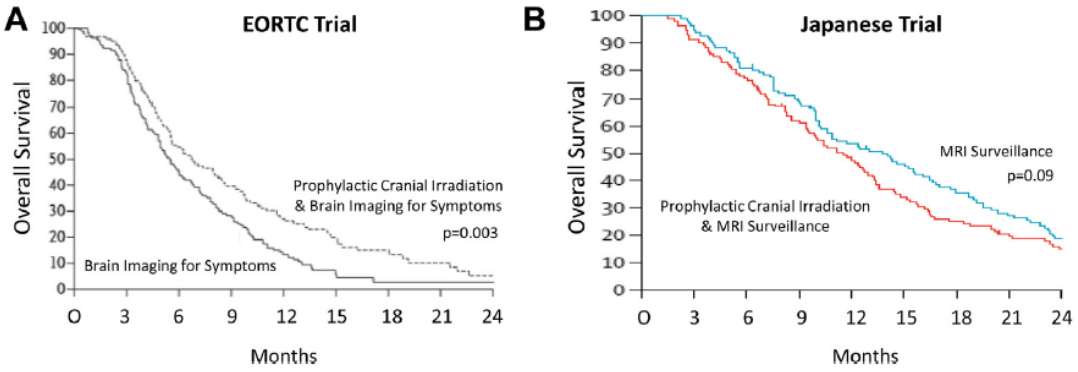
MAVERICK (SWOG S1827)

MRI Brain Surveillance Alone versus MRI Surveillance and Prophylactic Cranial Irradiation: A Randomized Phase III Trial in Small-Cell Lung Cancer

PI: Chad Rusthoven, Radiation Oncology Chair: Paul Brown,
Cognitive Chair: Jeffrey Wefel, Statistics: Mary Redman,
Translational Medicine Chair: Abhijit Patel, Radiology Chair: Justin Honce,
NRG Champion: Daphna Gelblum, Alliance Champion: Jyoti Patel,
ECOG Champion: Jyoti Malhotra, CCTG Champion: Jonathan Greenland,
VA Champion: Drew Moghanaki

PCI Background

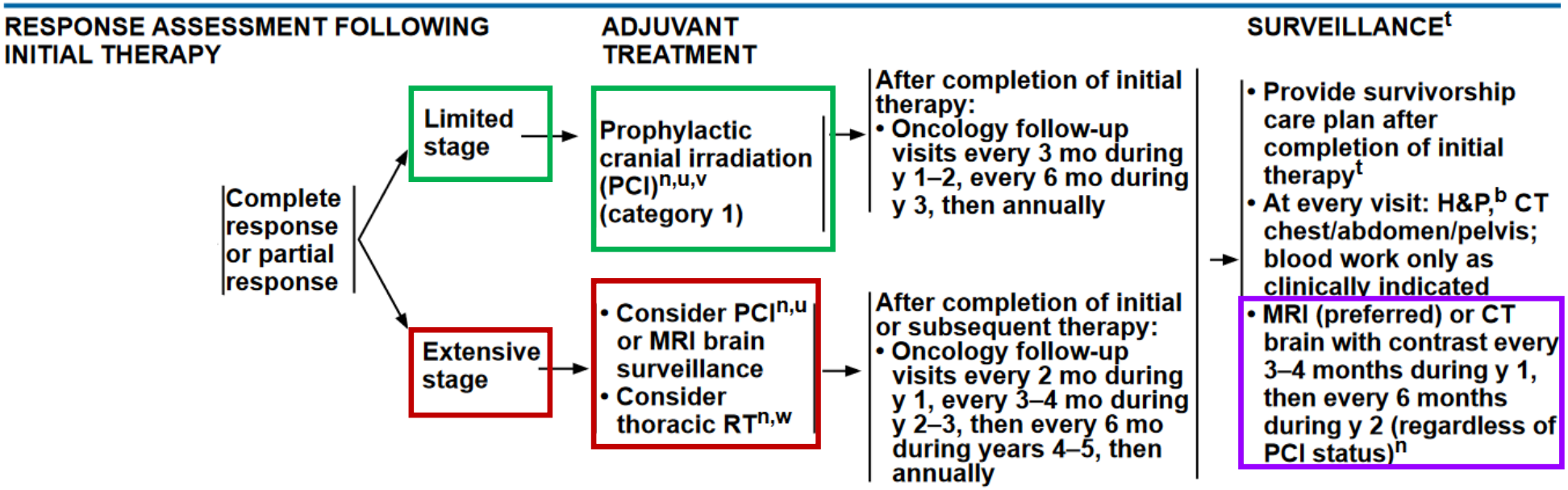
- PCI has historically been associated with ↓brain metastases and ↑neurologic toxicity
- PCI became the standard-of-care for SCLC following 2 landmark studies demonstrating ↑OS:
  - (1) Meta-analysis of primarily LS-SCLC (Auperin, *NEJM 1999*) and (2) an EORTC RCT in ES-SCLC (Slotman, *NEJM 2007*)
  - Both studies were limited by heterogeneous or absent brain staging and surveillance imaging
- Subsequently, a Japanese RCT in ES-SCLC (Takahashi, *Lancet Oncol 2017*) evaluated MRI surveillance +/- PCI
  - Reported no differences in PFS or OS with the addition of PCI (median OS 13.7 vs 11.6 mo, p=0.09, favoring no-PCI)
- Implications?
  - MRI surveillance (allowing for early salvage therapy for brain mets) may allow for the avoidance of PCI and its associated toxicities
  - The NCCN now categorizes PCI as 'optional' in ES-SCLC and recommends MRI surveillance for all patients regardless of PCI delivery



Auperin, *NEJM* 341.7 (1999): 476-484
Slotman, *NEJM* 357.7 (2007): 664-672
Takahashi, *Lancet Oncol* 18.5 (2017): 663-671

National Comprehensive Cancer Network®

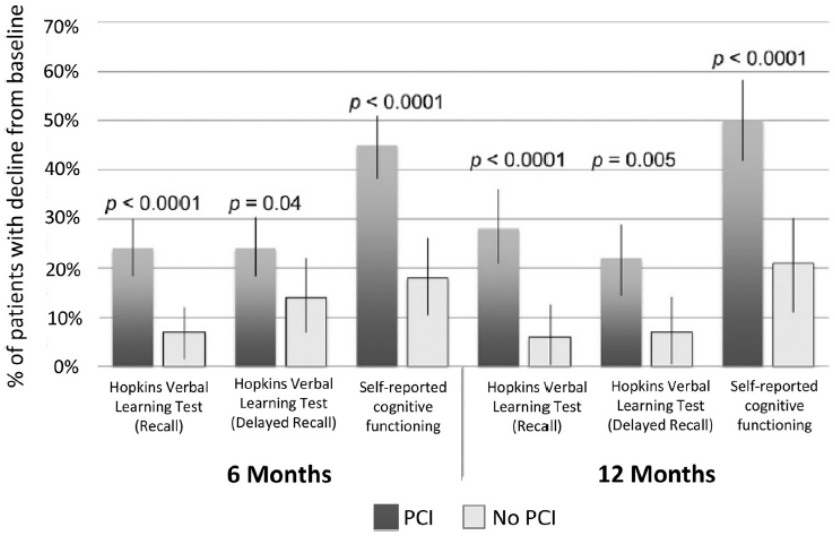
NCCN Guidelines Version 2.2021
Small Cell Lung Cancer



PCI is a NCCN category-1 recommendation for LS-SCLC and a standard option for ES-SCLC

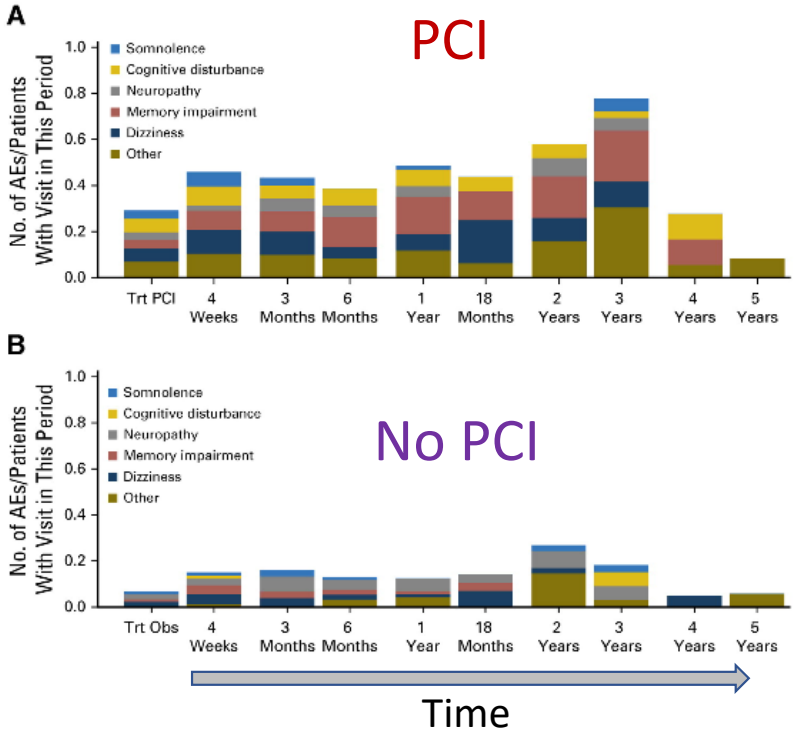
MRI surveillance is now recommended for <u>all patients</u> (regardless of PCI delivery)

Why does it matter? PCI is associated with neurocognitive toxicity



Tested and self-reported cognitive function with/without PCI in RTOG 0212 and 0214

Gondi, Vinai, et al *International Journal of Radiation Oncology* Biology* Physics* 86.4 (2013): 656-664.



De Ruysscher, Dirk, et al. "Prophylactic Cranial Irradiation Versus Observation in Radically Treated Stage III Non–Small-Cell Lung Cancer: A Randomized Phase III NVALT-11/DLCRG-02 Study." *Journal of Clinical Oncology* (2018): JCO-2017.

Patterns of care and equipoise on PCI

- Although the NCCN considers PCI a category-1 recommendation for LS-SCLC, approx. 40% of LS-SCLC patients do not receive PCI primarily due to toxicity concerns (Giuliani 2010, Lok 2015).

- 2019 survey study of 487 radiation oncologists (Gjyishi 2019):
  - Following the Japanese PCI trial, routine recommendations for PCI dropped from 72% to 44% for ES-SCLC
  - 82% were willing to enroll patients on a trial of MRI surveillance +/- PCI for limited and/or extensive-stage

- Separate surveys of SWOG and Alliance members indicated equipoise regarding MRI surveillance +/- PCI for SCLC
  - 85% & 87% indicated they would enroll patients on a randomized trial of MRI surveillance +/- PCI
  - 68% & 75% wanted the study to include both limited and extensive-stage SCLC patients

Giuliani, Cancer 116.24 (2010): 5694-5699
Lok, *Advances in radiation oncology* 2.4 (2017): 548-554
Gjyishi, *JAMA network open* 2.8 (2019): e199135-e199135

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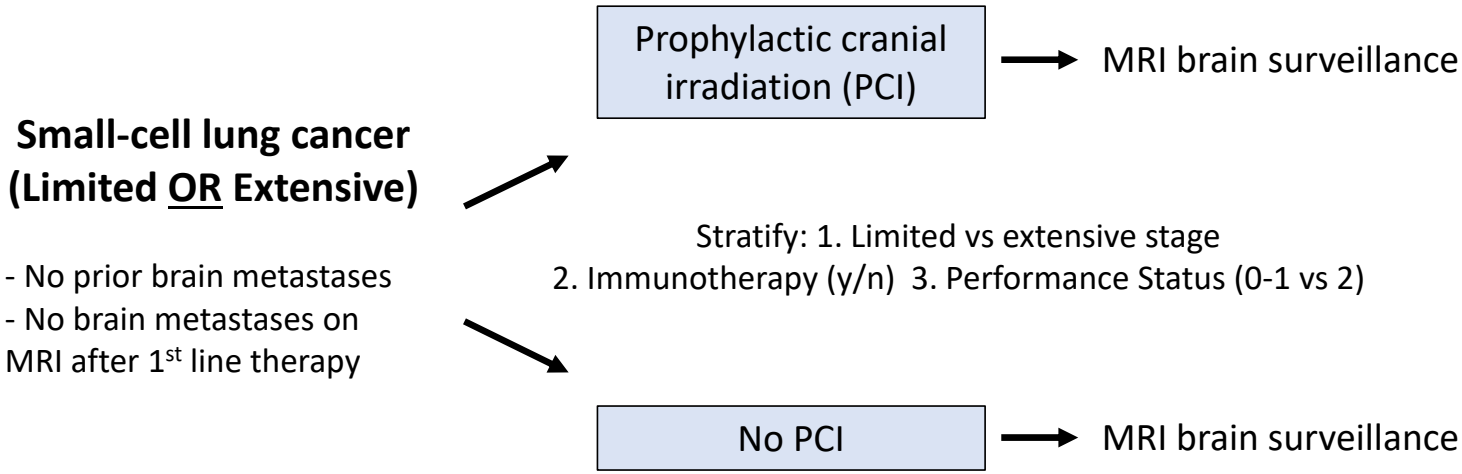


Primary Endpoint
- Overall survival (non-inferiority)

Secondary Endpoints
- Cognitive function
- OS in limited and extensive stage
- Brain metastases free survival

Translational Endpoints
-Longitudinal brain MRI changes
-ctDNA correlation to PFS, OS

Accrual goal: 600 analyzable pts

- MRI brain surveillance scheduled at 3, 6, 9, 12, 18, 24 months
- Hippocampal-avoidance PCI and WBRT are allowed
- Radiation therapy is recommended at the time of brain metastases (WBRT and SRS allowed)
- Patients managed with any/all NCCN-acknowledged first-line treatment strategies are eligible

PIs Chad Rusthoven and Paul Brown

Notes

- Open in SWOG, NRG, Alliance, ECOG, CCTG, and championed in the VA system

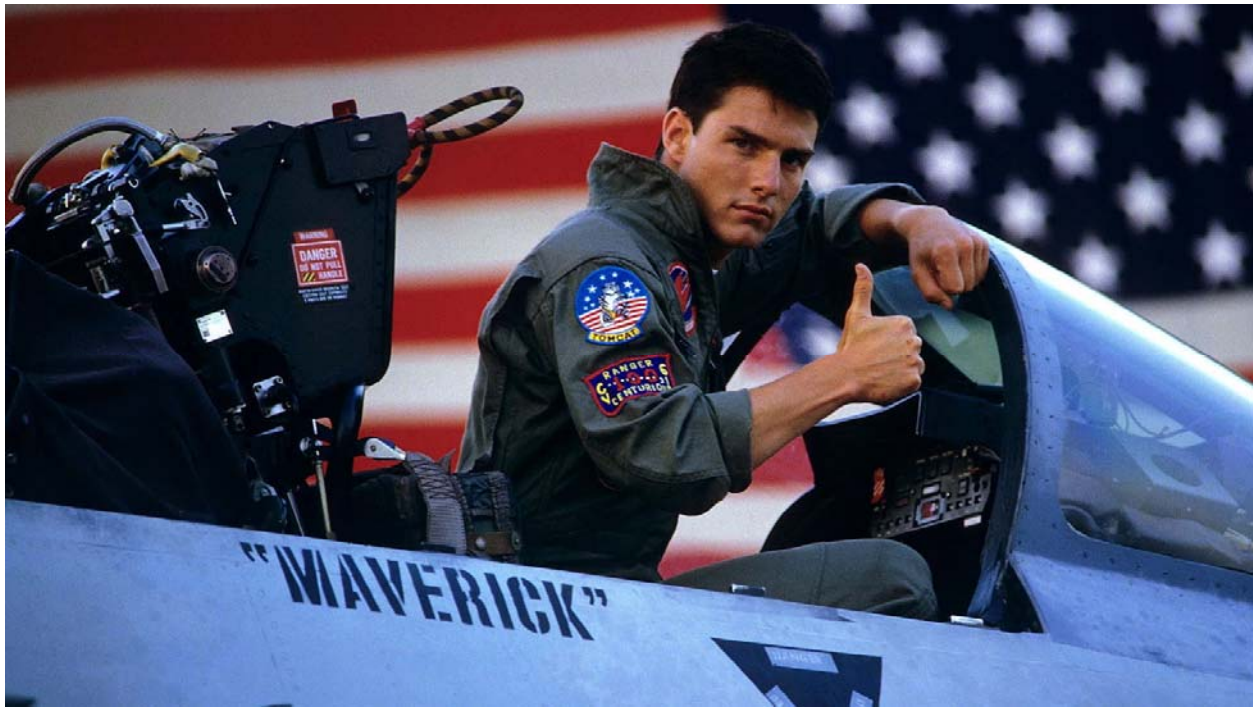
- The importance of community site participation
  - Successful comparable NRG trial of brain radiation including NRG CC001 (WBRT +/- hippocampal avoidance) and CC003 (PCI +/- hippocampal avoidance) exceeded their projected accrual rates, with NCORP community sites accounting for 20-30% of their accrual.

- Pragmatic design: any/all NCCN acknowledged treatment paradigms allowed
  - Allows immunotherapy, HA-PCI, salvage HA-WBRT & SRS, consolidative RT for ES, etc.
  - Our baseline approach is to allow dual trial enrollments wherever possible

- Cognitive testing
  - Same tests and neurocognitive leader (Dr. Jeff Wefel) as successful NRG trials CC001 & CC003
  - Financial ($) site incentives provided for completion

- Accrual is the key
  - Framing: PCI remains NCCN category-1 for LS-SCLC and a standard option for ES (with confliction RCT data)
  - Please consider opening/enrolling to help us answer this important question!

Thank you for your attention!



Contact: Chad.Rusthoven@CUanschutz.edu