Galera Therapeutics, Inc

Transforming Radiotherapy *with* Dismutase Mimetics

INTERIM DATA FROM PHASE 1/2 CLINICAL TRIAL OF GC4419 IN COMBINATION WITH SBRT FOR LOCALLY ADVANCED PANCREATIC CANCER

October 27, 2020

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Whenever the Company uses the terms "transform radiotherapy" or "transforming radiotherapy" in this presentation, it is referring to its mission statement.

Superoxide Dismutase Mimetics – Vision

Rapid elimination of Superoxide ($O_2^{\bullet-}$)

IMRT
Intensity Modulated RT

Potential to Reduce Toxicity

Severe Oral Mucositis Head & Neck Cancer (SOM in HNC)	Esophagitis NSC Lung Cancer (NSCLC)
	
Phase 3 ROMAN	Phase 2 Trial

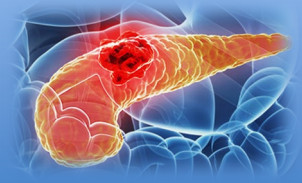
Normal tissue toxicity limits optimal radiotherapy treatment of tumor

Over half of cancer patients receive radiotherapy as part of their care[1, 2]

Increase H_2O_2 in tumors

SBRT
Stereotactic Body RT

Potential to Increase Efficacy

Pancreatic Cancer Locally Advanced (LAPC)	Lung Cancer Locally Advanced (LANSCLC)
	
Phase 1b/2a SBRT Combo	Phase 1b/2a SBRT Combo

Radiotherapy is SoC for many local tumors but need remains for greater efficacy

[1] *Delaney G, Jacob S, Featherstone C, Barton M. The role of radiotherapy in cancer treatment… Cancer. 2005;104:1129-1137*
[2] *Begg AC, Stewart FA, Vens C. Strategies to improve radiotherapy with targeted drugs. Nat Rev Cancer. 2011;11:239-253*

Randomized, Double-Blinded, Placebo-Controlled Multicenter Adaptive Phase 1-2 Trial of GC4419, a Dismutase Mimetic, in Combination with High Dose Stereotactic Body Radiation Therapy (SBRT) in Locally Advanced Pancreatic Cancer (PC)

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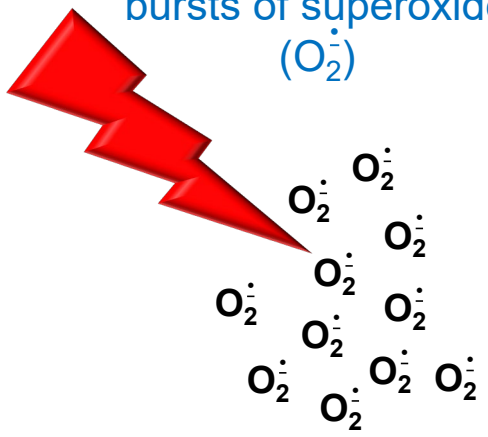
Superoxide Dismutase Mimetics (DM) Augment SBRT

Dismutase mimetics break down superoxide radicals → hydrogen peroxide

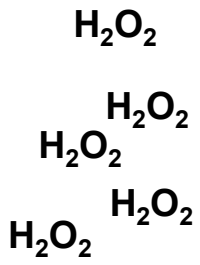
Radiation induces *dose-dependent* bursts of superoxide ($O_2^{\cdot-}$)



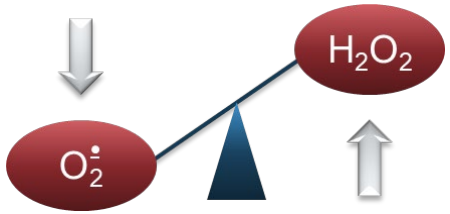
DM

SOD

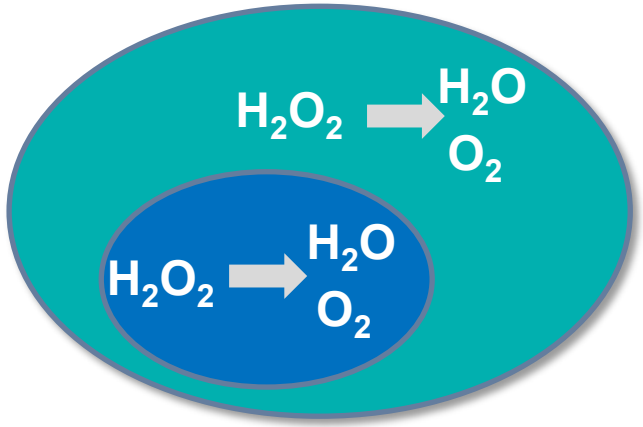
Dismutase mimetics convert the $O_2^{\cdot-}$ into bursts of H_2O_2



Alters the balance in cancer cells from $O_2^{\cdot-}$ to H_2O_2

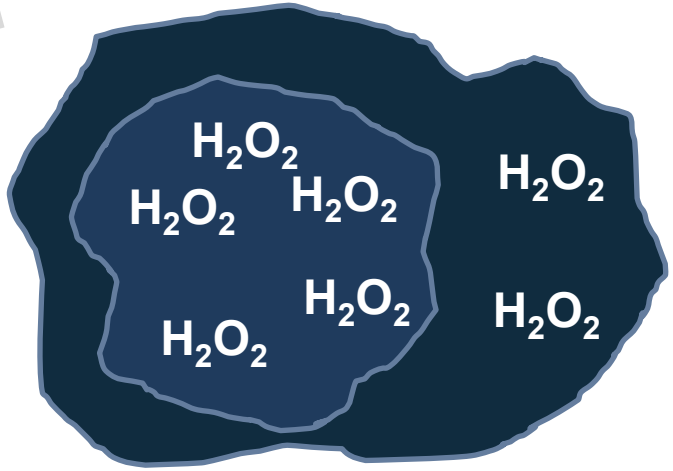


Normal Cell



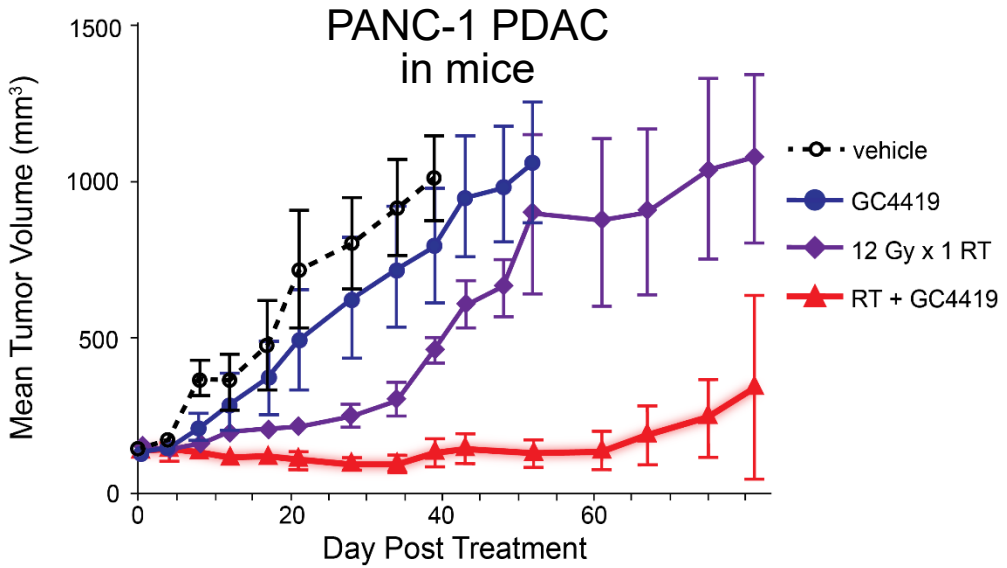
In normal cells, H_2O_2 is efficiently converted to O_2 and H_2O

Cancer Cell

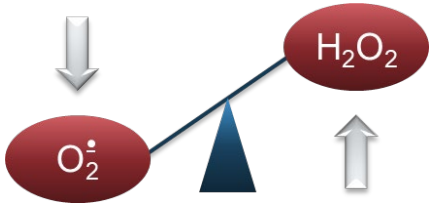


H_2O_2 more toxic to cancer cells than normal cells

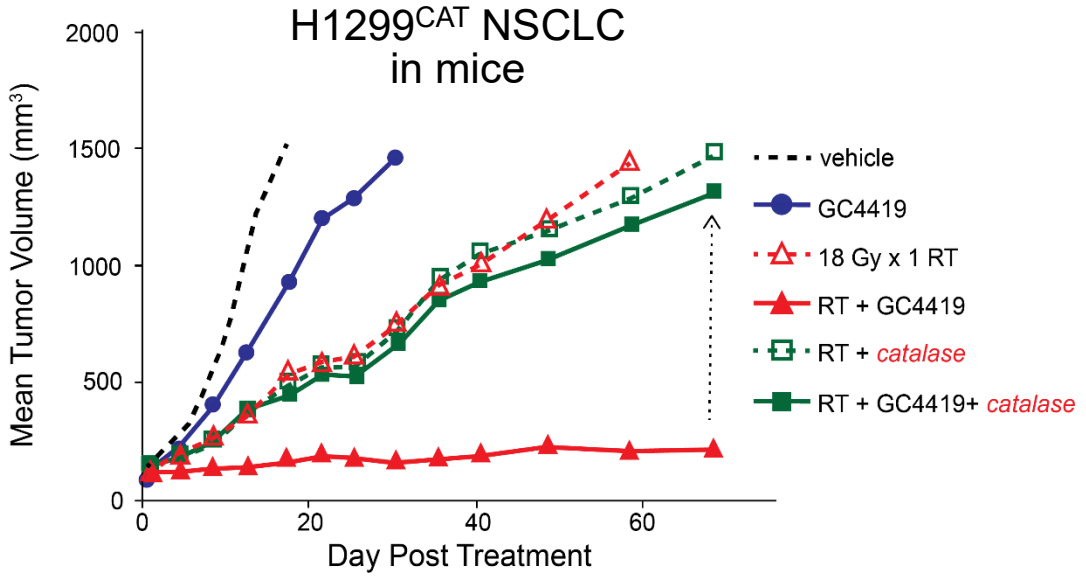
Hypofractionation Reveals an H_2O_2-Dependent Antitumor Synergy of Dismutase Mimetics with SBRT



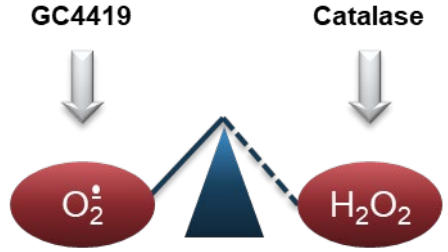
Larger RT fraction → more $O_2^{\bullet-}$
Dismutase Mimetics → more H_2O_2



Genetically modified H1299 tumor with doxycycline-inducible catalase



Tumor tissue H_2O_2 reduced when doxycycline added, losing the synergy



Hypothesis

A selective superoxide dismutase mimetic such as avasopasem (GC4419) will enable SBRT for pancreatic cancer by safely enhancing the radiation response, improving disease control and surgical resectability.

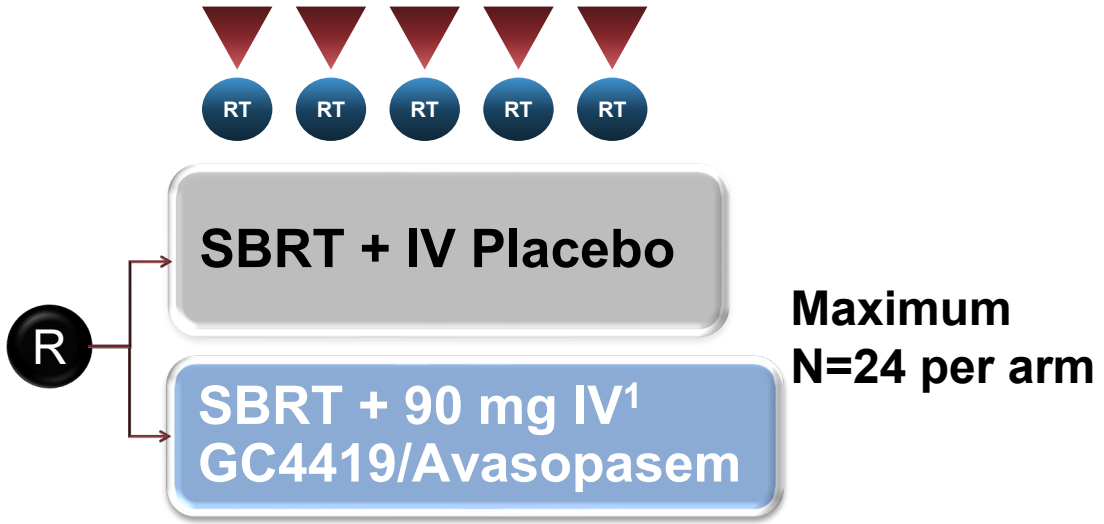
Dismutase Mimetic + SBRT Pilot Trial in Pancreatic Cancer

Randomized, Placebo-Controlled, Double-Blind Trial (NCT03340974)

Locally advanced or borderline resectable pancreatic cancer

Completed initial chemotherapy

M0 disease



Maximum N=24 per arm

SBRT dose: 10 Gy x 5 (BED_{10}= 100 Gy)
11 Gy x 5 (BED_{10}= 116 Gy)
12 Gy x 5 (BED_{10}= 132 Gy)

Dose assigned in real-time by adaptive Bayesian model[2]

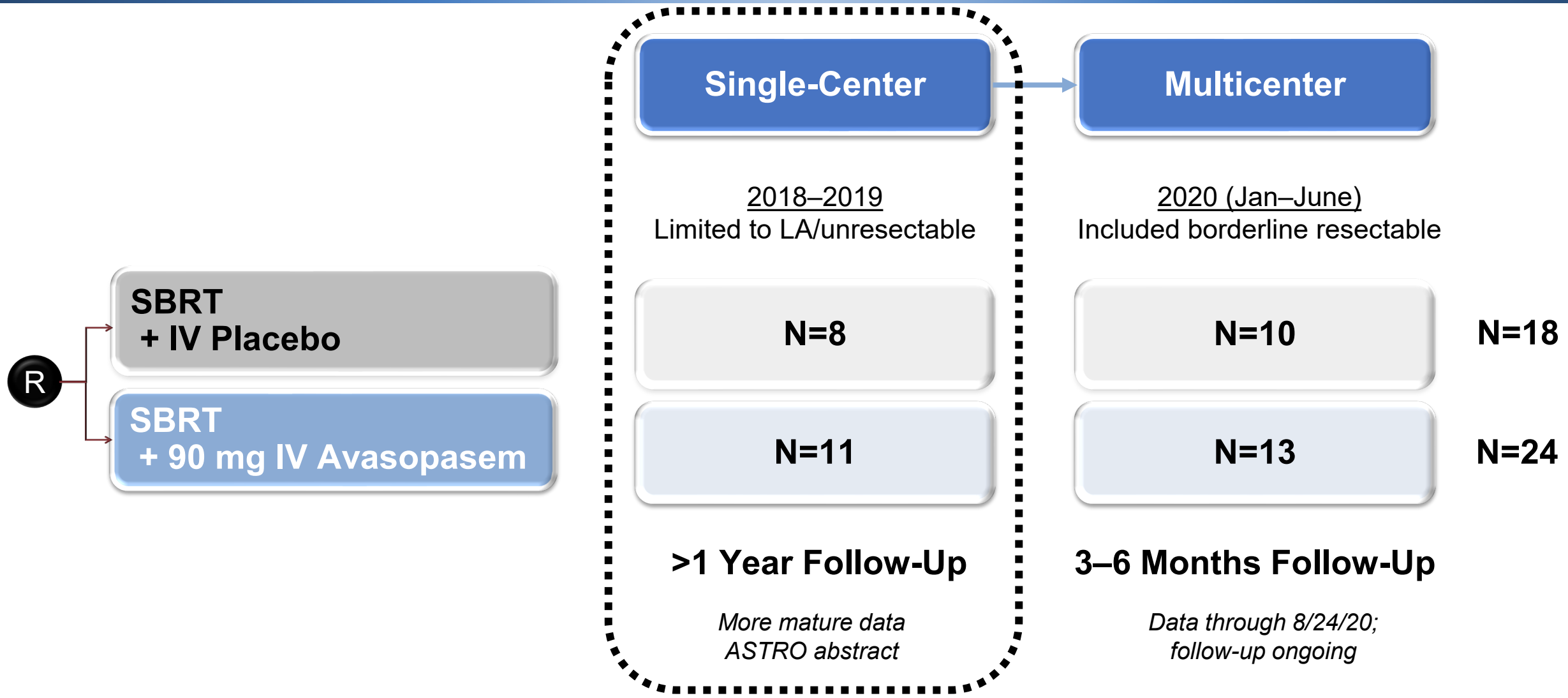
Endpoints

- 1° Recommended dose of SBRT with avasopasem or placebo based on:
  - GR 3-4 GI toxicity or death within 90 days post SBRT
  - Local SD or better at 90 days post SBRT
- 2° PFS, OS, local control, DM rate, ORR, resectability

IV = intravenous; PFS = progression-free survival; OS = overall survival; ORR = overall response rate; DM = distant metastasis; SBRT = stereotactic body radiation therapy; SD = stable disease.

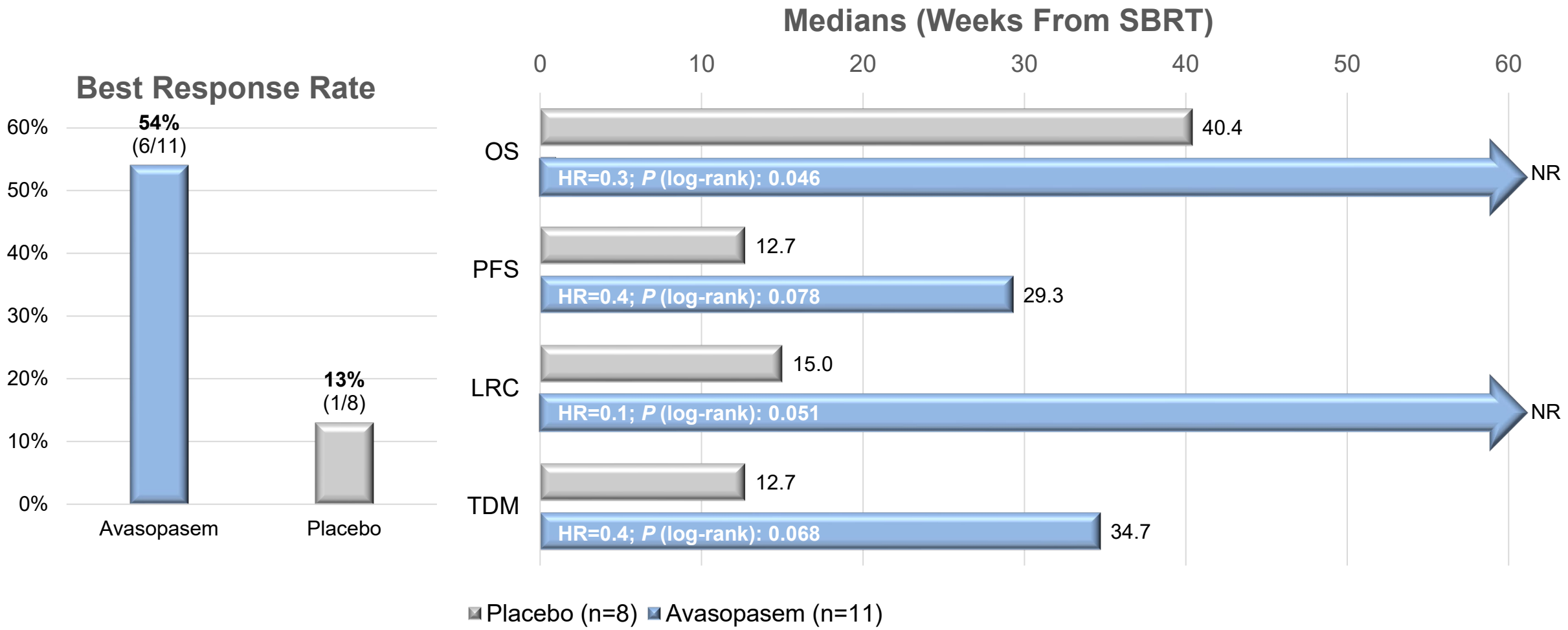
[1] **Anderson, et al, *Journal of Clinical Oncology* 2019 37(34):3256-3265** [2]**Yan et al, *Ann Onc* 2018 29(3):694-699**

Trial Timeline



IV = intravenous; LA = locally advanced; SBRT = stereotactic body radiation therapy.

Efficacy Endpoints for Patients Followed for >1 year
(ITT, n=19)

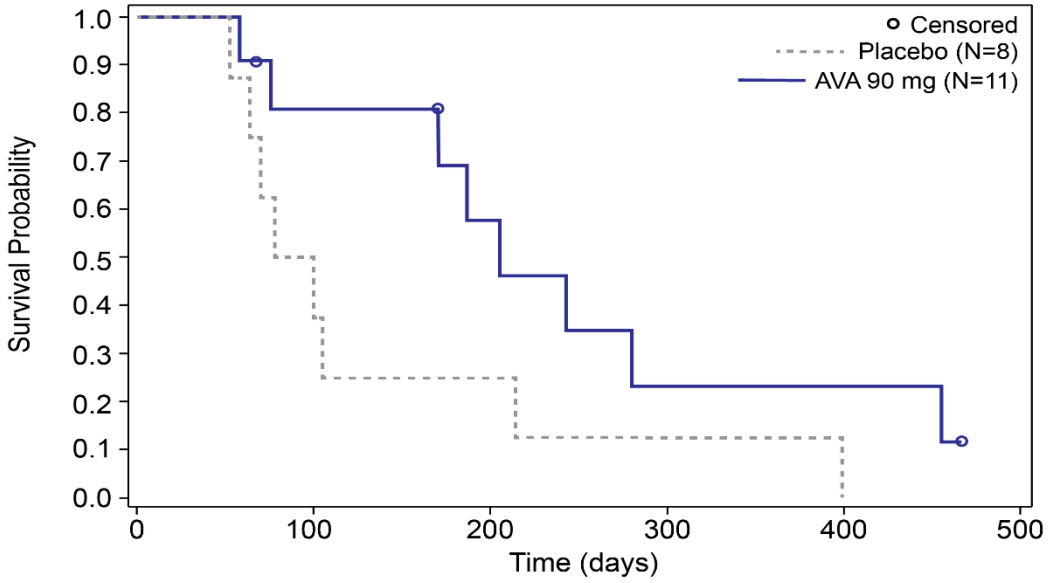


HR = Hazard ratio; LRC = locoregional control; OS = overall survival, PFS = progression-free survival, TDM = time to distant metastases.

Kaplan-Meier Analysis for Patients Followed for >1 Year

Kaplan-Meier Analysis by Treatment (ITT, n=19)

Progression-Free Survival (PFS)

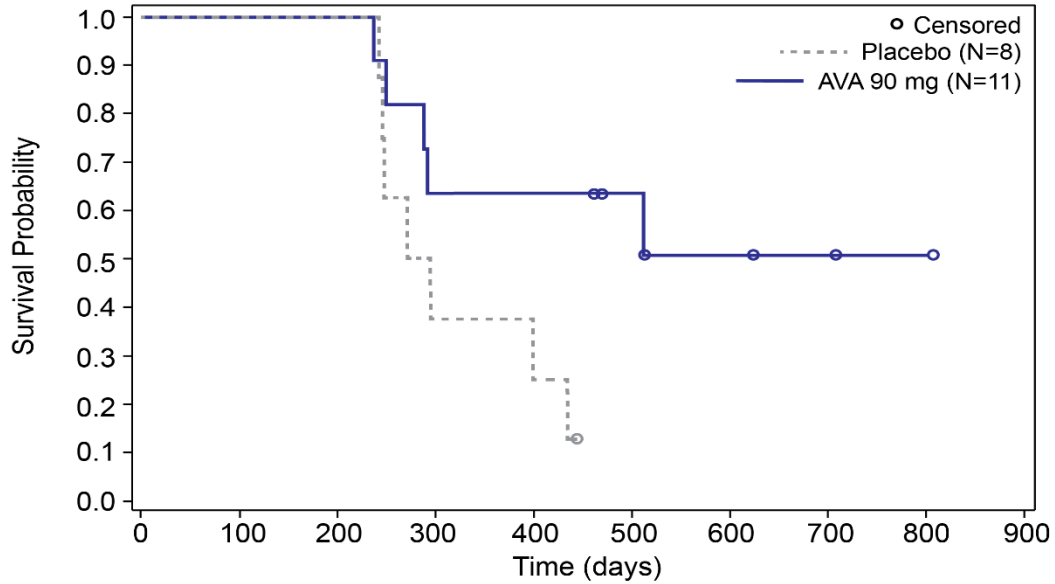


Number of Patients at Risk

Placebo	8	4	2	1	0	
AVA 90 mg	11	8	5	2	2	0

Log Rank *P* value = 0.078

Overall Survival (OS)

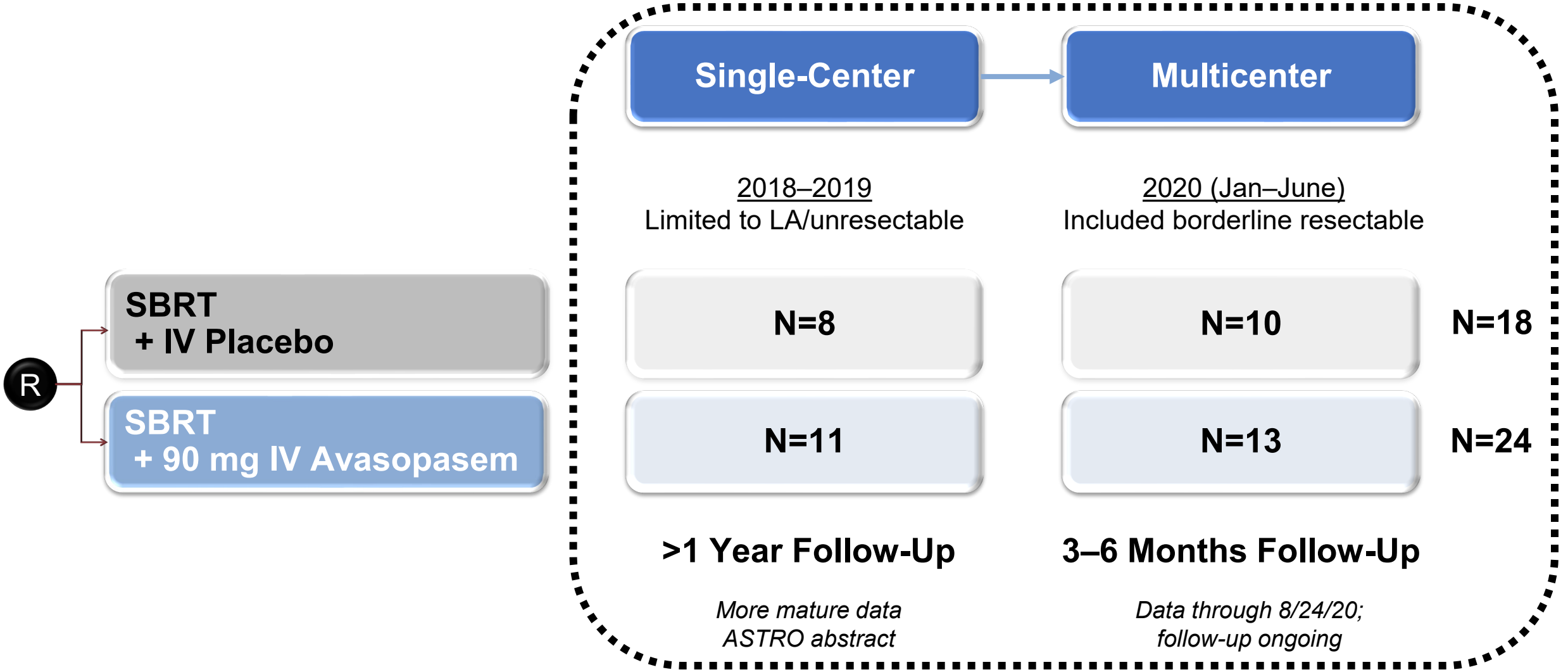


Number of Patients at Risk

Placebo	8	8	8	3	2	0				
AVA 90 mg	11	11	11	7	7	5	3	2	1	0

Log Rank *P* value = 0.0463

Trial Timeline



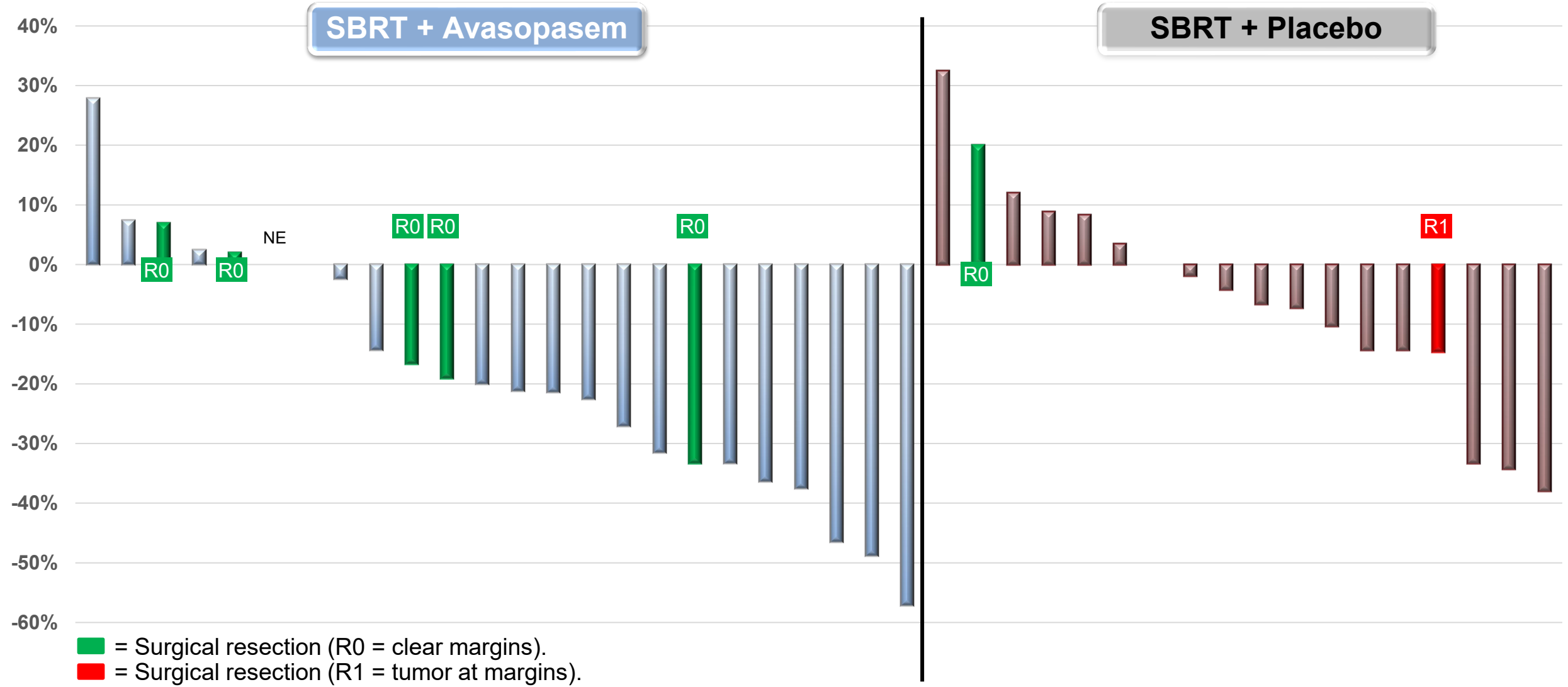
IV = intravenous; LA = locally advanced; SBRT = stereotactic body radiation therapy.

Baseline Characteristics

	Placebo (n=18)	Avasopasem (n=24)
Median age (range), yrs	68 (48–82)	72 (41–83)
Male/Female	7/11	16/8
Borderline resectable/Locally advanced	2/16	7/17
Performance status 0/1/2	9/9/0	12/11/1
Prior chemotherapy duration median (range), wks	21.9 (12.0–36.3)	17.9 (9.1–67.1)
CA19-9 at randomization, median (range)	26.25 (0.5–2186)	28.5 (0.3–70)
Smokers/Nonsmokers	3/15	2/22

Best Response from Baseline Tumor in SBRT Field

Data through August 24, 2020; follow-up ongoing



Patients Who Underwent Resection Post SBRT

Surgical Decision Based on Multiple Factors (n=7)

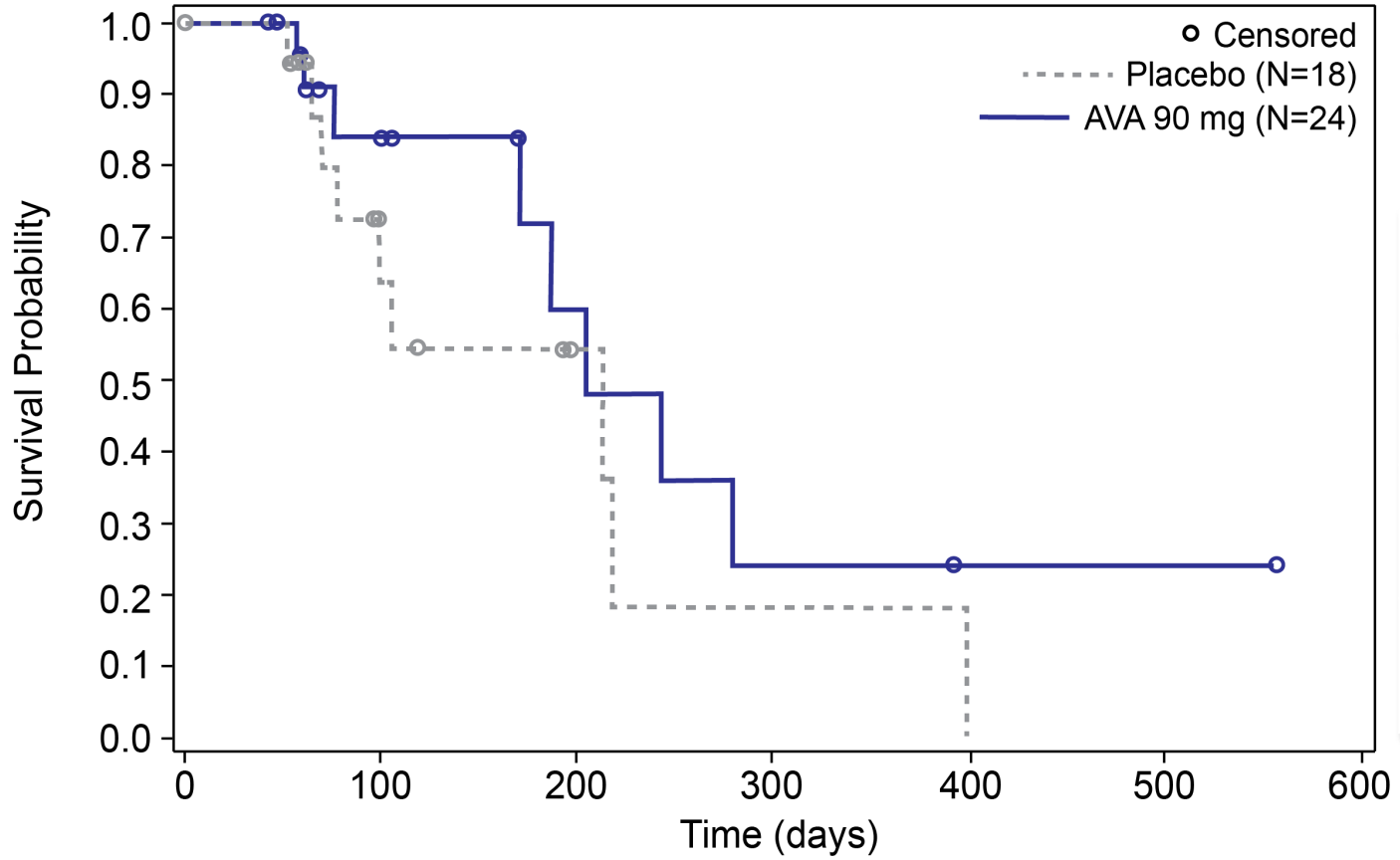
Treatment SBRT Arm	Initial Tumor Staging LA or BR		Margins Post Resection R0/R1		Histopath Analysis Post Resection		
Avasopasem (n=5)	LA		R0		**pCR**		
		BR	R0				pPR
		BR	R0				pPR
		BR	R0				pPR
	LA		R0				pPR
Placebo (n=2)		BR	R0				pPR
	LA			R1		pNR	

- No significant perioperative complications after SBRT for all 7 patients

AVA/PBO = avasopasem or placebo arm; LA/BR = locally advanced or borderline resectable; pCR/pNR/pPR = pathological complete, near, or partial response; R0/R1 = resectable results: R0 = clear margins; SBRT = stereotactic body radiation therapy.

Progression-Free Survival From Randomization (N=42)

Kaplan-Meier Analysis of PFS by Treatment (ITT)—Resected Patients Censored at Time of Surgery



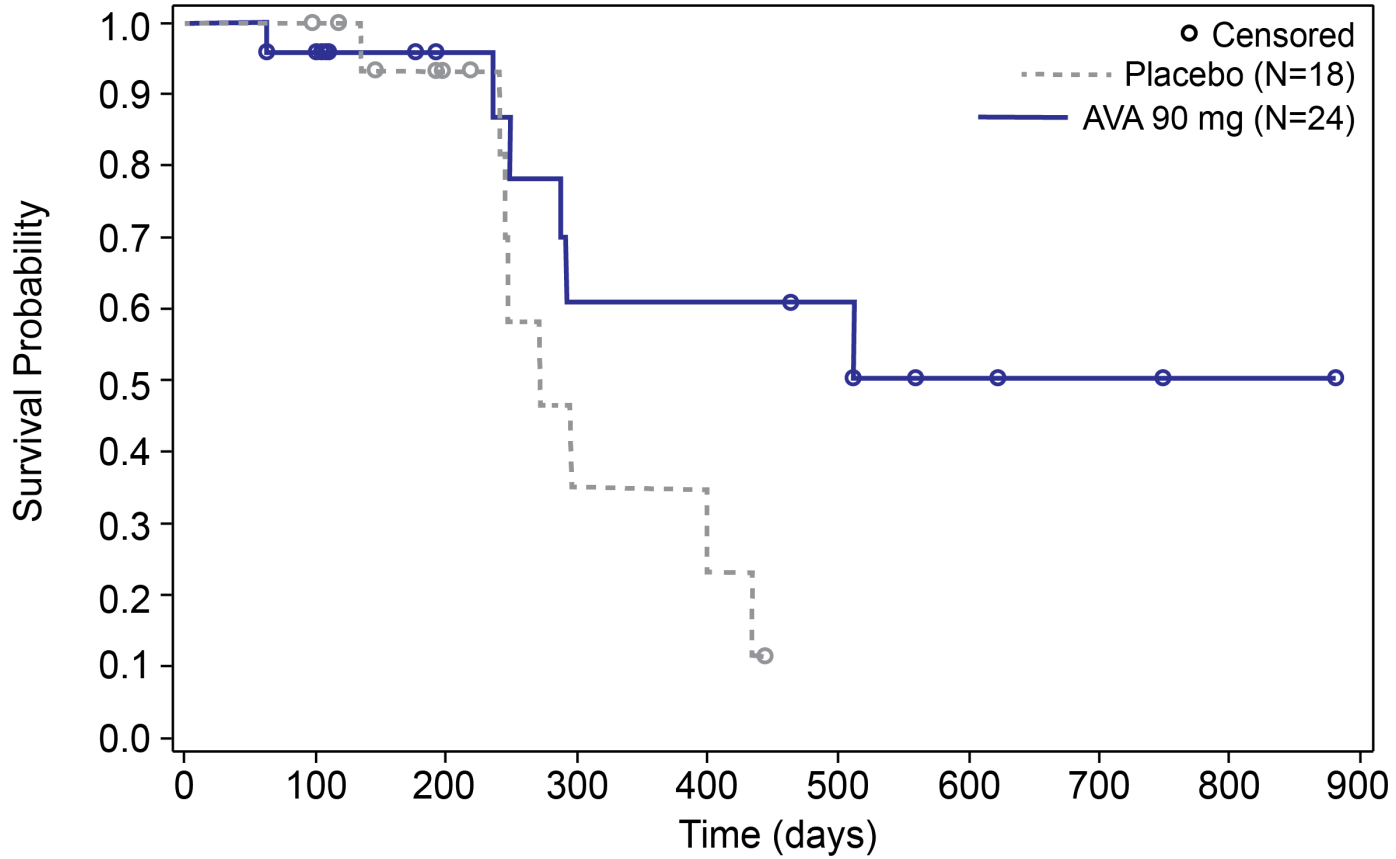
Number of Patients at Risk

Placebo	18	8	3	1	0		
AVA 90 mg	24	12	5	2	1	1	0

	Placebo (n=18)	Avasopasem (n=24)
Median PFS (wks)	30.6	29.3
P value (log-rank)	0.2852	
Hazard Ratio (95% CI)	0.6 (0.23–1.56)	

Overall Survival From Randomization (N=42)

Kaplan-Meier Analysis of OS by Treatment (ITT)



Number of Patients at Risk

Placebo	18	16	9	3	2	0				
AVA 90 mg	24	21	11	7	7	6	3	2	1	0

	Placebo (n=18)	Avasopasem (n=24)
Median OS (wks)	38.7	NR
P value (log-rank)	0.0643	
Hazard Ratio (95% CI)	0.4 (0.12–1.11)	

Grade 3+ Adverse Events
All Causalities

	Placebo (n=18)	Avasopasem (n=24)
Acute Adverse Events (up to 90 days post SBRT)		
• Any acute Grade 3+ AEs, n (%)	4 (22)	6 (25)
• Grade 3 or greater acute GI toxicity[a]	2 (11)	2 (8)
• Total number of Grade 3+ acute AEs	5	8
Late Adverse Events (91 days–1 year post SBRT)		
• Any Grade 3+ AEs, n (%)	5 (28)	7 (29)
• Total number of Grade 3+ late AEs	12	10

[a]No bleeding ulcers by 12-week endoscopy.

AE = adverse event; GI = gastrointestinal.

Conclusions

- This placebo-controlled pilot trial is the first to evaluate the combination of a superoxide dismutase mimetic (avasopasem/GC4419) with SBRT in patients with advanced pancreatic cancer.
- Demonstrated feasibility and preliminary safety of 5 days of avasopasem (90 mg/day) combined with SBRT (10-11 Gy x 5), including subsequent surgical resections in 7 patients.
- In these early analyses, avasopasem appeared to improve tumor responses to SBRT without increasing acute and late toxicity to patients.
- These interim data warrant further studies of dismutase mimetics to enhance responses to SBRT in pancreatic cancer.

Acknowledgements

We thank the patients, their families and caregivers for their contribution to this trial

Sarah E. Hoffe[1], Jessica Frakes[1], Todd Anthony Aguilera[2], Brian Czito[3], Manisha Palta[3], Melissa Brookes[4], Lauren Elizabeth Colbert[5], Shalini Moningi[5], Manoop S. Bhutani[5], Shubham Pant[5], Ching-Wei D. Tzeng[5], Rebecca Slack Tidwell[5], Peter F. Thall[5], Elizabeth Charlotte Moser[4], Jon Holmlund[4], Joseph M. Herman[5], Cullen M. Taniguchi[5]

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