Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Tumors (SABR-COMET): Results of A Randomized Trial

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Disclosure for Dr. Palma

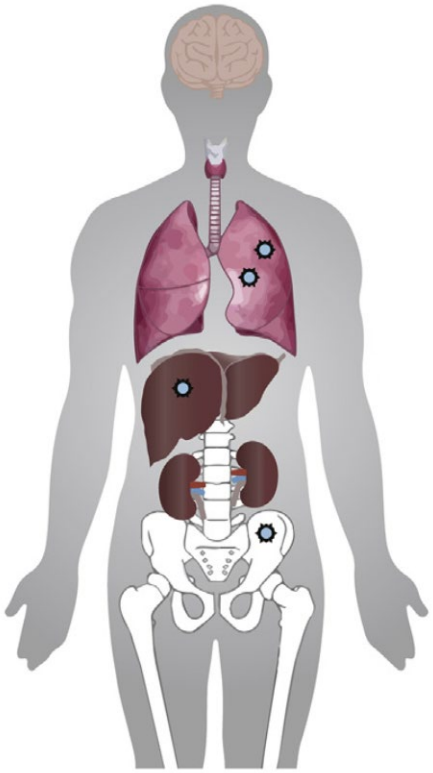
- I have no conflicts of interest to disclose.

Background

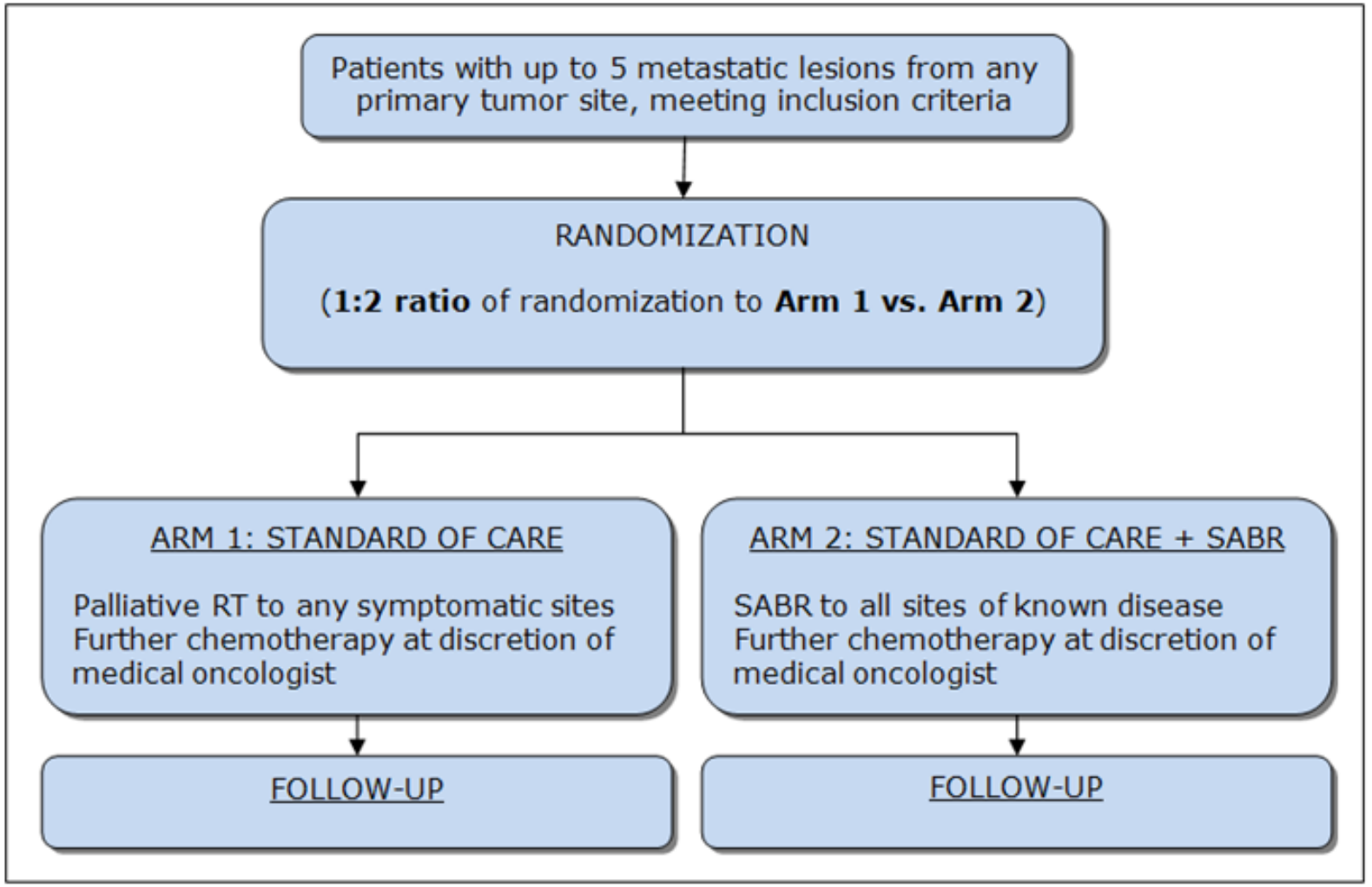
- Patients with metastatic cancer are generally considered incurable, but oligometastatic theory proposes that a few, small spots can be eliminated with radiation/surgery

- Stereotactic radiation (e.g., SABR, SBRT) delivers substantially higher doses of radiation very precisely to the tumor site in 1-5 treatment sessions

- This is the first RCT to directly test the oligometastatic paradigm
    - Directly compares OS after ablative vs. palliative approaches for patients with up to 5 metastatic lesions



SABR-COMET Schema



Primary Endpoint

- Overall survival

Secondary Endpoints

- Progression-free survival
- Toxicity (CTC-AE 4.0)
- Quality of life (FACT-G)
- Lesional control rate
- Number of cycles of further systemic therapy
  - Changed to binary variable "Receipt of systemic therapy" (Y/N)

Baseline Patient Characteristics

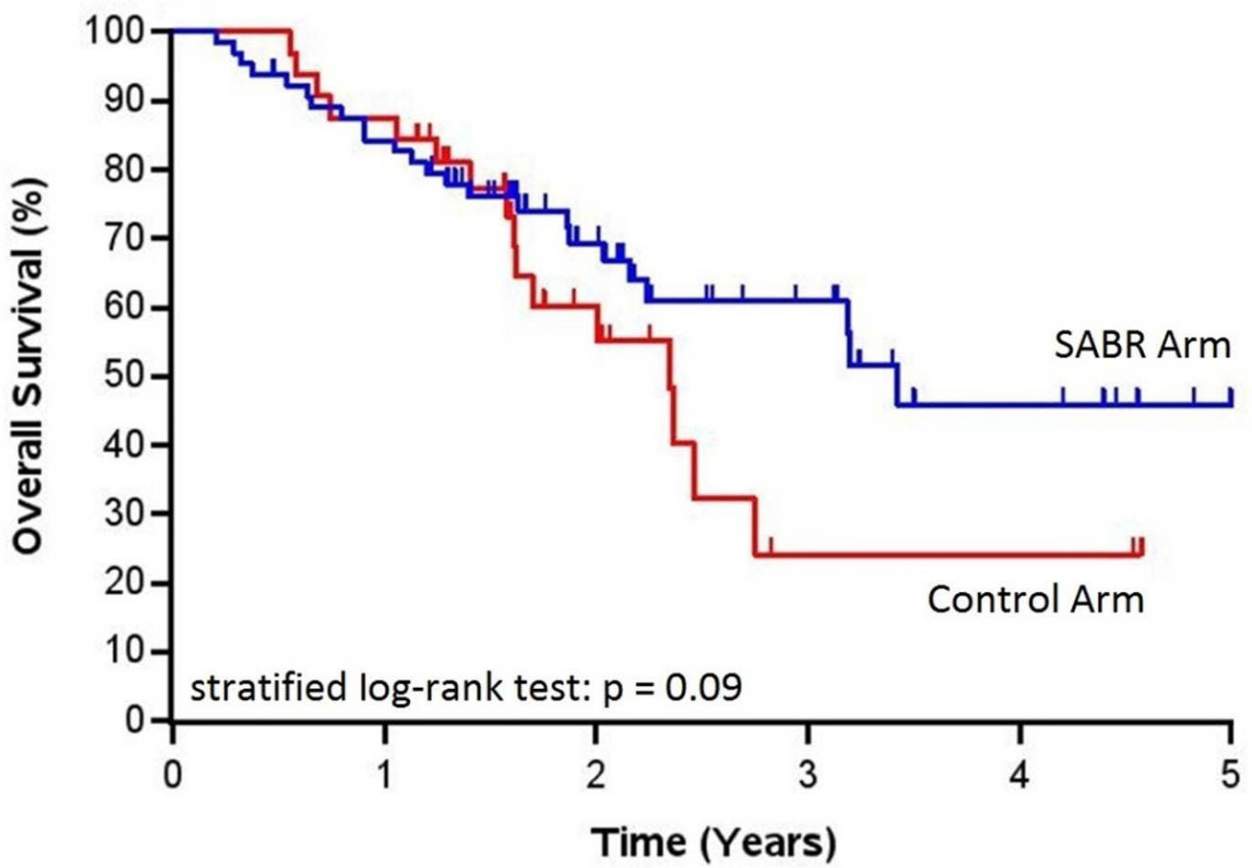
Between February 2012 and August 2016, 99 patients were randomized at centers in Canada, Scotland, Netherlands and Australia

Characteristic	All Patients (n=99)	Control Arm (n=33)	SABR Arm (n=66)	p-value
Age – median, (min, max)	68 (43, 89)	69 (44, 87)	67 (43, 89)	0.494
Sex – n(%)				0.772
Male	59 (59.6)	19 (57.6)	40 (60.6)	
Female	40 (40.4)	14 (42.4)	26 (39.4)	
Site of Original Primary Tumor – n(%)				0.204
Breast	18 (18.2)	5 (15.2)	13 (19.7)	
Colorectal	18 (18.2)	9 (27.3)	9 (13.6)	
Lung	18 (18.2)	6 (18.2)	12 (18.2)	
Prostate	16 (16.2)	2 (6.1)	14 (21.2)	
Other	29 (29.3)	11 (33.3)	18 (27.3)	

Baseline Patient Characteristics

Characteristic	All Patients (n=99)	Control Arm (n=33)	SABR Arm (n=66)	p-value
Number of Metastases – n(%)				0.591
1	42 (42.4)	12 (36.4)	30 (45.5)	
2	32 (32.3)	13 (39.4)	19 (28.8)	
3	18 (18.2)	6 (18.2)	12 (18.2)	
4	4 (4.0)	2 (6.1)	2 (3.0)	
5	3 (3.0)	0 (0.0)	3 (4.6)	
Location of Metastases – n(%)				0.181
Adrenal	9 (4.7)	2 (3.1)	7 (5.5)	
Bone	65 (34.0)	20 (31.3)	45 (35.4)	
Liver	19 (10.0)	3 (4.7)	16 (12.6)	
Lung	89 (46.6)	34 (53.1)	55 (43.3)	
Other	9 (4.7)	5 (7.8)	4 (3.2)	

Results: Overall Survival



Number at risk:

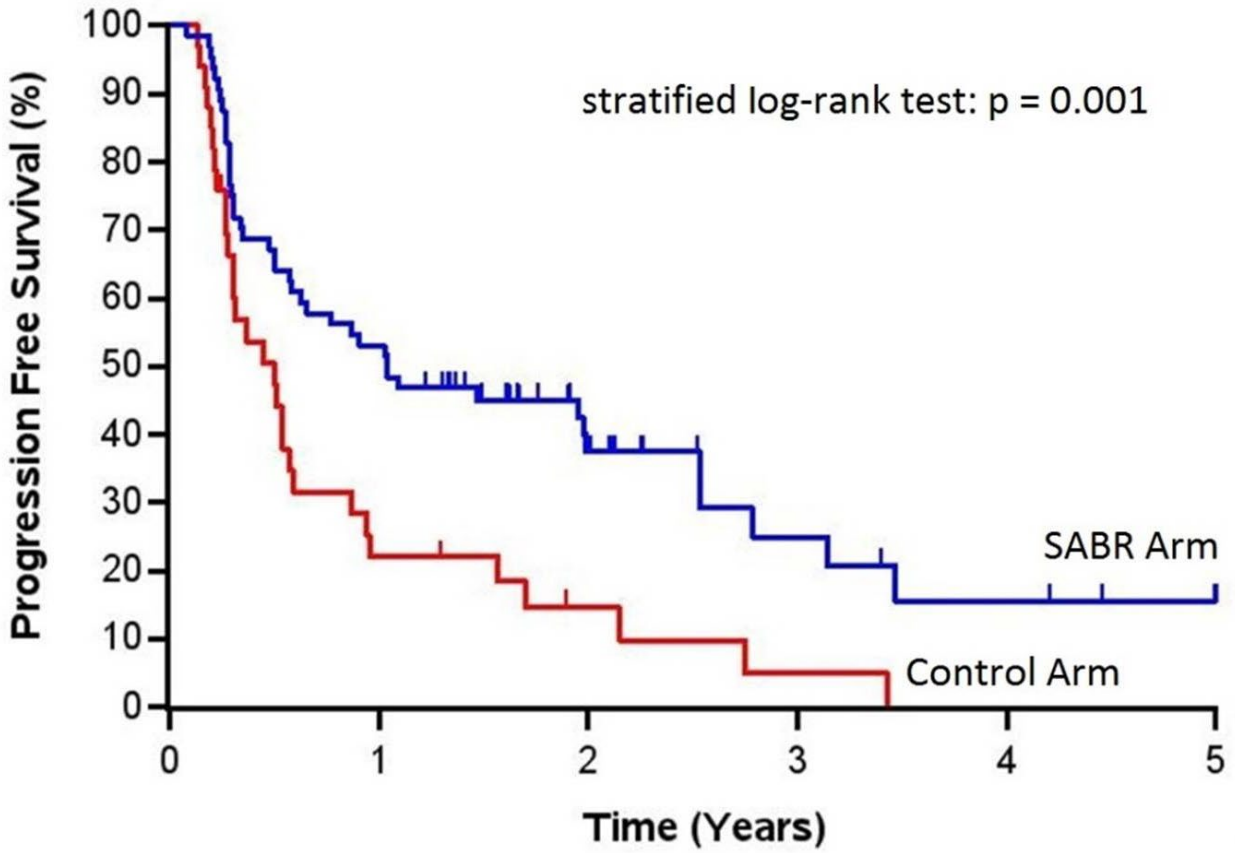
Control	33	28	12	2	2	
SABR	66	53	29	15	7	1

Median Overall Survival

Control Arm: 28 months
(95% CI: 19-33 months)

SABR Arm: 41 months
(95% CI: 26 months to 'not reached')

Results: Progression-free Survival



Number at risk:

Control	33	7	3	1		
SABR	66	34	15	6	3	1

Median PFS

Control Arm: 6 months
(95% CI: 3.4-7.1 months)

SABR Arm: 12 months
(95% CI: 6.9-30 months)

Results: Adverse Events

Characteristic	All Patients (n=99)	Control Arm (n=33)	SABR Arm (n=66)	p-value
Related AE Grade ≥ 2 – n(%)	22 (22.2)	3 (9.1)	19 (28.8)	0.03
AE Associated with Death (Grade 5) – n(%)	3 (3.0)	0 (0.0)	3 (4.5)	0.55
Fatigue – n(%)				
Grade 2	6 (6.1)	2 (6.1)	4 (6.1)	0.45
Grade 3	1 (1.0)	1 (3.0)	0 (0.0)	
Dyspnea – n(%)				
Grade 2	1 (1.0)	0 (0.0)	1 (1.5)	1.00
Grade 3	1 (1.0)	0 (0.0)	1 (1.5)	
Pain (any type) – n(%)				
Grade 2	5 (5.1)	0 (0.0)	5 (7.6)	0.14
Grade 3	3 (3.0)	0 (0.0)	3 (4.6)	

Related events were determined by the treating investigator (Possibly, Probably, or Definitely related)

Results: Additional Secondary Endpoints

	Control	SABR	P-value
Quality of Life FACT-G @ 6 months (mean ± SD)	82.5 ± 16.4	82.6 ± 16.6	0.99
Lesional Control Rate (i.e. absence of progression in lesions present at randomization)	49%	75%	p<0.001
Receipt of Systemic Therapy	58%	52%	0.57

Conclusions

- SABR was associated with improved OS, meeting the primary endpoint of this trial, and PFS was doubled. Toxicities were more common with SABR, with a 4.5% risk of treatment-related death, but no decrease in QOL.
- This is a higher level of evidence than exists for any surgical intervention for oligometastatic disease.
- The clinical question: Is clear PFS benefit enough to treat?
  - OS data are promising but need to mature; Study amended to follow patients for 10 years
  - Majority of FDA approvals for cancer drugs are not based on OS.[1,2]
- Next steps: phase III RCTs for 1-3 and 4-10 metastatic lesions

[1]Brooks et al, Drugs Context, 2017, [2]Kim et Prasad, JAMA Internal Medicine 2015