NRG CC003

Phase IIR/III Trial of Prophylactic Cranial Irradiation with or without Hippocampal Avoidance for Small Cell Lung Cancer

PIs: Minesh Mehta, MD, and Vinai Gondi, MD
Neurocog: Jeffrey Wefel, PhD Physics: Wolfgang Tome, PhD
QOL: Shannon Fogh, MD, Ben Movsas, MD, Ben Corn, MD
Stats: Stephanie Pugh, PhD TRP: Andrew Lassman, MD
Lung: Alex Sun, MD SWOG: Laurie Gaspar, MD ECOG: Kristin Redmond, MD
Imaging: Joseph Bovi, MD, Cliff Robinson, MD, Tammie Benzinger, MD, PhD

Background

- Building on positive results of NRG CC001

Hippocampal avoidance prevents cognitive function failure

Adjusted Hazard ratio = 0.74 (p=0.020)
Independent of age

Separation of the curves starting at 3 months and maintained through the follow-up period

Effect on memory function (HVLT-R) and executive function (TMT B)

Preserves patient-reported symptoms assessed using MDASI-BT

Benefits in fatigue (p=0.036), difficulty speaking (p=0.049) and problems remembering things (p=0.013)

Variable	Estimate	p	Estimate	p
	Complete Data		Imputed Data	
Symptom	-0.36	0.16	-0.37	0.19
Interference	**-0.93**	**0.011**	**-1.02**	**0.0080**
Cognitive factor	**-0.50**	**0.027**	**-0.63**	**0.011**
Neurologic factor	-0.16	0.54	-0.22	0.45

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Brown, Gondi et al. JCO 2020

Conflicting Data from Europe

PREMER Trial

- 150 pts PCI vs PCI-HA 25 Gy/10 tx
- Primary endpt: Delayed Recall on Free & Cued Selective Reminding Test at 3 mos
- 3 Month decline in delayed free recall:
  23.5% PCI vs 5.8% HA-PCI p=0.003
- 6 Month decline in delayed free recall:
  33.3% PCI vs 6.0% HA-PCI p = 0.005
- HA-PCI arm less likely to have decline in delayed free recall at 6, 12 and 24 mos
- No difference in intracranial relapse rts or overall survival

de Dios et.al. JCO 2021

NKI Trial

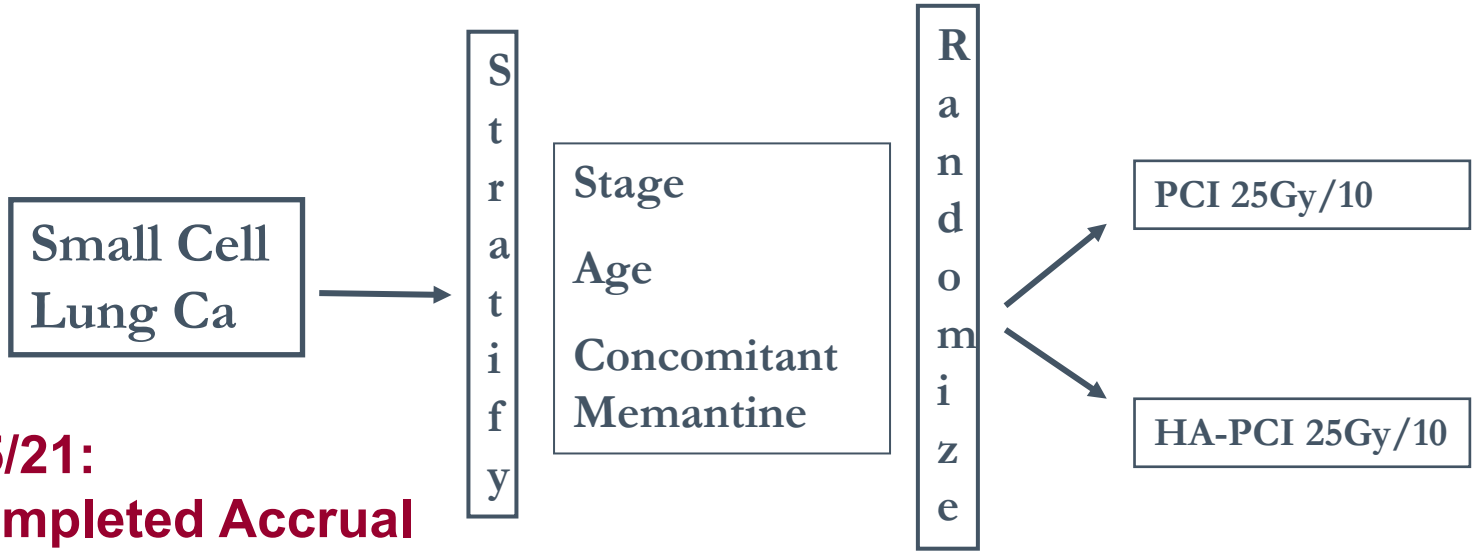
- 168 pts PCI vs PCI-HA 25 Gy/10 tx
- Primary endpt: HVLT total recall decline at 4 mos
- 4 Month HVLT total recall decline:
  29% PCI vs 28% HA-PCI p=0.99
- Risk of neurocognitive toxicity was higher in the HA-PCI arm vs the PCI arm (HR 1.75; p= 0.0088)
- No difference in intracranial relapse rates or overall survival

J Belderbos et.al. JTO 2021

NRG CC003: Phase IIR/III Trial Prophylactic Cranial Irradiation with or without Hippocampal Avoidance for Small Cell Lung Cancer

PIs: Minesh Mehta (Miami Cancer Institute) + Vinai Gondi (Northwestern)

Basic Eligibility: Small cell lung cancer; PR or CR to chemo; ECOG PS≤70; MRI scan



6/5/21:
Completed Accrual
N=393 pts

Sample Size:	Phase IIR:	172 patients	Phase III:	392 patients

Primary endpts: Phase IIR—Intracranial relapse rate at 12 months
Phase III—HVLT-R delayed recall deterioration at 6 months

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Post-Treatment Compliance

NRG-CC003 - Neurocognitive Assessment - HVLT						
	Baseline[1]	Month 3[3]	Month 6[4]	Month 12[5]	Month 18[6]	Month 24[6]
Forms expected	392	325	268	203	142	118
% completed of forms expected	392 (100.0%)	253 (77.8%)	203 (75.7%)	133 (65.5%)	92 (64.8%)	80 (67.8%)
% with reason missing supplied by site	0 (0.0%)	72 (22.2%)	64 (23.9%)	64 (31.5%)	46 (32.4%)	30 (25.4%)
Discontinued due to patient illness	0 (0.0%)	2 (2.8%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Not tested due to patient illness	0 (0.0%)	12 (16.7%)	3 (4.7%)	9 (14.1%)	5 (10.9%)	3 (10.0%)
Not tested due to neurologic disability	0 (0.0%)	2 (2.8%)	1 (1.6%)	2 (3.1%)	0 (0.0%)	1 (3.3%)
Not tested due to patient refusal	0 (0.0%)	22 (30.6%)	33 (51.6%)	29 (45.3%)	27 (58.7%)	17 (56.7%)
Not tested due to institutional error	0 (0.0%)	6 (8.3%)	10 (15.6%)	5 (7.8%)	4 (8.7%)	4 (13.3%)
Not completed due to COVID-related issue and remote testing was NOT attempted	0 (0.0%)	4 (5.6%)	4 (6.3%)	8 (12.5%)	5 (10.9%)	4 (13.3%)
Not completed due to COVID-related issue but remote testing was attempted	0 (0.0%)	0 (0.0%)	1 (1.6%)	0 (0.0%)	1 (2.2%)	0 (0.0%)
Unknown	0 (0.0%)	7 (9.7%)	5 (7.8%)	8 (12.5%)	3 (6.5%)	1 (3.3%)
Assessment completed too early	0 (0.0%)	3 (4.2%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Assessment completed too late	0 (0.0%)	14 (19.4%)	5 (7.8%)	3 (4.7%)	1 (2.2%)	0 (0.0%)
% missing of forms expected	0 (0.0%)	0 (0.0%)	1 (0.4%)	6 (3.0%)	4 (2.8%)	8 (6.8%)

Remote NCF testing no longer permitted

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