

# Addition of prophylactic cranial irradiation in extensive small -cell lung cancer patients

## Editorial

Small-cell lung cancers (SCLC) make up approximately 15%-20% of all newly diagnosed cases of lung cancer. Compared to non-small-cell lung cancer, SCLC can be a more aggressive malignancy. Due to the high rate of metastatic dissemination of SCLC, the 5-year survival rate is only 5-6%. A small-cell lung cancer is classified as either limited stage (LS-SCLC) or extensive stages (ES-SCLC) of disease.<sup>1</sup> Thoracic radiotherapy (TRT) brings benefits to LS-SCLC patients, as well as extensive stage of disease by improvement of local control and overall survival. The current standard of care for LS-SCLC is the use of concurrent chemotherapy (CHT) and TRT, followed by prophylactic cranial irradiation (PCI) for patients who have a good response to the previous treatment. Historically, the standard of care for ES-SCLC has consisted of CHT only. Radiotherapy has been indicated for site-specific symptom palliation.<sup>2</sup> However, first randomized trial in 2007 demonstrated survival benefit from the addition of PCI in ES-SCLC patients who had any response to CHT.<sup>3</sup> Previously, Auperin meta-analysis showed the benefit associated with PCI for group of patients with ES-SCLC as in the limited disease group.<sup>4</sup> In 2007, Slotman et al.<sup>3</sup> showed the results of a phase III trial with ES-SCLC patients who have been randomized to the two groups of patients with addition of PCI or observation.<sup>2</sup> After 1 year of follow-up, the PCI patients were found to have a significantly lower rate of symptomatic brain metastases (15 vs. 40 %,  $p < 0.001$ ). Of course, greater importance had improvements in 1-year (27 vs. 13 %) and median (6.7 vs. 5.4 months,  $p = 0.003$ ) survivals, compared to the patients without PCI.<sup>3</sup> In view of these benefits, PCI is now increasingly being routinely offered to any ES-SCLC patient who showed a response to the CHT. However, patients who were receiving PCI had not clinically significant benefits on global health condition nine months after treatment.<sup>5</sup> A warning of the EORTC trial in 2009 is that brain imaging was not mandatory prior to PCI.<sup>1</sup>

A randomized trial from Japan in 2014 showed that patients with ES-SCLC who had any response to first-line platinum doublet CHT were randomized to either PCI (25 Gy/10 fractions) or observation. Magnetic resonance imaging has been performed to prove the absence of brain metastases prior the enrollment into the trial.<sup>6</sup> With a median follow-up of 9.4 months and 111 observed deaths, the median survival was 10.1 and 15.1 months for the PCI and the observation patients, respectively ( $p = 0.091$ ). PCI significantly reduced the risk of brain metastases as compared to observation (32.4 vs. 58.0 % at 12 months,  $p < 0.001$ ). Although there was no demonstrated improvement in survival, the previously recognized improvement in primary brain control afforded by PCI was confirmed. Therefore, PCI should be considered for ES-SCLC patients who demonstrated clinical benefits from their primary systemic therapies.<sup>6</sup> Although routine use of TRT to treat ES-SCLC should not yet be integrated into the standard care of patients, there is more convincing evidence for offering PCI to patients with ES-SCLC.<sup>1</sup> The treatment of patients with SCLC remains a clinical challenge. It seems that both therapies TRT, as well as PCI contributed to improve of outcomes in SCLC patients. Therefore, the current standards in limited disease are use of TRT concurrently with CHT and PCI because they improve local control and overall

survival. In extensive disease, growing evidence suggests that the use of TRT and PCI in selected patients completing CHT successfully will likely also improve local control and survival.<sup>2</sup> Therefore, standard of care for patients with ES-SCLC should be consisted PCI after good response on CHT.

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## Conflicts of interest

The authors declare that there is no conflict of interest.

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