

# A Retrospective Review of Stage III Unresectable and Stage IV Extracranial Cancers Treated with Concurrent and Sequential PD-1 Inhibitors and Ablative Radiation Therapy at LVHN

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# A Retrospective Review of Stage III Unresectable and Stage IV Extracranial Cancers Treated with Concurrent and Sequential PD-1 Inhibitors and Ablative Radiation Therapy at LVHN

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## Background

- Radiation therapy has long been used in treating unresectable cancer or reducing the risk of local recurrence after surgery<sup>1</sup>.
- Checkpoint blockade immunotherapy has gained increasing attention for treating patients with metastatic cancer, specifically in conjunction with radiation therapy<sup>2</sup>.
- Previous studies of combined therapy have shown improved local control of tumor burden with minimal adverse events (AEs) ( $\leq$  Grade 3)<sup>3</sup>.
- Our institution has been treating patients with concurrent ablative (stereotactic or hypofractionated) radiation therapy (ART) and anti-PD1 immunotherapy for various oligometastatic malignancies.
- Long term local and distant treatment response, autoimmune adverse events, and survival outcomes in our patient cohort are unknown.

## Problem Statement

**Primary Aim:** Report local and distant treatment response in patients with stage IV/unresectable stage III solid tumors treated with concurrent and sequential hypofractionated ablative radiation therapy and anti-PD-1.

**Secondary Aim:** Report overall health outcomes and safety profiles of patients treated with this modality.

## Methods

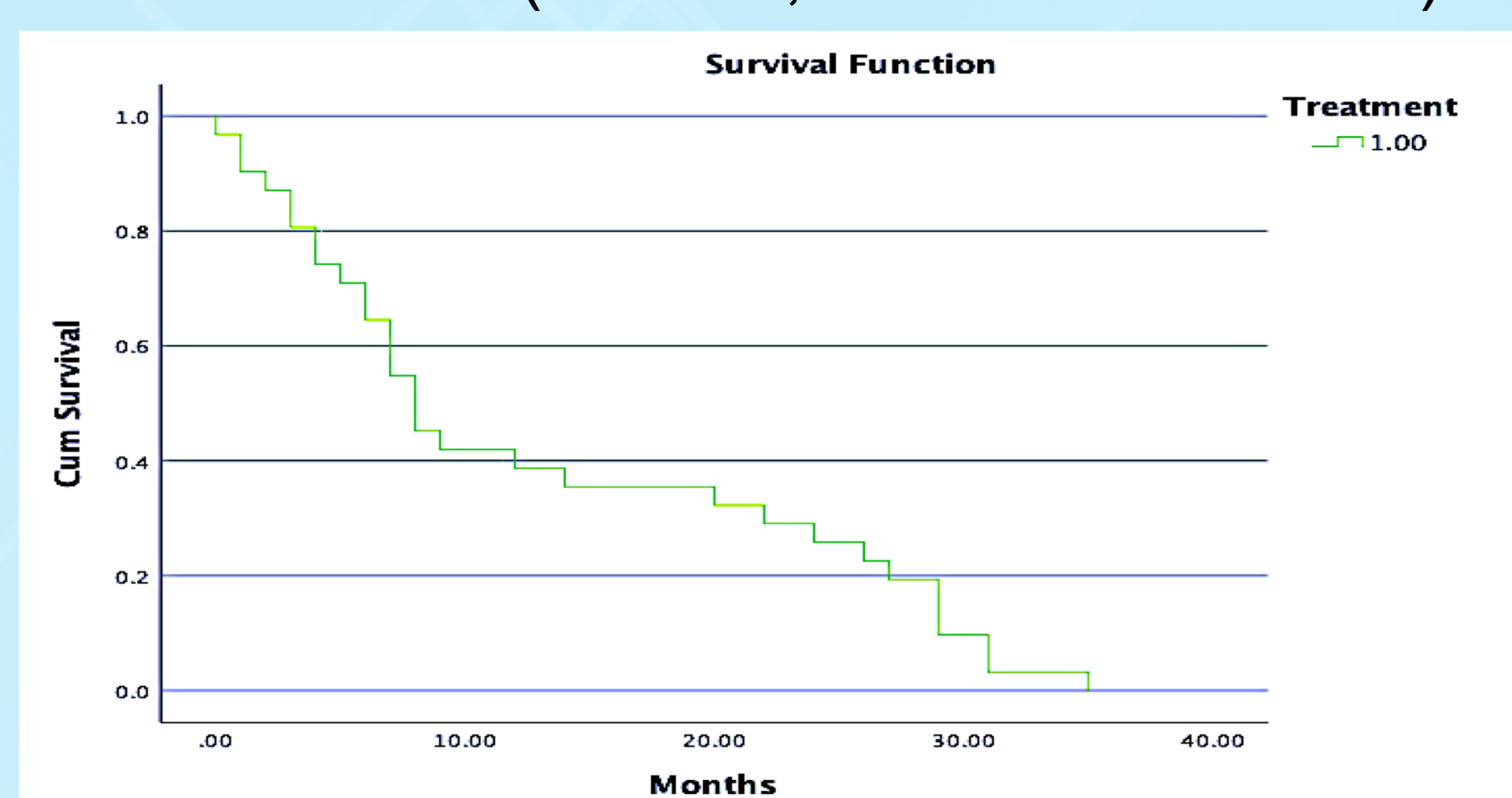
- This is an IRB approved retrospective cohort study of patients with extra-cranial metastases who received treatment with concurrent ablative radiotherapy and anti-PD-1 immunotherapy at LVHN.
- Patients with stage III and stage IV unresectable malignancies 18 years or older treated with combined hypofractionated ablative radiation therapy and anti-PD-1 from 1/1/2015 to 12/31/2016 were included.
- Patients who have received chemotherapy prior to concurrent treatment, and patients who received radiation therapy in same region as concurrent treatment location were excluded.
- 29 patients with oligometastatic lesions including sarcoma (7%), renal cell carcinoma (24%), melanoma (59%), and lung cancer (10%), were treated with concurrent radiation and anti-PD1 therapy.
- The data was statistically analyzed through SPSS to determine outcomes as stated in the primary and secondary aims.

## Results

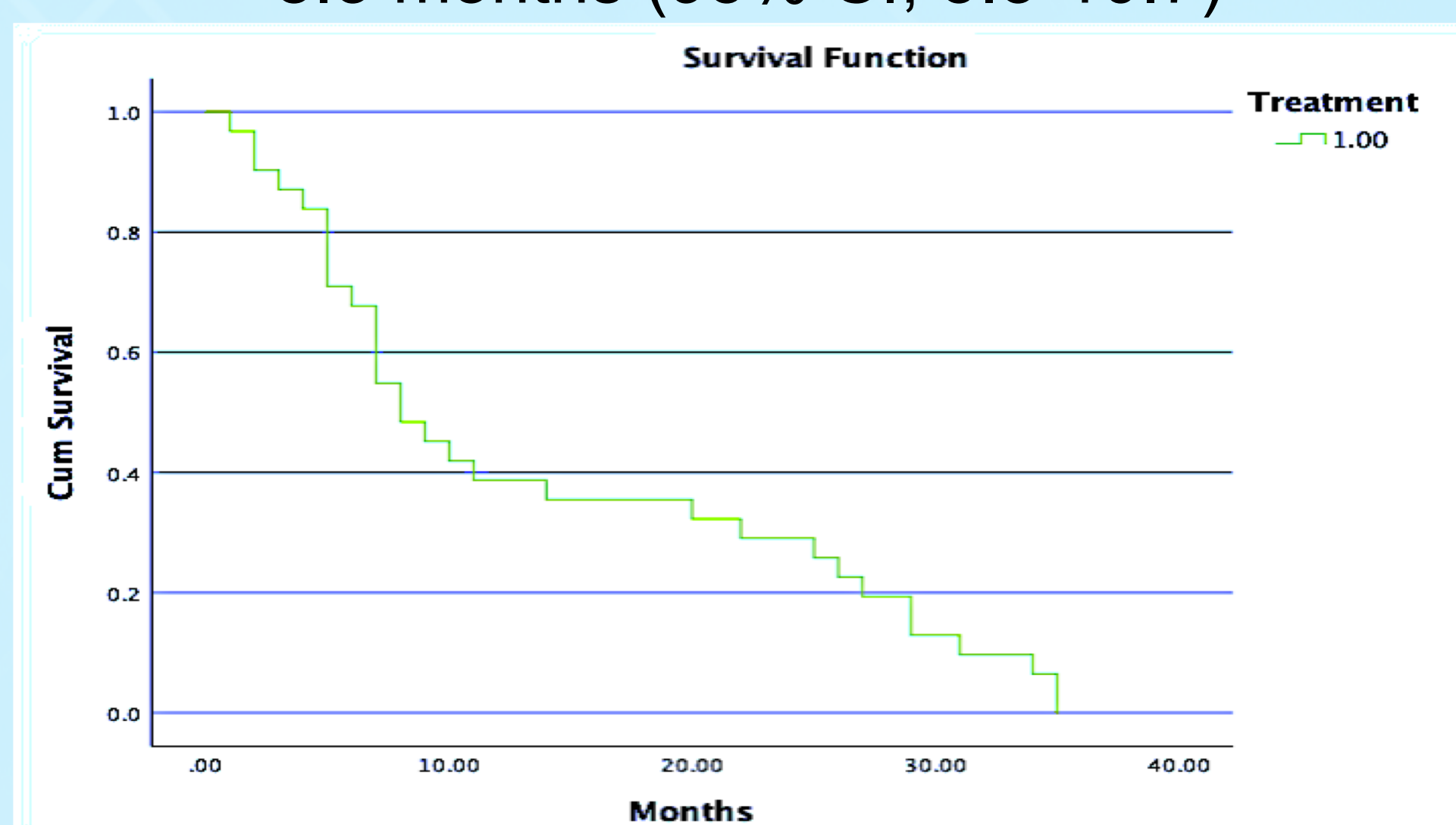
Of 37 oligometastatic sites, 68% reached local clinical benefit and 30% reached distant benefit:

Local and Distant Tumor Response Outcomes			
<b>Local Response</b>			
Complete Response	8	22%	
Partial Response	8	22%	
Stable Disease	9	24%	
Progressive Disease	12	32%	
<b>Distant Response</b>			
Complete Response	3	8%	
Partial Response	5	14%	
Stable Disease	3	8%	
Progressive Disease	26	70%	

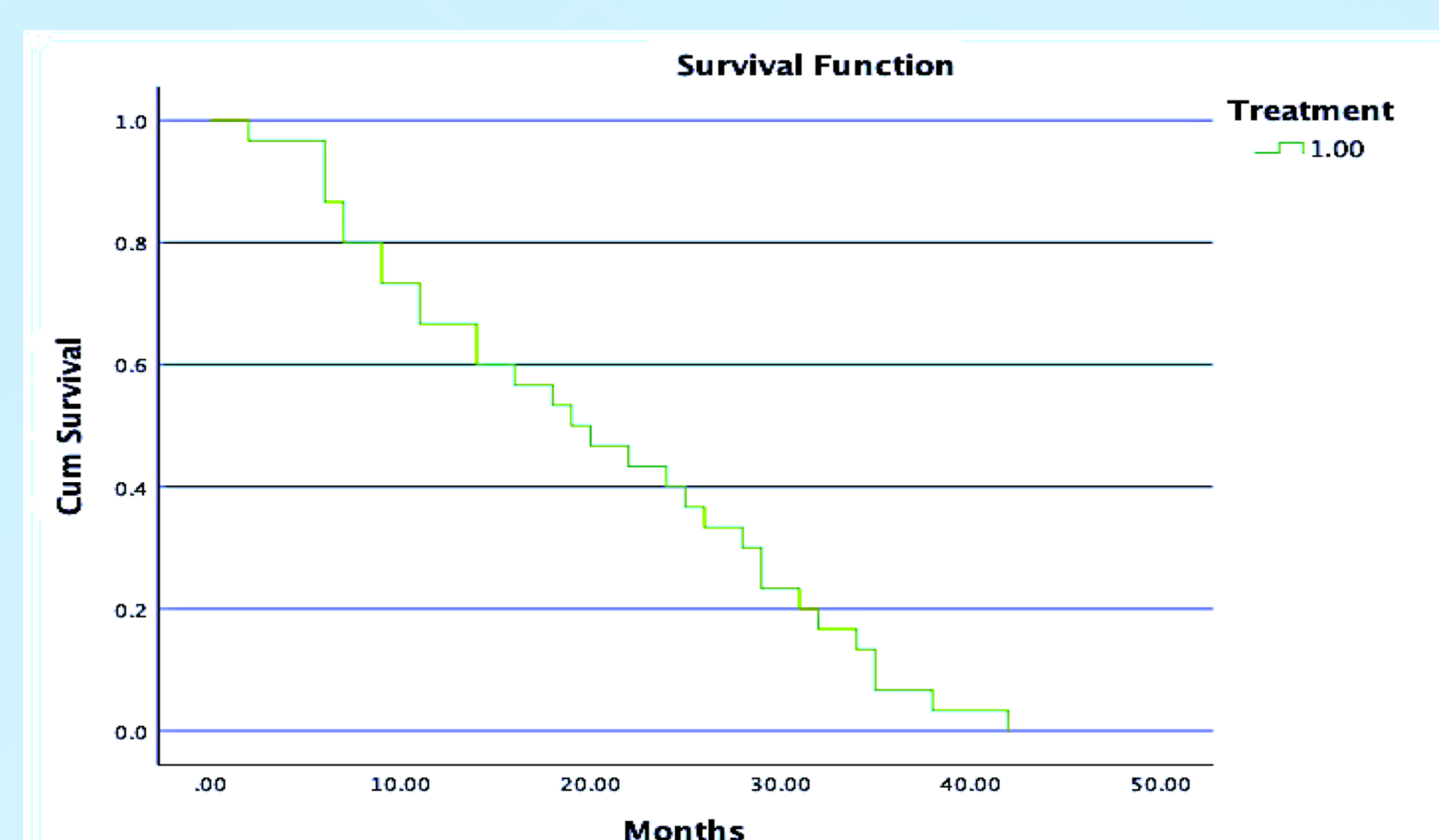
Median Local Progression-Free Survival  
8.1 months (95% CI, 5.7 to not reached)



Median Distant. Progression-Free Survival  
8.3 months (95% CI, 5.3-10.7)



Median Overall Survival  
19.5 months (95% CI, 10.3 to not reached).



Grade  $\geq$  3 toxicity occurred in 8 patients (28%) in 13 instances including nephritis (17%) hypophysitis (8%) colitis (25%) pneumonia (25%) and arthritis (25%).

## Conclusions/SELECT Implications

- In this series, concurrent immunotherapy and ablative radiotherapy to oligometastases yielded some improvement in tumor control and overall survival and moderate rates of Grade 3 autoimmune toxicity compared to historic controls (monotherapy with immunomodulation) and previous studies.
- This treatment is unique as it focuses on combining immunotherapy and radiation therapy, the success of which heavily relies upon the integration of medical oncology, radiation oncology, and at the epicenter, the patient and their families.<sup>4</sup>
- This process involved multiple SELECT competencies, including peer-to-peer mentorship, communicating on a multidisciplinary platform, and evaluating the safety and efficacy of an increasingly utilized modality of treating cancer.

## Limitations/ Future Directions

- Our patient population is extremely heterogenous (various primary cancer diagnoses, prior radiation in other regions, other treatments such as chemotherapy during or after combined treatment, and location and number of metastases). Additionally our study was retrospective, nonblinded and nonrandomized.
- These limitations warrant future prospective, randomized studies as this treatment modality could yield clinical benefit for patients with oligometastatic disease.
- Ongoing Phase II studies are evaluating the combination of anti-pd1 therapy with hypofractionated radiation compared to anti-pd1 monotherapy in terms of tumor response rates, overall survival, safety profiles, and the molecular basis of the synergistic effect between the combined modalities<sup>5</sup>.
- Future studies could utilize quality of life measures<sup>6</sup> to better capture symptom burden from the patient's perspective.

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