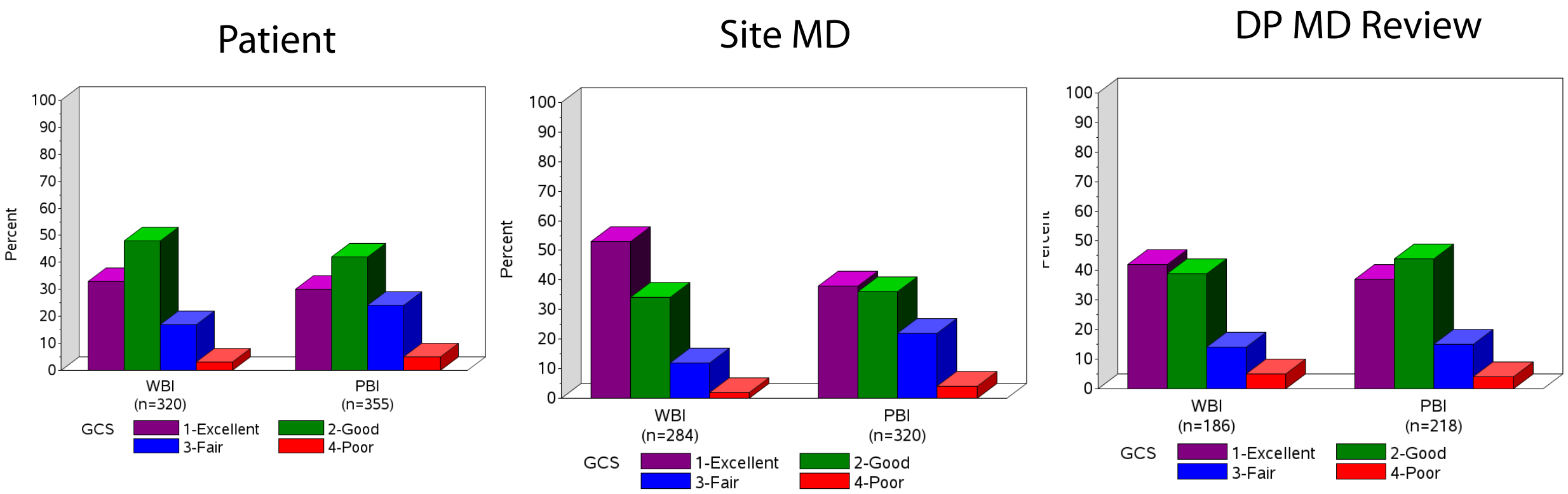
Change in GCS at 36 months

NRG/NSABP B39-RTOG 0413: Comparing Cosmetic Outcome between Treatment Arms - PBI and WBI

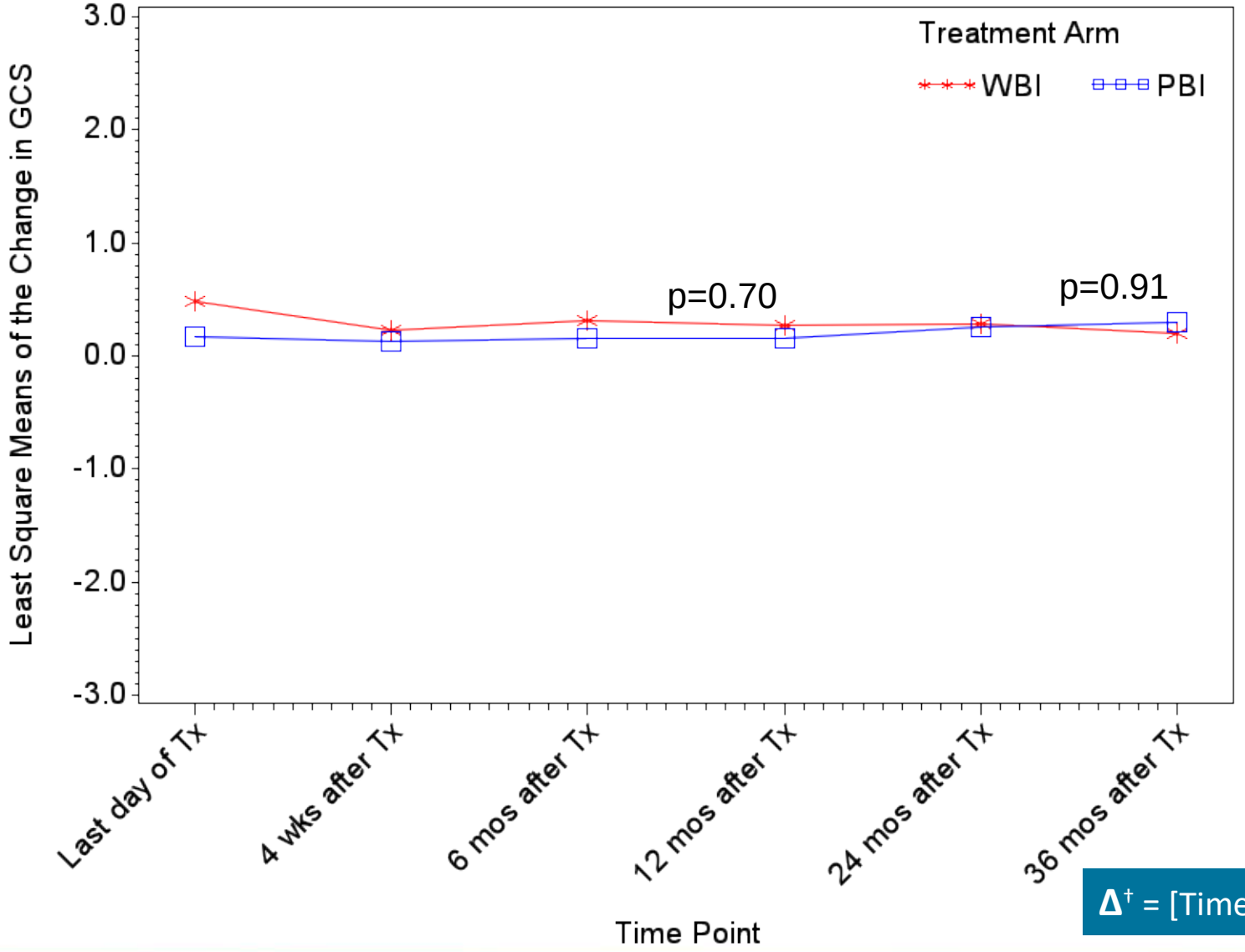
$\Delta^{\dagger}$ = [36-Month Scores - Baseline Scores]		$\Delta^{\dagger}$ in GCS by Patient	$\Delta^{\dagger}$ in GCS by Site MD	$\Delta^{\dagger}$ in GCS by DP Central MD Review
Chemo	Diff (μPBI- μWBI): 95%CI: Bound: Effect Size:	n=307 0.06 **(-0.14 to 0.25)** **-0.35 to 0.35** **Equivalent** **0.06**	n=261 0.27 **(0.02 to 0.53)** **-0.42 to 0.42** **NOT Equivalent (PBI worse)** **0.26**	n=191 0.18 **(-0.09 to 0.44)** **-0.37 to 0.37** **NOT Equivalent (PBI worse)** **0.19**
Non-Chemo	Diff (μPBI- μWBI): 95%CI: Bound: Effect Size	n=368 0.04 **(-0.15 to 0.22)** **-0.35 to 0.35** **Equivalent** **0.04**	n=343 0.16 **(-0.01 to 0.33)** **-0.33 to 0.328** **NOT Equivalent (PBI worse)** **0.19**	n=213 -0.20 **(-0.42 to 0.01)** **-0.31 to 0.31** **NOT Equivalent (WBI worse)** **-0.26**
Combined*	Diff (μPBI- μWBI): 95%CI: Bound: Effect Size	n=675 0.04 **(-0.09 to 0.17)** **-0.35 to 0.35** **Equivalent** **0.045**	n=604 0.20 **(0.05 to 0.35)** **-0.37 to 0.37** **Equivalent** **0.22**	n=404 -0.024 **(-0.19 to 0.14)** **-0.34 to 0.34** **Equivalent** **-0.028**

*Chemo Use Groups

36-Month Global Cosmetic Score (GCS) by Treatment Arm
All Patients

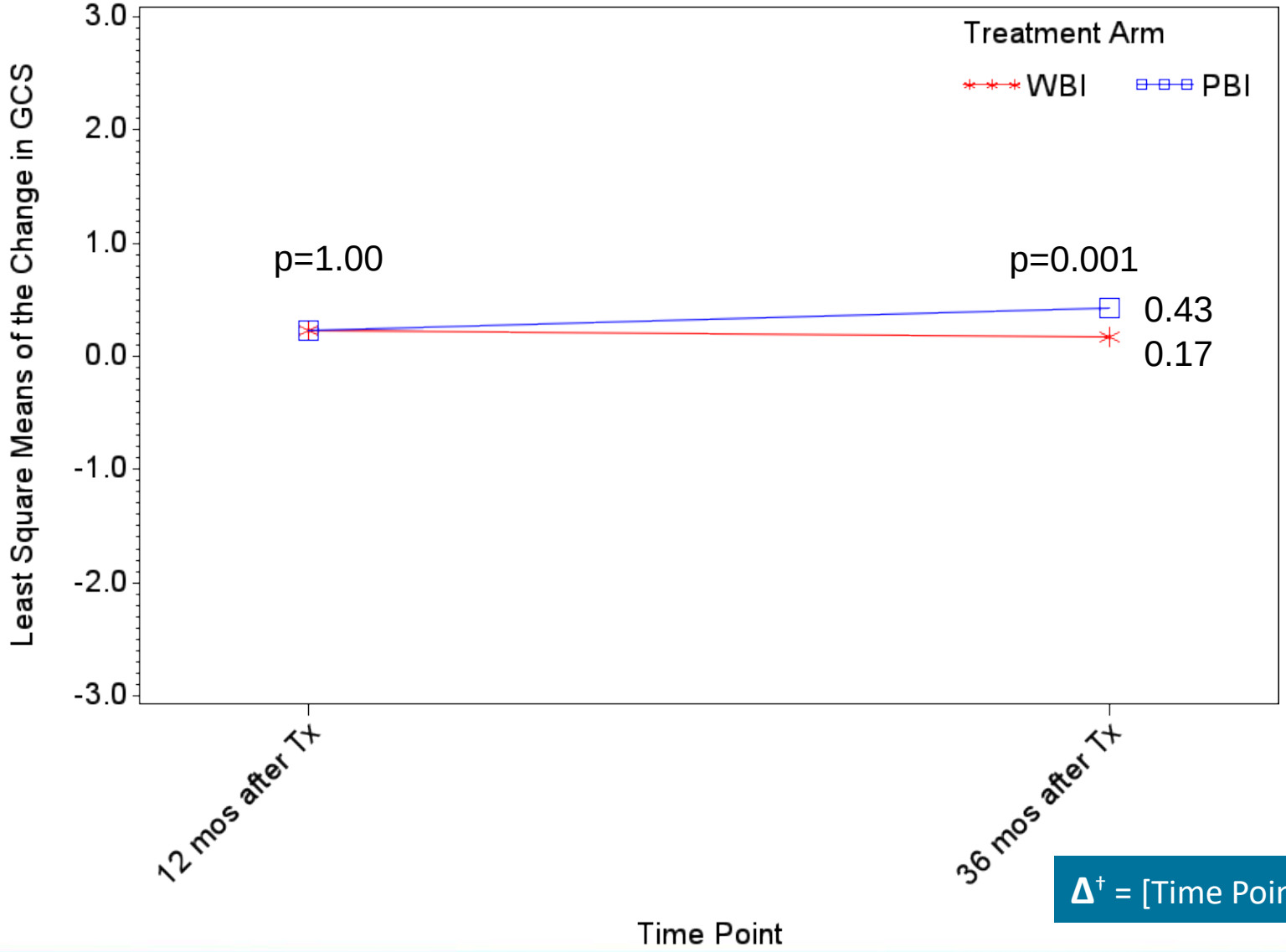


Adjusted Mean Change ($\Delta^{\dagger}$) in GCS by Patient at Each Time Point



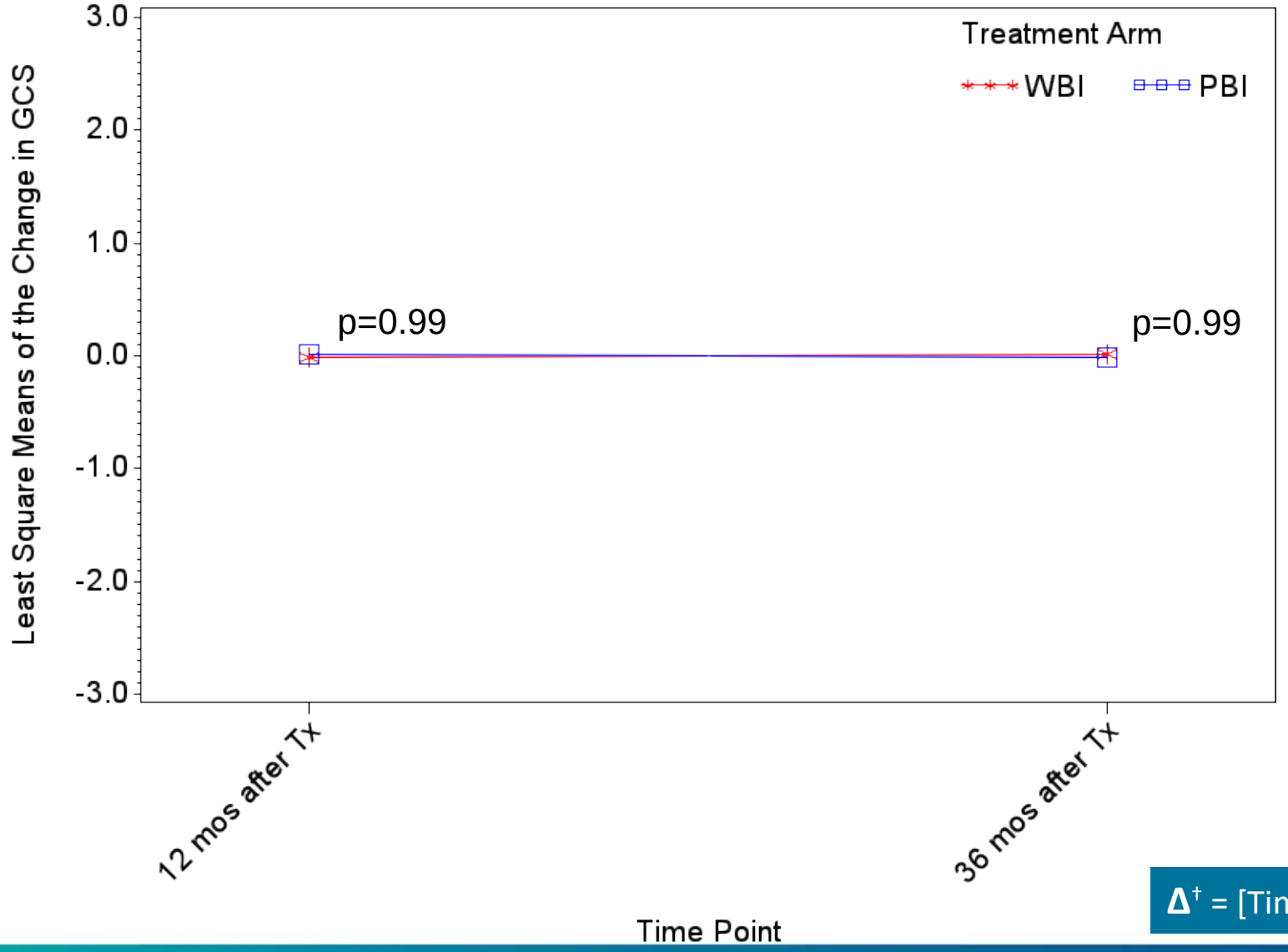
$\Delta^{\dagger}$ = [Time Point Scores - Baseline Scores]

Adjusted Mean Change ($\Delta^{\dagger}$) in GCS by Site MD at Each Time Point



$\Delta^{\dagger}$ = [Time Point Scores - Baseline Scores]

Adjusted Mean Change ($\Delta^{\dagger}$) in GCS by MD Central Digital Photo Review at Each Time Point

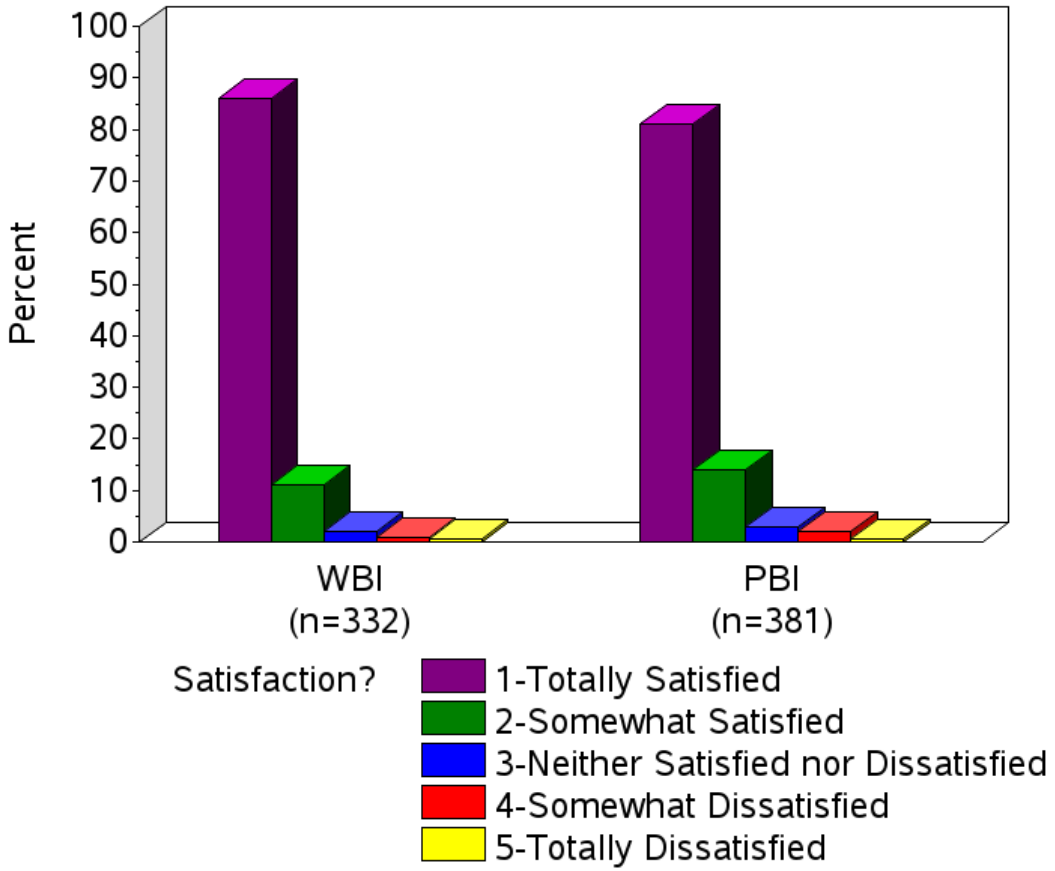


$\Delta^{\dagger}$ = [Time Point Scores - Baseline Scores]

Chemo Use Groups Combined

Patients' Satisfaction with Treatment and Cosmetic Outcome

At 36 Months



Change ($\Delta^{\dagger}$) in Patients' Satisfaction

Chemo	Diff (μPBI- μWBI): 95%CI: Bound: Effect Size:	n=327 0.013 **(-0.18 to 0.21)** **-0.36 to 0.36** **Equivalent** 0.014
Non-Chemo	Diff (μPBI- μWBI): 95%CI: Bound: Effect Size:	n=386 0.045 **(-0.13 to 0.22)** **-0.34 to 0.34** **Equivalent** 0.053
Combined	Diff (μPBI- μWBI): 95%CI: Bound: Effect Size:	n=713 0.03 **(-0.10 to 0.16)** **-0.35 to 0.35** **Equivalent** **0.035**

$\Delta^{\dagger}$ = [36-Month Scores - Baseline Scores]

Conclusions

- Patient rated cosmetic outcome based on the GCS was equivalent for PBI and WBI.
- Accruing site MDs rated cosmetic outcome worse at 36 months for PBI. The change in cosmetic outcome over time was equivalent for PBI and WBI.
- Digital photo cosmetic outcome rated by MDs blinded to treatment arm and time point was equivalent for PBI and WBI.
- Patient Satisfaction was equivalent for PBI and WBI.

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Expert Perspective

Wendy Woodward, MD

Chief of Clinical Breast Radiotherapy,
The University of Texas MD Anderson Cancer Center

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Longer Term Results from a Phase I/II Study of EP-guided Noninvasive Cardiac Radioablation for Treatment of Ventricular Tachycardia (ENCORE-VT)

Clifford Robinson, MD

Washington University School of Medicine in St. Louis

Disclosures for Dr. Robinson

- **Employer**: Washington University
- **Stock**: Radialogica
- **Research Grants**: Varian, Elekta, Merck
- **Consulting**: Varian, AstraZeneca, EMD Serono
- **Speaking**: Varian, ViewRay

- Results discussed here involve off-label use of linear accelerators outside of their current 510(k) intended use

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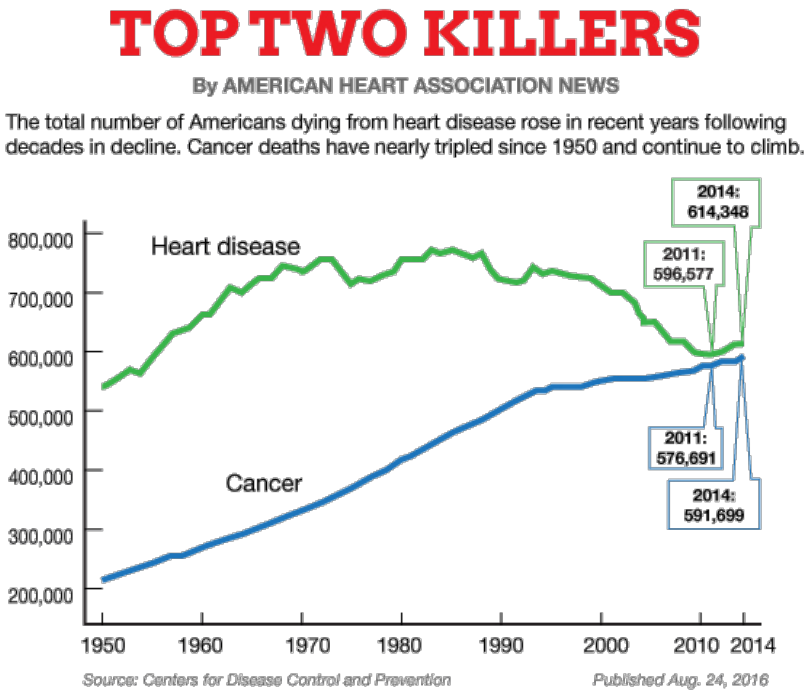
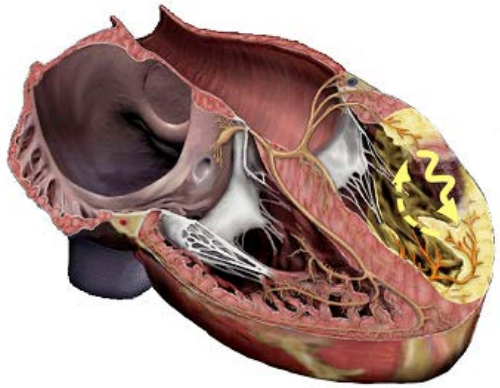
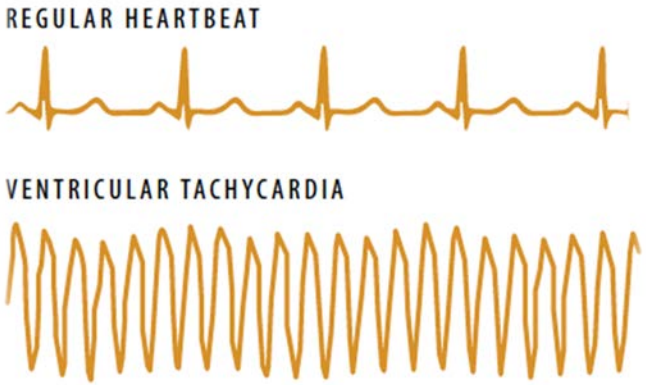
Background

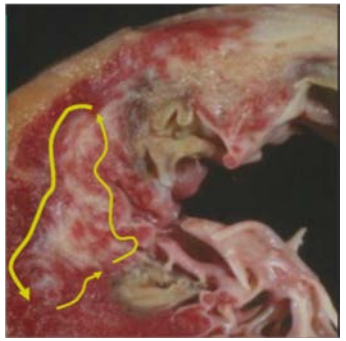




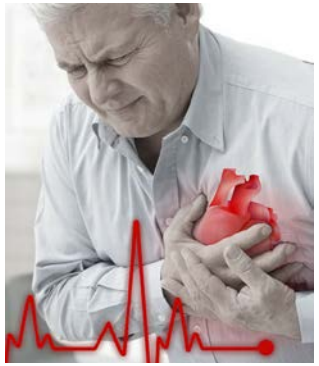


Implantable Cardiac Defibrillator (ICD)

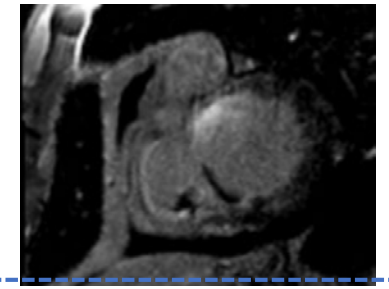
Medications (Amiodarone)

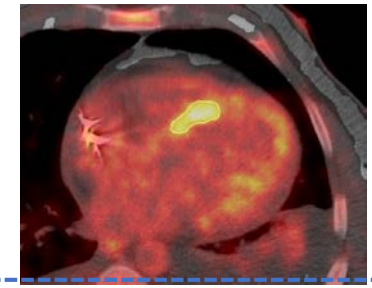


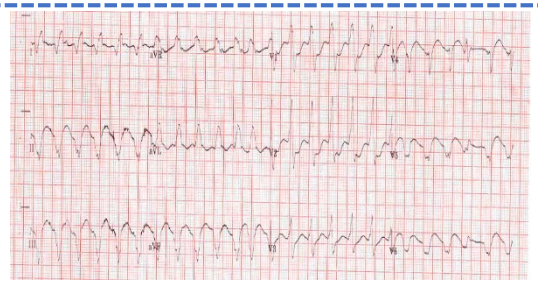
Catheter Ablation

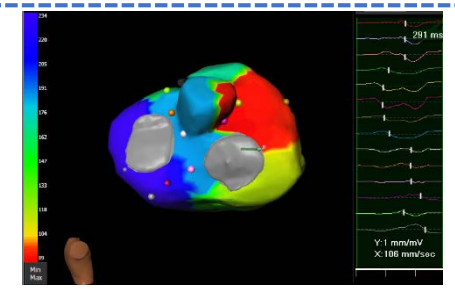


Patient selection





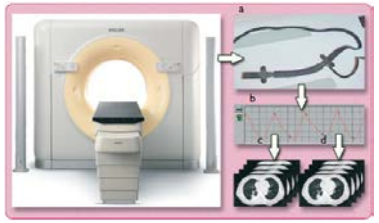




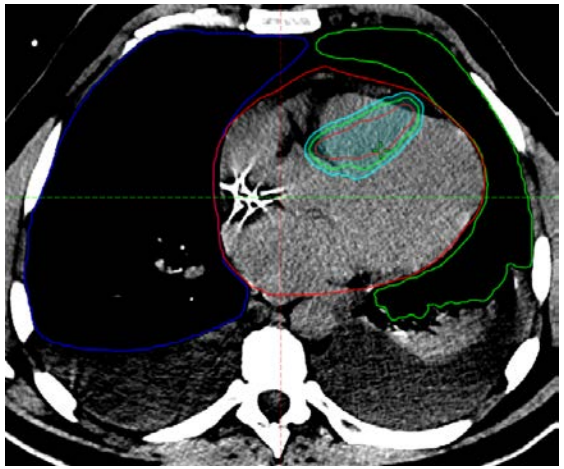
Workup / Targeting

Imaging

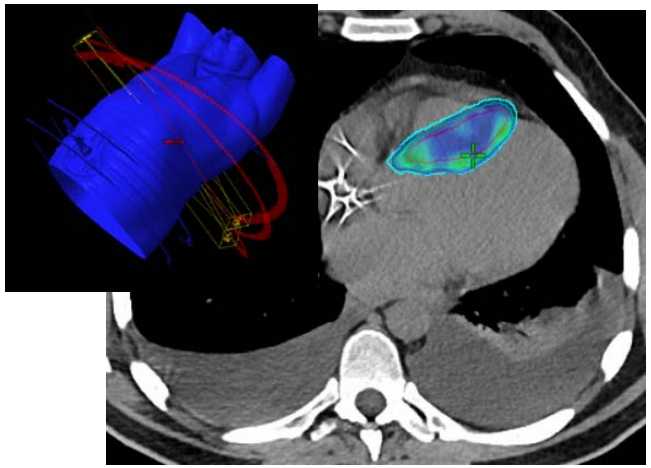
EP



Imaging / Simulation



Segmentation



Treatment Planning

Delivery

ORIGINAL ARTICLE

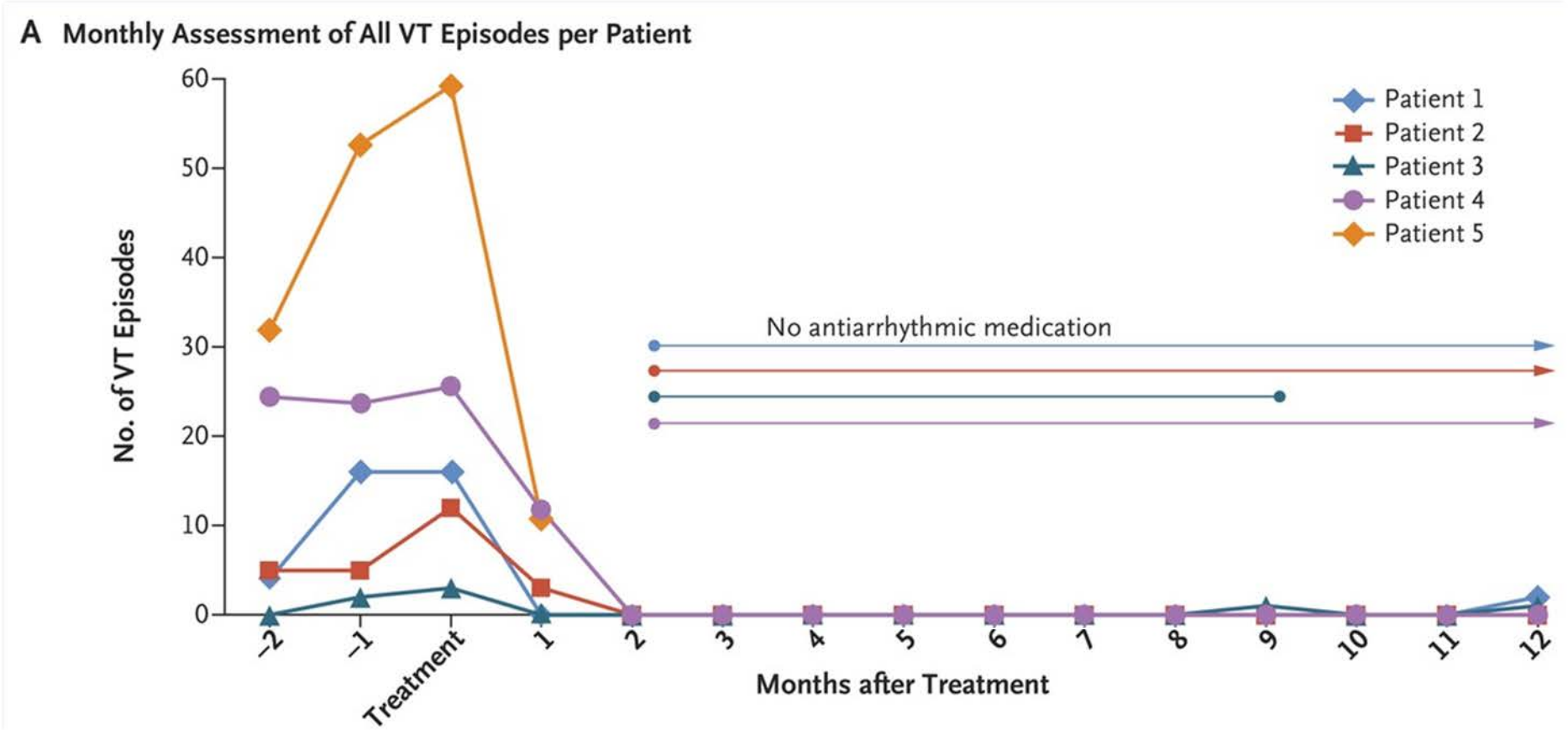
Noninvasive Cardiac Radiation for Ablation of Ventricular Tachycardia

Phillip S. Cuculich, M.D., Matthew R. Schill, M.D., Rojano Kashani, Ph.D., Sasa Mutic, Ph.D., Adam Lang, M.D., Daniel Cooper, M.D., Mitchell Faddis, M.D., Ph.D., Marye Gleva, M.D., Amit Noheria, M.B., B.S., Timothy W. Smith, M.D., D.Phil., Dennis Hallahan, M.D., Yoram Rudy, Ph.D., and Clifford G. Robinson, M.D.

5 patients w/refractory VT treated off-label for clinical need in 2015

Single SBRT treatment, 25 Gy

Average treatment time 14 min



3 month pre treatment = **6577** 6 week blanking = **680** Next 10.5 months = **4**

Phase I/II Trial – "ENCORE-VT"

- **Inclusion**
  - ≥3 VT episodes over 6 months
  - Failed medication
  - Failed (or too sick for) at least one catheter ablation
- **Phase I - Safety**
  - Serious toxicity in first 90 days
- **Phase II – Efficacy**
  - Any reduction in VT, 6 months before vs after

- **19 patients** - 90% Male and Caucasian
- **Significant cardiac impairment** – Average heart function (EF) less than half of normal
- **High burden of VT** – 53% presented in "storm"
- **Heavily medicated** – 58% on 2+ drugs and >300 mg of amiodarone
- **Average treatment time - 15 min as outpatient**

Phase I – Safety

Serious adverse events, *probably or definitely* related to SBRT

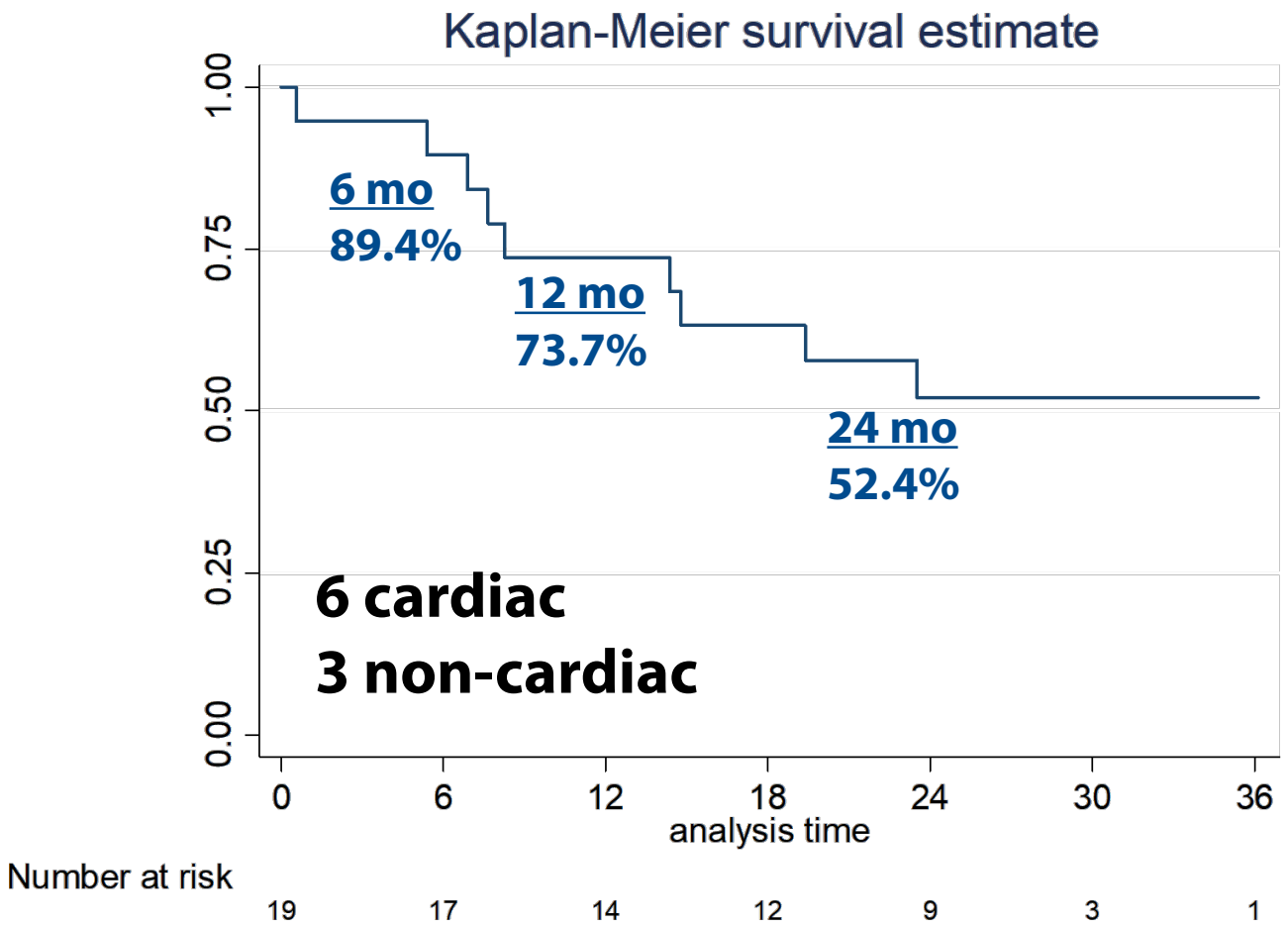
<90 days

- Grade 3
  - **1 pericarditis** (80d)

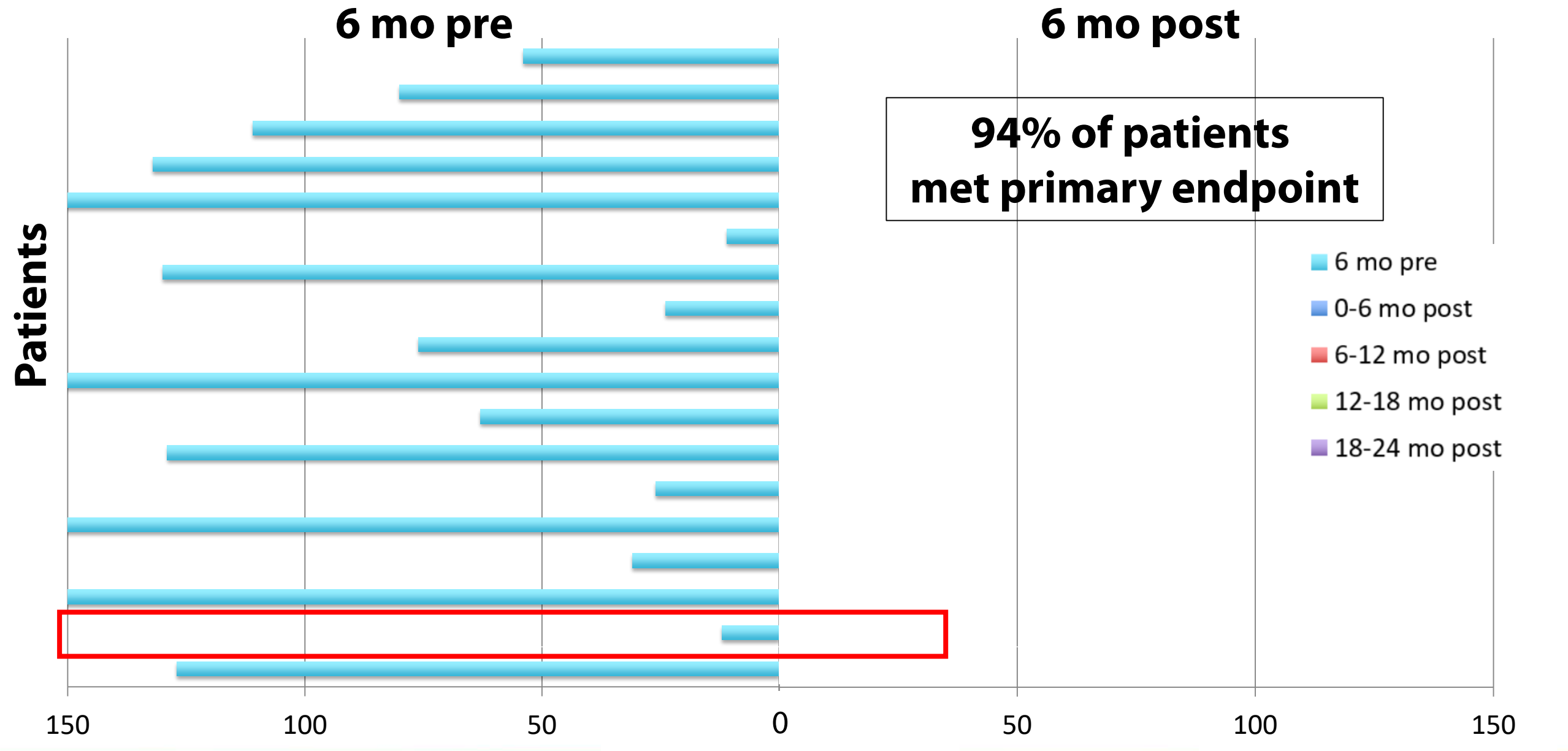
>90 days

- Grade 3
  - **2 pericardial effusions** (2.2y and 2.4y)
- Grade 4
  - **1 gastropericardial fistula** (2.4y)

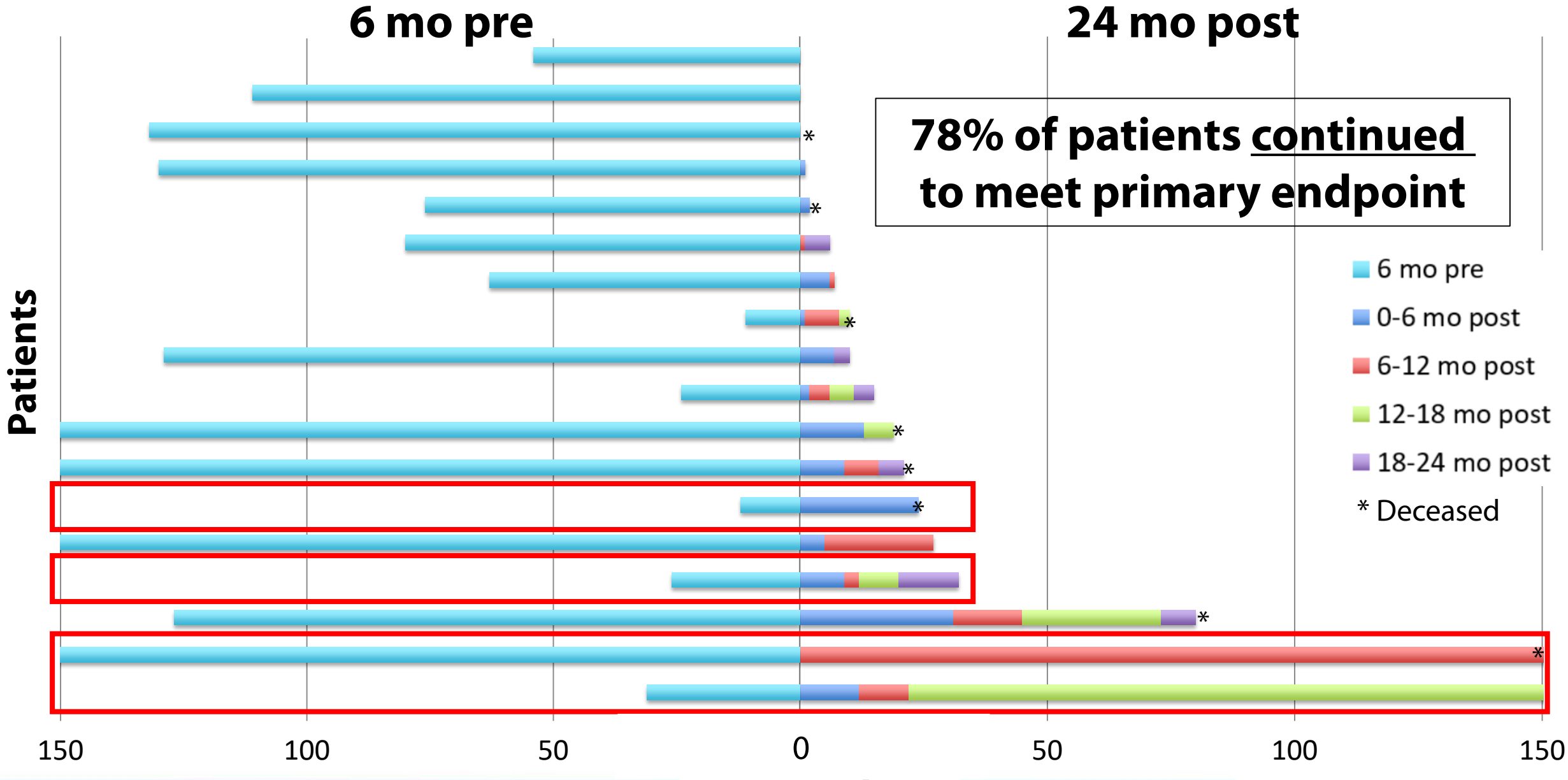
Median follow-up, 23.5 mo (range, 0.6-36.1)



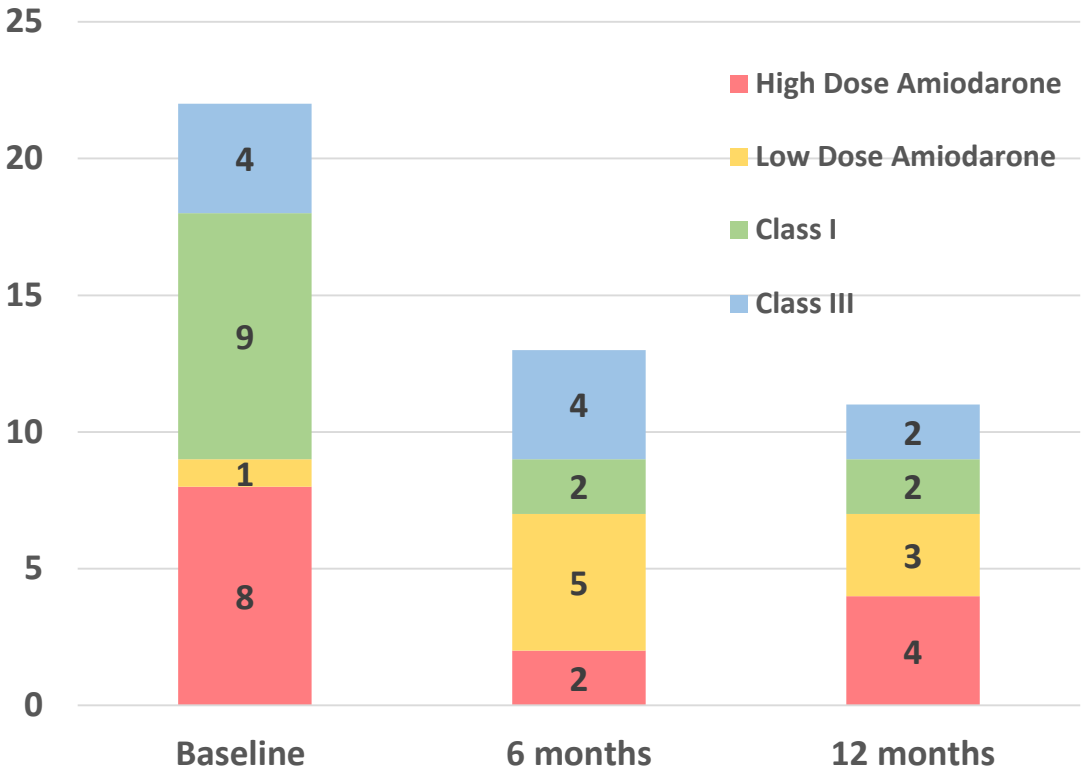
Phase II – Primary Efficacy Endpoint (n=18)



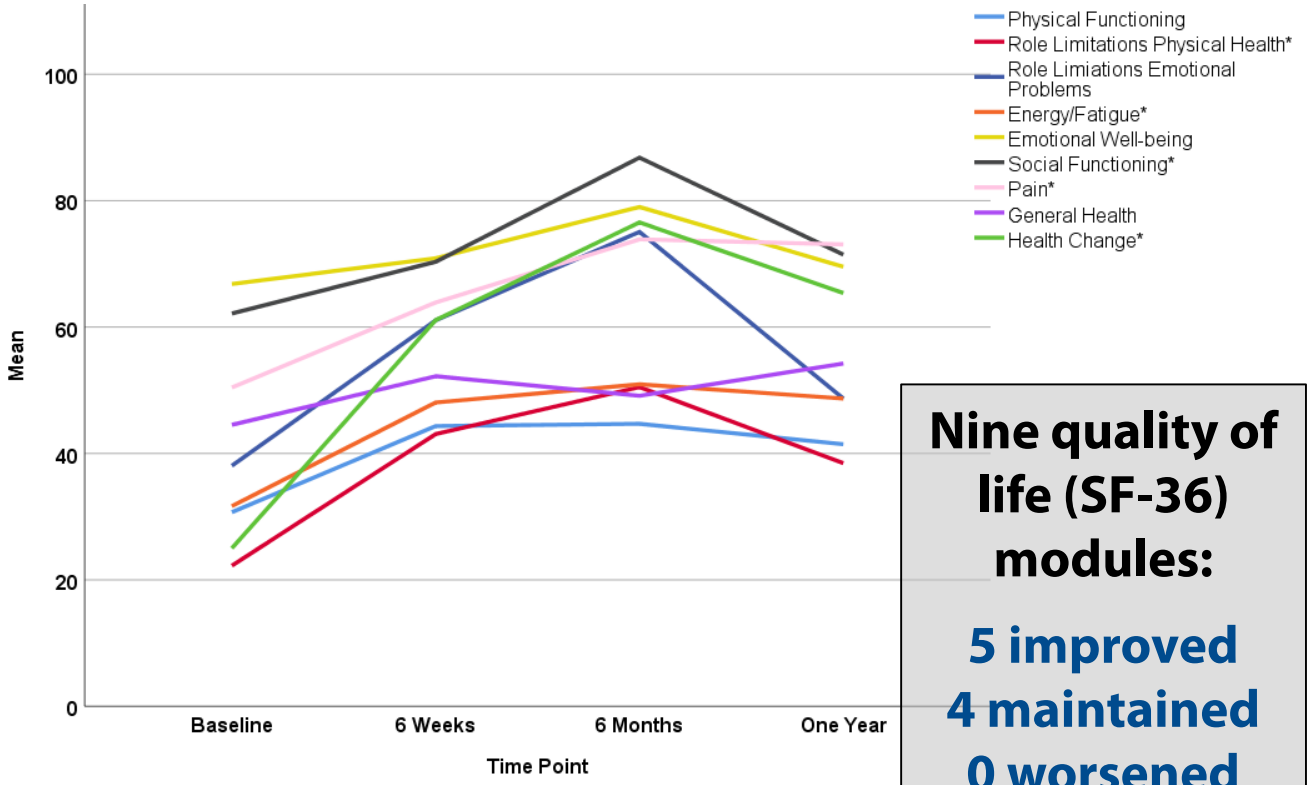
Phase II – Efficacy over time



Medications and QoL



N=14



Nine quality of life (SF-36) modules:

5 improved
4 maintained
0 worsened

Conclusion

We were able to **significantly reduce VT** using a workflow combining **noninvasive** imaging with a single noninvasive radiation therapy treatment

The **effect persisted for 2 years** in most patients

Serious toxicity was low, but may occur after 2 years. Long term follow-up is needed

ENCORE is currently **best suited for high-risk patients** who have failed conventional treatments for VT, and ideally on study

ASTRO ANNUAL MEETING 2019

Expert Perspective

Joost Verhoeff, MD, PhD

Assistant Professor of Radiotherapy,
University Medical Center Utrecht, Netherlands

ASTRO ANNUAL MEETING 2019

Q & A

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