

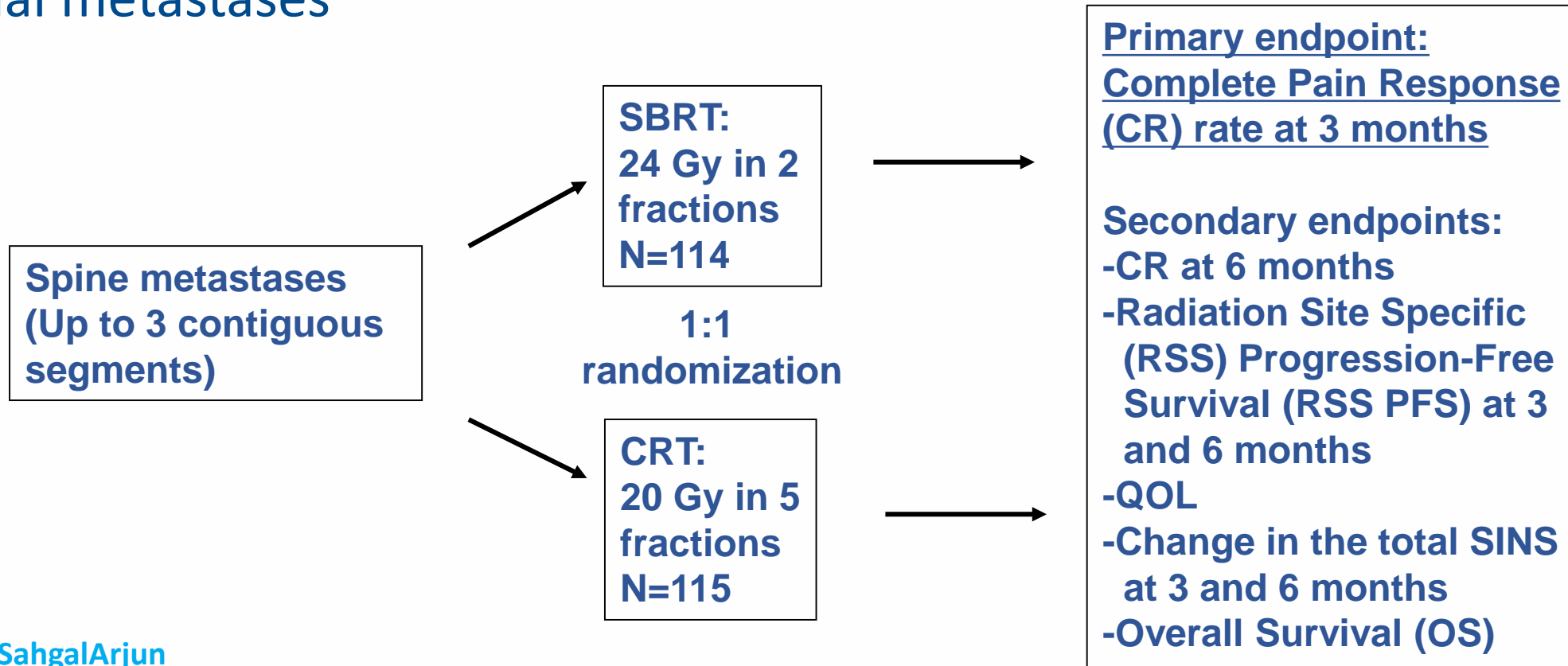
CCTG SC.24/TROG 17.06:

A Randomized Phase II/III Study Comparing 24Gy in 2 Stereotactic Body Radiotherapy (SBRT) Fractions Versus 20Gy in 5 Conventional Palliative Radiotherapy (CRT) Fractions for Patients with Painful Spinal Metastases (NCT02512965)

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Overview

- Tested in a Phase 2/3 randomized controlled trial (RCT) a Canadian spine SBRT fractionation scheme of 24 Gy in 2 fractions*, to a standard of care CRT regimen of 20 Gy in 5 fractions, to determine if the complete pain response rate (CR) can be improved with spine SBRT vs. CRT for patients with painful spinal metastases



Statistical Considerations

- Initial Phase 2 RCT that was converted to a Phase 3 RCT without interruption of accrual
- A priori assumption of a CR to pain in the SBRT arm was 34% vs 17% in the CRT arm
 - 15% drop out/in-evaluable rate per month, 2-sided 5% level test and 80% power
 - Sample size was determined at 228 patients
 - Accrual period: Jan 2016-September 2019
 - Patients in-evaluable at outcome assessment time points of 3 and 6 months considered non-responder

	SBRT	CRT	Total
Total patients randomized	114	115	229
Did not receive study treatment	4	0	4
In-evaluable at 3 months	16	22	38
Intent to treat (ITT) analyses	114	115	229
Safety/QA Analyses (as-treated)	110	115	225

Radiation Target Volume Pain Response Rates

Response	CRT (N=115)	SBRT (N=114)
3 month assessment		
Complete response	14 %	35%
Partial response	25%	18%
Stable disease	30%	24%
Progressive disease	12%	6%
Indeterminant	19%	18%
Mean change in total SINS (standard deviation)	-0.49 (1.61)	-0.94 (1.69)

Response	CRT (N=115)	SBRT (N=114)
6 month assessment		
Complete response	16%	32%
Partial response	16%	9%
Stable disease	27%	23%
Progressive disease	7%	4%
Indeterminant	34%	32%
Mean change in total SINS (standard deviation)	-0.74 (1.99)	-0.73 (1.86)

Multivariable Analyses for CR at 3 and 6 months

Variable	3-month Odds Ratio	3-month 95% Confidence Interval	3- month P Value	6-month Odds Ratio	6-month 95% CI	6- month P Value
SBRT CRT	3.47 1.0	1.77-6.80	0.0003	2.45 1	1.28-4.71	0.007
Age ≥ 65 Age < 65	1.58 1.0	0.82-3.06	0.17	0.65 1	0.34-1.25	0.20
Male Female	1.33 1.0	0.54-3.26	0.54	1.39 1	0.56-3.45	0.48
ECOG 2 ECOG 0 or 1	0.74 1.0	0.19-2.89	0.67	0.39 1	0.08-1.86	0.24
Pain Score at Baseline 8 to 10 5 to 7 2 to 4	0.92 0.74 1.0	0.39-2.20 0.36-1.54	0.85 0.43	1.39 0.94 1	0.60-3.21 1.45-1.96	0.44 0.86
Primary Cancer: GU (excluding RCC) Lung Other Breast	1.22 1.49 0.58 1	0.32-4.65 0.54-4.08 0.09-3.77	0.77 0.44 0.57	0.99 0.96 0.74 1	0.26-3.79 0.36-2.63 0.14-3.86	0.99 0.95 0.72
Total baseline SINS 7 to 12 ≤ 6	1.12 1	0.58-2.15	0.57	0.91 1	0.48-1.71	0.78

Conclusions

- Spine SBRT is superior to CRT and achieved a 21% absolute increase in the CR to pain at 3 months which was durable at the 6 month and final assessment and statistically significant
- 1st Phase 3 RCT trial to show dose escalation with modern RT improves pain outcomes for patients with spinal bone metastases
- 24 Gy in 2 SBRT fractions was safe, non-destabilizing and associated with better patient financial perception and should be considered a standard of care