2022 ASCO ANNUAL MEETING

ONCO NOUVELLE-AQUITAINE
Réseau Régional de Cancérologie

BRIO
BORDEAUX | Recherche Intégrée Oncologie

Les « Scoops » en Soins Oncologiques de Support

Dr Sophie MORIN

Institut Bergonié Bordeaux

Bergonié
UNICANCER
NOUVELLE-AQUITAINE

Liens d’intérêts

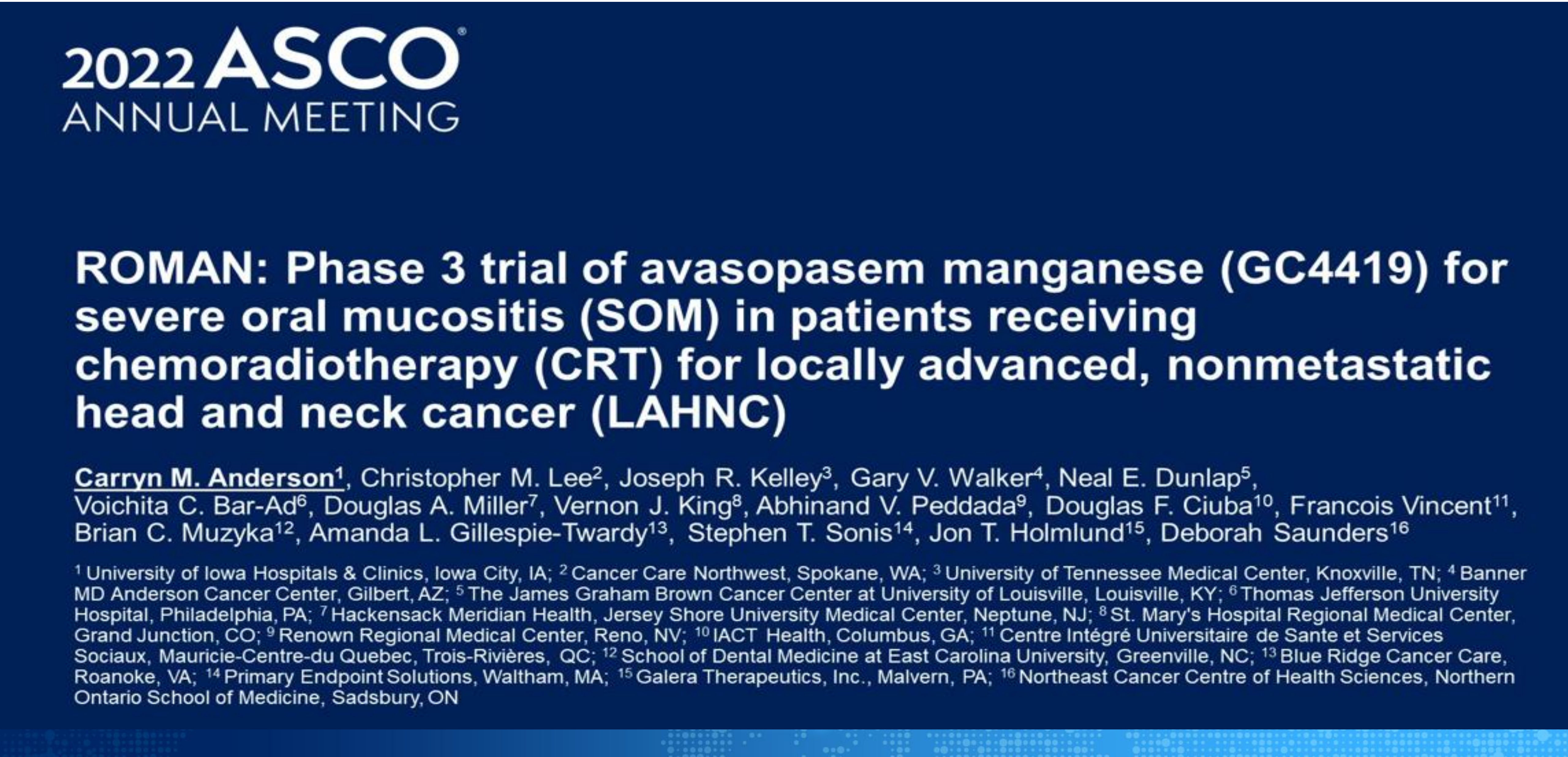
- Aucun

SCOOP !?

SOS dans le Parcours SEIN – Gestion des toxicités aux ADC

Des nouveautés ?

Gestion des toxicités en ORL, effet immunomodulateur du paracétamol, alopécie et le chemobrain



2022 ASCO ANNUAL MEETING

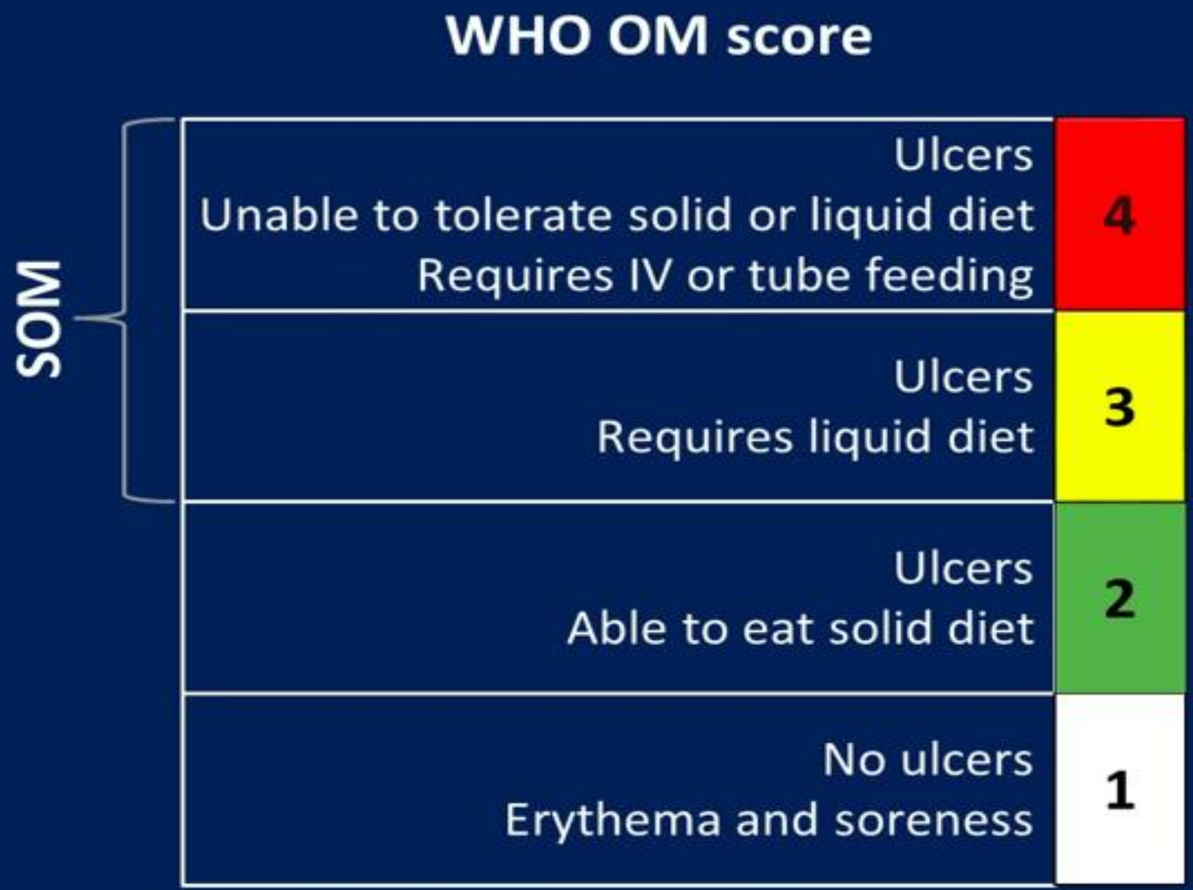
ROMAN: Phase 3 trial of avasopasem manganese (GC4419) for severe oral mucositis (SOM) in patients receiving chemoradiotherapy (CRT) for locally advanced, nonmetastatic head and neck cancer (LAHNC)

Carryn M. Anderson[1], Christopher M. Lee[2], Joseph R. Kelley[3], Gary V. Walker[4], Neal E. Dunlap[5], Voichita C. Bar-Ad[6], Douglas A. Miller[7], Vernon J. King[8], Abhinand V. Peddada[9], Douglas F. Ciuba[10], Francois Vincent[11], Brian C. Muzyka[12], Amanda L. Gillespie-Twardy[13], Stephen T. Sonis[14], Jon T. Holmlund[15], Deborah Saunders[16]

[1] University of Iowa Hospitals & Clinics, Iowa City, IA; [2] Cancer Care Northwest, Spokane, WA; [3] University of Tennessee Medical Center, Knoxville, TN; [4] Banner MD Anderson Cancer Center, Gilbert, AZ; [5] The James Graham Brown Cancer Center at University of Louisville, Louisville, KY; [6] Thomas Jefferson University Hospital, Philadelphia, PA; [7] Hackensack Meridian Health, Jersey Shore University Medical Center, Neptune, NJ; [8] St. Mary's Hospital Regional Medical Center, Grand Junction, CO; [9] Renown Regional Medical Center, Reno, NV; [10] IACT Health, Columbus, GA; [11] Centre Intégré Universitaire de Sante et Services Sociaux, Mauricie-Centre-du Quebec, Trois-Rivières, QC; [12] School of Dental Medicine at East Carolina University, Greenville, NC; [13] Blue Ridge Cancer Care, Roanoke, VA; [14] Primary Endpoint Solutions, Waltham, MA; [15] Galera Therapeutics, Inc., Malvern, PA; [16] Northeast Cancer Centre of Health Sciences, Northern Ontario School of Medicine, Sadsbury, ON

Background

- IMRT + cisplatin SoC for LAHNC
- ~70% of patients develop SOM (WHO grade 3 or 4)
  - Grade 4 OM: ~20–25%
  - Median duration: 3–4 weeks
  - Median onset: ~40 Gy
- No FDA-approved HNC SOM drugs

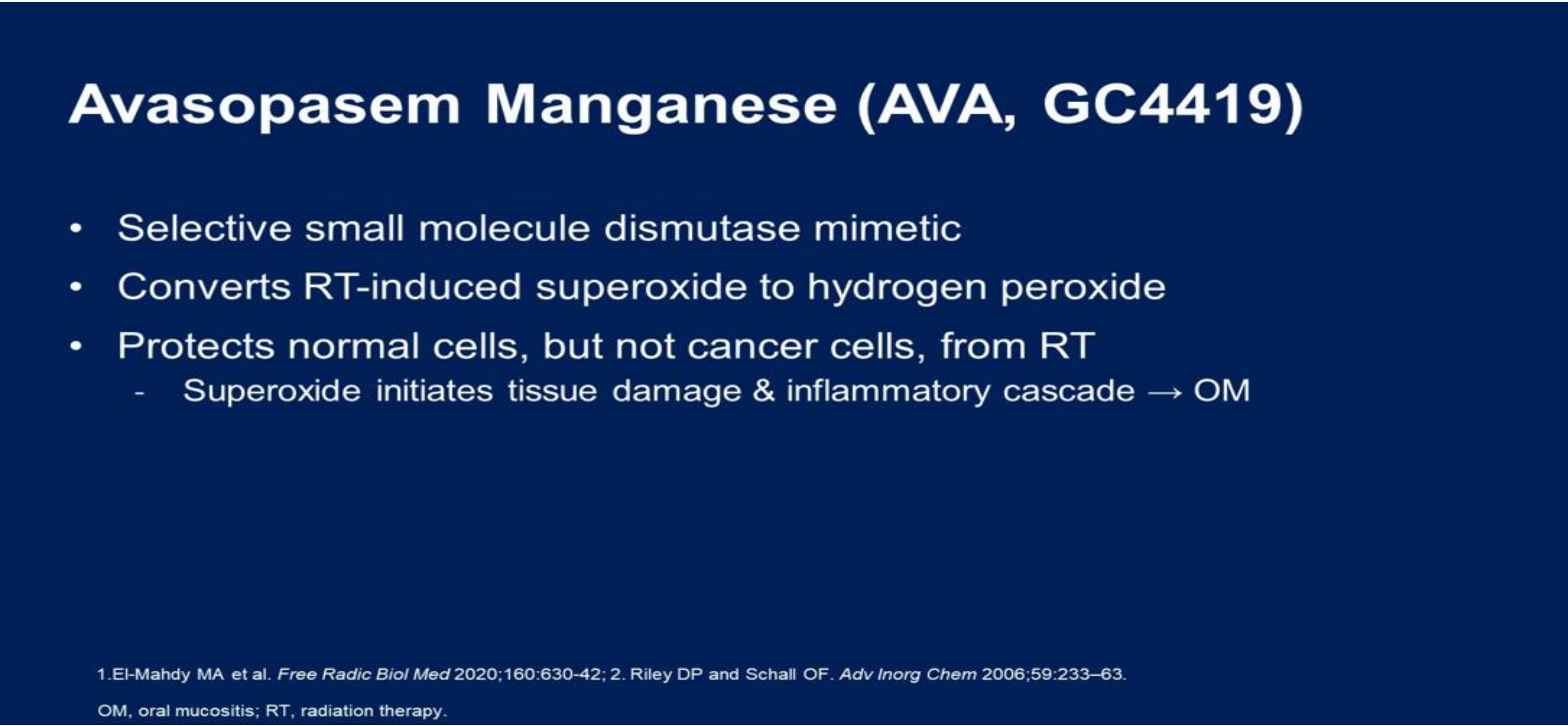


WHO OM score

SOM	Ulcers Unable to tolerate solid or liquid diet Requires IV or tube feeding	4
SOM	Ulcers Requires liquid diet	3
	Ulcers Able to eat solid diet	2
	No ulcers Erythema and soreness	1

1. Henke M et al. *J Clin Oncol* 2011;29:2815-20; 2. Le QT et al. *J Clin Oncol* 2011;29:2808-14; 3. Kudrimoti MA et al. *J Biotechnol* 2016;239:115-25.

FDA, United States Food and Drug Administration; IMRT, intensity-modulated radiation therapy; LAHNC, locally advanced head and neck cancer; OM, oral mucositis; SoC, standard of care; SOM, severe OM; WHO, World Health Organization.

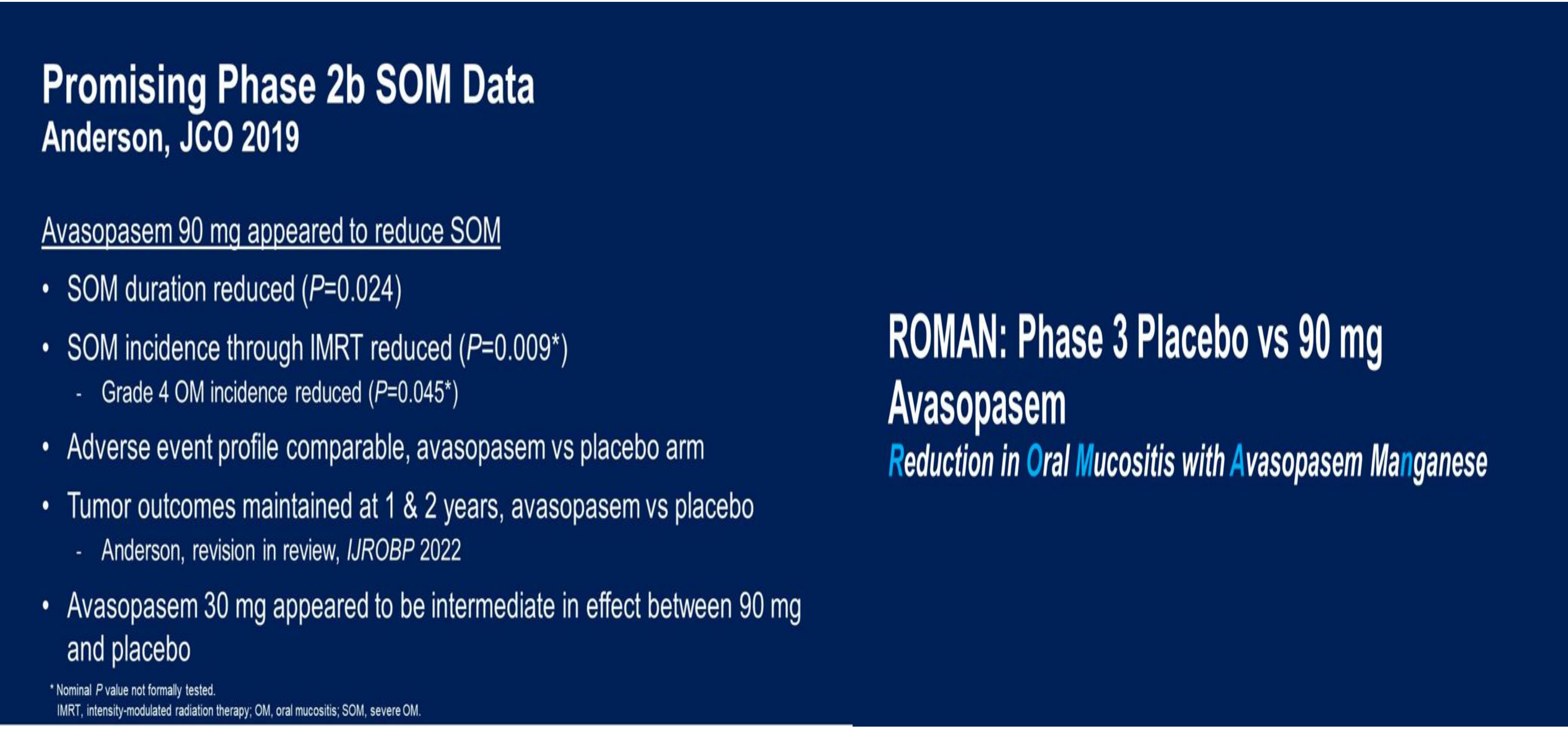


Avasopasem Manganese (AVA, GC4419)

- Selective small molecule dismutase mimetic
- Converts RT-induced superoxide to hydrogen peroxide
- Protects normal cells, but not cancer cells, from RT
  - Superoxide initiates tissue damage & inflammatory cascade → OM

1.El-Mahdy MA et al. *Free Radic Biol Med* 2020;160:630-42; 2. Riley DP and Schall OF. *Adv Inorg Chem* 2006;59:233–63.

OM, oral mucositis; RT, radiation therapy.



Promising Phase 2b SOM Data

Anderson, JCO 2019

Avasopasem 90 mg appeared to reduce SOM

- SOM duration reduced (*P*=0.024)
- SOM incidence through IMRT reduced (*P*=0.009*)
  - Grade 4 OM incidence reduced (*P*=0.045*)
- Adverse event profile comparable, avasopasem vs placebo arm
- Tumor outcomes maintained at 1 & 2 years, avasopasem vs placebo
  - Anderson, revision in review, *IJROBP* 2022
- Avasopasem 30 mg appeared to be intermediate in effect between 90 mg and placebo

* Nominal *P* value not formally tested.
IMRT, intensity-modulated radiation therapy; OM, oral mucositis; SOM, severe OM.

ROMAN: Phase 3 Placebo vs 90 mg Avasopasem

Reduction in Oral Mucositis with Avasopasem Manganese

GT-301: The ROMAN Trial

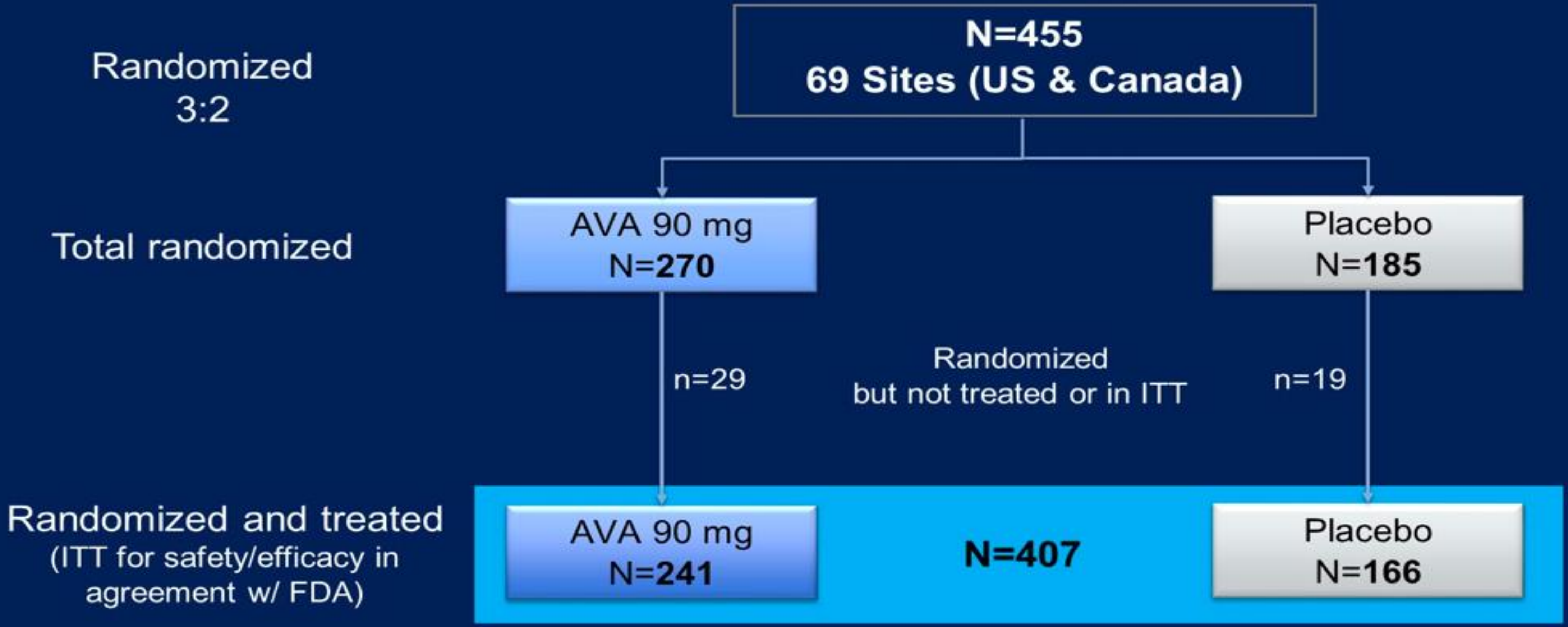
Population	• Oral cavity/oropharynx tumor • Locally advanced, squamous cell • Eligible for SoC: 7 weeks IMRT + cisplatin
Treatment	• Avasopasem 90 mg or placebo • 60-minute IV infusion, Mon-Fri • Ending ≤60 mins pre-RT
Stratification factors	• Surgery status: post-op or definitive • Cisplatin schedule: q3wks or weekly

Randomize (3:2)

- **Avasopasem 90 mg x 7 weeks**
- **Placebo x 7 weeks**

IMRT, intensity-modulated RT; RT, radiation therapy; SoC, standard of care.

Consort Diagram



Randomized
3:2

N=455
69 Sites (US & Canada)

Total randomized

AVA 90 mg
N=**270**

Placebo
N=**185**

n=29

Randomized
but not treated or in ITT

n=19

Randomized and treated
(ITT for safety/efficacy in agreement w/ FDA)

AVA 90 mg
N=**241**

N=407

Placebo
N=**166**

AVA, avasopasem; FDA, United States Food and Drug Administration; ITT, intent-to-treat population.

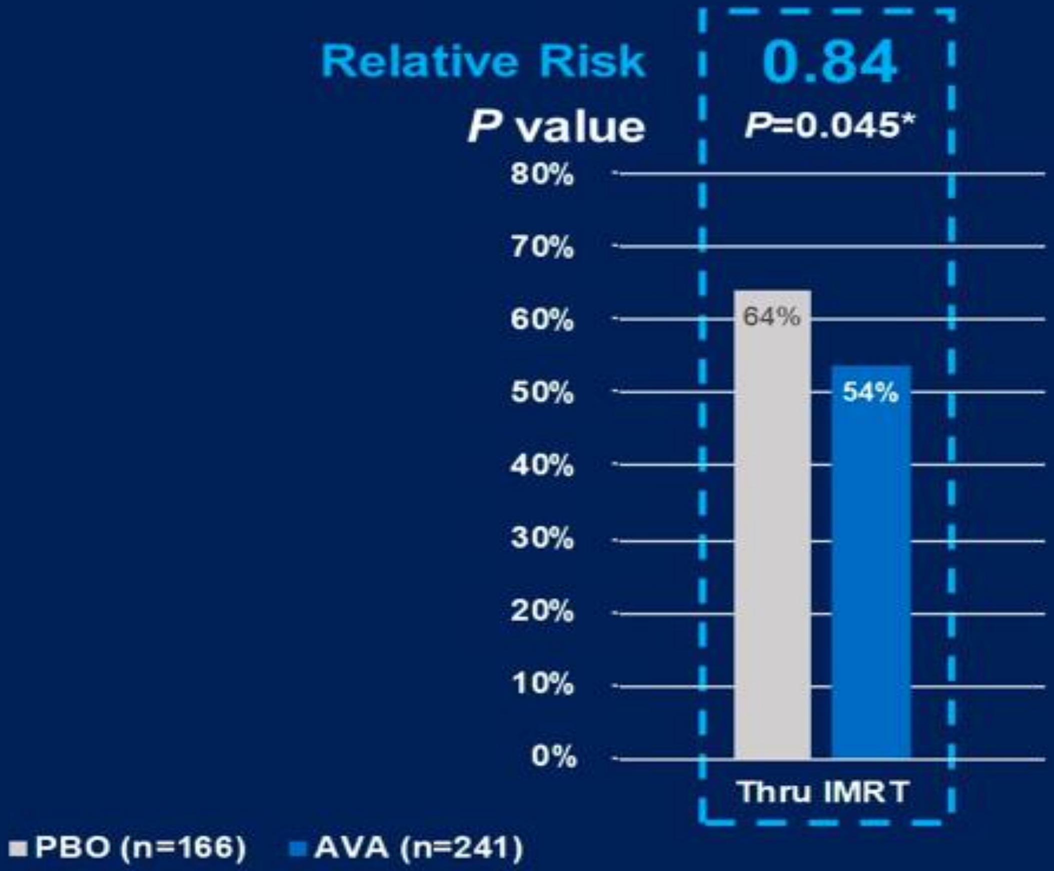
Patient Characteristics

ITT population, N=407

		Avasopasem (N=241)	Placebo (N=166)
Oropharyngeal (%)		80	85
Oral cavity (%)		16	13
Unknown (%)		4	2
HPV positive (%)		80	81
negative (%)		18	16
unknown		2	3
Definitive (%)		81	81
Post-operative treatment (%)		19	19
Cisplatin q3wks (%)		42	45
qw (%)		58	55
Normal mucosa sites $\geq$50 Gy (%)	2	5	3
	3–4	49	45
	5+	48	52

HPV, human papillomavirus; ITT, intent-to-treat population; qw, once weekly; q3wks, once every three weeks.

SOM Incidence Reduced



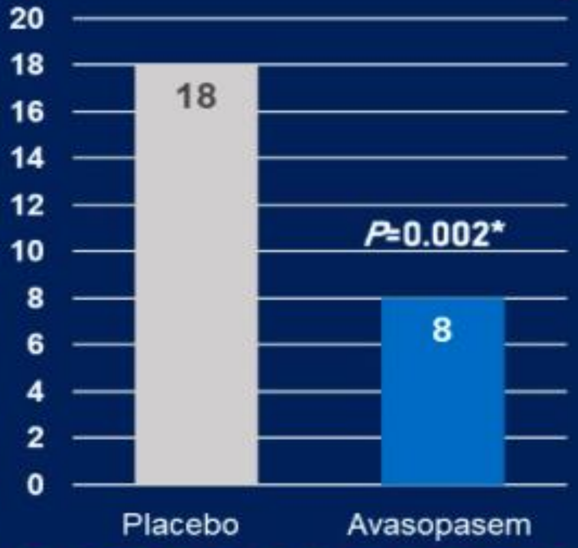
- Statistically significant per SAP.

AVA, avasopasem; IMRT, intensity-modulated radiation therapy; PBO, placebo; SAP, statistical analysis plan; SOM, severe oral mucositis.

Improvement Across Other Key SOM Parameters

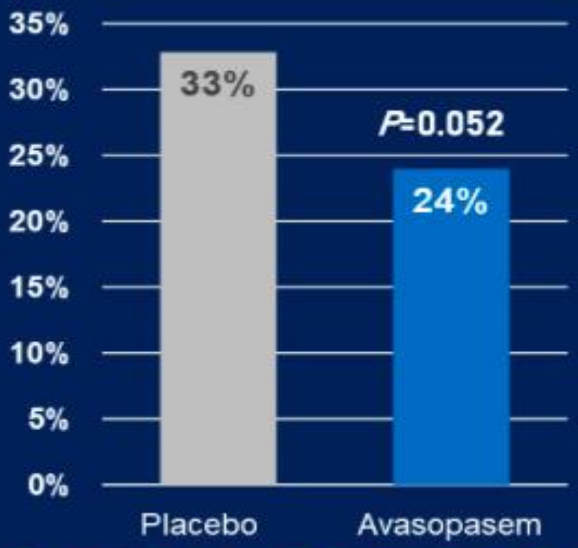
SOM days

56% **Reduction** in median days of SOM



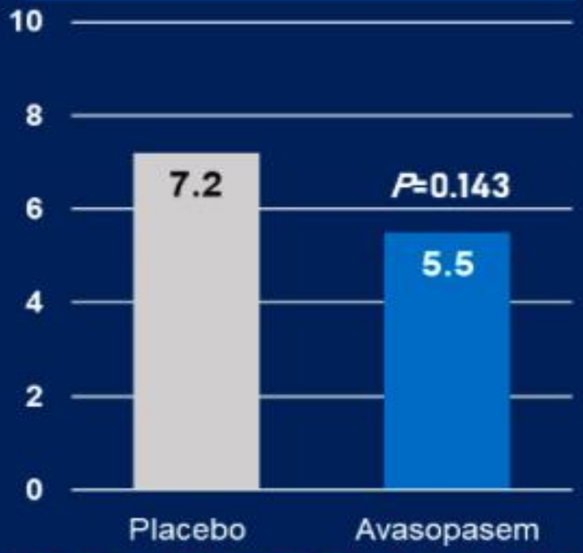
Grade 4 OM incidence

27% **Reduction** in incidence of grade 4 OM



Grade 4 days

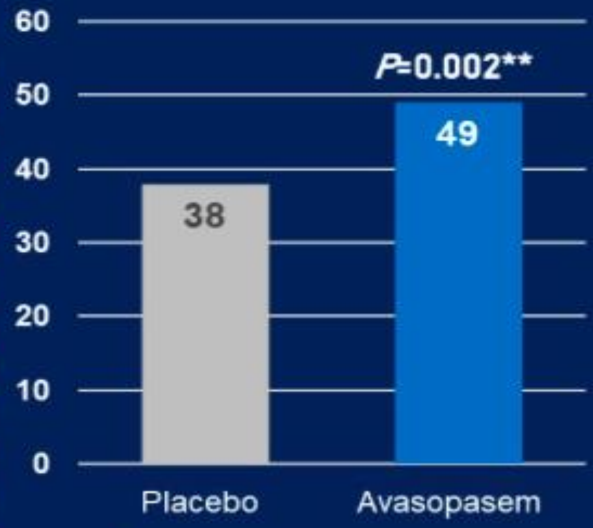
24% **Reduction** in mean days of SOM



Secondary endpoints

SOM onset

29% **Delay** in median days to 1st SOM



Exploratory endpoint

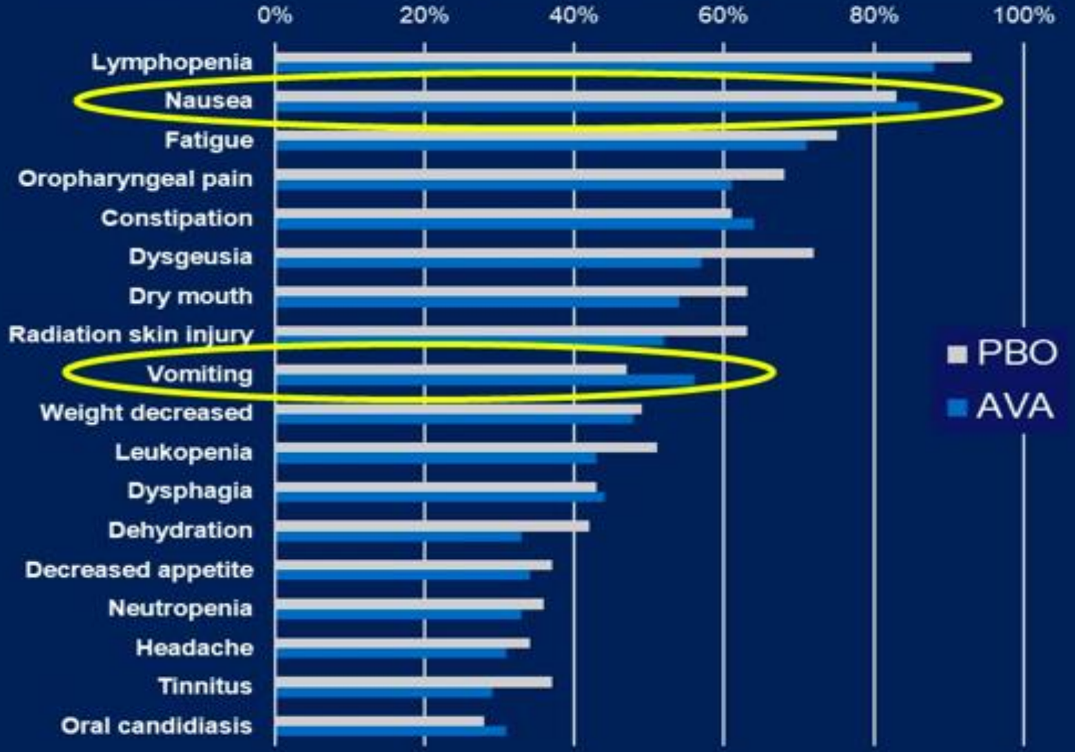
* Statistically significant per SAP.
** Nominal P value; time to onset exploratory endpoint.

OM, oral mucositis; SAP, statistical analysis plan; SOM, severe OM.

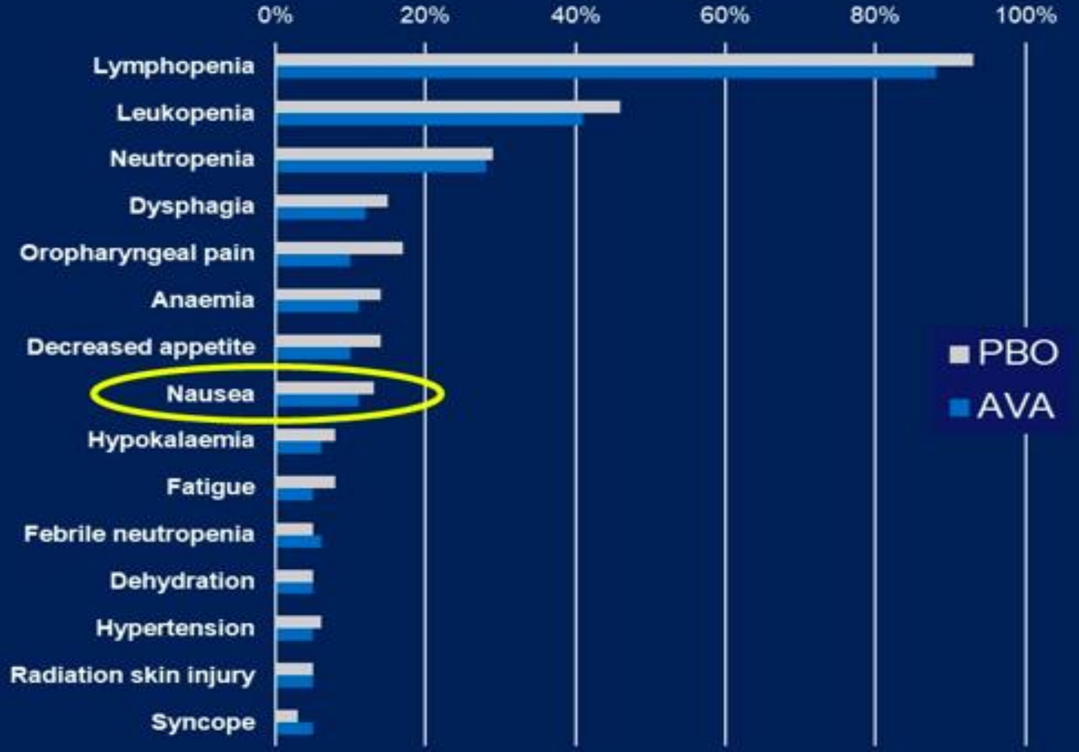
Most Frequent Adverse Events

Avasopasem 90 mg appears generally well tolerated, consistent with phase 2b

Adverse events[1] (all grades, all causes)



Adverse events[1] grade ≥3



[1] ITT population: 166 patients on placebo; 241 on 90 mg avasopasem.
AVA, avasopasem; ITT, intent-to-treat; PBO, placebo.

Conclusions

- Avasopasem 90 mg first drug to show statistically significant and clinically meaningful reduction in SOM
  - Incidence
  - Days of SOM (duration)
- Nominal, meaningful improvements
  - Severity (grade 4 OM incidence)
  - Onset of SOM
- Consistent with randomized, double-blind phase 2b results
- Future analyses include
  - Tumor control and overall survival
  - Chronic kidney disease
- Galera preparing FDA submission
- Safety profile comparable, avasopasem vs placebo

FDA, United States Food and Drug Administration; OM, oral mucositis; SOM, severe OM.

A Phase III, Randomized, Sham-controlled Trial of Acupuncture for Treatment of Radiation-Induced Xerostomia in Patients with Head and Neck Cancer: Wake Forest NCI Community Oncology Research Program Research Base

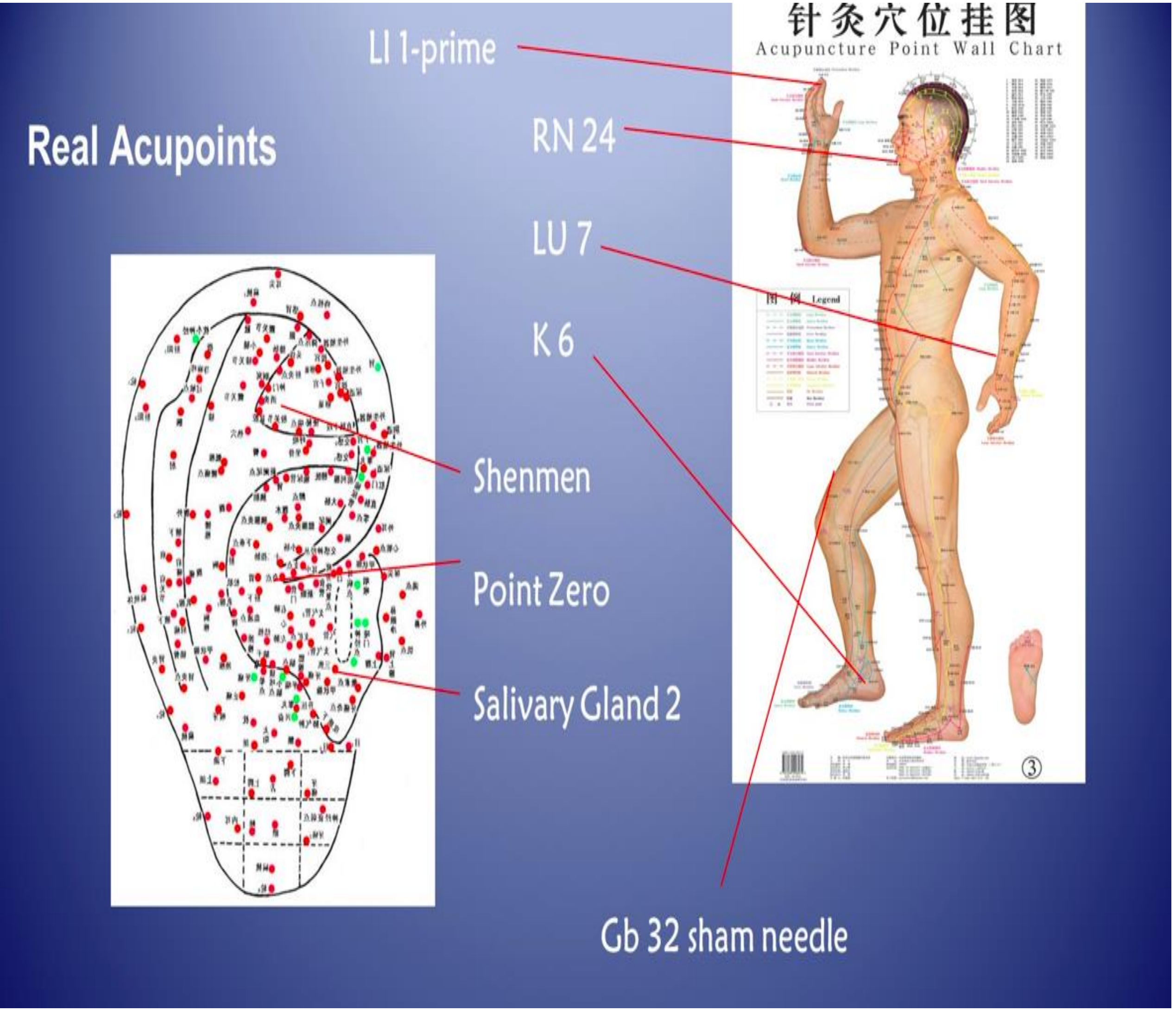
Lorenzo Cohen, PhD
Richard E Hayes Distinguished Professorship for Clinical Cancer Prevention
Director, Integrative Medicine Program
MD Anderson Cancer Center

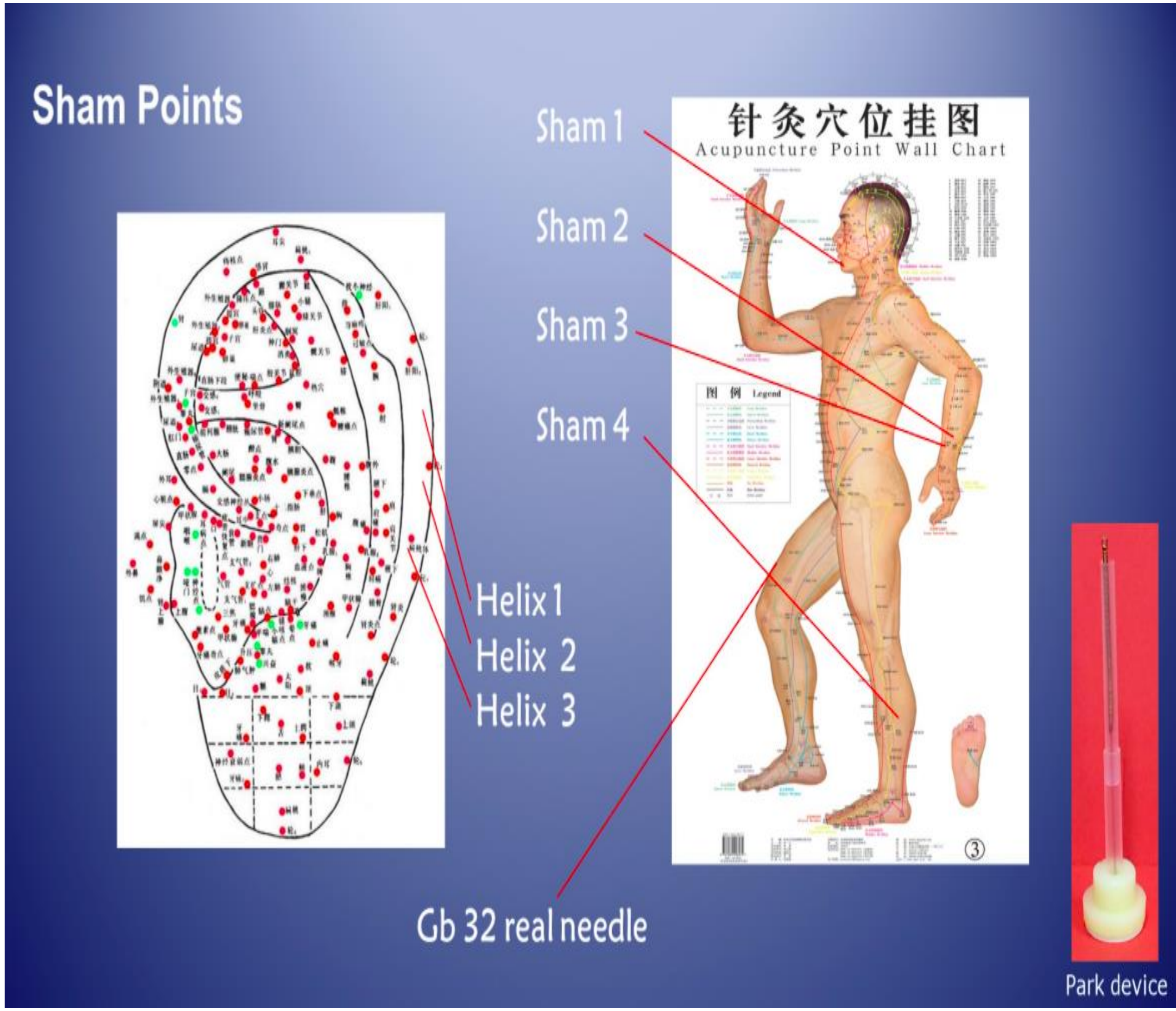
Suzanne Danhauer, David I. Rosenthal, Mark Chambers, Kay Garcia, Andrew Cusimano, W. Mark Brown, Emily V. Dressler, Jewel Ochoa, Peiying Yang, Joseph Chiang, Ora Gordon, Rhonda Crutcher, Jung K. Kim, Michael P. Russin, Joshua Lukenbill, Mercedes Porosnicu, Kathleen J. Yost, Kathryn E. Weaver, Glenn J. Lesser

THE UNIVERSITY OF TEXAS
MD Anderson ~~Cancer~~ Center
Making Cancer History®

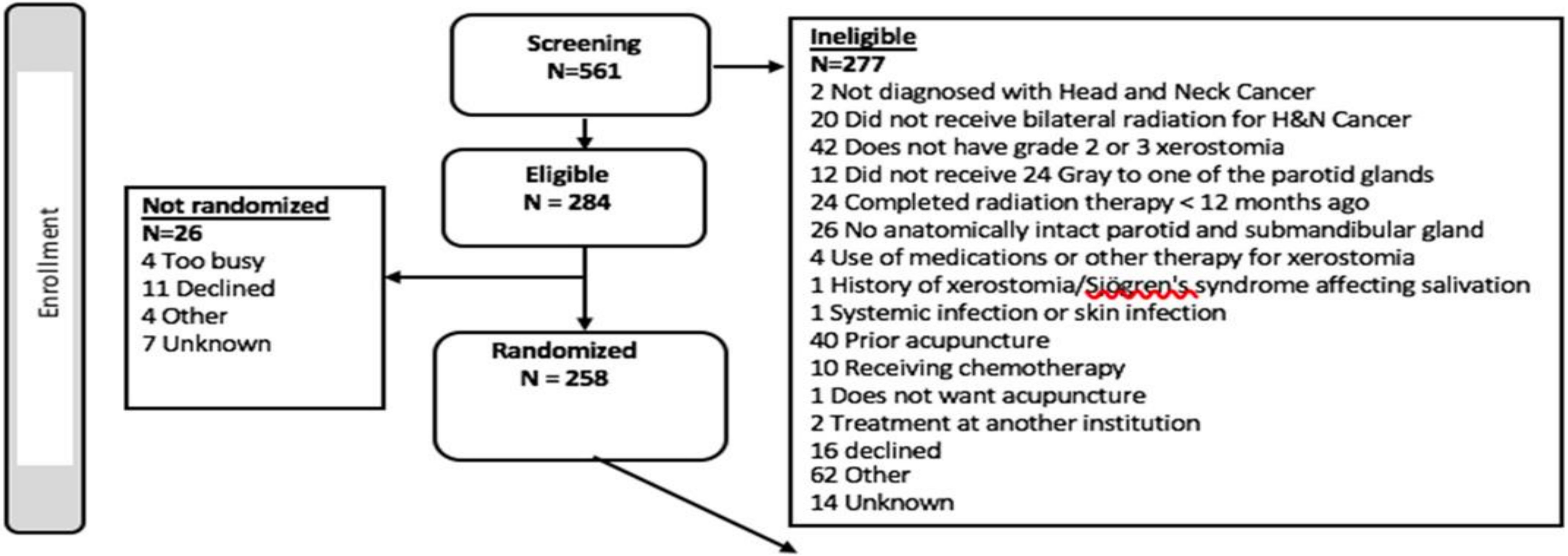
Wake Forest
NCORP RESEARCH BASE

Wake Forest University
School of Medicine


Real Acupoints
LI 1-prime
RN 24
LU 7
K 6
Shenmen
Point Zero
Salivary Gland 2
Gb 32 sham needle
针灸穴位挂图
Acupuncture Point Wall Chart


Sham Points
Sham 1
Sham 2
Sham 3
Sham 4
Helix 1
Helix 2
Helix 3
Gb 32 real needle
Park device
针灸穴位挂图
Acupuncture Point Wall Chart

CONSORT: Recruitment from over 30 sites



Screening
N=561

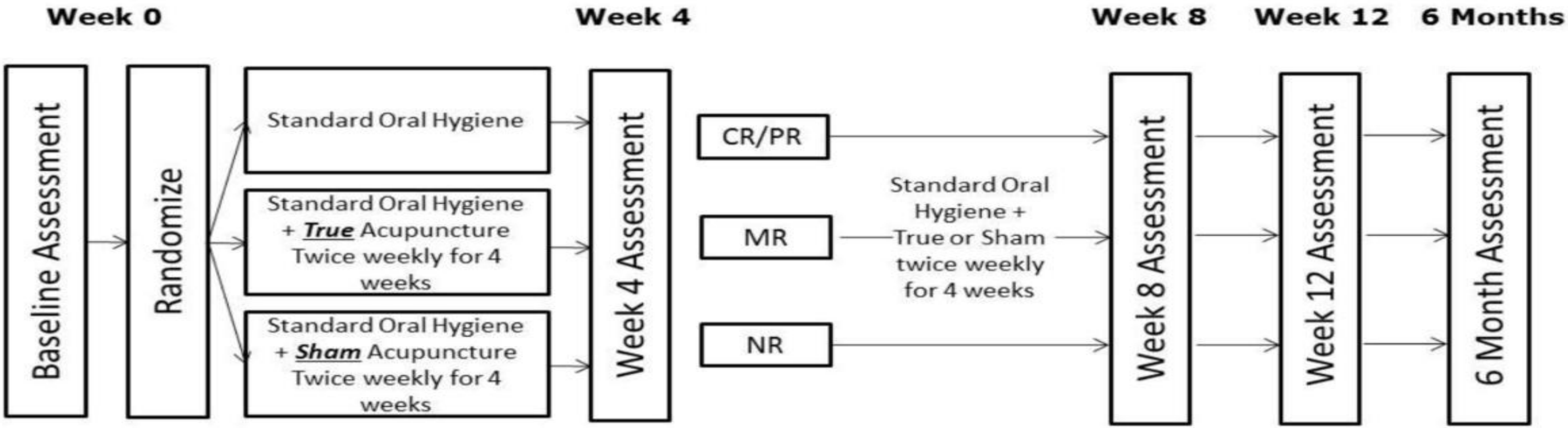
Eligible
N = 284

Randomized
N = 258

Not randomized
N=26
4 Too busy
11 Declined
4 Other
7 Unknown

Ineligible
N=277
2 Not diagnosed with Head and Neck Cancer
20 Did not receive bilateral radiation for H&N Cancer
42 Does not have grade 2 or 3 xerostomia
12 Did not receive 24 Gray to one of the parotid glands
24 Completed radiation therapy < 12 months ago
26 No anatomically intact parotid and submandibular gland
4 Use of medications or other therapy for xerostomia
1 History of xerostomia/Sjögren's syndrome affecting salivation
1 Systemic infection or skin infection
40 Prior acupuncture
10 Receiving chemotherapy
1 Does not want acupuncture
2 Treatment at another institution
16 declined
62 Other
14 Unknown

Study Design & Schema



Week 0

Baseline Assessment

Randomize

Standard Oral Hygiene

Standard Oral Hygiene + ***True*** Acupuncture Twice weekly for 4 weeks

Standard Oral Hygiene + ***Sham*** Acupuncture Twice weekly for 4 weeks

Week 4

Week 4 Assessment

CR/PR

MR

NR

Standard Oral Hygiene + True or Sham twice weekly for 4 weeks

Week 8

Week 8 Assessment

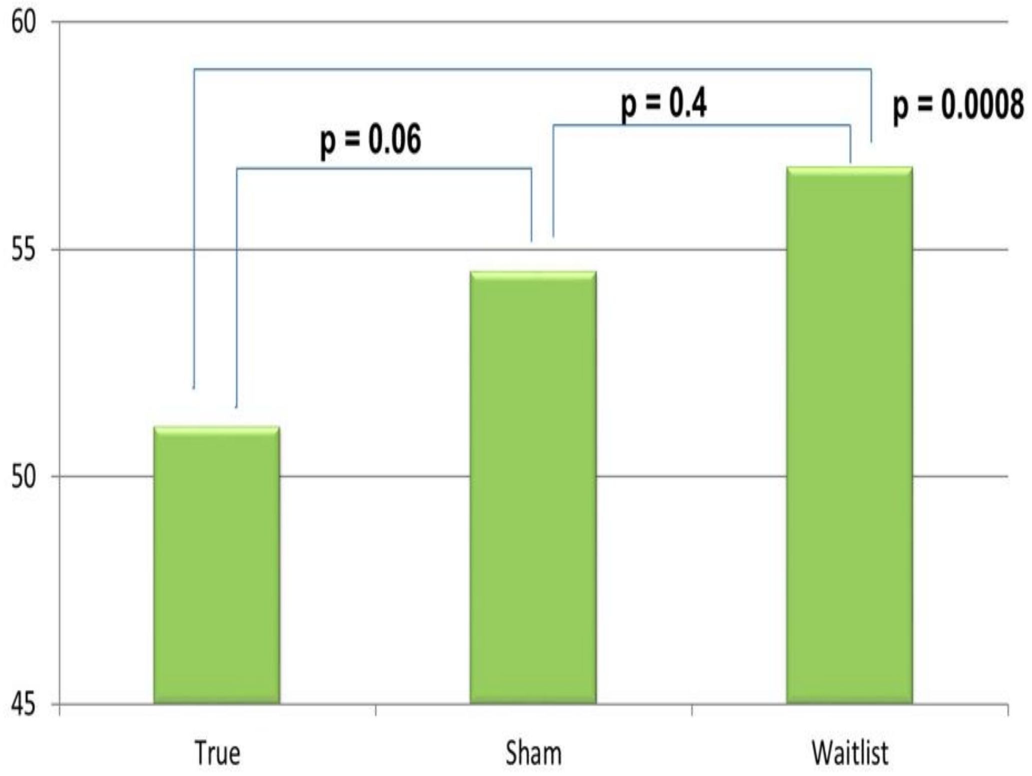
Week 12

Week 12 Assessment

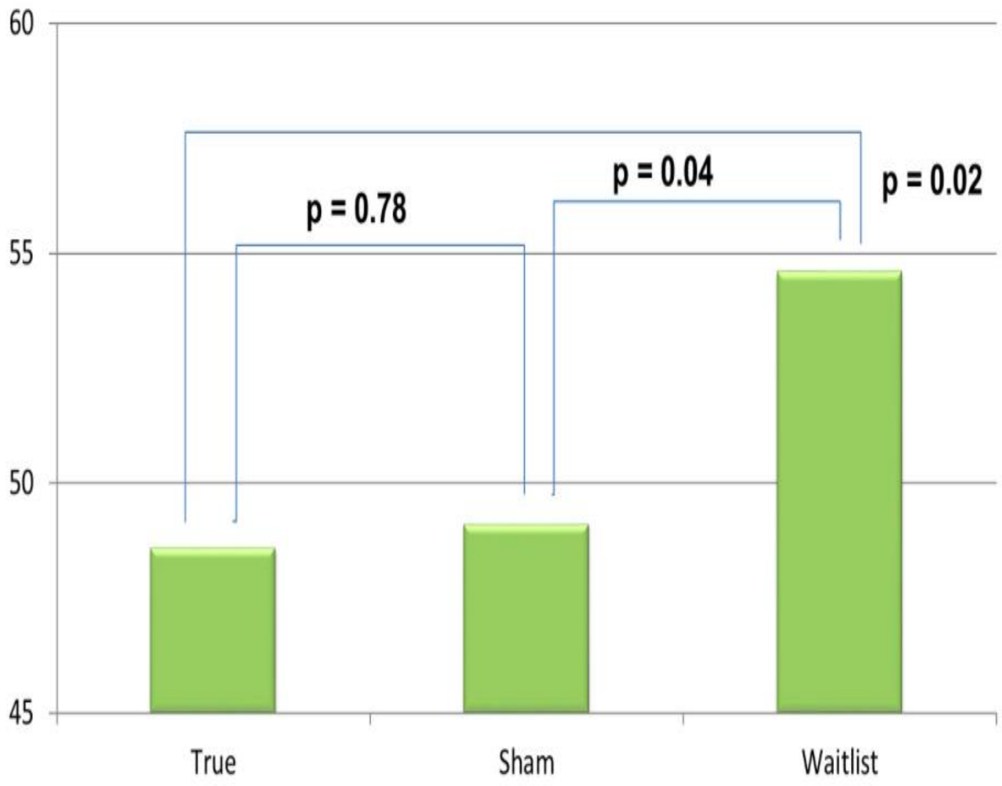
6 Months

6 Month Assessment

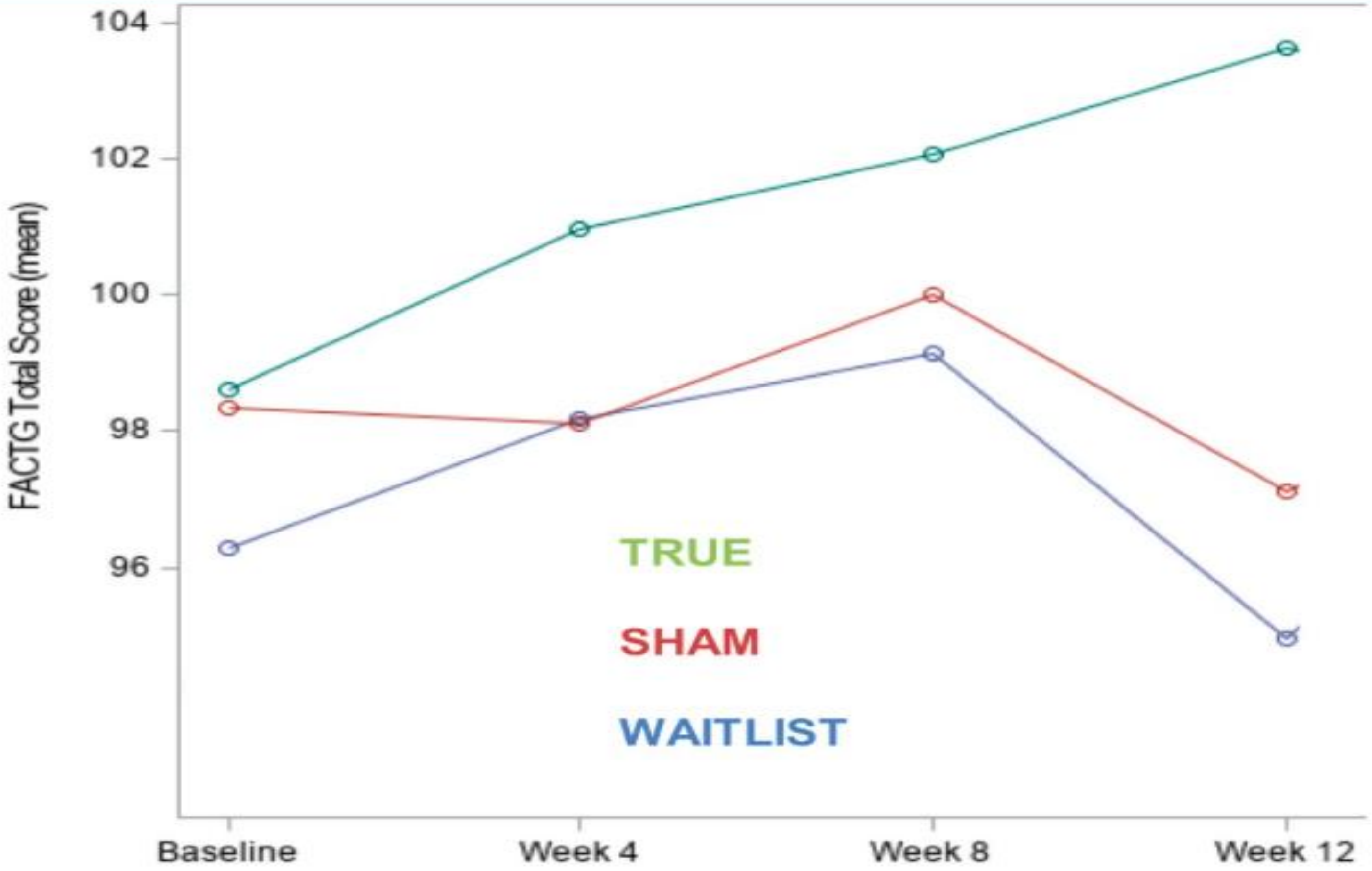
XQ Week 4 (↑= worse symptoms)



XQ Week 12 (↑ = worse symptoms)



FACT-G Total



True v WLC P = 0.001

True v Sham P = 0.02

Sham v WLC P = 0.26

Patient Comments

- I can lick my lips for the first time in over 10 years!
- When he put that needle in my ear, I suddenly felt a big gush of saliva.
- This is the first time I've been able to enjoy a chocolate chip cookie in a long time.
- I'm thrilled with the acupuncture results. I have regained some taste buds in a good way. This is huge for me.
- I could only taste really sour foods or the burn from acidy foods. So I didn't enjoy eating....Now there are some foods that actually taste good.
- I look forward to dinner and have even gone out to dinner a few times, which I haven't done in almost 2 years..... Thanks to you all!

2022 ASCO ANNUAL MEETING

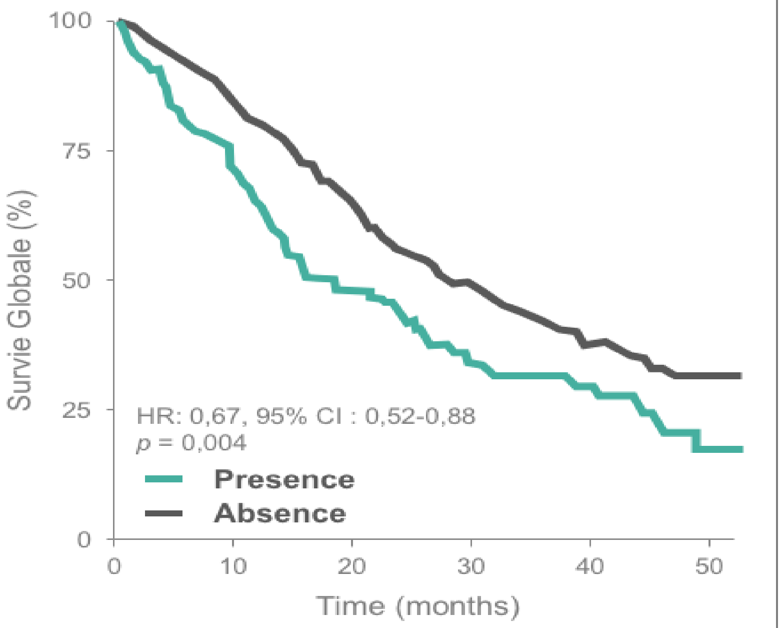
2022 ASCO ANNUAL MEETING

Impact of acetaminophen on the efficacy of immune checkpoint blockers in cancer patients

Pr Antoine ITALIANO
University of Bordeaux, France

Impact du paracétamol sur l'efficacité des Inhibiteurs de checkpoint

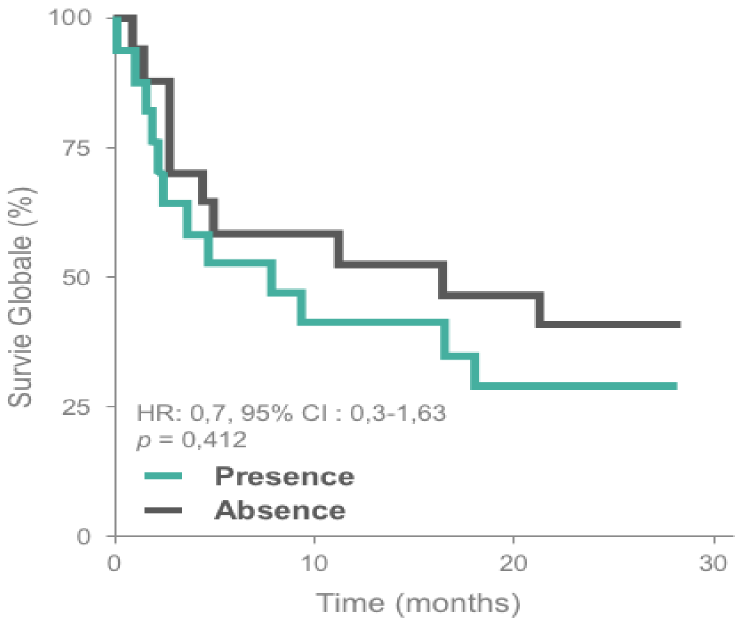
CheckMate-025
Phase 3 Nivo RCC avancé n=297, approche Métabolomique



Nb à risque

101 (0)	72 (29	48 (52)	34 (66)	26 (70)	5 (77)
291 (0)	240 (46)	184 (100)	135 (146)	95 (174)	17 (185)

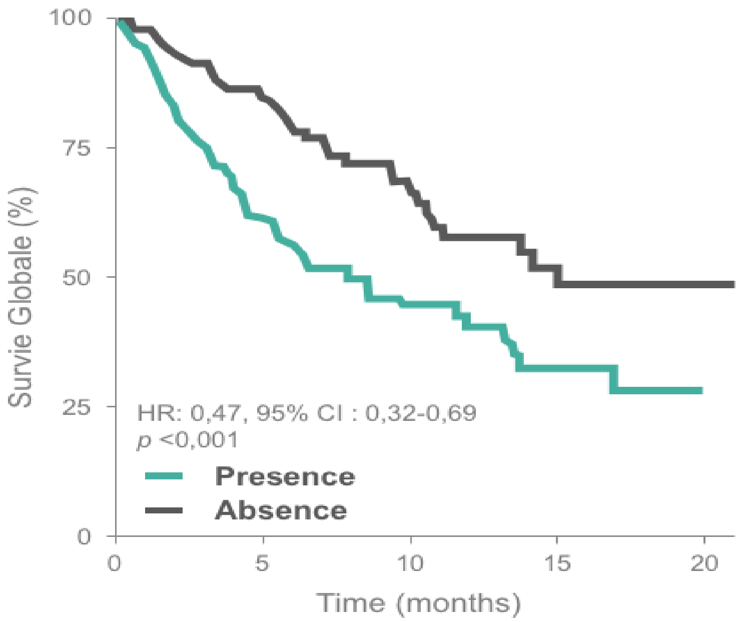
BIP
Anti-PD-L1 +/- CTLA4 cancer avancés (n=34), Approche Métabolomique



Nb à risque

17 (0)	7 (10)	5 (12)	0 (12)
17 (0)	10 (7)	8 (9)	0 (10)

PREMIS
Anti-PD-L1 +/- CTLA4 cancer avancés (n=297) Approche quantitative



Nb à risque

167 (0)	78 (60)	27 (77)	9 (82)	0 (83)
130 (0)	84 (18)	33 (32)	14 (39)	2 (39)

A. Italiano, et al., ASCO® 2022, Abs. #12000

Impact du paracétamol sur l'efficacité des Inhibiteurs de checkpoint

Phase 3 Nivo RCC avancé n=297, approche Quantitative

Survie Sans Progression

Independent variables	Hazard ratio	IC 95%	*p*
Age (≥ 61.2 ans)	0,71	0,54-0.94	0,018
Exposition APAP (Oui)	1,43	1,07-1.91	0,015
Taux de LDH (≥ 207 UI)	1,55	1,17-2.06	0,002
ECOG (≥ 2)	2,05	1,41-2.96	< 0,001
Métastases hépatiques (Oui)	2,10	1,54-2.87	< 0,001

Survie Globale

Independent variables	Hazard ratio	95% CI	*p*
Sex (Male)	1,45	0.99-2.11	0,056
Exposition APAP (Oui)	1,78	1.18-2.68	0,006
Taux de LDH (≥ 207 UI)	1,91	1.30-2.81	0,001
ECOG (≥ 2)	3,57	2.27-5.60	< 0,001
Métastases hépatique (Oui)	2,60	1.76-3.85	< 0,001

ADAP=Acétaminophène

- En analyse multivariée, la présence d'acétaminophène ou de glucuronide d'acétaminophène est indépendamment associée à une moins bonne PFS et OS.
- La corrélation a été faite sur un modèle animal murin
- Le modèle humain sur 4 volontaires sains a confirmé l'implication du paracétamol avec un effet sur Treg

› **L'acétaminophène (paracétamol) a un effet délétère sur l'efficacité des inhibiteurs de checkpoint.**

A. Italiano, et al., ASCO® 2022, Abs. #12000

Memorial Sloan Kettering Cancer Center

Oral Minoxidil for the Treatment of Late Alopecia in Cancer Survivors

Alyce M. Kuo, Rachel E. Reingold, Kwami F. Ketosugbo, Alexander Pan, Stephen Dusza, Lukas Kraehenbuehl, Devika Gajria, Diana E. Lake, Jacqueline F. Bromberg, Shari B. Goldfarb, Tiffany A. Traina, Monica N. Fornier, Ayca Gucalp, Megan Dauscher, Alina Markova, Mario E. Lacouture

Memorial Sloan Kettering Cancer Center, New York, NY

Minoxidil oral contre l'alopécie persistante

- Minoxidil : stimule les canaux potassiques → vasodilatateur et entrée précoce des follicules en phase de croissance
- Autorisation FDA comme antihypertenseur à la posologie de 10 à 100 mg/j
- Utilisation hors AMM à la posologie de 0,25 à 5 mg/j dans l'alopécie

Patientes présentant une alopécie persistante
Traitement par Minoxidil oral 1,25 mg/j

N=216

Evaluation de la réponse Clinique par comparaison photographique avant et après traitement

Quantification de la réponse par trichoscopie
(HairMetrix® Canfield Scientific, Inc)

AM. Kuo, et al., ASCO®2022, Abs. #12022

On standardized photography (n=119), 74% of patients showed clinical improvement

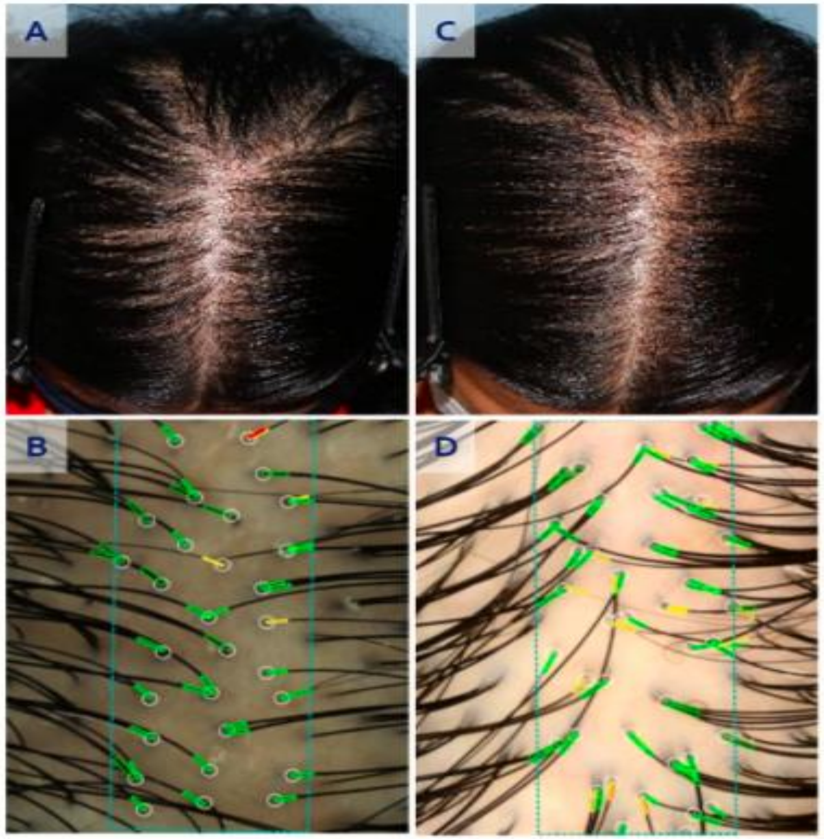


Figure 1. A) Standardized photo and B) occipital trichoscopy of a patient on tamoxifen, **before** oral minoxidil. C) Standardized photo and D) occipital trichoscopy **after** 131 days of oral minoxidil 1.25 mg daily.

Table 1. Trichoscopy assessments (*n*=42) before and after a median of 91 (IQR=136) days on oral minoxidil

	Baseline Value (95% CI)	Follow-up Value (95% CI)	Median Percent Change (IQR)	*p*
Hair Density (hairs/cm²)				
Frontal	124.2 (109.7-138.7)	153.2 (137.3-169.1)	**20.4%** (46.8)	**0.008**
Occipital	100.3 (89.2-111.3)	123.5 (112.1-134.9)	**21.4%** (59.3)	**0.004**
Follicle Density (follicles/cm²)				
Frontal	96.5 (86.5-106.4)	115.8 (105.7-125.9)	**22.5%** (37.1)	**0.007**
Occipital	77.4 (69.4- 85.4)	93.0 (85.5-100.5)	**20.9%** (39.6)	**0.005**
Hair Shaft Diameter (µm)				
Frontal	69.3 (66.7-71.9)	67.3 (65.4-69.2)	**-2.0%** (10.7)	0.22
Occipital	70.3 (67.8-72.7)	69.9 (67.2-75.6)	**0%** (13.4)	0.84

A single-arm feasibility trial of memantine to prevent chemotherapy related cognitive decline in patients with early breast cancer

Z. Nakamura, et al., ASCO® 2022, Abs. #12109

2022 ASCO® ANNUAL MEETING

ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

BRIO BORDEAUX | Recherche Intégrée Oncologie

Merci pour votre écoute

Merci au Réseau OncoNA