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Targeting Provider Wellness

FOR EXCEPTIONAL PATIENT CARE

News Briefing: Tuesday, October 1

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Abstract 2: A prospective, phase II study of ^{177}Lu-Dotatate in patients with surgery- and radiation-refractory meningioma: Results of the WHO grade II/III cohort

Presented by Kenneth Merrell, MD, Mayo Clinic Alix School of Medicine

Comments from Lia M. Halasz, MD, ASTRO CNS Resource Panel Chair; Fred Hutchinson Cancer Center, and from Hyun Kim, MD, ASTRO Radiopharmaceutical Therapy Committee member; Washington University School of Medicine

Abstract 150: Evaluating neurocognitive recovery following stereotactic radiosurgery and whole brain radiation therapy: Insights from a pooled analysis of three phase III trials

Presented by Hua-Ren Ryan Cherng, MD, University of Maryland Medical Center

Comments from Dr. Halasz

Abstract 215: Centering Black voices: Factors influencing a cancer patient's decision to join a clinical trial

Presented by Charlyn Gomez, BS, University of Maryland School of Medicine

Comments from Chika Madu, MD, ASTRO Community Engagement & Advocacy Committee Chair; Staten Island University Hospital

Moderator: Andrea K. Ng, MD, MPH, FASTRO, Dana-Farber/Brigham and Women's Cancer Center, incoming ASTRO Education Council Vice Chair

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A prospective, phase II study of ^{177}Lu-Dotatate in patients with surgery- and radiation-refractory meningioma: Results of the WHO grade II/III cohort

Kenneth Merrell, MD

Mayo Clinic Alix School of Medicine

Disclosure & Study Team

- Employer: Mayo Clinic
- This study was supported by Novartis.
- Full author list:

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Meningioma Background

- Most common brain tumor, > 25,000 cases annually in the US.
- **Recurrence and Prognosis:**
  - WHO Grade 2-3: **40-80%** recurrence rates.
  - WHO Grade 2-3: **2-3x** ↑ mortality risk compared to WHO Grade 1
- **Tumor behavior at recurrence is often more aggressive.**
  - Limited options post-surgery and radiation.
  - Systemic therapy remains off-label with no proven efficacy.

Clinical Outcomes Benchmark

- **Response Assessment in Neuro-Oncology (RANO)**: Systematic review of 47 studies to establish 6-Month Progression-Free Survival (PFS-6) benchmarks for future trial designs.

Kaley, Neuro-Oncology, 2014

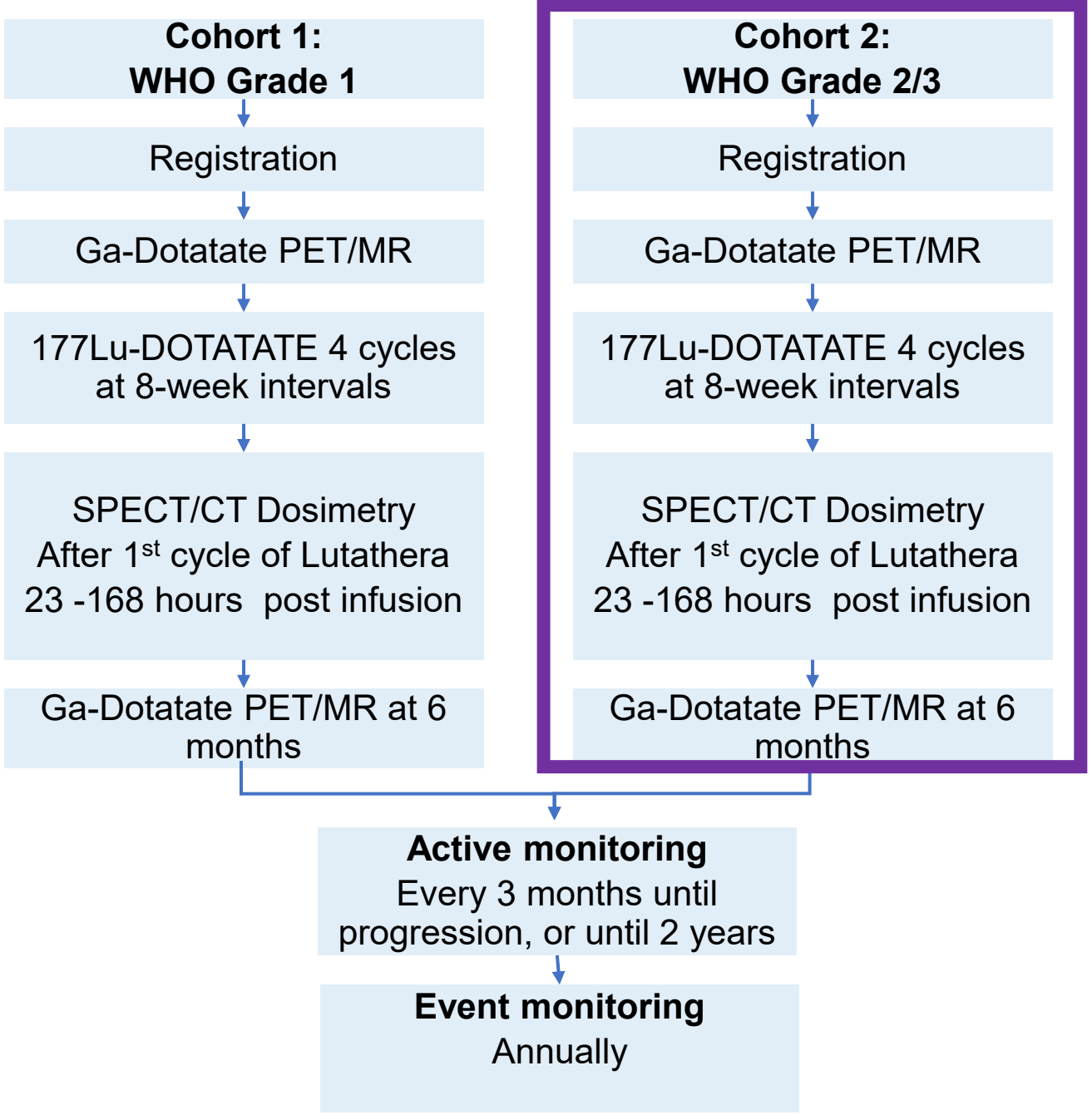
PFS-6 Rate	WHO Grade 2 and 3
Benchmark	26%
Rate not of interest	<30%
Rate probably of interest	>35%

Peptide Receptor Radionuclide Therapy (PRRT)

- **Somatostatin Receptors in Meningioma:**
  - **SSTR2** is expressed in **80-100%** of meningiomas across all grades.
- **PRRT uses a peptide (somatostatin analog) linked to a radionuclide**
  - **177Lu-DOTATATE** binds with high affinity to SSTR2.
  - Emits β-radiation, targeting SSTR2-expressing tumor cells.
  - FDA-approved for GEP-NET based on the Netter Trial.

Strosberg, NEJM, 2017

177Lu-DOTATATE : specific and targeted radiation for refractory meningioma with potential broad applicability



Simon's two-stage design with interim analysis for futility.

20 patients in **Grade 2/3** Cohort

Significance & Power: 0.07 significance (one-sided) ≥ 80% power

Primary Objectives:

1. Estimate the efficacy of 177Lu-DOTATATE by PFS-6 by grade cohort

Secondary Objectives:

1. Determine OS by grade cohort
2. Determine PFS by grade cohort
3. Determine the toxicity of 177Lu-DOTATATE in CNS population

Patient Demographics

Variable		Total (N=20)
Age years	Median (r)	66.8 (39-85)
Gender	Female	35%
ECOG Performance Status	0	55%
	1	35%
	2	10%
Neuro deficit	Yes	65%
Seizure History	Yes	60%
Corticosteroid	Yes	15%

Tumor Characteristics

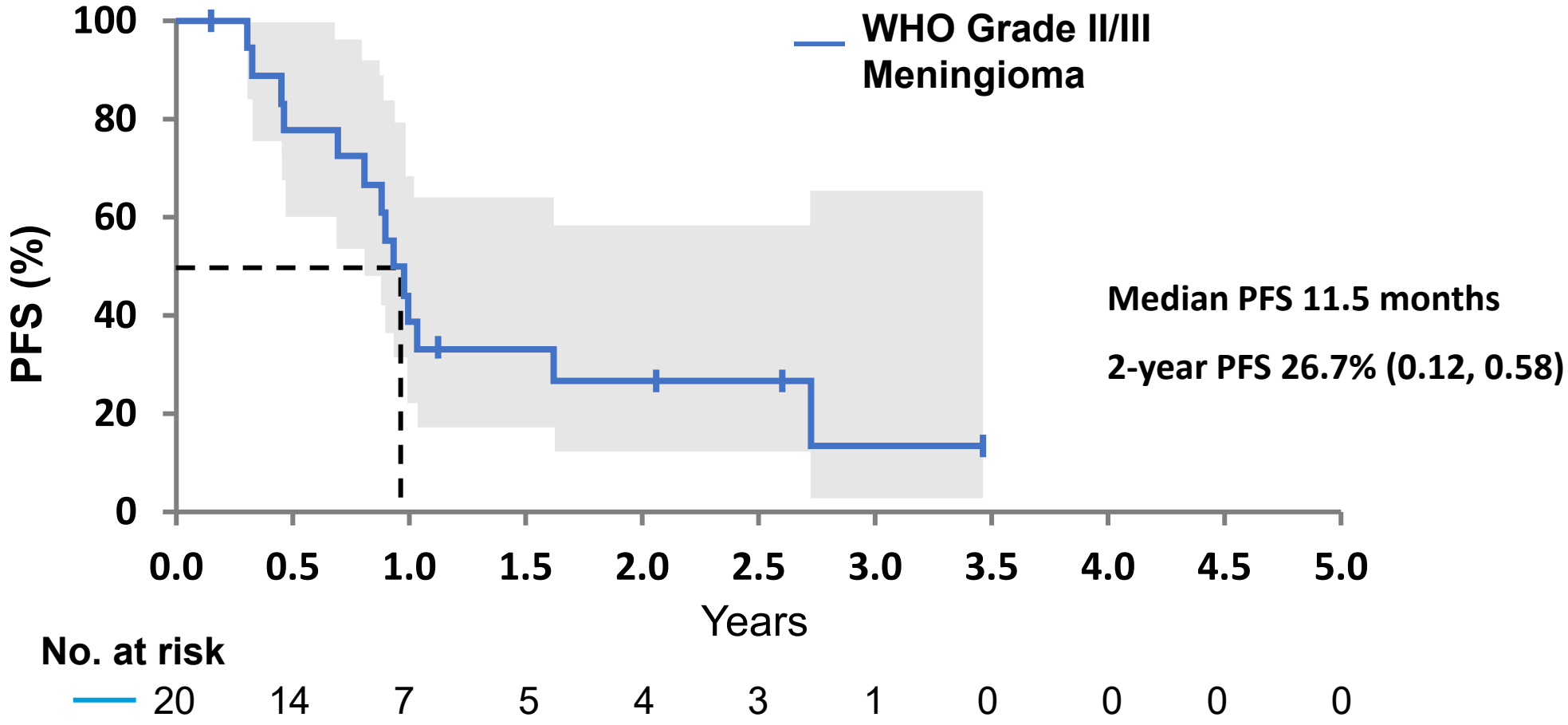
Variable		Total (N=20)
WHO Grade	2	95%
Krenning Score	2	45%
	>2	55%
Largest Tumor Dimension (cm)	Mean (SD)	3.5 (1.6)
	Range	1.8-7.5
Multifocal	Yes	75%
Prior Surgery	Yes	100%
Prior Courses of RT	Median	2
	Range	1-7
Prior Chemo	Yes	15%

Study Completion and Safety

- 70% of patients received all 4 infusions
  - For those < 4 cycles (10% AE, 10% other medical problems, 10% progression)
- No AE > grade 3 attributed to 177Lu-DOTATATE
  - Rate of grade 3 non-hematologic AE was 10%
- Overall, ^{177}Lu-DOTATATE was well tolerated

Primary Endpoint Met: PFS-6 of 77.8%

Best RECIST response achieved: Stable Disease

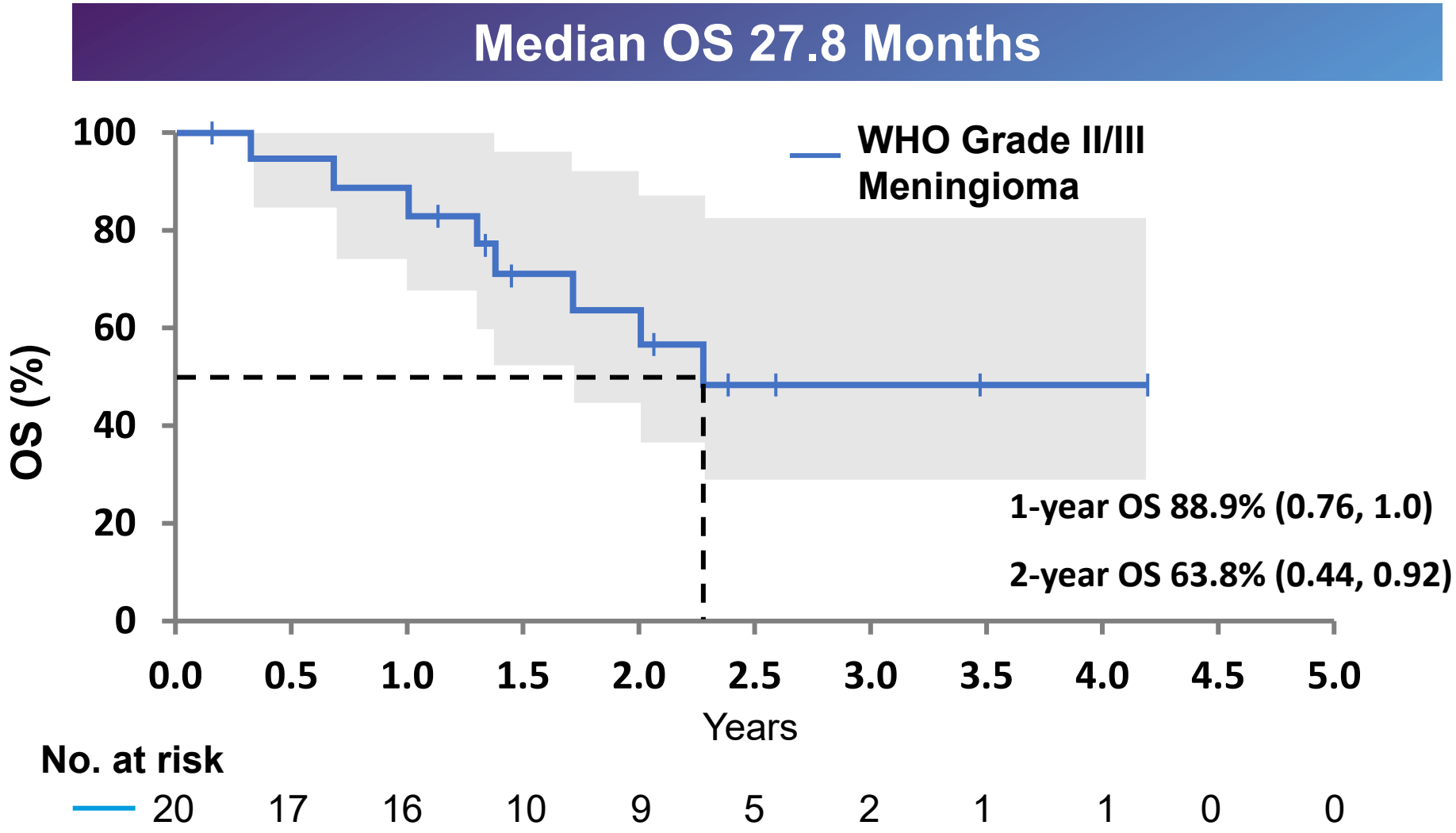


Best RECIST response achieved: Stable Disease

Measurable progression over 6 months; stable disease > 2 years

Diagnostic Imaging	Therapeutic Imaging

Overall Survival



Conclusions

Phase II Trial on 177Lu-DOTATATE for Refractory Meningioma:

- **Primary Endpoint Met:** PFS-6 (77.8%), surpassing established RANO benchmarks (>26%).
- **Clinical Efficacy:** Demonstrated clinically meaningful outcomes across a **broad patient population**, marking a significant milestone for refractory meningioma.
- **Safety:** Reasonable safety profile in CNS population.

Considering limited alternative therapies, our results support 177Lu-Dotatate as a rational therapeutic choice

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Expert Perspective

Lia Halasz, MD

Chair, ASTRO CNS Resource Panel

University of Washington-Fred Hutchinson Cancer Center

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Expert Perspective

Hyun Kim, MD

ASTRO Radiopharmaceutical Therapy Committee

Washington University School of Medicine in St. Louis

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Evaluating neurocognitive recovery following stereotactic radiosurgery and whole brain radiation therapy: Insights from a pooled analysis of three phase III trials

Hua-Ren Ryan Cherng, MD
University of Maryland Medical Center

Disclosure & Study Team

- Disclosure: I have no conflicts of interest to disclose.
- This study was supported by study was supported by grant P30CA134274 from the National Cancer Institute.
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Background

- While there are data describing the onset and incidence of cognitive side effects following brain radiation for brain metastases, there is not as much research with regards to the long-term cognitive changes and potential functional recovery that patients may experience after they experience their initial cognitive toxicities
- Our study sought to estimate the incidence of full neurocognitive function recovery after side effects of brain radiation and to assess whether certain types of radiation techniques confer higher chances of this recovery

Method

- A pooled analysis of three large phase III randomized clinical trials (N107C, N0574, CC001) was performed. 288 patients with long term cognitive testing data and who met pre-specified trial criteria for cognitive toxicity were included in this analysis.
- Full cognitive recovery was defined as patients no longer exhibiting a 1 or more standard deviation decline from baseline on any cognitive test.

Postoperative stereotactic radiosurgery compared with whole brain radiotherapy for resected metastatic brain disease (NCCTG N107C/CEC·3): a multicentre, randomised, controlled, phase 3 trial

Paul D Brown, Karla V Ballman, Jane H Cerhan, S Keith Anderson, Xiomara W Carrero, Anthony C Whitton, Jeffrey Greenspoon, Ian F Parney, Nadia N I Laack, Jonathan B Ashman, Jean-Paul Bahary, Costas G Hadjipanayis, James J Urbanic, Fred G Barker II, Elana Farace, Deepak Khuntia, Caterina Giannini, Jan C Buckner, Evanthia Galanis, David Roberge

Original Investigation

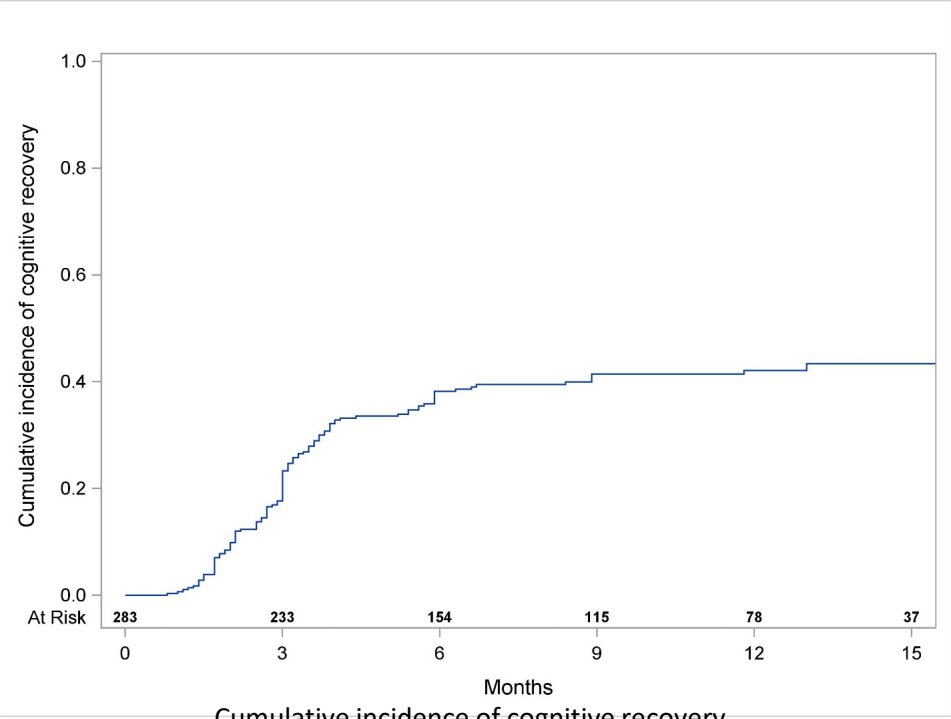
Effect of Radiosurgery Alone vs Radiosurgery With Whole Brain Radiation Therapy on Cognitive Function in Patients With 1 to 3 Brain Metastases
A Randomized Clinical Trial

Paul D. Brown, MD; Kurt Jaeckle, MD; Karla V. Ballman, PhD; Elana Farace, PhD; Jane H. Cerhan, PhD; S. Keith Anderson, MS; Xiomara W. Carrero, BS; Fred G. Barker II, MD; Richard Deming, MD; Stuart H. Burri, MD; Cynthia Ménard, MD; Caroline Chung, MD; Volker W. Stieber, MD; Bruce E. Pollock, MD; Evanthia Galanis, MD; Jan C. Buckner, MD; Anthony L. Asher, MD

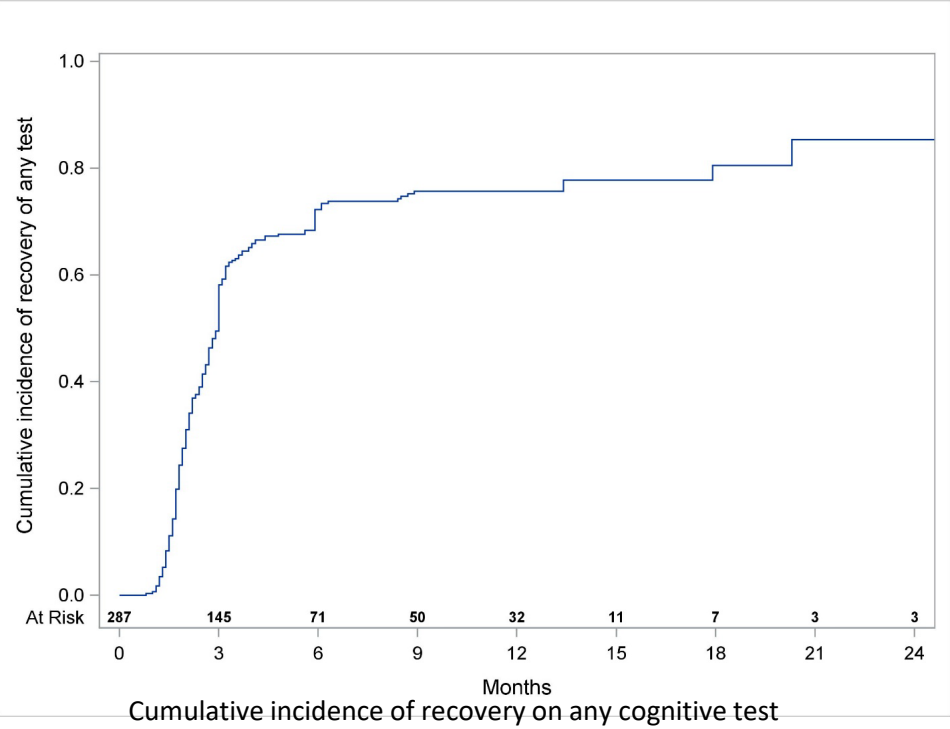
Hippocampal Avoidance During Whole-Brain Radiotherapy Plus Memantine for Patients With Brain Metastases: Phase III Trial NRG Oncology CCO01

Paul D. Brown, MD[1]; Vinai Gondi, MD[2]; Stephanie Pugh, PhD[3]; Wolfgang A. Tome, PhD[4]; Jeffrey S. Wefel, PhD[5]; Terri S. Armstrong, PhD[6]; Joseph A. Bovi, MD[7]; Cliff Robinson, MD[8]; Andre Konski, MD, MBA[9]; Deepak Khuntia, MD[10]; David Grosshans, MD, PhD[5]; Tammie L. S. Benzinger, MD, PhD[8]; Deborah Bruner, PhD[11]; Mark R. Gilbert, MD[6]; David Roberge, MD[12]; Vijayananda Kundapur, MD[13]; Kiran Devisetty, MD[14]; Sunjay Shah, MD[15]; Kenneth Usuki, MD[16]; Bethany Marie Anderson, MD[17]; Baldassarre Stea, MD, PhD[18]; Harold Yoon, MD[19]; Jing Li, MD[5]; Nadia N. Laack, MD[1]; Tim J. Kruser, MD[20]; Steven J. Chmura, MD, PhD[21]; Wenyin Shi, MD[22]; Snehal Deshmukh, MS[3]; Minesh P. Mehta, MD[23]; and Lisa A. Kachnic, MD[24] for NRG Oncology

Results – pooled incidence of cognitive recovery



Cumulative incidence of cognitive recovery

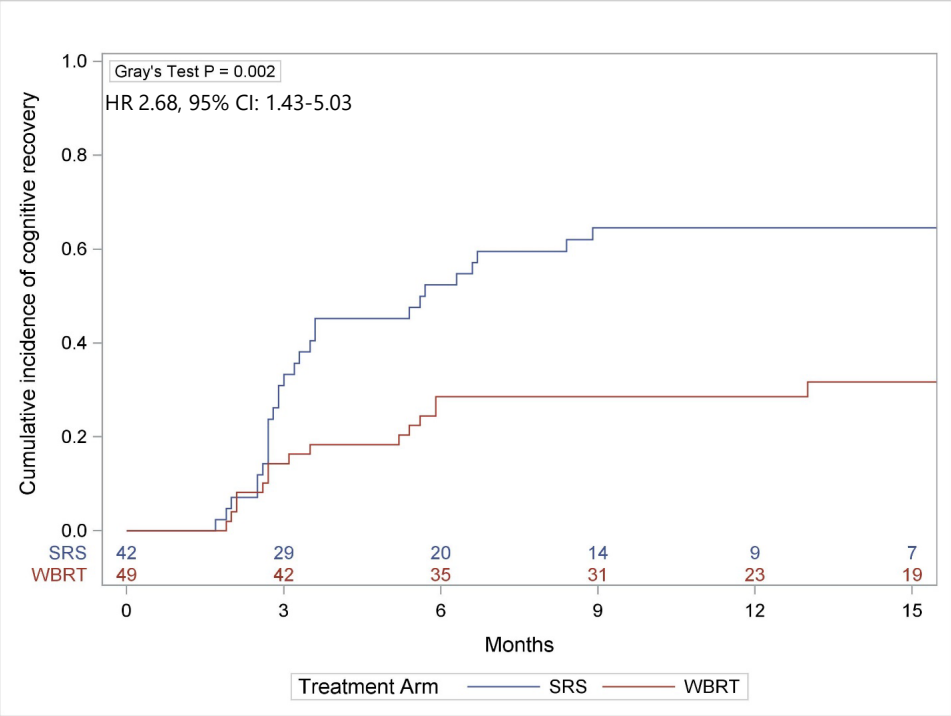


Cumulative incidence of recovery on any cognitive test

- 288 patients who experienced trial-defined neurocognitive function failure were included. Pooled incidence of full CR was 38% and 42% at 6- and 12-months after onset of neurocognitive failure, respectively.

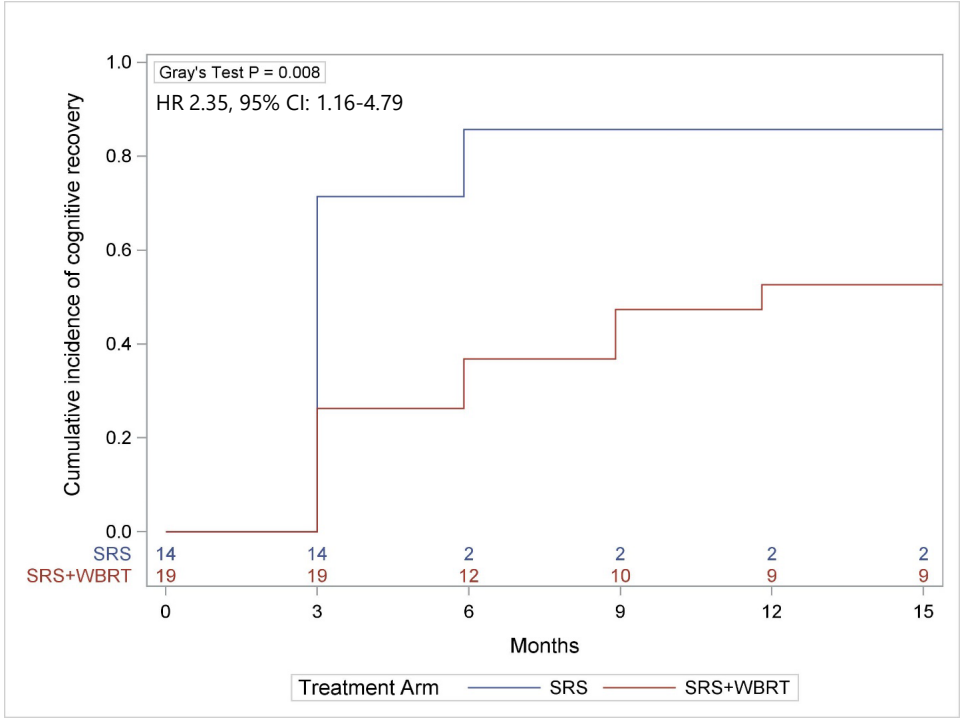
Results – Cognitive Recovery by Trial (N107C and N0574)

N107C



Cumulative incidence of cognitive recovery by arm (postoperative SRS vs WBRT)

N0574



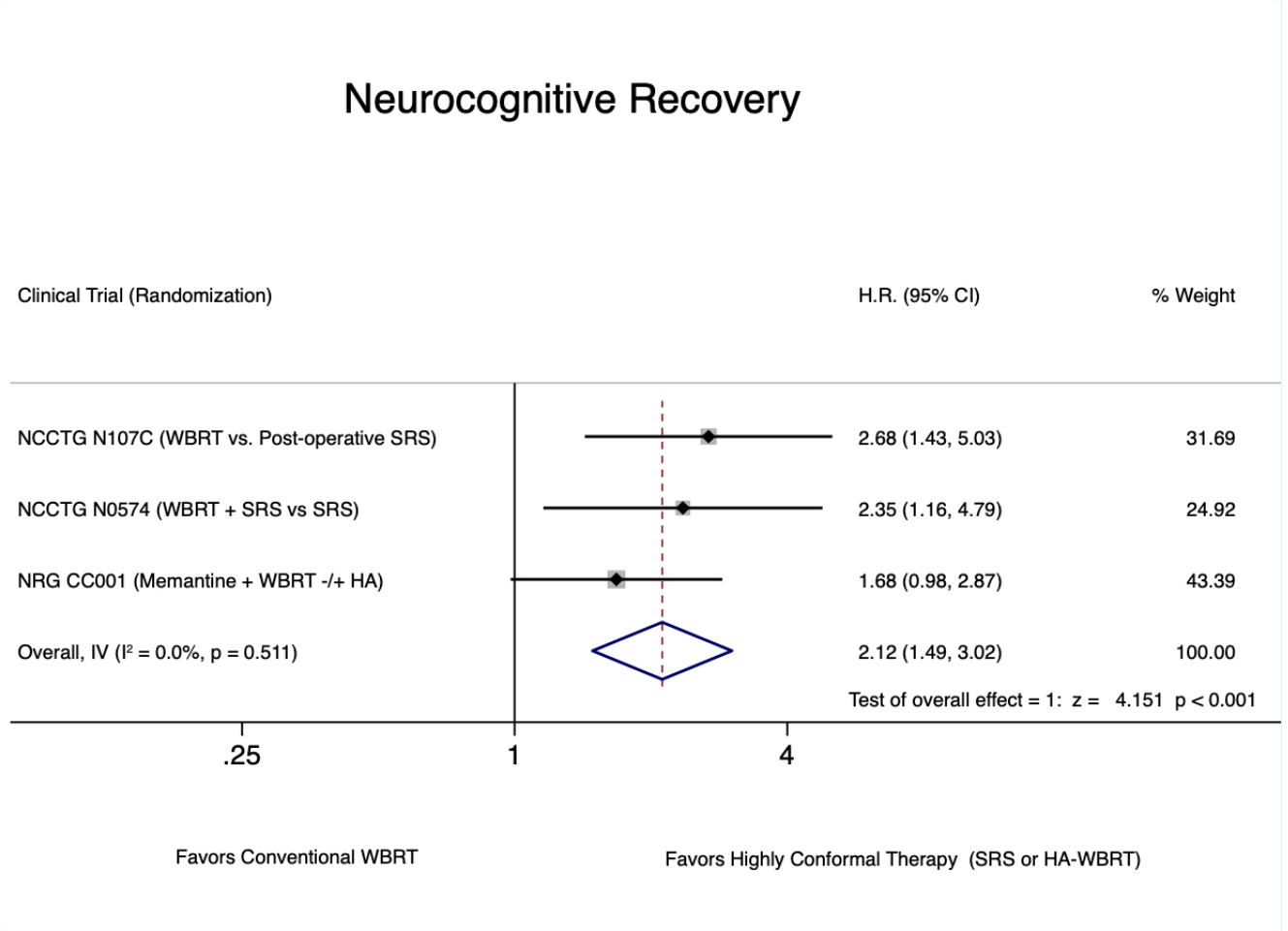
Cumulative incidence of cognitive recovery by arm (SRS vs SRS + WBRT for intact BM)

- Cumulative incidence of full CR was significantly greater with more conformal radiation techniques (SRS vs WBRT, SRS vs. SRS+WBRT)

Results – prognostic factors associated with cognitive recovery

Factor	Hazard Ratio	95% CI	p-value
Treatment arm (SRS vs WBRT [R])	2.42	1.70, 3.45	**<0.0001**
Age (≤ 60 vs > 60 [R])	1.29	0.91, 1.84	0.15
Histology (lung vs non-lung [R])	0.79	0.55, 1.13	0.20
Performance status (0 vs 1-2 [R])	1.26	0.88, 1.84	0.19

Time to cognitive failure: pooled multivariate Cox proportional hazards model comparing SRS and WBRT



Conclusions

- This is the first description of a novel concept of *cognitive recovery* (defined as the absence of cognitive failure [no longer exhibiting a 1 or more SD decline from baseline on any cognitive test])
- Our analysis reveals that a sizeable proportion (~40%) of patients who experience neurocognitive function failure following brain radiation therapy eventually demonstrate full cognitive recovery. Nearly 2/3 of patients with longer term cognitive testing data maintained cognitive recovery.
- At the individual trial level and on pooled meta-analysis, conformal radiation techniques (ie. SRS and/or HA-WBRT compared to conventional WBRT) confers substantial benefit with regards to cognitive recovery
- These findings may help counsel patients about their likelihood of meaningful cognitive improvement after radiation and underscore that neurocognitive decline is not necessarily permanent which may also affect clinical trial design

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Expert Perspective

Lia Halasz, MD

Chair, ASTRO CNS Resource Panel

University of Washington-Fred Hutchinson Cancer Center

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Centering Black voices: Factors influencing a cancer patient's decision to join a clinical trial

Charlyn Gomez, BS
University of Maryland School of Medicine

Disclosure & Study Team

I have no conflicts of interest to disclose.

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Background

- Longstanding issue of **underrepresentation of diverse populations** in clinical trials
- Black cancer patients face worse clinical outcomes due to poor social determinants of health
- Our first study on breast cancer patients showed that Black females were **less likely to trust their cancer team**, more likely to believe that **research harms minorities**, and that **God determines health, not research**

Method

Cross-Sectional Study

45-Item Questionnaire

- Cancer Type: Thoracic, Head & Neck, Gynecologic, Gastrointestinal
- 1 month - 5 years post-treatment

UMMC

BWMC

1. Illness and death are God's will and are not necessarily affected by research.

1-Strongly Agree 2-Agree 3-Neither Agree or Disagree 4- Disagree 5- Strongly Disagree

13. It would be difficult to find time to participate in a research study.

1-Strongly Agree 2-Agree 3-Neither Agree or Disagree 4- Disagree 5- Strongly Disagree

14. These roles sometimes occupy much of people's time. Please indicate which roles apply to you:

___Student ___Full-time employee ___Part-time employee ___Spouse/"significant other"

___Parent ___Grandparent ___Adult-Caregiver ___Child-Caregiver

___Church leader ___Other major role that I haven't mentioned:_____

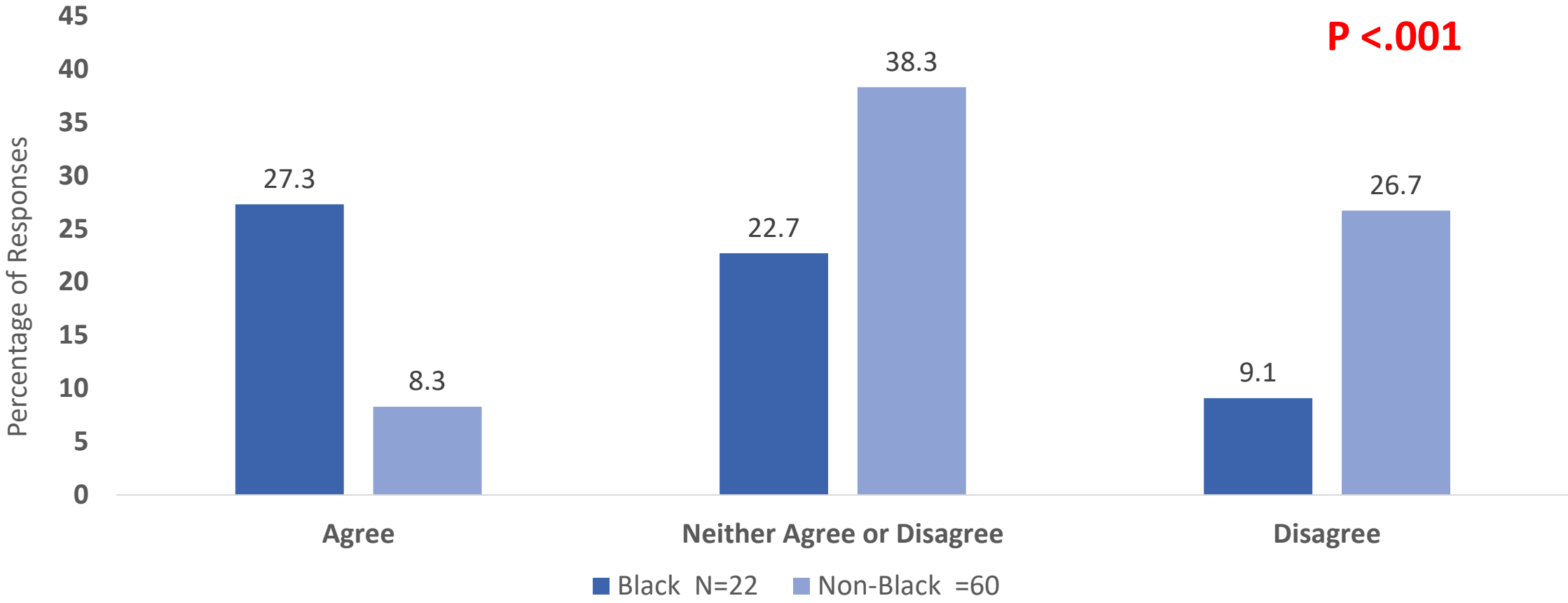
Results

1. Non-Black Patient Demographics (%):
   a. White: 88 (92.6)
   b. Asian: 4 (4.2)
   c. Other: 3 (3.2)

Characteristic	Black (N=42)	Non-Black (N=95)[1]	p-value
Survey compliance (%)	27 (64.3)	69 (72.6)	NS
Prior clinical trial participation (%)	3 (15.8)	10 (18.2)	NS
Age			
Median (Range)	69 (49-88)	68 (29-91)	NS
Sex			
Female (%)	29 (69)	45 (47.4)	0.019
Marital status			
Married (%)	10 (37)	62 (74)	0.002
Household Income			
Median (Range)	69,318 (34,884-171,848)	111,378 (31,947- 250,001)	<0.001
Household Composition			
Lives with family (%)	6 (33.3)	7 (12.7)	.004
Charlson Comorbidity Index			
Mean (Range)	3.63 (1-7)	2.80 (0-6)	0.017
Insurance			
Private (%)	10 (23.8)	38 (40)	NS
Medicare/Medicaid (%)	31 (73.8)	52 (54.7)	NS
Other Government (%)	1 (2.4)	5 (5.3)	NS

Results

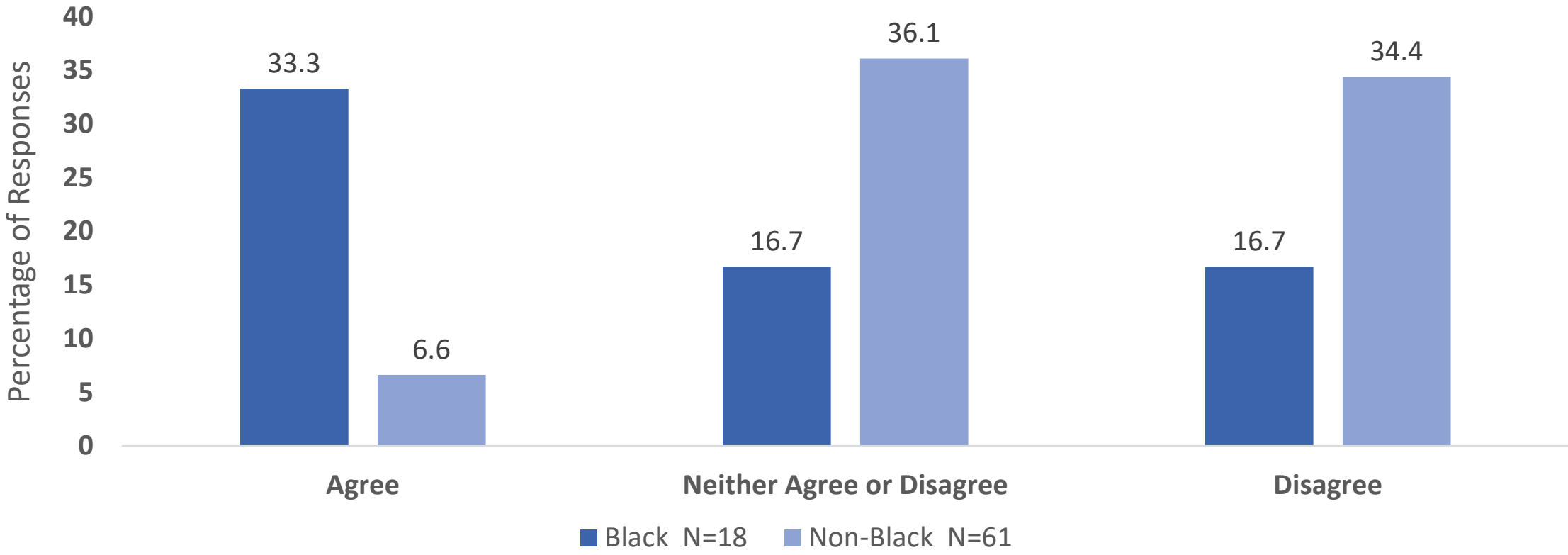
Figure 1: "God determines wellness, not results of research."



Results

Figure 2: "Illness and death are God's will and not necessarily affected by research."

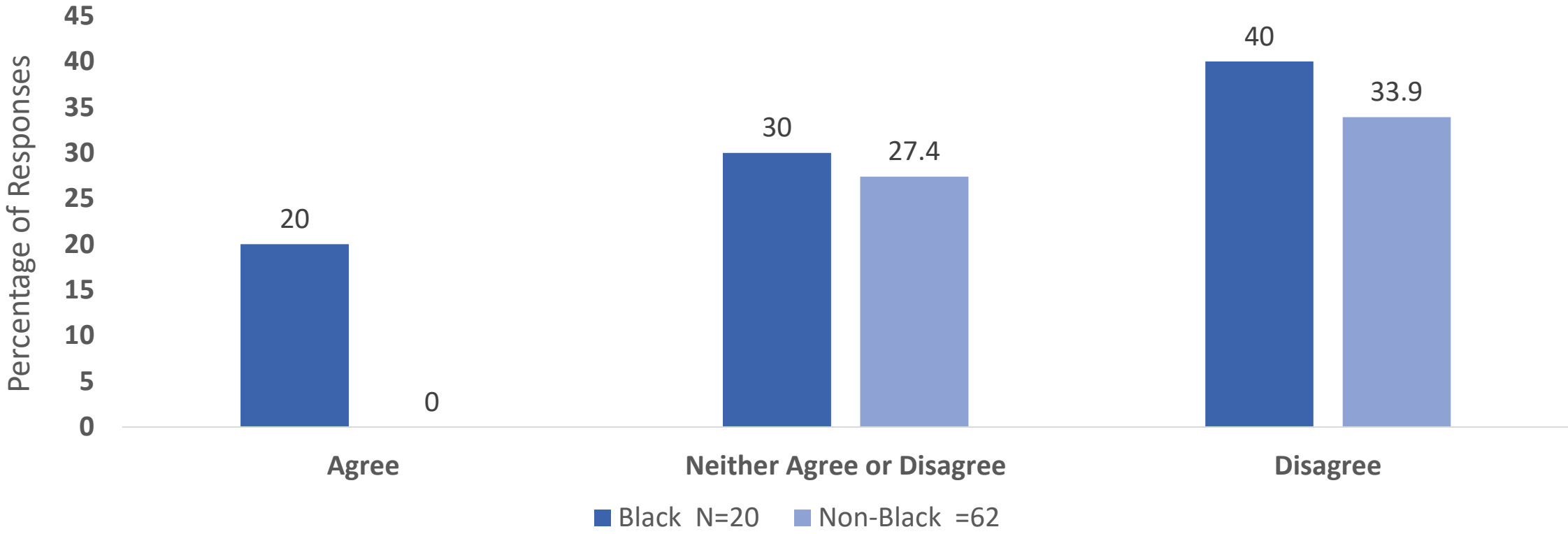
P= 0.001



Results

Figure 3: "Research is part of a conspiracy to negatively impact the health of minority groups."

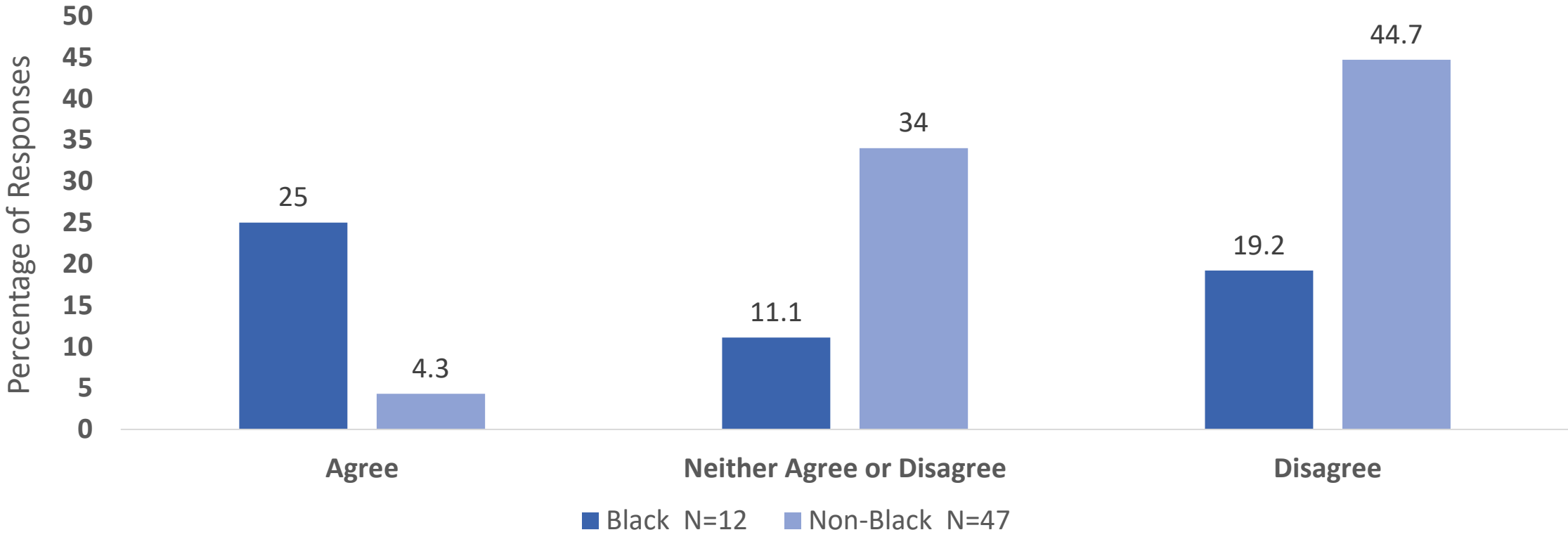
P <.001



Results

Figure 4: "Research could provide information about my health I would rather not know about."

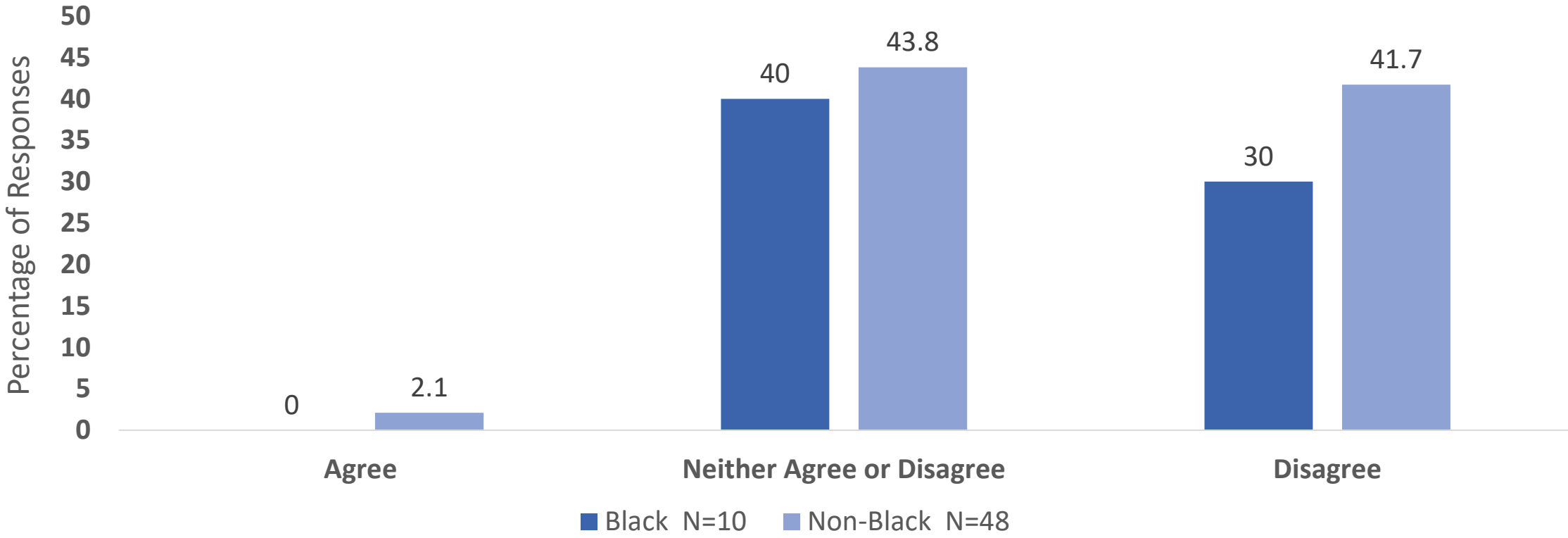
P=0.037



Results

Figure 5: "There isn't anything for me to gain by participating in research."

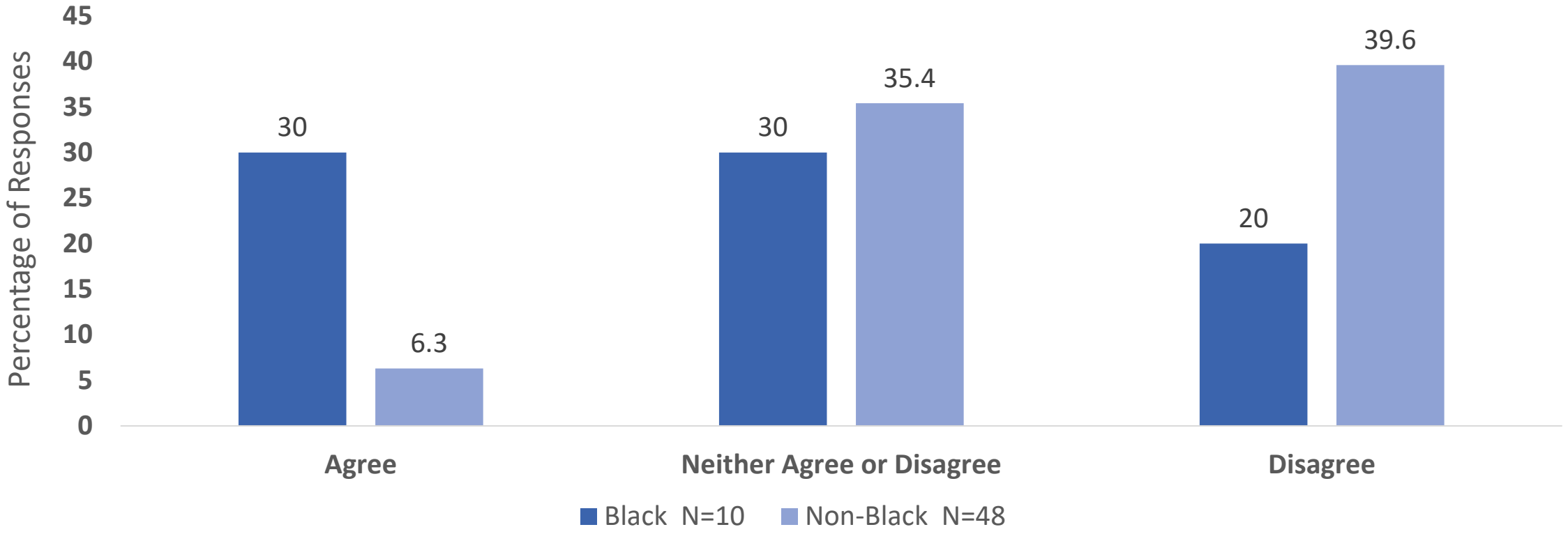
P=0.038



Results

Figure 6: "There isn't anything for my community to gain by participating in research."

P=0.031



Conclusions

- Clinicians and their research team should **be prepared to address the spiritual themes** which impact Black participants' decision-making
  - What training and resources do we need to do so?
- There is a difference between a patient's trust in their care team *versus* clinical research
  - Avoid compromising physician-patient relationship
  - Opportunity for patient-centered education

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Expert Perspective

Chika Madu, MD

Chair, ASTRO Community Engagement & Advocacy Committee

Staten Island University Hospital/Northwell Health

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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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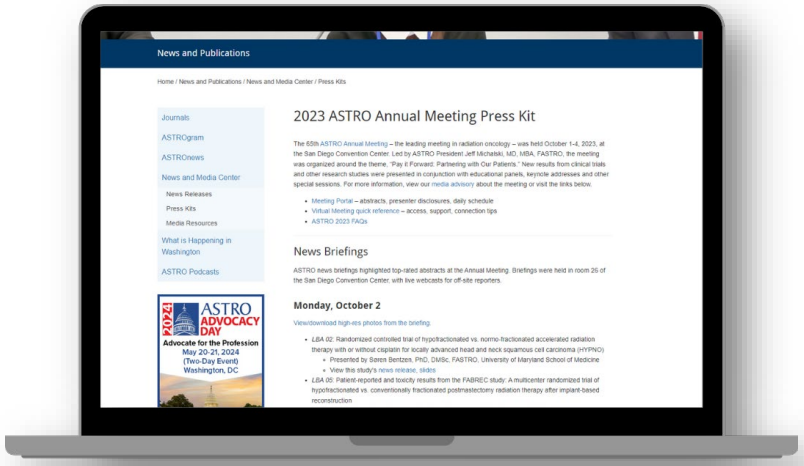
Targeting Provider Wellness

FOR EXCEPTIONAL PATIENT CARE



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