

Prophylactic cranial irradiation: Improvements for advanced NSCLC

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Prophylactic cranial irradiation (PCI), a technique used to prevent the clinical development of brain metastases, is established as a standard approach for many patients with small cell lung cancer (SCLC) after initial therapy. While studies established that PCI decreases the incidence of brain metastases for patients with locally advanced non-small cell lung cancer (LA-NSCLC), there is no established indication for its use for such NSCLC patients.

Cumulative [brain](#) metastases (BM) rates are high for [patients](#) with LA-NSCLC. NRG Oncology conducted the NRG-RTOG 0214 trial to address this high incidence of brain metastases and determine if the addition of PCI following primary treatment improved [overall survival](#) (OS) in patients with LA-NSCLC. This trial also evaluated changes in disease-free survival (DFS) and brain metastases rates. At 5 and 10 years, PCI did not improve survival in patients with stage III LA-NSCLC without progression of disease after therapy, however, DFS increased and BM rates decreased considerably, thus providing important information that could benefit future trials. The long-term update of this trial was recently published in *JAMA Oncology*.

Patients in NRG-RTOG 0214 were randomly assigned either to observation or to receive PCI in 2Gy per fraction over five days a week up to 30Gy. This occurred at 291 institutions globally. Patients in the PCI study arm were followed beginning at 3 and 6 months from the start of PCI, then every 6 months for 2 years, then yearly. Brain imaging with MRI or CT was performed at 6 and 12 months, then yearly

340 patients were evaluable at 5 and 10 years. OS rates on the study arm that received PCI were not statistically better than the observation arm (HR=0.82, p= 0.12, 10-year rates: 17.6% and 13.3%, respectively), however, DFS improved significantly (HR=0.76, p= 0.003, 10-year rates

12.6% vs. 7.5% for PCI vs. observation) as well as BM rates (p=0.0004, 10-year rates 16.7% vs. 28.3% for PCI vs. observation). Patients in the PCI study arm were 57% less likely to develop BM than those in the observation arm (HR=0.43, 95% CI=0.24-0.77).

A subgroup analysis of 225 patients on this trial who did not have surgery of their primary lung tumor exhibited statistically significant differences in OS, DFS, and BM rates between the PCI treatment arm and the observation arm. This analysis suggests PCI may prolong OS in this subgroup, as the median survival time of 2.3 years on the PCI arm compared favorably to 1.9 years on the observation arm (p=0.027). Multivariable analysis within this patient population suggests PCI may effectively prolong OS (HR=0.73, p=0.004) and DFS (HR=0.70, p=0.001), and decreases BM (HR=0.34, p=0.0002).

"As the incidence of brain metastases rise in patients living longer with improved control of loco-regional and distant disease, the need to establish an accepted means of prevention of brain metastases remains important. Researchers need to identify the appropriate patient population and a safe intervention on future trials," stated Alexander Sun, MD, of the Department of Radiation Oncology at the University Health Network's Princess Margaret Cancer Centre and corresponding author of NRG-RTOG 0214.

More information: Alexander Sun et al, Prophylactic Cranial Irradiation vs Observation in Patients With Locally Advanced Non-Small Cell Lung Cancer, *JAMA Oncology* (2019). [DOI: 10.1001/jamaoncol.2018.7220](https://doi.org/10.1001/jamaoncol.2018.7220)

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