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)

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Disclosures

- Employment – University of Iowa Hospitals & Clinics
- Uncompensated Research Advisor for Galera Therapeutics, Inc.
- Will discuss Investigational Use of a drug

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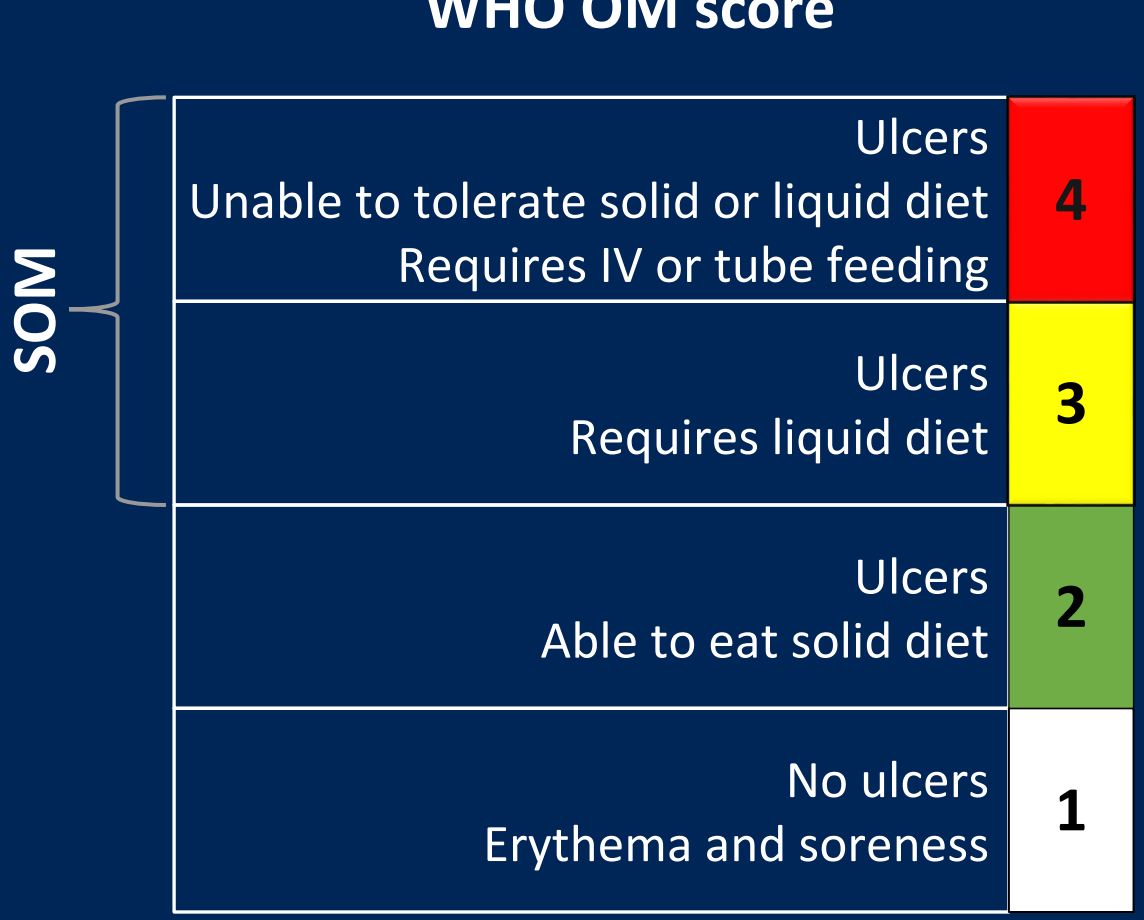
Background

- 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



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.

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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.

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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.

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ROMAN: Phase 3 Placebo vs 90 mg Avasopasem

Reduction in Oral Mucositis with Avasopasem Manganese

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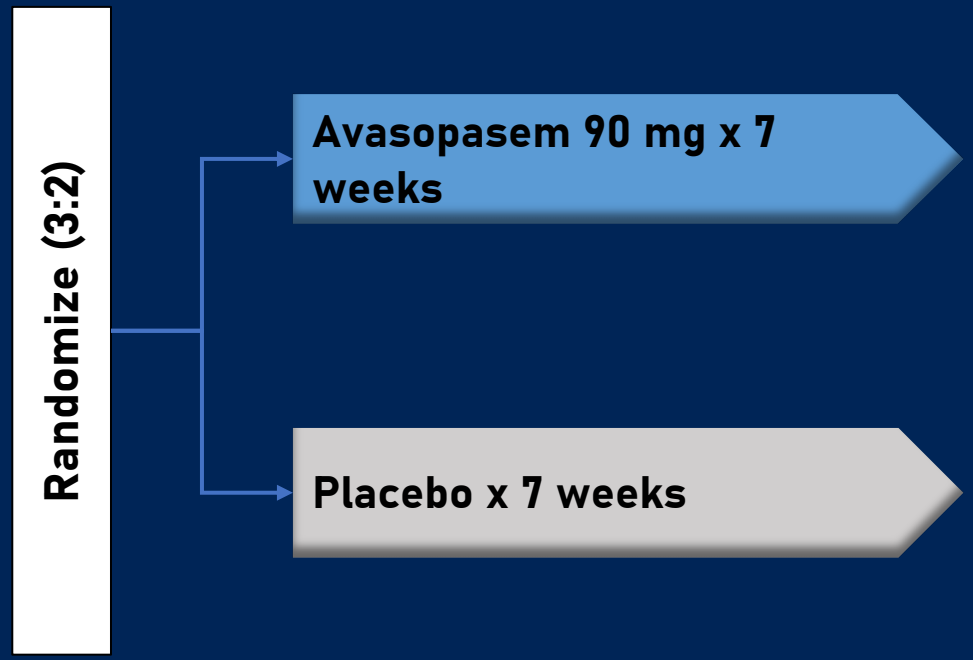
GT-301: The ROMAN Trial

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



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

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ROMAN Endpoints

Primary endpoint

- Incidence of SOM through IMRT
  - Cochrane-Mantel-Hansel relative risk calculated

Secondary efficacy endpoints

(Holm-Bonferroni correction for multiple comparisons)

- Total number of days of SOM ("duration" in phase 2b)
  - In all patients
  - 0 days for patients w/o SOM
- Incidence & total number of days of grade 4 SOM

Additional endpoints

- Safety and tolerability
- Tumor outcomes at 1–2 years – LRC, DM, PFS, OS
  - In progress

DM, distant metastasis; IMRT, intensity-modulated radiation therapy; LRC, locoregional control; OS, overall survival; PFS progression free survival; SOM, severe oral mucositis.

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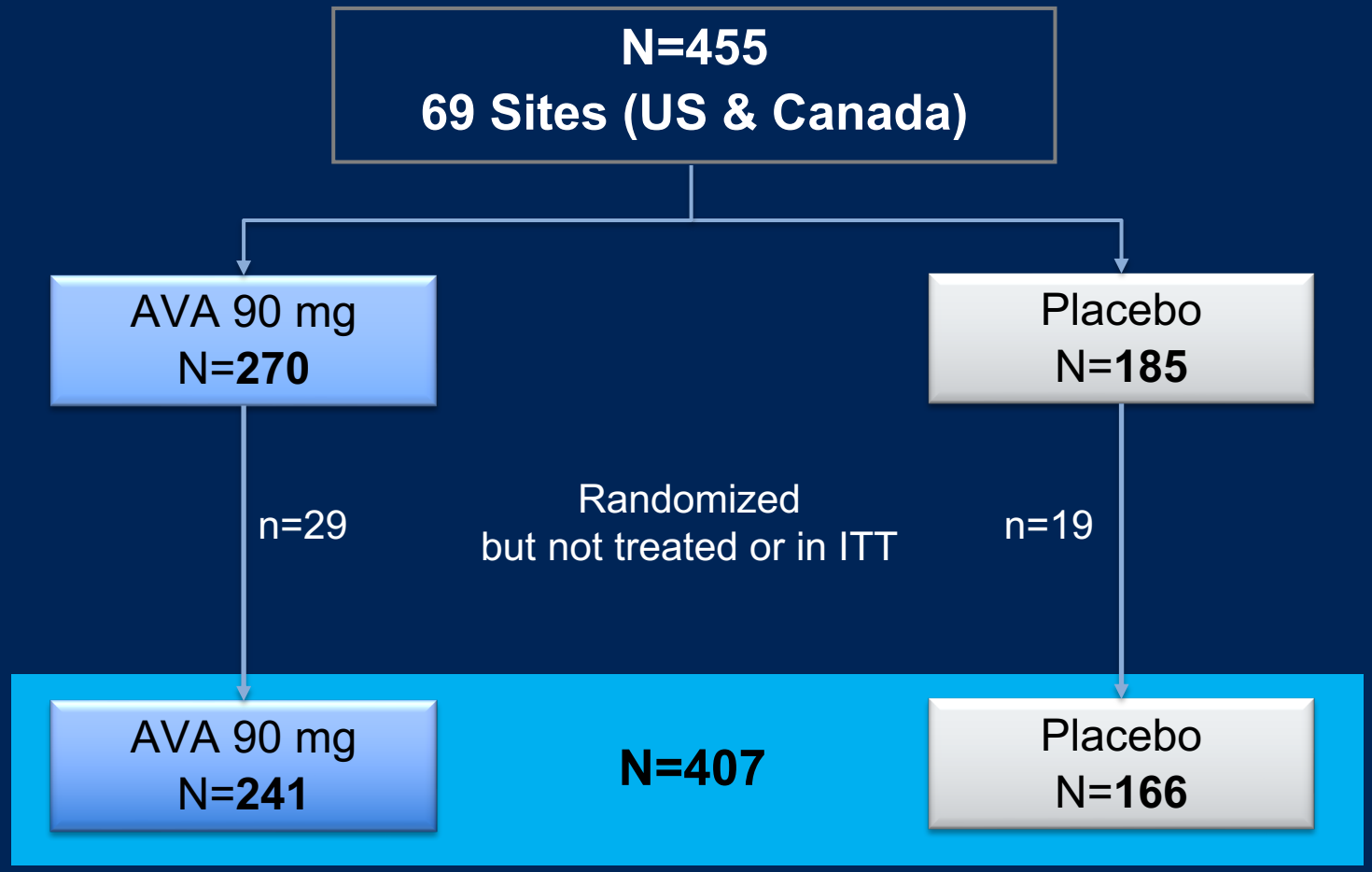
Consort Diagram



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

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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 ≥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.

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RESULTS

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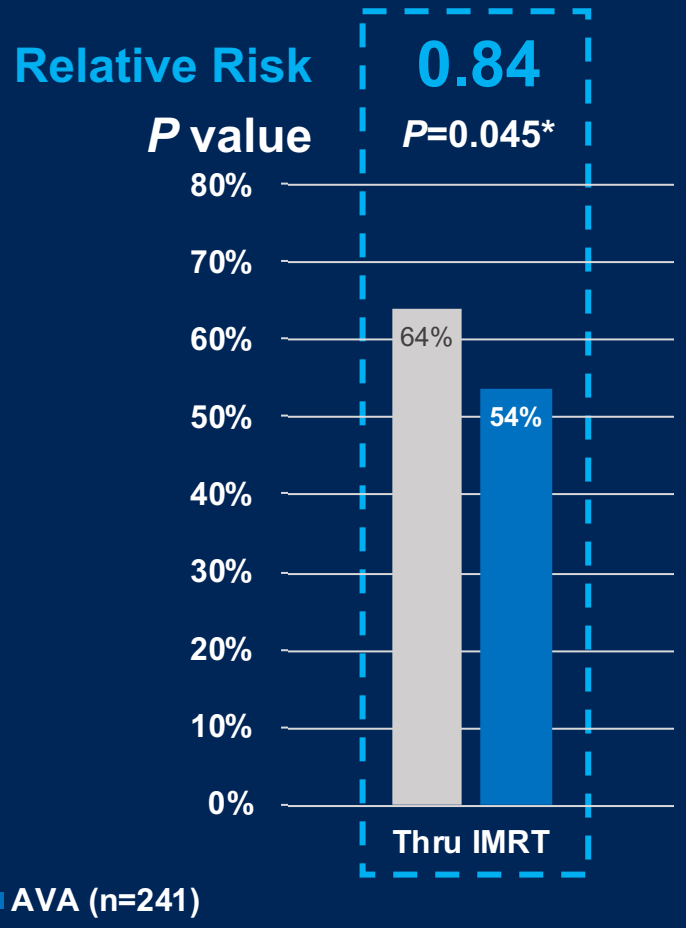
SOM Incidence Reduced



- Statistically significant per SAP.

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

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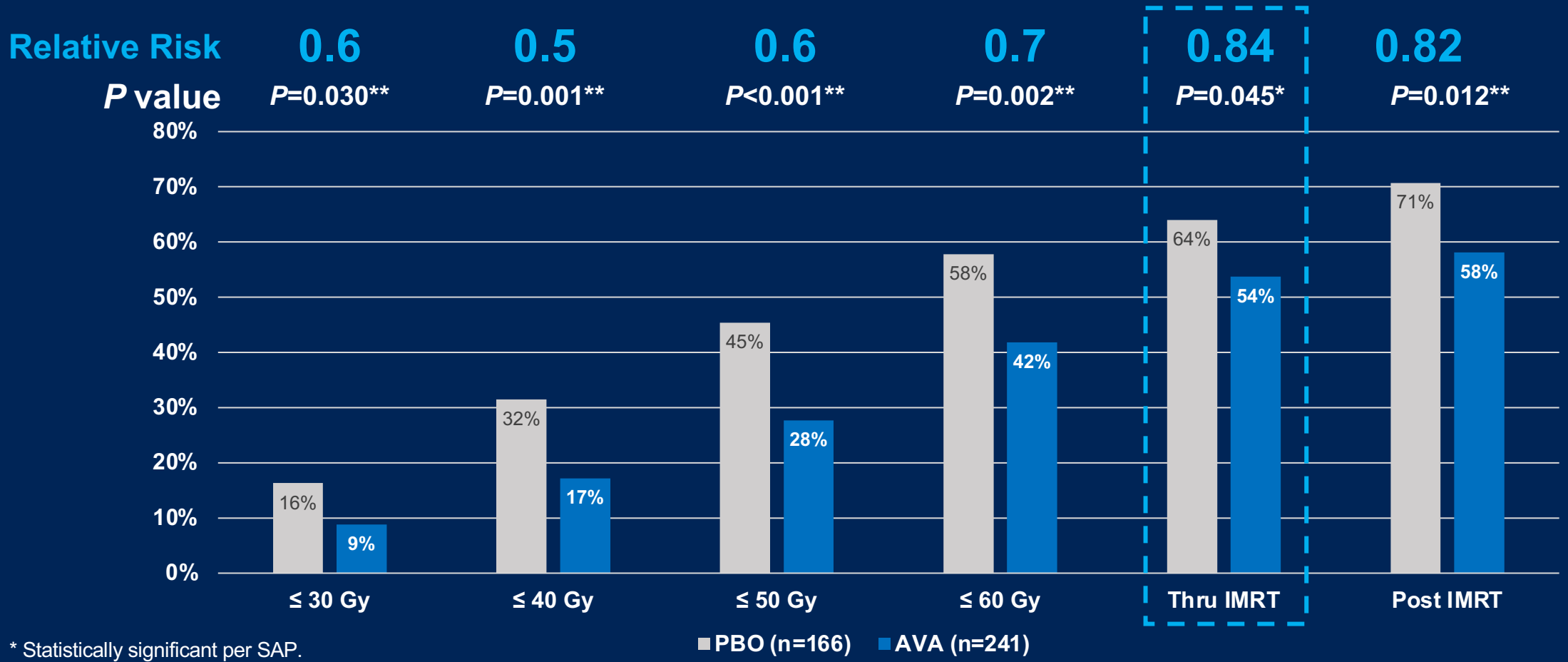
SOM Incidence Reduced at All IMRT Landmarks

Primary endpoint



* Statistically significant per SAP.
** Exploratory endpoints, not formally tested as part of SAP.
AVA, avasopasem; IMRT, intensity-modulated radiation therapy; PBO, placebo; SAP, statistical analysis plan; SOM, severe oral mucositis.

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Incidence Doesn't Tell Full Story

Real patient examples with very different SOM burdens

OM evaluation	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	1° endpoint	2° endpoints		Exploratory
Cumulative RT	→ 10 Gy		→ 20 Gy		→ 30 Gy		→ 40 Gy		→ 50 Gy		→ 60 Gy		→ 65–70		Follow-up		SOM incidence	# Days of SOM	Grade 4 incidence	Days to onset
ROMAN patient examples A	0	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	0	0	>62
B	0	0	0	0	0	0	0	0	0	0	0	1	1	3	0	0	1	7	0	46
C	0	0	2	2	3	2	2	2	2	2	2	2	0	0	2	2	1	3	0	17
D	0	0	0	0	3	3	3	3	3	3	3	3	3	3	3	3	1	44	0	16
E	0	0	0	1	2	3	3	4	4	4	4	4	4	4	4	3	1	45	1	20

OM, oral mucositis; RT, radiation therapy; SOM, severe OM.

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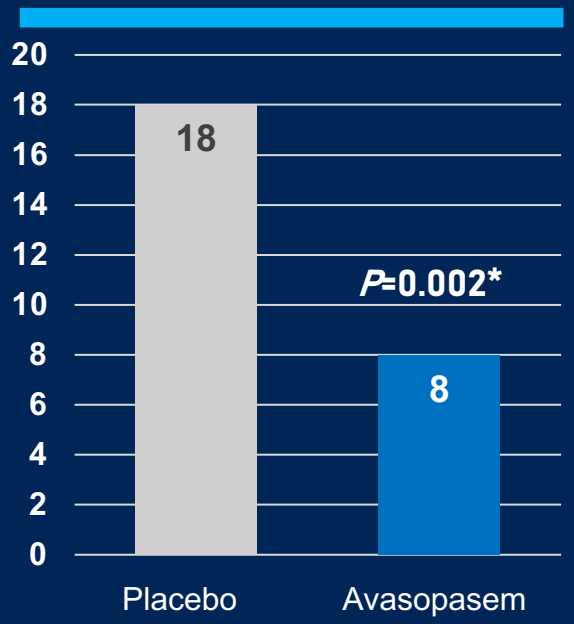
Improvement Across Other Key SOM Parameters

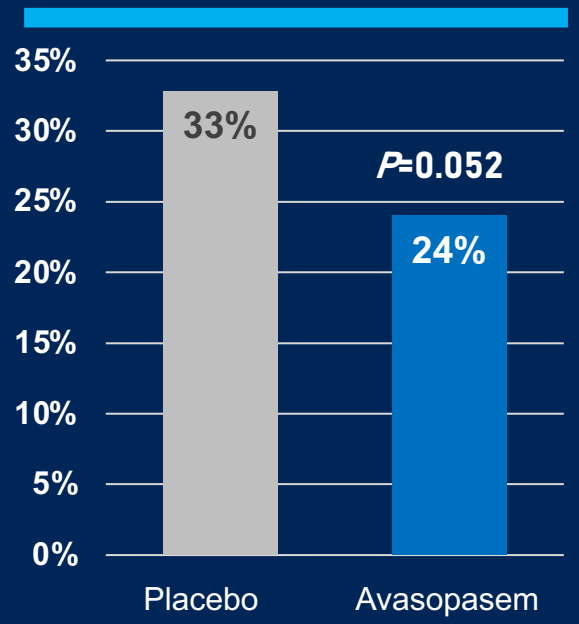
SOM days

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



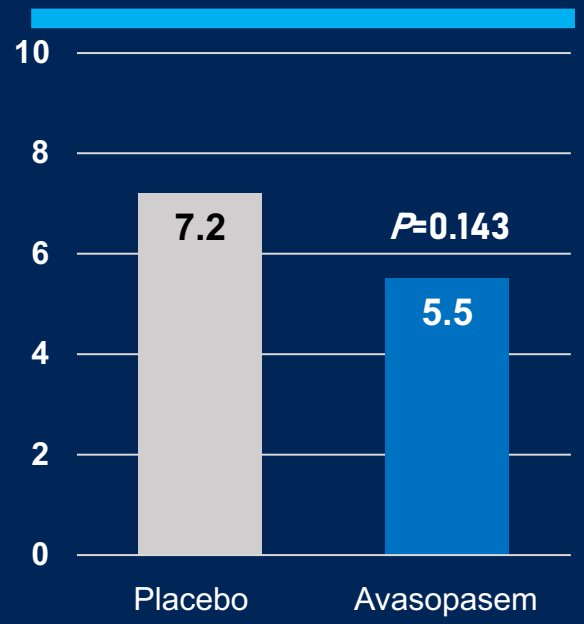
Grade 4 OM incidence

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



Grade 4 OM days

24% **Reduction** in mean days of Gr 4 OM



Secondary endpoints

* Statistically significant per SAP.

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

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Improvement Across Other Key SOM Parameters

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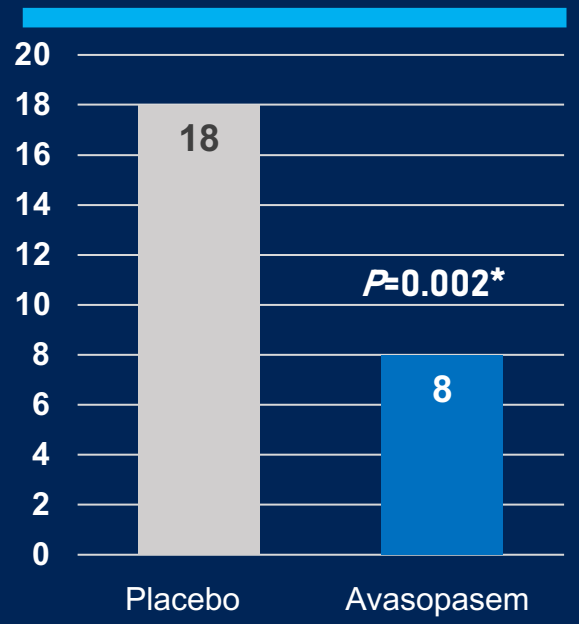

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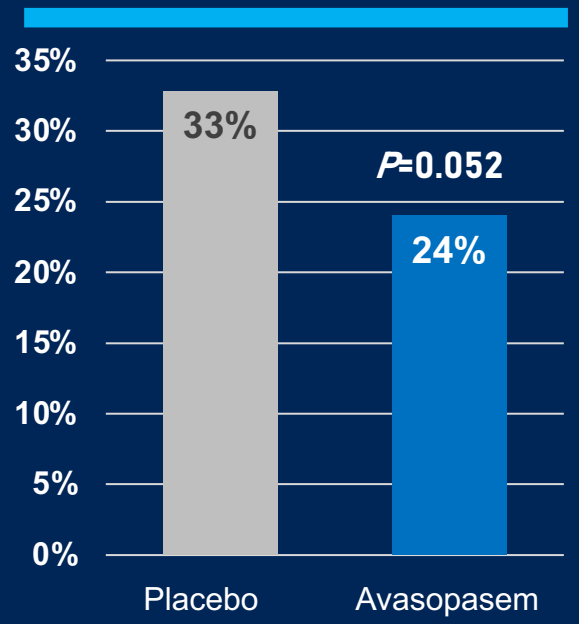

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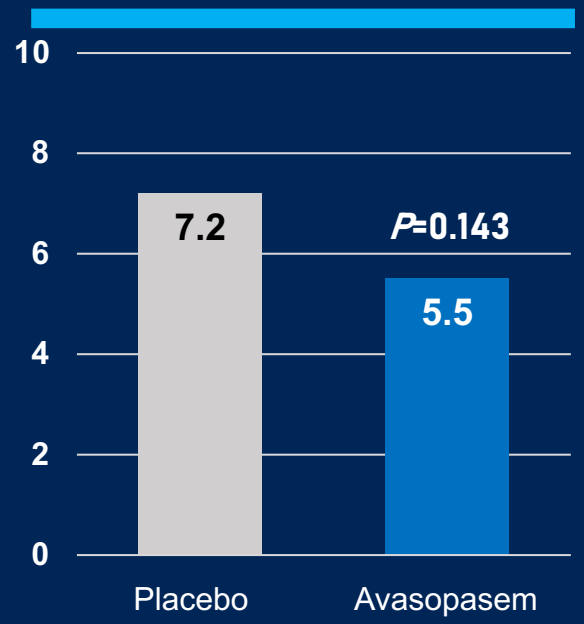
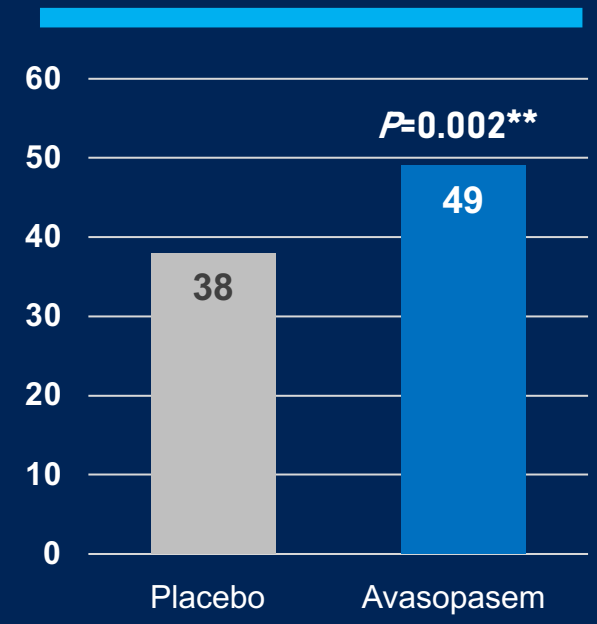


SOM onset

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



Secondary endpoints

Exploratory endpoint

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

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

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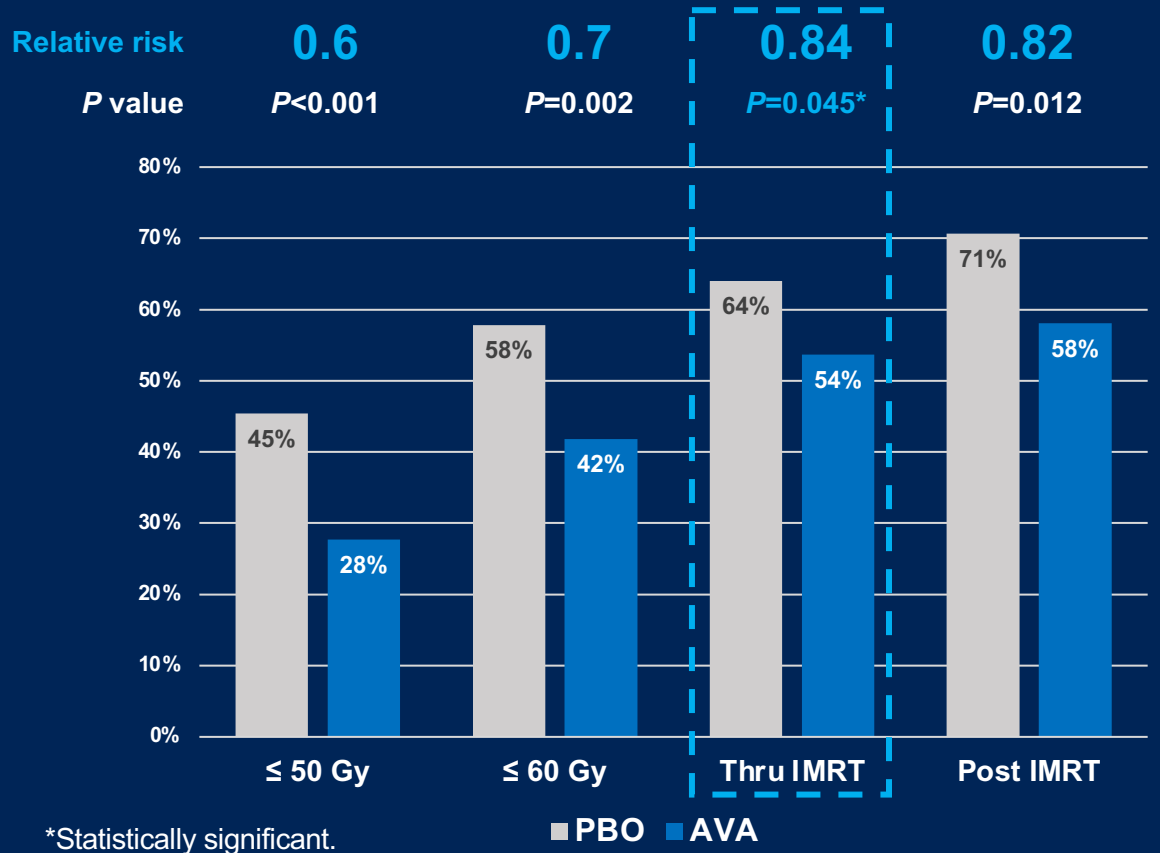
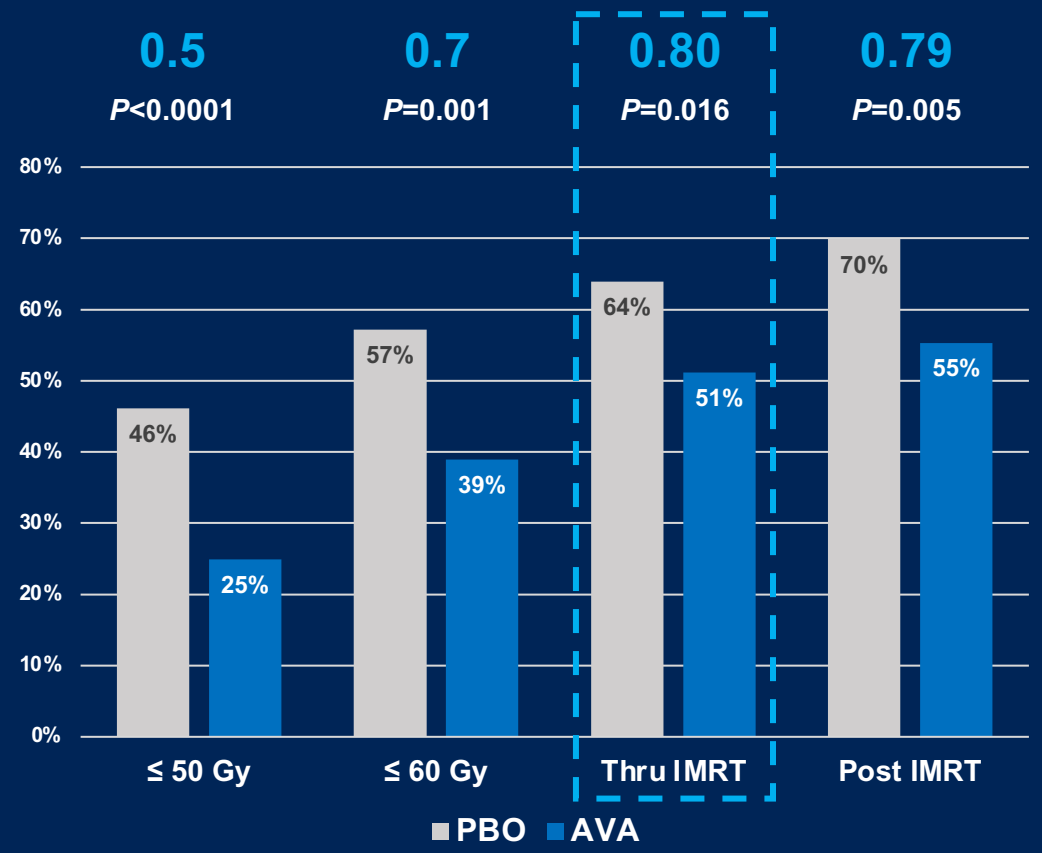
Greater Reduction with Full Treatment

Full courses of avasopasem demonstrated greater SOM incidence reduction

ITT



Full treatment[1]



*Statistically significant.

AVA, avasopasem; IMRT, intensity-modulated radiation therapy; ITT, intent-to-treat population; PBO placebo; SOM, severe oral mucositis.

[1] Per protocol population: patients who received ≥60 Gy of radiotherapy and ≥25 infusions of placebo or avasopasem.

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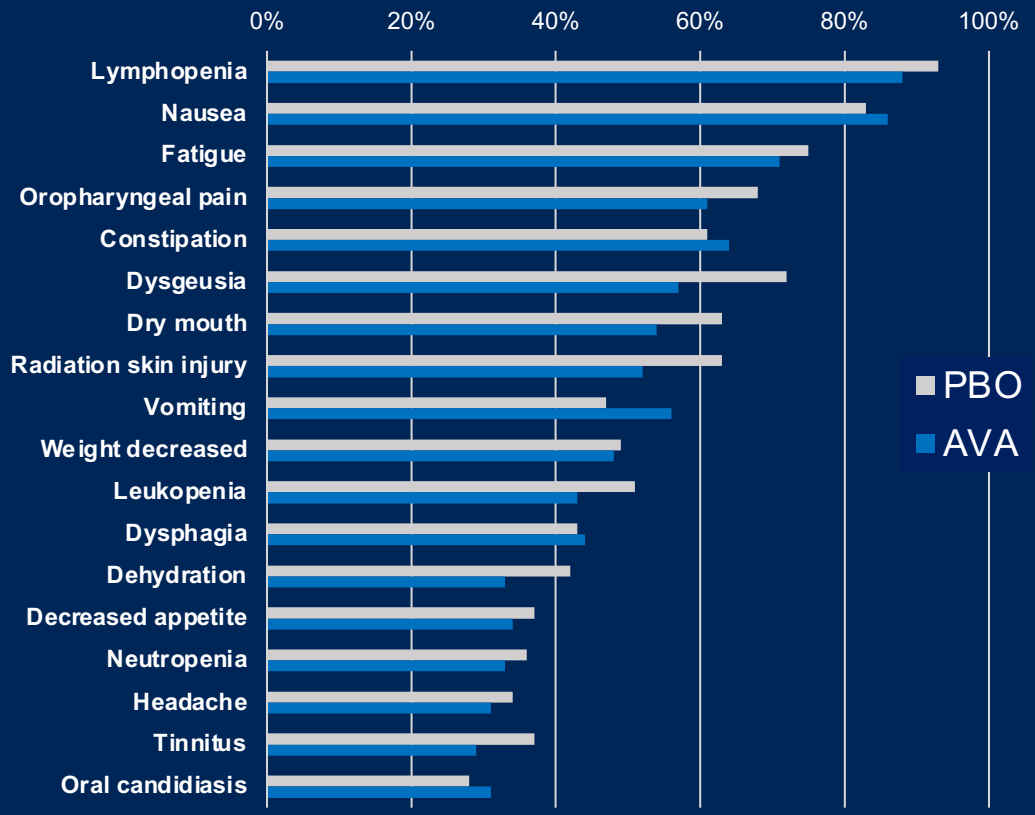
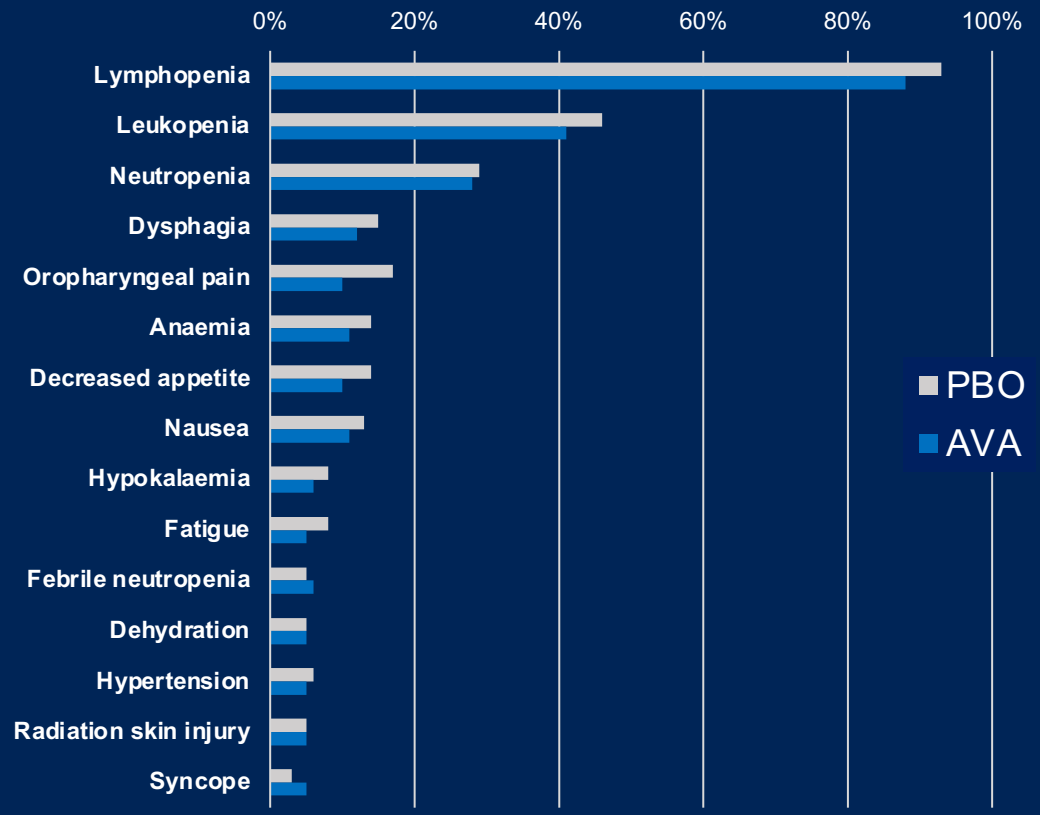
Most Frequent Adverse Events

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.

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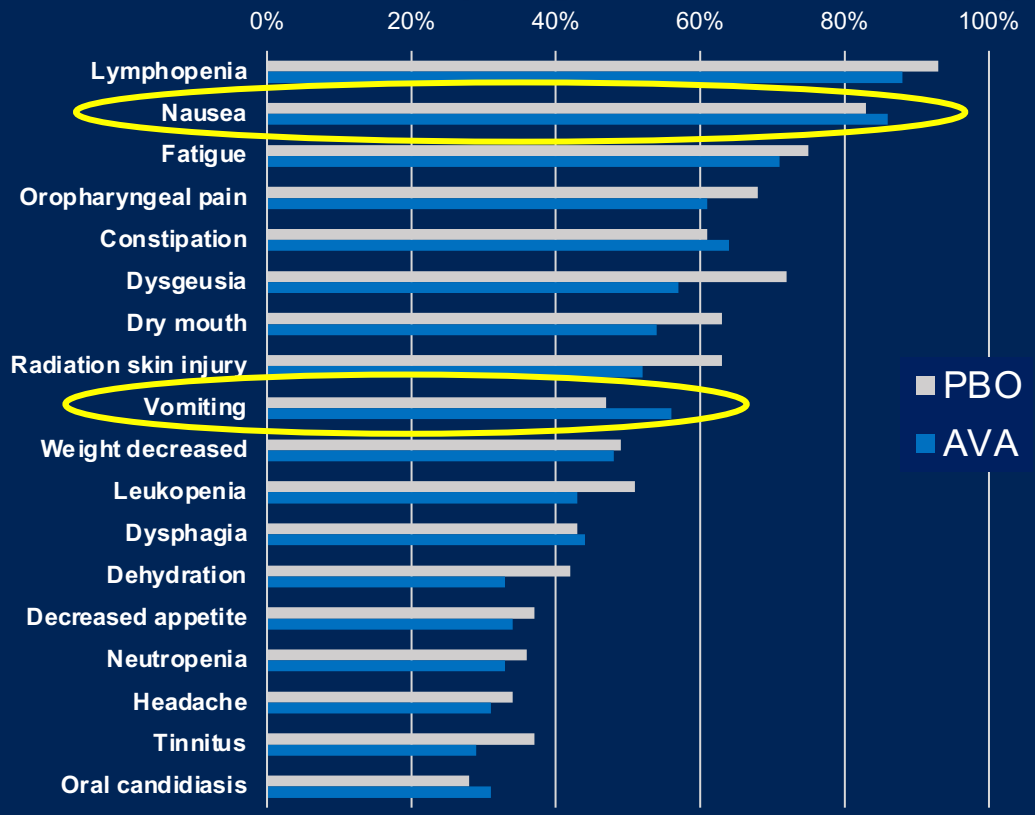

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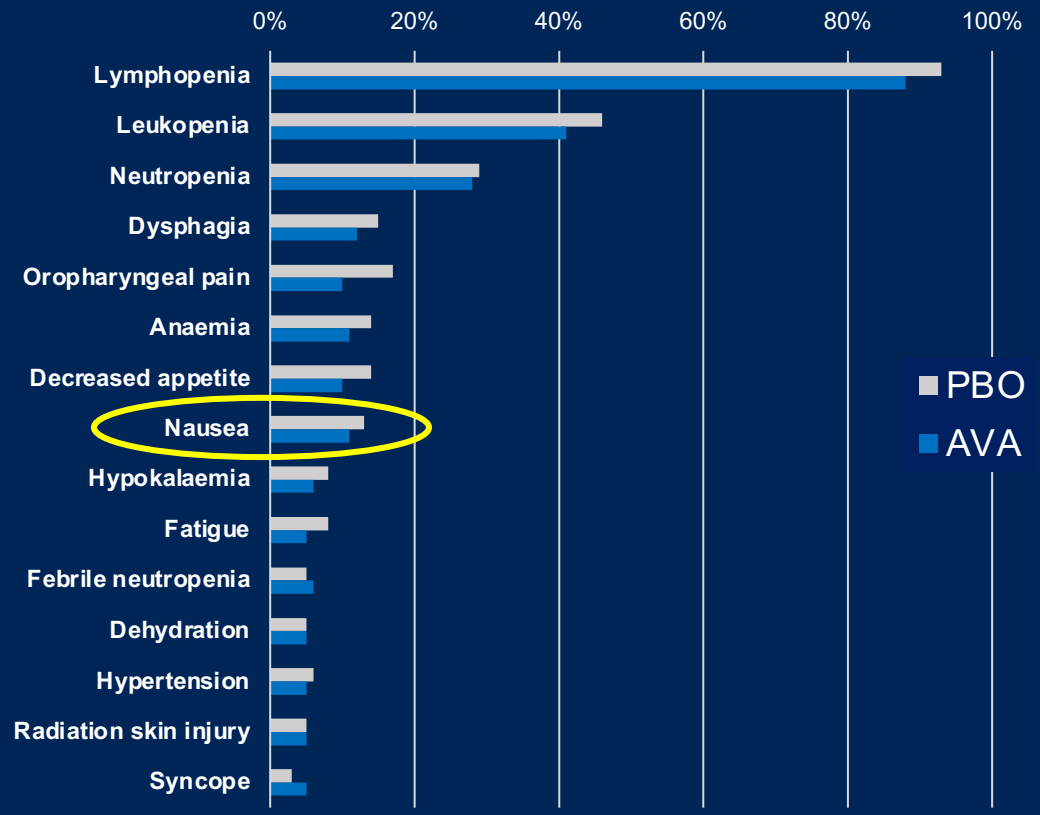

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Conclusions

- 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.

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Thank you

For more information, contact:

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