ASTRO 2024

Targeting Provider Wellness

FOR EXCEPTIONAL PATIENT CARE

News Briefing: Monday, September 30

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Abstract 1: A randomized trial of hypofractionated post-mastectomy radiation therapy (PMRT) in women with breast reconstruction (RT CHARM, Alliance A221505)

Presented by Matthew Poppe, MD, FASTRO, University of Utah

Comments from Rachel Jimenez, MD, Massachusetts General Hospital; Vice Chair of ASTRO's forthcoming PMRT guideline update

LBA 01: Prostate Advanced Radiation Technologies Investigating Quality of Life (PARTIQoL): Phase III randomized clinical trial of proton therapy vs. IMRT for localized prostate cancer

Presented by Jason Efstathiou, MD, PhD, FASTRO, Massachusetts General Hospital

Comments from Sameer Keole, MD, FASTRO, Mayo Clinic, ASTRO President-elect (*Moderator*)

LBA 02: Concurrent chemoradiation +/- atezolizumab (atezo) in limited-stage small cell lung cancer (LS-SCLC): Results of NRG Oncology/Alliance LU005

Presented by Kristin A. Higgins, MD, City of Hope Cancer Center Atlanta

Comments from Kenneth Rosenzweig, MD, Mount Sinai Icahn School of Medicine; Chair of ASTRO's SCLC guideline

LBA 03: Interim futility results of NRG-HN005, a randomized, phase II/III non-inferiority trial for non-smoking p16+ oropharyngeal cancer patients

Presented by Sue Yom, MD, PhD, FASTRO, University of California, San Francisco

Comments from Danielle Margalit, MD, MPH, Dana-Farber Cancer Institute; Vice Chair of ASTRO's recent oropharyngeal cancer guideline update

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A randomized trial of hypofractionated post-mastectomy radiation therapy (PMRT) in women with breast reconstruction

(RT CHARM, Alliance A221505)

Matthew M. Poppe, MD, FASTRO

University of Utah Huntsman Cancer Institute

Disclosure & Study Team

- Employer: Huntsman Cancer Institute, University of Utah
- Alliance Breast Committee Vice-Chair
- NCI Breast Cancer Steering Committee – BOLD Member
- I have no financial conflicts of interest.
- This study was supported by funding from UG1CA189823, U10CA180821; https://acknowledgments.alliancefound.org. Clinical Trials.gov: NCT03414970
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Background

- More than 100,000 mastectomies performed in the U.S. each year for breast cancer, approx. 50% will get breast reconstruction[1]
- Radiation after mastectomy improves survival for certain patients, such as those with larger tumors or involved lymph nodes[2]
- Standard radiation after mastectomy takes 4-5 weeks of daily treatment
- Many forgo radiation and compromise survival given the time involved
- Hypofractionation, or short course radiation, has become standard practice in lumpectomy patients based on multiple randomized trials[3,4]

[1]Steffen et al. Plast Surg Nurs. 2017 Oct/Dec;37(4):146-153.
[2]EBCTCG. Lancet. 2014 Jun 21;383(9935):2127-35.
[3]NCIC. Whelan et al. JNCI. 94(15).2002.
[4]UK Start A/B. Haviland et al. Lancet Oncol. 14(11). 2013.

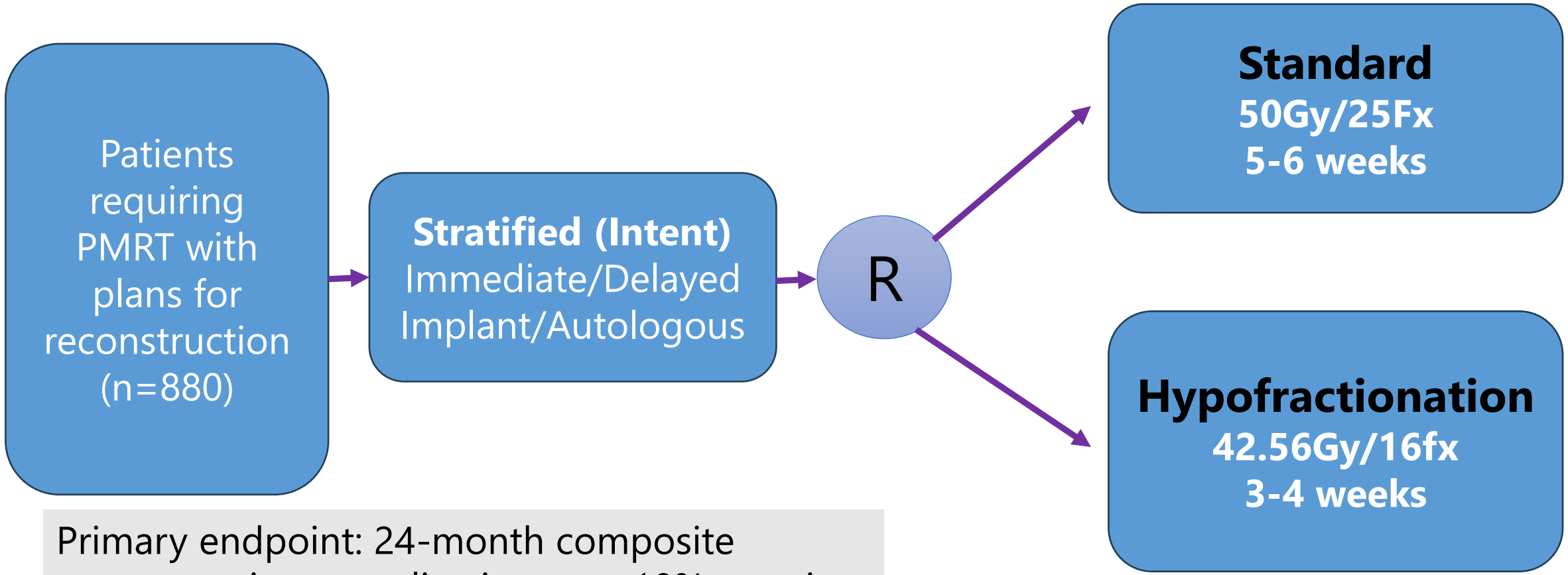
Breast Reconstruction

- Limited to NO prospective, randomized data regarding radiation and breast reconstruction complications. Mostly = retrospective, institutional
- Complex factors: Implant, Autologous tissue, Tissue Expanders, Immediate, delay and immediate-delayed
- Available data – radiation after reconstruction increases (double?) complication rate. Estimated 20-30%.[1,2,3]
  - Wound healing
  - Re-Operation
  - Infection
  - Contracture
  - Loss of Reconstructed Breast

[1]Jagsi et al. Ann Surg. 2016 Feb;263(2):219-27.
[2]Manyam et al. Pract Radiat Oncol. 2019 Nov;9(6):e497-e505.
[3]Christante et al. Arch Surg. 2010 Sep;145(9):873-8.

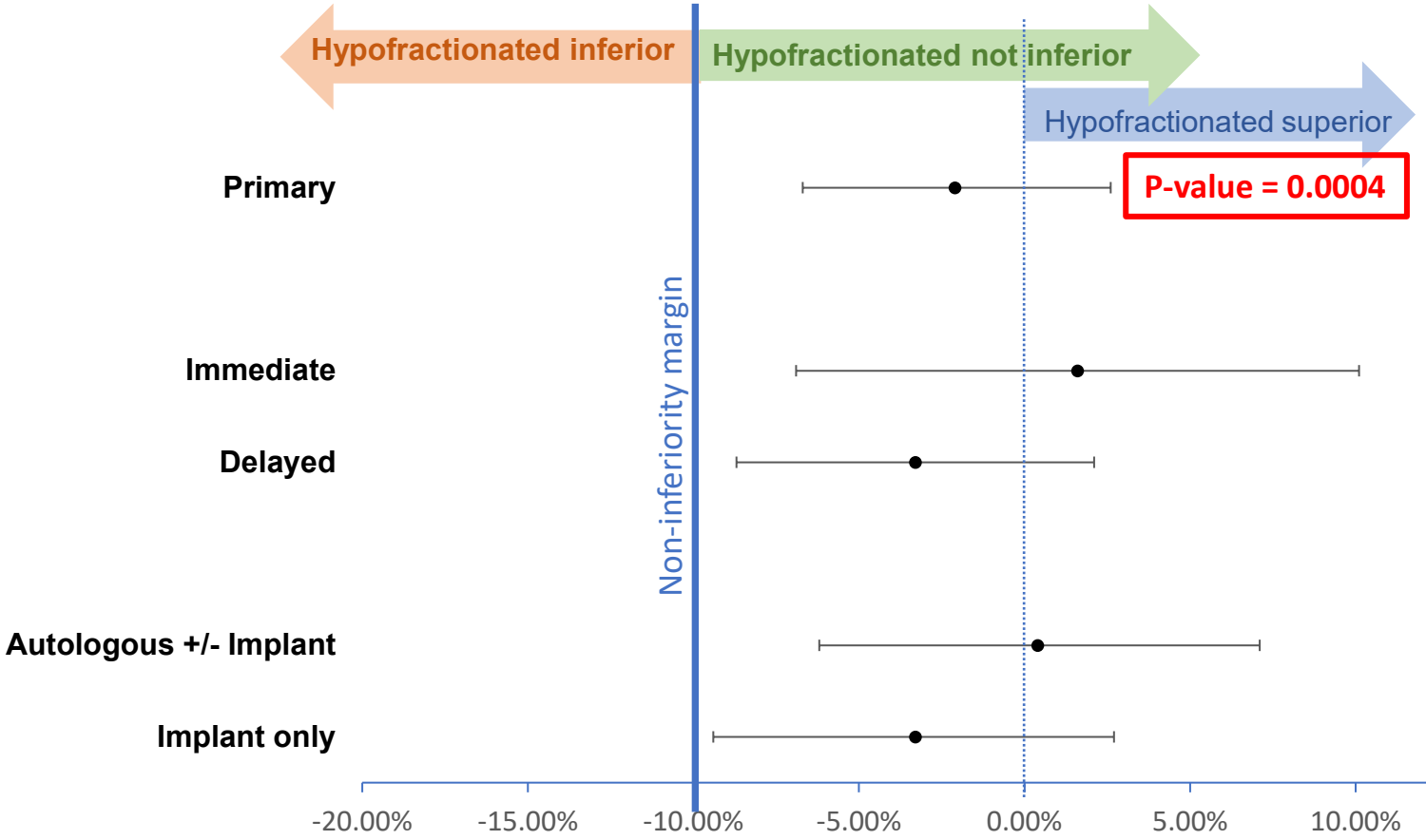
RT CHARM: Method

Phase 3 randomized non-inferiority trial



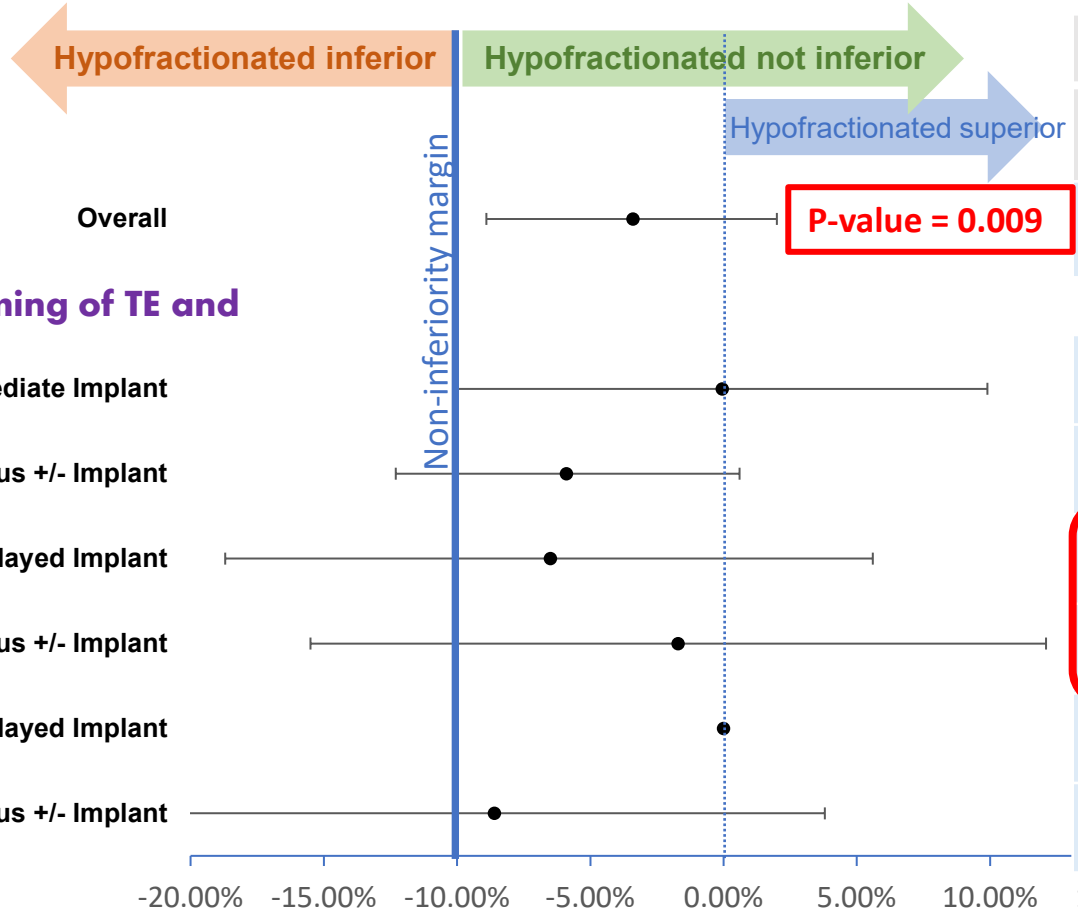
Primary endpoint: 24-month composite reconstruction complication rate, 10% margin

Primary endpoint: Reconstruction Complications
Intention-to-Treat Analysis (N = 825)



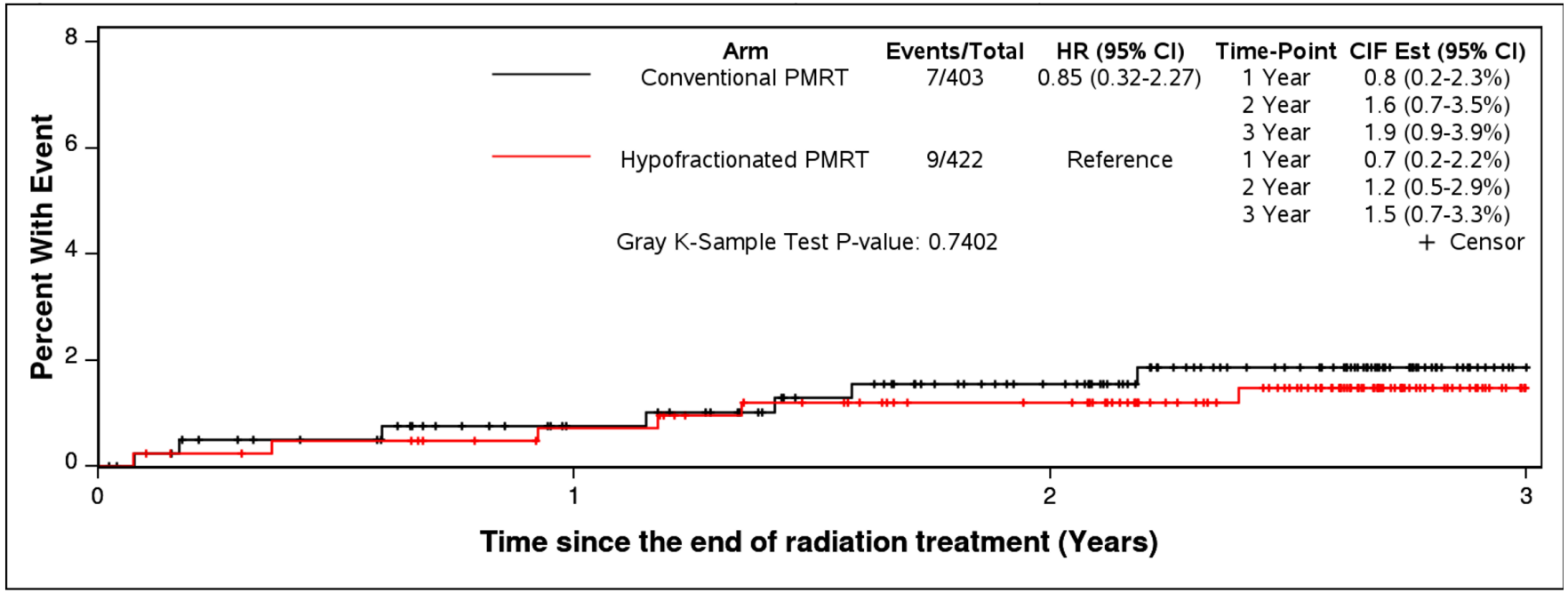
Proportion with 24-month Complications			
Conventional PMRT	Hypofractionated PMRT	Estimated Difference	95% CI
12.2% (n = 403)	14.2% (n = 422)	-2.1%	(-6.7%, 2.6%)
11.9% (n = 101)	10.3% (n = 107)	1.6%	(-6.9%, 10.1%)
12.3% (n = 302)	15.6% (n =. 315)	-3.3%	(-8.7%, 2.1%)
8.9% (n = 135)	8.5% (n = 142)	0.4%	(-6.2%, 7.1%)
13.8% (n = 268)	17.1% (n = 280)	-3.3%	(-9.4%, 2.7%)

Primary endpoint and planned subgroup: Reconstruction Complications As-Treated Analysis (N = 650)



Proportion with 24-month Complications			
Conventional PMRT	Hypofractionated PMRT	Estimated Difference	95% CI
13.1% (n = 312)	16.6% (n = 338)	-3.4%	(-8.9%, 2.0%)
13.0% (n = 92)	13.1% (n = 84)	-.05%	(-10.0%, 9.9%)
0.0% (n = 35)	5.9% (n = 51)	-5.9%	(-12.3%, 0.6%)
20.5% (n = 88)	27.0% (n = 100)	-6.5%	(-18.7%, 5.6%)
16.9% (n = 59)	18.6% (n = 59)	-1.7%	(-15.5%, 12.1%)
0% (n = 6)	0% (n = 10)	0%	Not estimable
3.1% (n = 32)	11.8% (n = 34)	-8.6%	(-21.0%, 3.8%)

Local and Local Regional recurrence



The Gray's test results indicates there was no evidence to conclude that the incidence of local and local regional recurrence differ between the two treatment arms.

Conclusions

- Hypofractionated radiation is non-inferior to standard radiation after mastectomy for reconstruction complications, toxicity and local control.
- Hypofractionated PMRT with reconstruction should become the new standard of therapy.
- This change will improve the lives of breast cancer patients.
- Implant only and 2-stage reconstruction ↑ toxicity (not randomized)
    - Await patient reported outcomes and photographic assessment

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Expert Perspective

Rachel Jimenez, MD

Vice Chair, ASTRO PMRT Guideline Update (forthcoming)

Massachusetts General Hospital

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Prostate Advanced Radiation Technologies Investigating Quality of Life (PARTIQoL):

Phase III randomized clinical trial of proton therapy vs. IMRT for localized prostate cancer

Jason A. Efstathiou, MD, PhD, FASTRO

Massachusetts General Hospital

Disclosures & Study Team

PARTIQoL
Prostate Advanced Radiation Technologies Investigating Quality of life

- Dr. Efstathiou's Disclosures: *Consultant/Honoraria*: Blue Earth Diagnostics, Boston Scientific, AstraZeneca, Genentech, Lantheus/Progenics, IBA, Astellas/Pfizer, Elekta, Uptodate; *Advisory Board*: Merck, Roivant Pharma, Myovant Sciences, EMD Serono, Bayer Healthcare, Janssen, Pfizer, Progenics Pharmaceuticals, Gilead, Lantheus, Blue Earth Diagnostics, Angiodynamics, Clarity Pharmaceuticals

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Mass General Brigham Mass General Cancer Center · Washington University in St. Louis · Penn · Rutgers Cancer Institute of New Jersey · Rutgers Health · Northwestern Medicine Chicago Proton Center · Mayo Clinic · University of Maryland · UFHealth Proton Therapy Institute · University Hospitals · Provision Healthcare · CentraState

Background

- People diagnosed with localized prostate cancer — about 70% of diagnoses or 200K in the U.S. each year —have several treatment options, including multiple options for external radiation treatments.
- Because many patients survive their cancer and live many years after treatment, quality of life is paramount.
- The PARTIQoL multi-center phase 3 randomized trial compared patient-reported quality of life after external radiation using photon/x-ray beams (IMRT) vs. proton beams, to determine which therapy best minimizes the side effects of treatment.

Study Design & Aims: Phase III RCT

Stratification

- Study site
- Age (<65 years vs. ≥ 65 years)
- Rectal spacer (No vs. Yes)
- Moderate hypofractionation* (No vs. Yes)

Planned fractionation schedule: 1.8 Gy (RBE) fractions to 79.2 Gy (RBE) vs. 2.5 Gy (RBE) fractions to 70.0 (RBE)

Randomization
450 men

Proton Beam Therapy (PBT)

versus

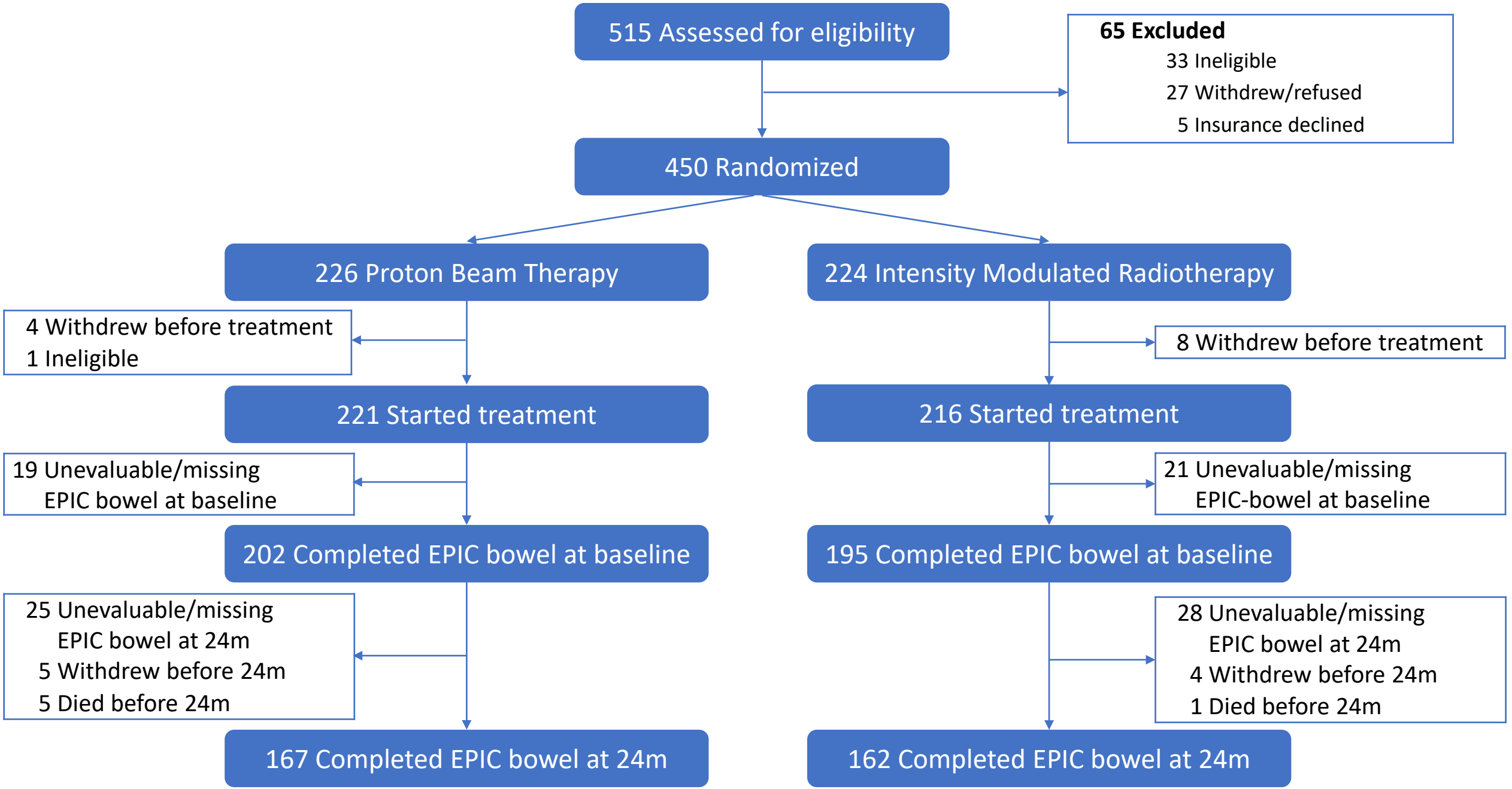
Intensity Modulated Radiotherapy (IMRT)

Timepoints (months)
0, 3, 6, 9, 12, 18, 24, 36, 48, 60

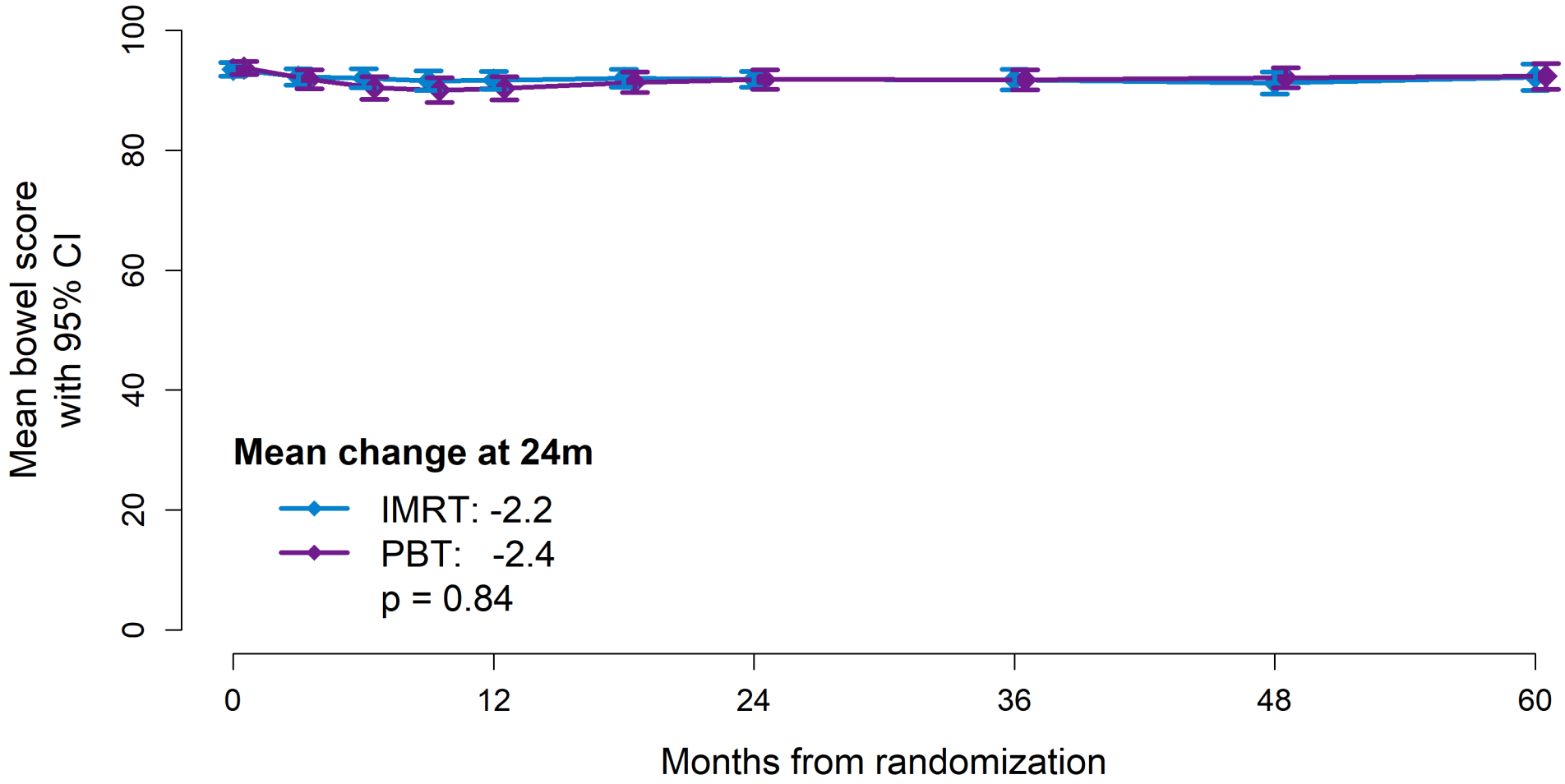
Primary Endpoint
Bowel Function at 24mo (EPIC)

Secondary Outcomes

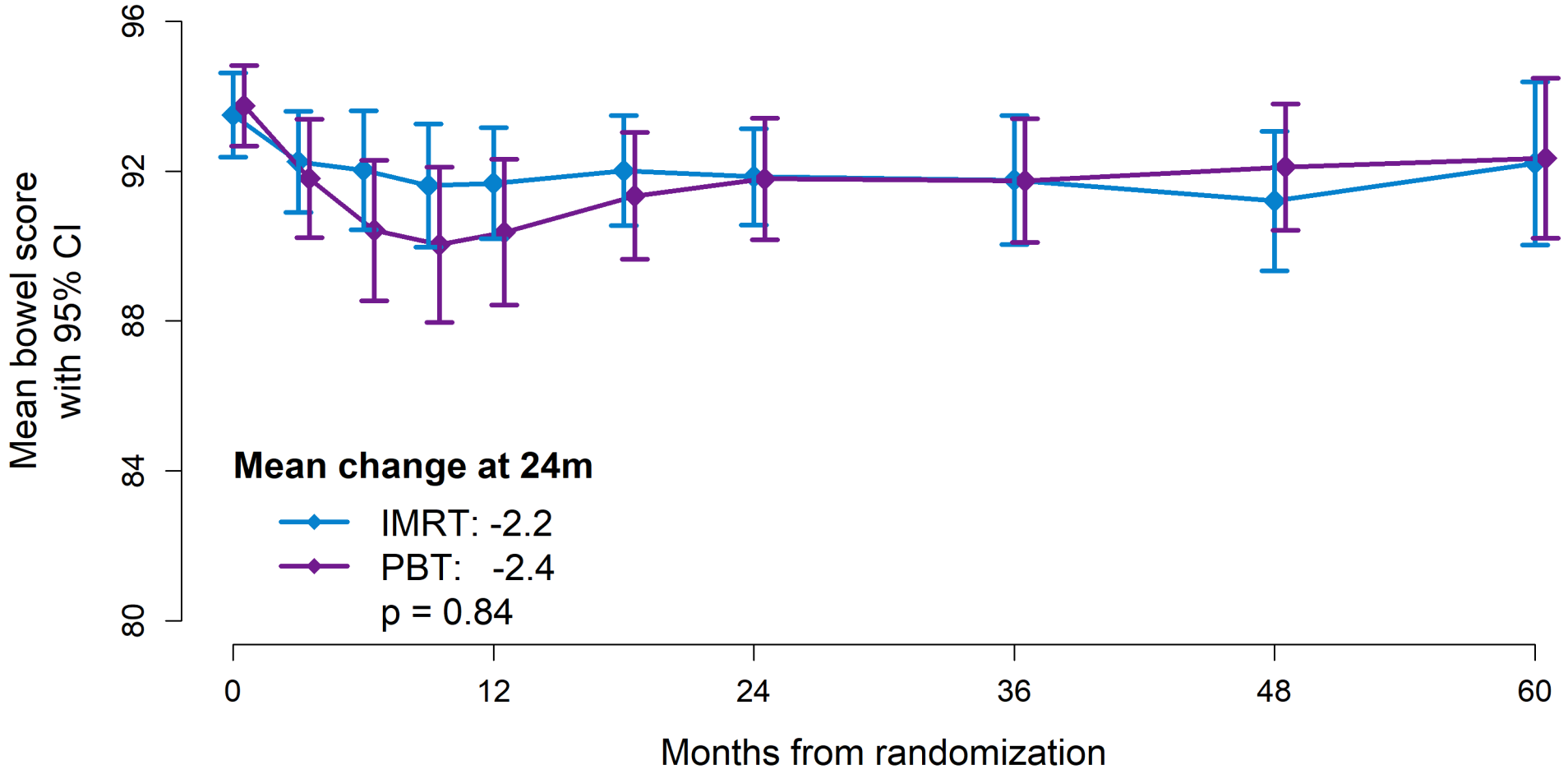
- Urinary & erectile function
- HRQoL & Utilities
- Perceptions of care
- Adverse events/toxicity
- Efficacy endpoints
- Economic endpoints
- Response Biomarkers


515 Assessed for eligibility
65 Excluded
33 Ineligible
27 Withdrew/refused
5 Insurance declined
450 Randomized
226 Proton Beam Therapy
224 Intensity Modulated Radiotherapy
4 Withdrew before treatment
1 Ineligible
8 Withdrew before treatment
221 Started treatment
216 Started treatment
19 Unevaluable/missing
EPIC bowel at baseline
21 Unevaluable/missing
EPIC-bowel at baseline
202 Completed EPIC bowel at baseline
195 Completed EPIC bowel at baseline
25 Unevaluable/missing
EPIC bowel at 24m
5 Withdrew before 24m
5 Died before 24m
28 Unevaluable/missing
EPIC bowel at 24m
4 Withdrew before 24m
1 Died before 24m
167 Completed EPIC bowel at 24m
162 Completed EPIC bowel at 24m

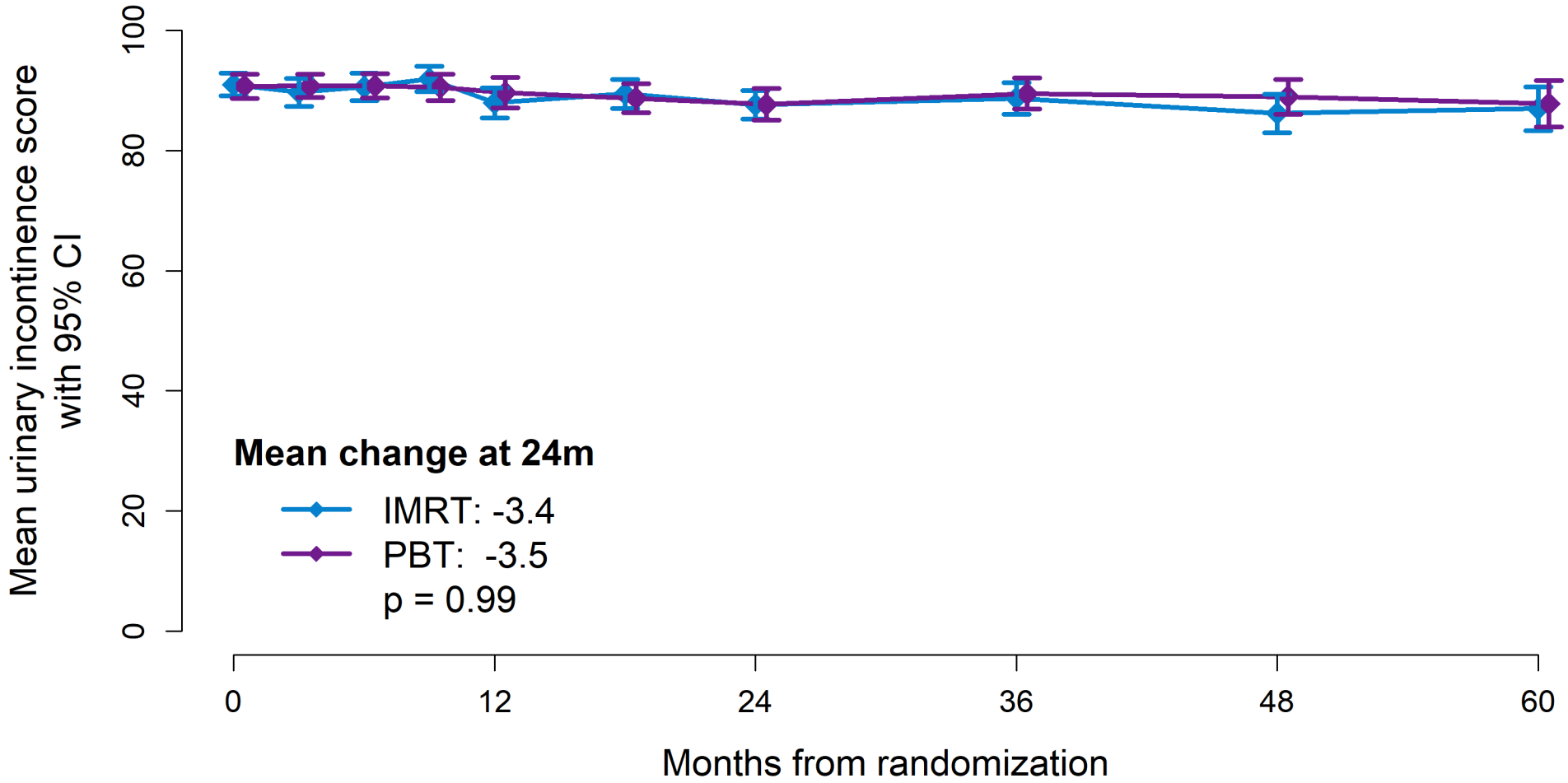
Quality of Life: Bowel (EPIC)



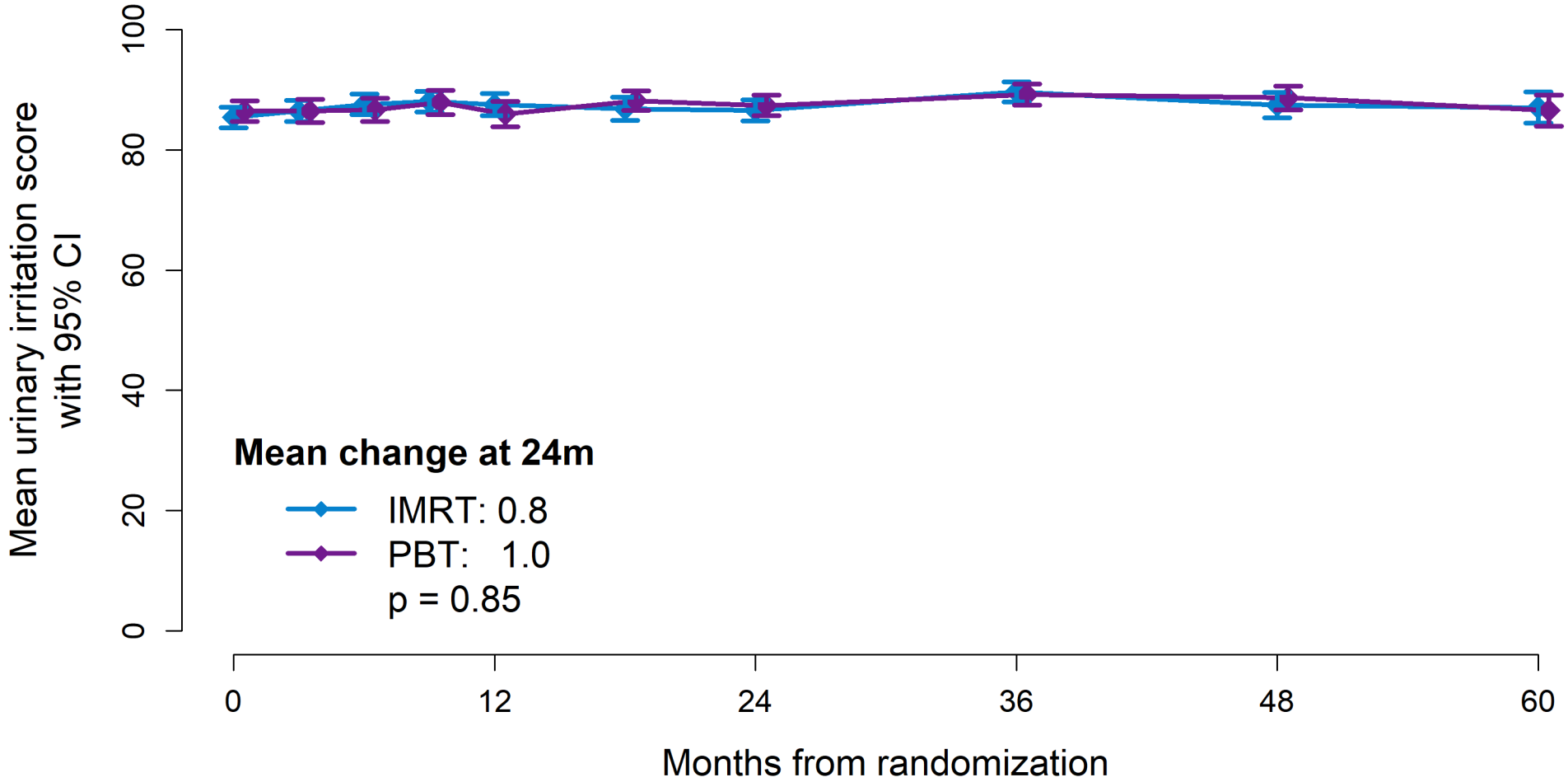
Quality of Life: Bowel (EPIC)



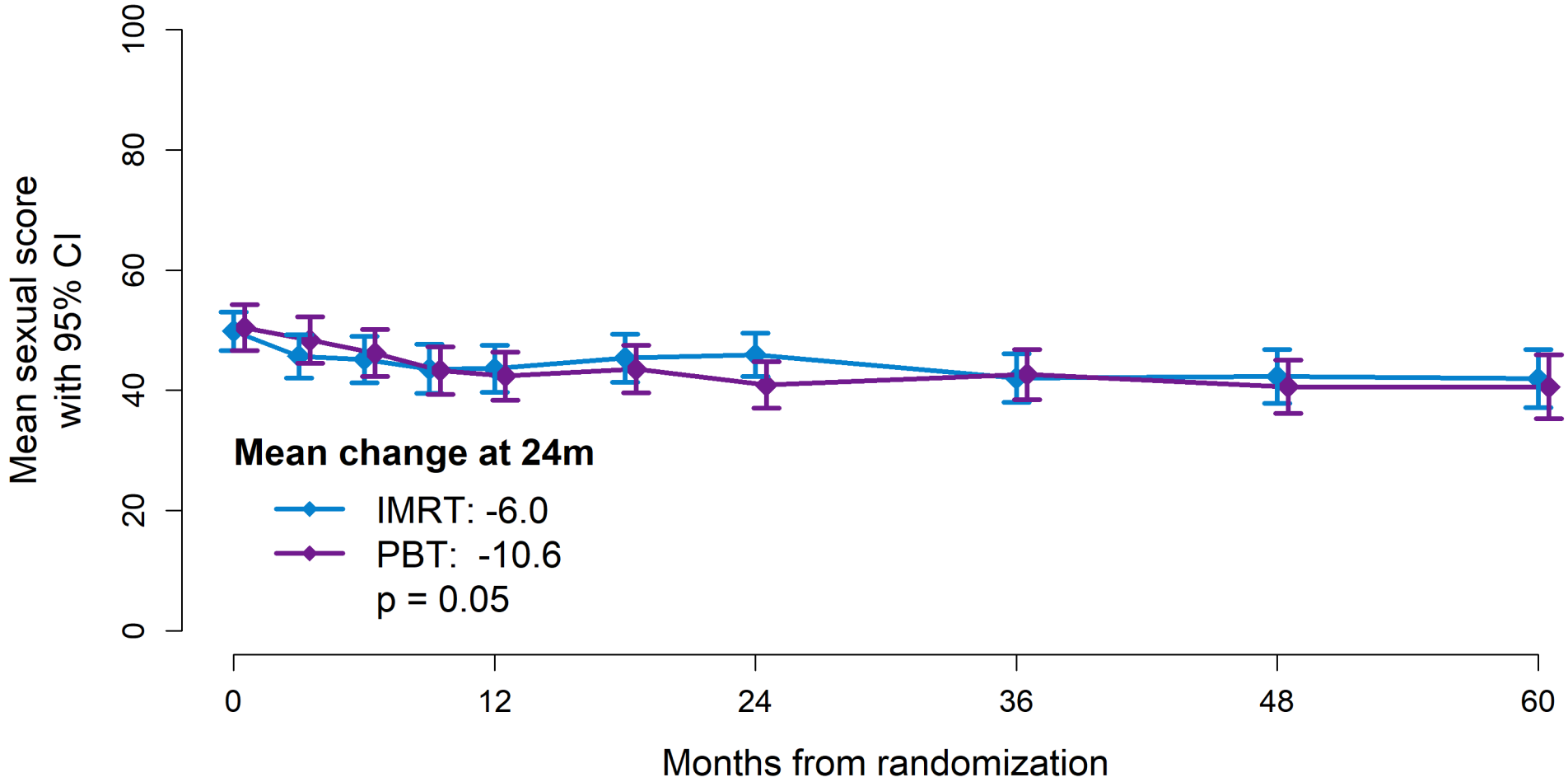
Quality of Life: Urinary Incontinence (EPIC)



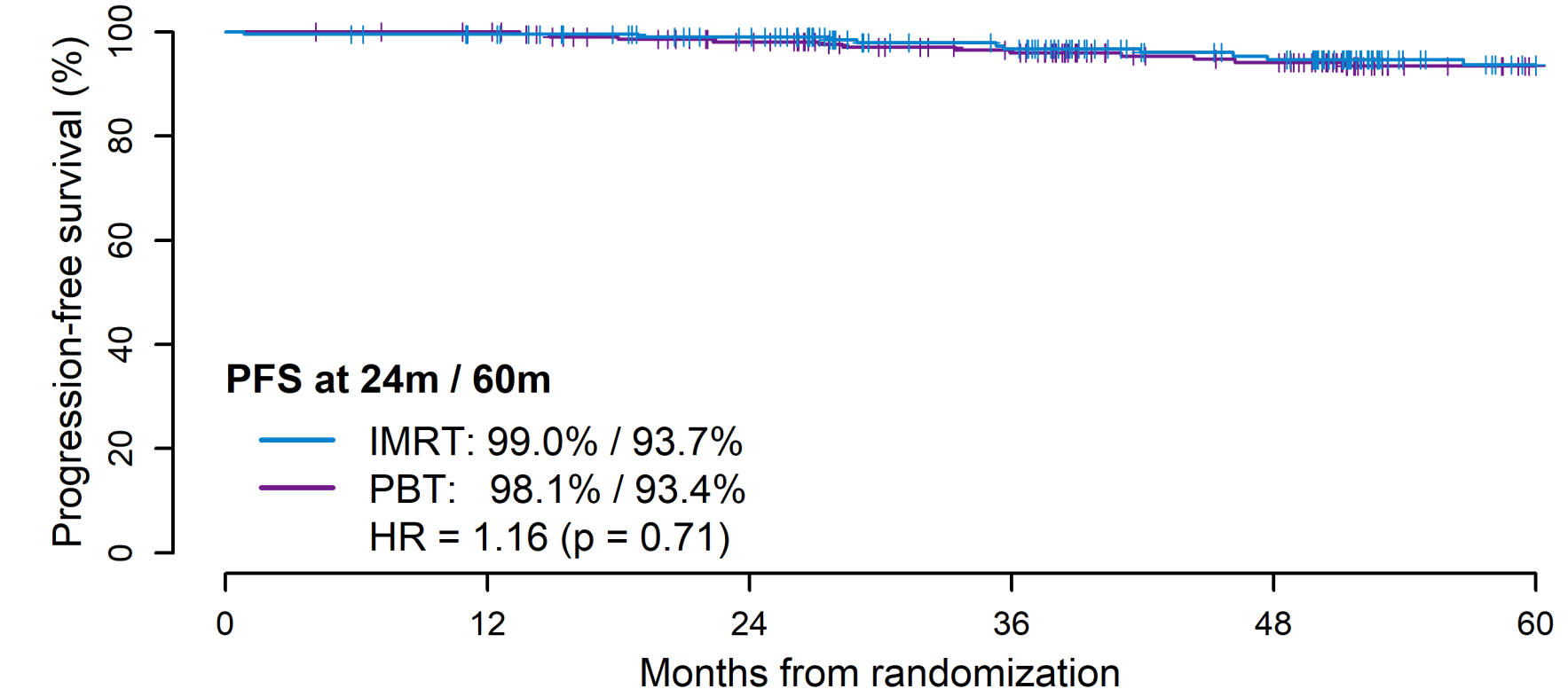
Quality of Life: Urinary Irritation (EPIC)



Quality of Life: Sexual (EPIC)



Progression-free Survival



No. at risk

IMRT	216	210	194	164	135	92
PBT	221	218	199	178	151	112

Subgroup Analyses

No differences in EPIC Bowel QoL by:

- Age group (≤65 years, >65 years)
- Disease risk (intermediate, low)
- Rectal spacer use (yes, no)
- Fractionation schedule (conventional, hypofractionation)

Conclusions

- IMRT and proton therapy offer patients with localized prostate cancer equally excellent quality of life outcomes with highly effective tumor control, without measurable differences between the two approaches.
- There were only small QoL declines from baseline levels for each arm.
  - For example, ~2% decrease on 100-point scale for bowel QoL after two years.
- We continue to monitor participants for longer followup and secondary endpoints, as well as the results from our companion registry.

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Expert Perspective

Sameer Keole, MD, FASTRO

ASTRO President-elect
(President as of Oct. 1)

Mayo Clinic

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Concurrent chemoradiation +/- atezolizumab (atezo) in limited-stage small cell lung cancer (LS-SCLC): Results of NRG Oncology/Alliance LU005

Kristin A. Higgins, MD,
City of Hope Cancer Center Atlanta

Disclosure & Study Team

- Disclosures: RefleXion Medical, Astra Zeneca, Janssen Pharmaceuticals, Genentech, Jazz Pharmaceuticals
- This project was supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), UG1CA189867 (NCORP), U24CA196067 (NRG Specimen Bank), U24CA180803 (IROC) from the National Cancer Institute and Genentech, member of the Roche Group. ClinicalTrials.gov Identifier: NRG-LU005, NCT03811002

- Full author list:

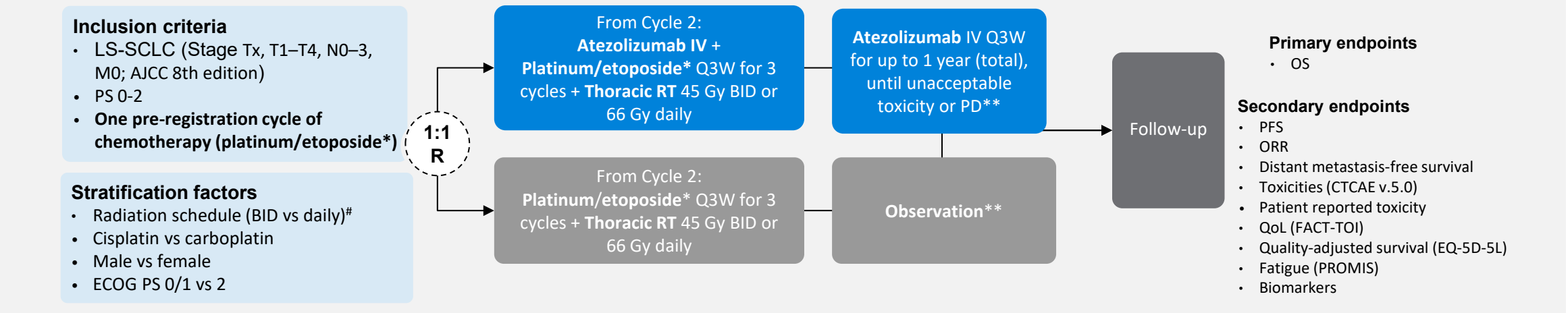
  Kristin A. Higgins, Chen Hu, Helen J. Ross, Salma K. Jabbour, David E. Kozono, Taofeek K. Owonikoko, Kyoichi Kaira, Amit K. Gupta, Pranshu Mohindra, Elie G. Dib, Jeremy Brownstein, Stephen Chun, Charles S. Kuzma, Rupesh R. Kotecha, Adedayo A. Onitilo, Yuhchyau Chen, Tom Stinchcombe, Xiaofei F. Wang, Rebecca Paulus, Jeffrey D. Bradley

Background

- Long term survival for LS-SCLC is ~ 30% at 5 years, with standard of care chemoradiation +/- PCI approaches
- Recent successes with the addition of immunotherapy to chemotherapy has improved survival in ES-SCLC
- NRG/Alliance LU005 tested the addition of atezolizumab to concurrent chemoradiation in LS-SCLC

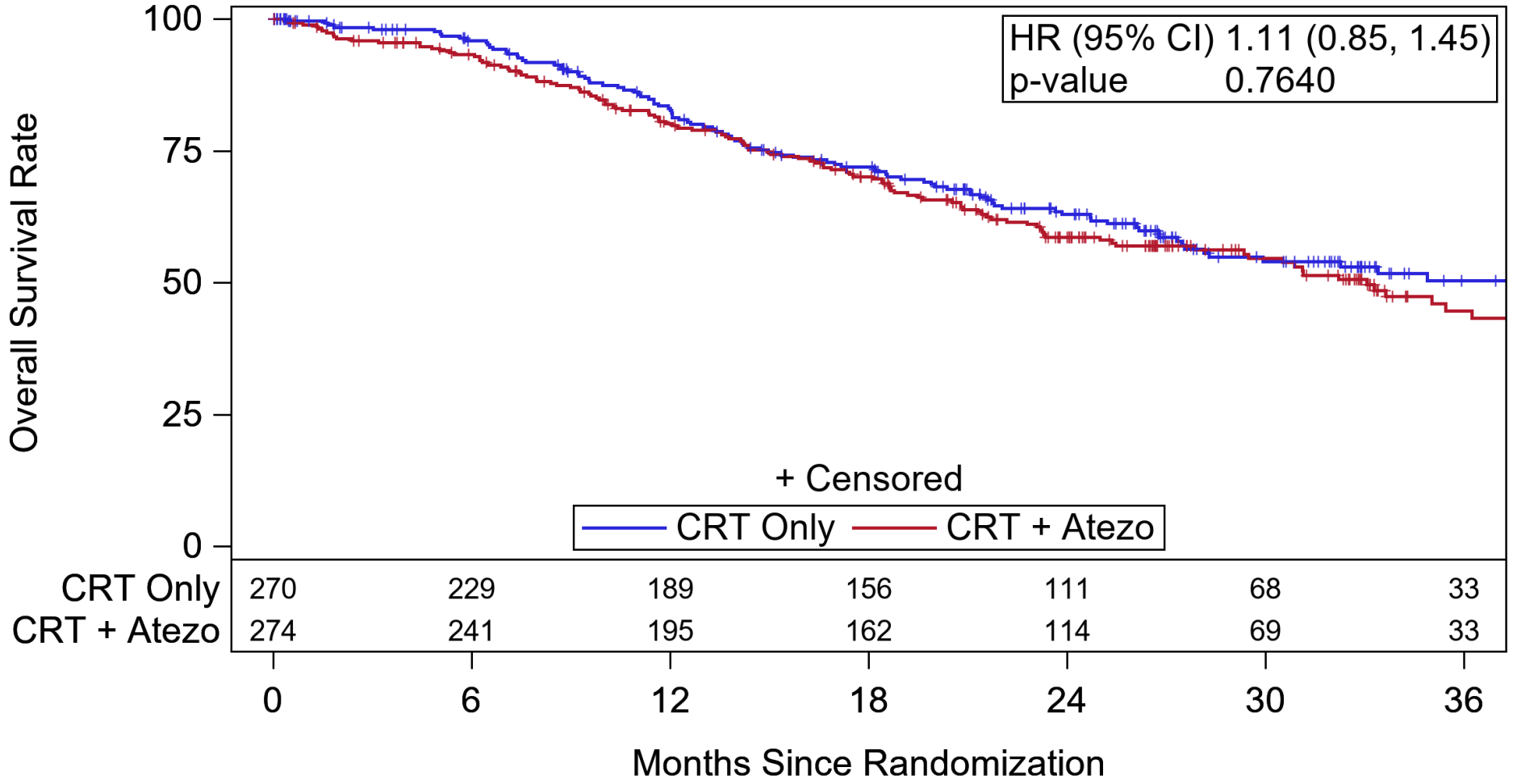
NRG LU005 Schema

Phase III (N = 544; US & Japanese sites) NCT03811002



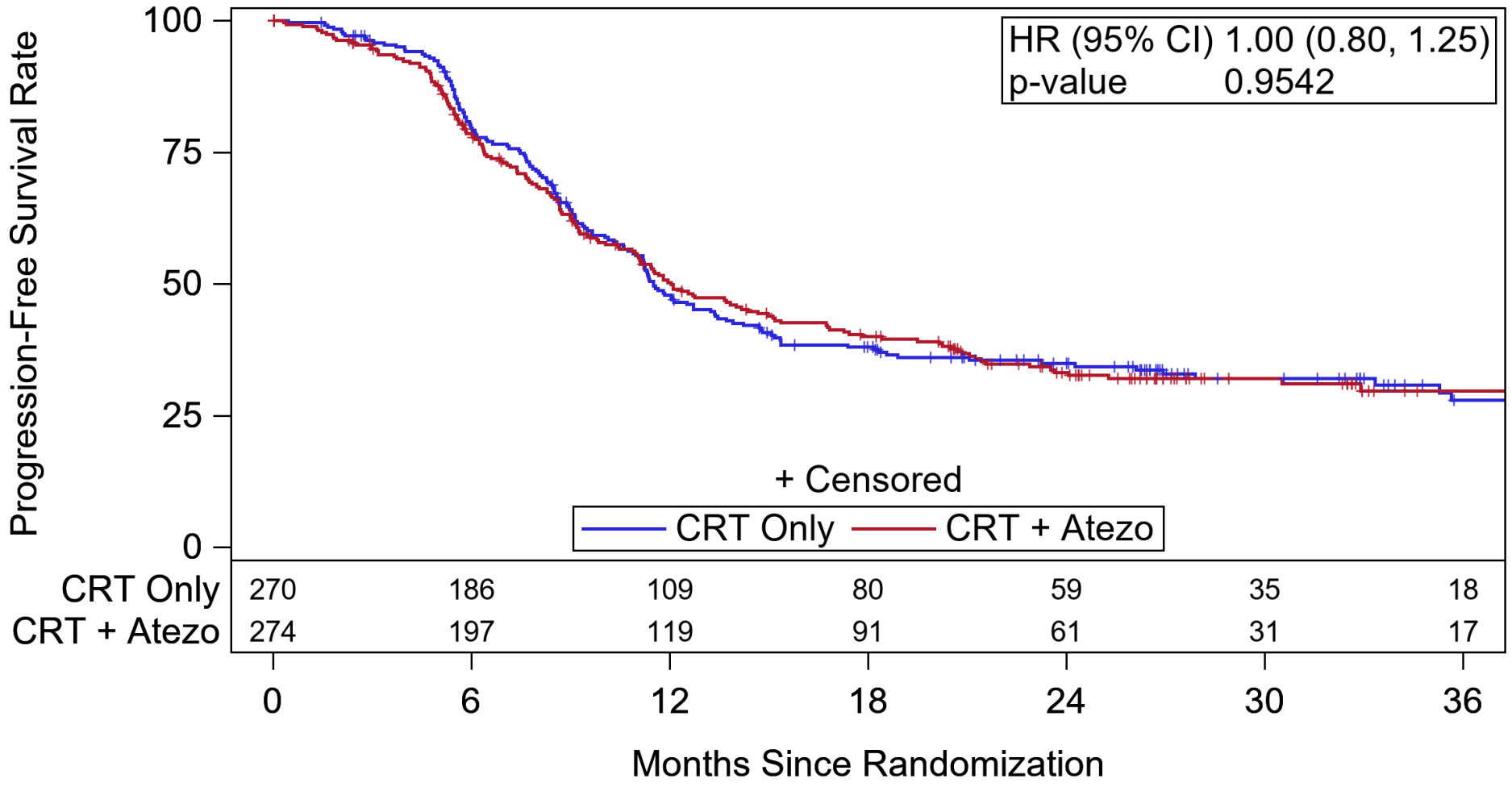
#Thoracic RT 45 Gy BID (1.5 Gy x 30 fractions ->3 weeks) or 66 Gy daily (2 Gy x 33 fractions ->6.5 weeks) beginning with cycle 2 of chemotherapy; *cisplatin (preferred) or carboplatin; first cycle of chemotherapy given prior to study entry, 3 given on study (for a total of 4 cycles); **All patients with a CR or near CR are strongly recommended to receive prophylactic cranial irradiation (PCI; 25 Gy)

Overall Survival



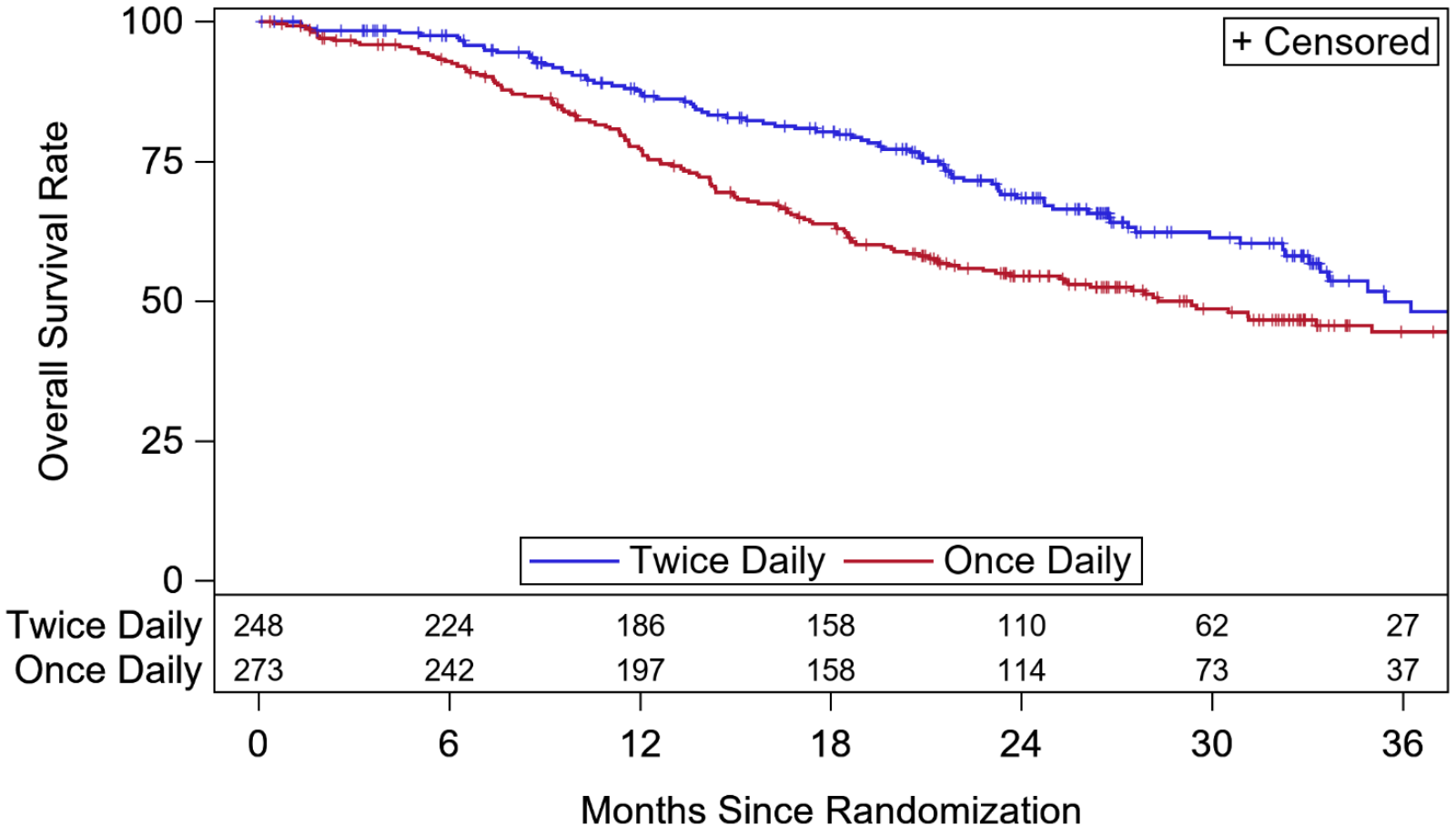
Hazard ratio and one-sided p-value stratified by RT schedule, chemotherapy, and sex

Progression-Free Survival



Hazard ratio and p-value stratified by RT schedule, chemotherapy, and sex

Overall Survival: Unadjusted RT Schedule Comparison



Note: Preliminary findings. Patients may have received twice daily RT over once daily for a number of reasons, including better performance status. Excludes patients who received no RT.

Conclusions

- Concurrent Atezolizumab did not improve survival for patients with LS-SCLC compared with standard chemoradiation.

- Twice daily radiation may be associated with improved survival compared to daily RT and could be considered the optimal choice for RT fractionation. Additional analysis is warranted.

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Expert Perspective

Kenneth Rosenzweig, MD, FASTRO

Chair, ASTRO SCLC Guideline

Icahn School of Medicine at Mount Sinai

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Interim futility results of NRG-HN005, a randomized, phase II/III non-inferiority trial for non-smoking p16+ oropharyngeal cancer patients

Sue S. Yom, MD, PhD, FASTRO
University of California, San Francisco

Disclosure & Study Team

- Disclosures: EMD Serono, Nanobiotix, Bristol-Myers Squibb, Merck, UpToDate, Springer, Elsevier
- This study was supported by funding from NCI and Bristol-Myers Squibb

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Background

- 70% of new oropharynx cancer patients in the U.S. are HPV+
- Long-term side effects of chemoradiation are a concern in this population because of their long survival times
- RTOG 1016 previously established excellent results from standard cisplatin and radiation therapy in all HPV+ patients
- NRG-HN002 was a randomized phase 2 that tested 60 Gy with or without concurrent cisplatin in nonsmoking HPV+ patients with less extensive disease
- NRG-HN005 was a phase II/III randomized study comparing two experimental arms adapted from NRG-HN002 against the control arm from RTOG 1016

NRG-HN005 Phase II Schema

- **Oropharyngeal squamous cell carcinoma, p16-positive**
- **≤ 10 pack-year history of smoking**
- **8th ed. clinical stages T1-2N1M0 or T3N0-N1M0 (8th ed. stage I-II excluding T0, T1-2N0, or any N2)**

↓

STRATIFICATION
Zubrod Performance Status: 0 vs.1

RANDOMIZE 1:1:1

Arm 1	**Arm 2**	**Arm 3**
70 Gy radiation in 6 weeks using 6 fractions per week	**60 Gy radiation in 6 weeks using 5 fractions per week**	**60 Gy radiation in 5 weeks using 6 fractions per week**
+	**+**	**+**
Cisplatin x 2 cycles	**Cisplatin x 2 cycles**	**Nivolumab x 6 cycles**

Stratified by Zubrod performance status and randomized (1:1:1) to 70 Gy IMRT over 6 weeks + Cisplatin at 100 mg/m^2 every 3 weeks (Arm 1) vs 60 Gy IMRT over 6 weeks + Cisplatin at 100 mg/m^2 every 3 weeks (Arm 2) vs 60 Gy IMRT over 5 weeks with nivolumab (Arm 3)

Method

- In phase II, for each comparison, an analysis to test for futility would be triggered when 11 events were reported
- The phase III trial would proceed if 1 or both experimental arms from phase II were not eliminated

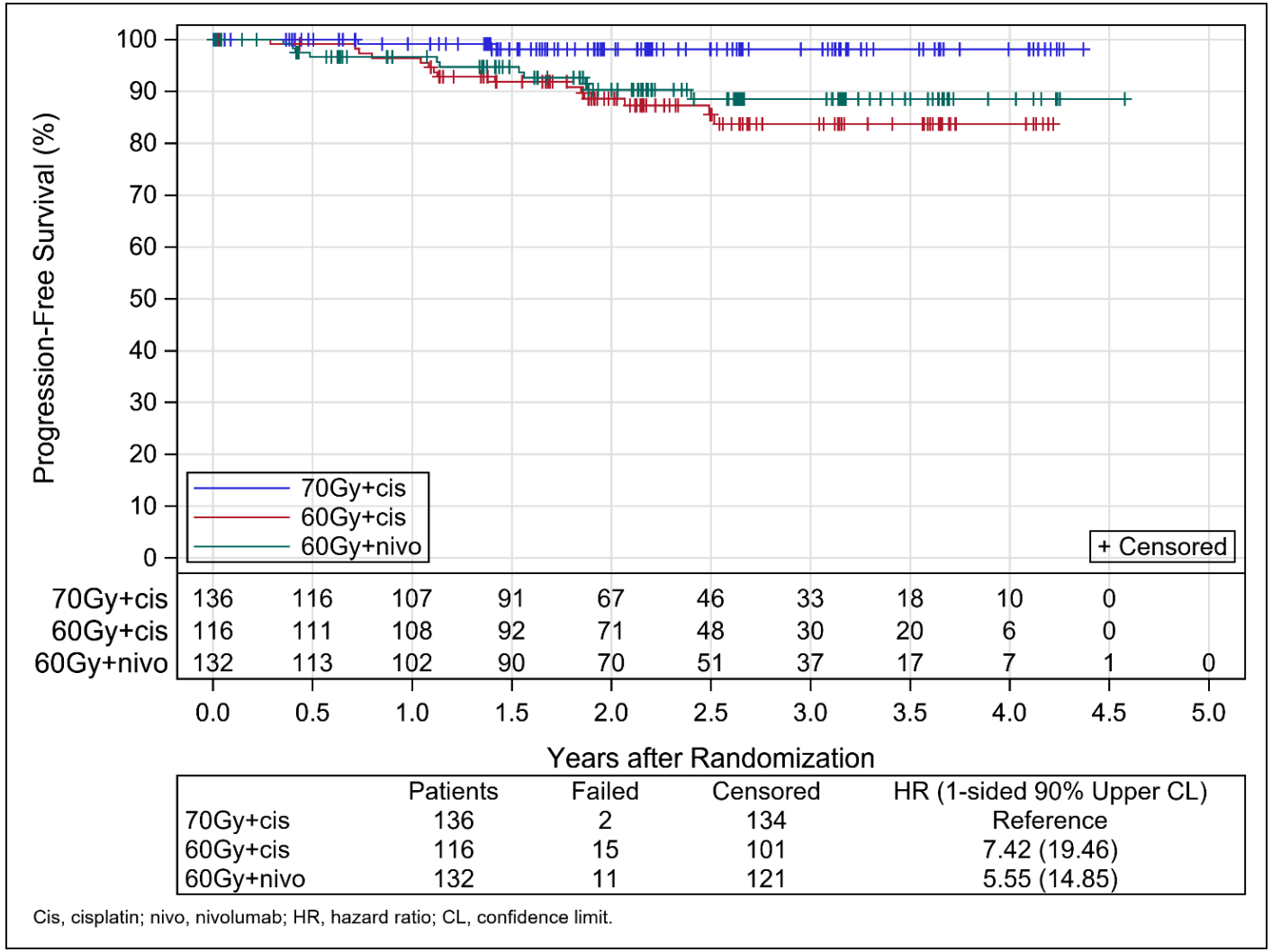
Results

- Median age was 60 years, 90.6% were male, 87.5% were White, 79.4% were never smokers
- The two futility analyses for Arm 2 and then Arm 3 both resulted in elimination of the arm
- Hazard ratios for both futility analyses were over 4 clearly exceeding the preset boundary of HR<2.4 required for noninferiority

2-Year Progression-Free Survival

At median follow-up of 2.2 years,
2-year PFS estimates are:

- Arm 1: **98.1%** (95%CI 95.4, 100)
- Arm 2: 88.6% (95%CI 82.4, 94.7)
- Arm 3: 90.3% (95%CI 84.5, 96.1)



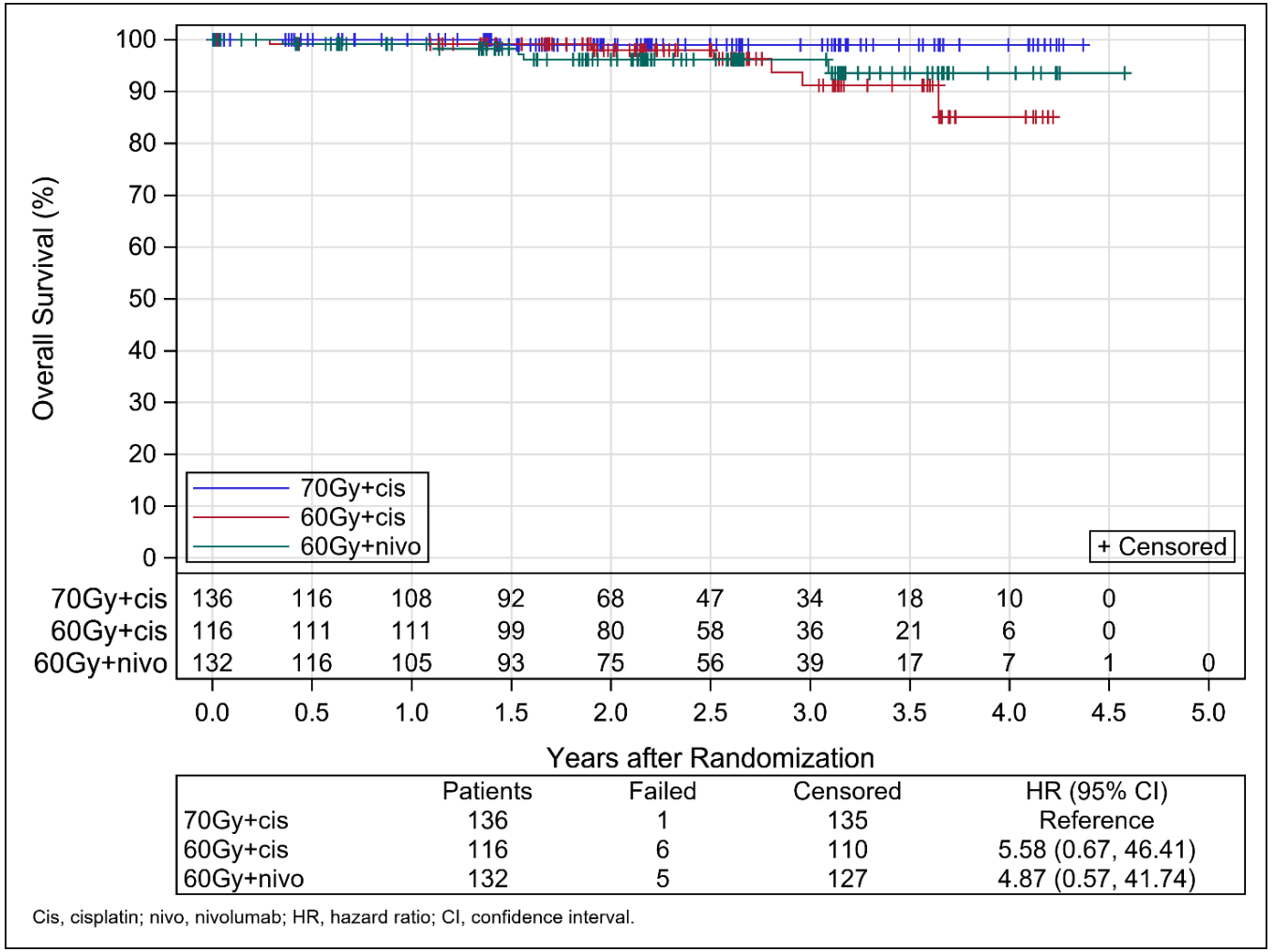
	Patients	Failed	Censored	HR (1-sided 90% Upper CL)
70Gy+cis	136	2	134	Reference
60Gy+cis	116	15	101	7.42 (19.46)
60Gy+nivo	132	11	121	5.55 (14.85)

Cis, cisplatin; nivo, nivolumab; HR, hazard ratio; CL, confidence limit.

2-Year Overall Survival

2-year OS estimates are:

- Arm 1: 99.0% (95% CI 97.0, 100)
- Arm 2: 98.0% (95% CI 95.2, 100)
- Arm 3: 96.1% (95% CI 92.3, 99.9)



	Patients	Failed	Censored	HR (95% CI)
70Gy+cis	136	1	135	Reference
60Gy+cis	116	6	110	5.58 (0.67, 46.41)
60Gy+nivo	132	5	127	4.87 (0.57, 41.74)

Cis, cisplatin; nivo, nivolumab; HR, hazard ratio; CI, confidence interval.

Conclusions

- While deintensified radiation regimens work well in the large majority of these patients, current eligibility criteria are not selective enough
- The highest rate of cure now documented in the national trial literature comes from this study
  - Phase 2 trials are not valid until tested against a contemporary standard of care
  - These results set a new benchmark for PFS expectations in this population
  - Further deintensification trials should be held to this very high standard going forward

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Expert Perspective

Danielle Margalit, MD, MPH

Vice Chair, ASTRO Oropharyngeal Cancer Guideline Update

Dana-Farber Cancer Institute

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Q&A

Submit questions in the chat, including your name/outlet, or raise your hand to ask via audio.

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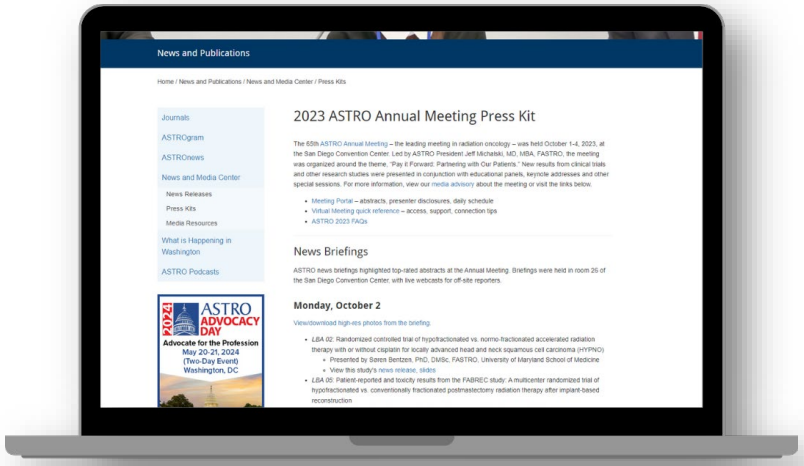
Targeting Provider Wellness

FOR EXCEPTIONAL PATIENT CARE



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