# Management of Brain Metastases from Small Cell Lung Cancer using SRS

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## BACKGROUND

- Small Cell Lung Cancer is avidly metastatic with a significant tropism for the brain
- Nonetheless the natural history tends to be that patients succumb to systemic disease burden rather than intracranial burden
- In the pre-MRI era, CNS metastasis was documented in ~50% of patients and discovered in ~65% at autopsy, with incidence increased to ~80% among those surviving at least 2 years from Dx. Median survival: 9 months without and 8.4 months with documented CNS mets, NSS (1).
- Current NCCN guidelines: "Brain metastases should typically be treated with WBRT; however, selected patients with a small number of metastases may be appropriately treated with stereotactic radiotherapy (SRT)/radiosurgery (SRS)" (2).
- EORTC 22952 found for 1-3 brain mets from solid tumors **(excluding SCLC)** no survival advantage to addition of WBRT to SRS but significantly greater neurocognitive toxicity, and greater intracranial progression with omission of WBRT but equivalent survival and better QOL, establishing upfront SRS as standard of care for limited intracranial disease/high performance status (3).
- For SCLC, management of CNS disease poses unique challenge: assumer greater disease extent than radiographically apparent and risk neurocognitive toxicity to give WBRT? Or treat focally to maximize QOL with risk of florid progression?
- Combination of MRI surveillance and SRS intervention is attractive to many radiation oncologists. Data to guide practice are scarce, but utilization is rising. Per one review of 489 patients at a European center between 1990 and 2018, first line treatment for brain mets in SCLC was 43.4% SRS vs. 36% WBRT (4).
- Retrospective FIRE-SCLC cohort study showed decreased time to CNS progression with SRS vs. WBRT without compromised survival, similar to findings in other histologies (5).

## PURPOSE/OBJECTIVES

- In the SCLC setting, what is the relationship between progression of intracranial disease, neurologically symptomatic disease, and survival?
- We examine our institutional experience treating patients with SCLC with CNS involvement with SRS.
- We hypothesize that an SRS strategy in well-selected patients who undergo close MRI surveillance will result in acceptable tumor control, and without disproportionate future neurological symptoms associated with progression of disease.

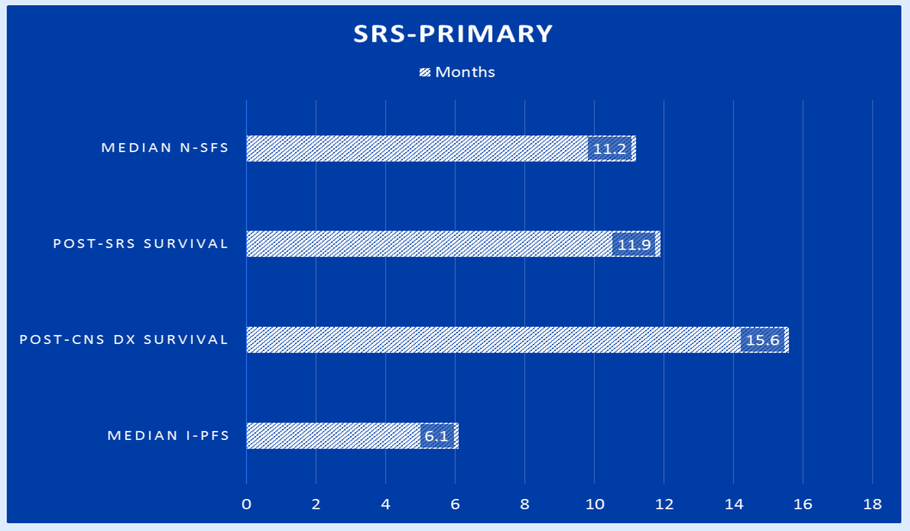
## MATERIALS/METHODS

- Institutional EMR queried to identify patients with a diagnosis of high grade neuroendocrine lung cancer who had undergone SRS between 2013 and 2019
- 20 total patients divided into two groups
- SRS-primary: patients who, at time of SRS, had not received previous PCI or WBRT
- SRS-salvage: patients who had received previous PCI or WBRT
- Primary outcome: neurologic symptom-free survival (N-SFS), defined as time to development of neurologic symptoms attributed to disease progression
- Secondary outcomes: intracranial progression-free survival (I-PFS), survival from CNS diagnosis, survival from initial CNS therapy

## RESULTS

| | SRS-primary (n=11) |
|---|---|
| ES | 9 |
| LS | 2 |
| Focal neuro Sx at CNS Dx | 3 |
| Focal neuro Sx post-SRS | 3 |
| Salvage | 3 SRS, 2 WBRT |
| Death d/t intracranial disease | 0 |

| | SRS-salvage |
|---|---|
| PCI | 6 |
| ES | 4 |
| LS | 5 |
| Focal neuro Sx at CNS Dx | 4 |
| Focal neuro Sx post-therapeutic intervention (WBRT or SRS) | 3 |
| Salvage | 9 SRS |
| Death d/t intracranial disease | 1 |




## RESULTS (continued)

| | SRS-primary | SRS-salvage |
|---|---|---|
| Median I-PFS | 6.1 mos (0.9-14.5) | 9.8 mos (1.8-23.6) post-WBRT/PCI<br>*2.5 mos (0.6-12.8) post-salvage SRS* |
| Survival | 15.6 mos (4.1-43.5) post-CNS Dx<br>*11.9 mos (1.5-43.0) post-SRS* | 5.5 mos (1.1-27.8) post-CNS Dx<br>*15.9 mos (5.1-34.6) post-WBRT/PCI* |
| N-SFS | 11.2 mos (3.6-40.0) | 17.2 mos (1.1-42.9) |

## DISCUSSION

- Symptomatic intracranial disease following SRS was uncommon
- SRS salvage of SRS-primary patients did not have deleterious outcomes
- No patients undergoing upfront SRS died from intracranial disease
- Both radiographic and neurologic outcomes from upfront SRS are favorable
- **In particular post-SRS survival and N-SFS are nearly identical in SRS-primary group**
  - **i.e. upfront SRS does not sacrifice length or quality of life in this cohort**
- Caveats: data are not randomized, confounders clearly present, SRS-salvage cohort weighted towards LS presentation vs. SRS-primary group, study is under-powered
- Neurocognitive toxicities not well-documented, but can safely be assumed to favor upfront SRS
- Prior NCDB studies have shown better OS with SRS vs. WBRT+SRS, and generally poor post-WBRT survival (6,7)
- To our knowledge direct comparison of neurocognitive and QOL outcomes between focal and whole brain approaches in either prospective or retrospective settings is lacking
- Because we know that SCLC patients are unlikely to die from intracranial disease, asymptomatic intracranial progression should not be chief concern and can be successfully salvaged
- In well-selected patients, with but only with MRI surveillance, SRS may be a reasonable primary management strategy
- Prospective data will be needed to validate these results

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