Impact of early prophylactic cranial irradiation with hippocampal avoidance on neurocognitive function in patients with limited disease small cell lung cancer: A multicenter phase II trial (SAKK 15/12)


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Background: In limited disease small-cell lung cancer (LD SCLC) prophylactic cranial irradiation (PCI) is the standard of care following chemotherapy (CHT) and thoracic radiotherapy (tRT) in patients with a good clinical response. It is unknown if PCI concomitant with CHT and tRT has an impact on neurocognitive function (NCF) and clinical outcome.

Methods: In a phase II trial, patients with LD SCLC received hippocampal avoidance (HA)-PCI concomitant to the 2nd cycle of CHT (cisplatin or carboplatin and etoposide) and tRT. All patients underwent objective NCF testing before starting HA-PCI (baseline), at 6 weeks, and at 6 and 12 months after HA-PCI. NCF tests included the Hopkins Verbal Learning Test Revised (HVLT-R) for verbal learning and memory, the Controlled Oral Word Association (COWAT) for verbal fluency, and Trail Making Tests A and B (TMT A&B) for visual search, scanning, speed of processing and executive function. The primary endpoint was NCF decline at 6 months after HA-PCI, defined as a decrease of two standard error of measurement in any of the tests. We assumed a rate of ≤ 30% of patients with no NCF decline as unpromising and a rate of ≥ 50% as promising. Secondary endpoints included overall survival (OS) and quality of life.

Results: Among the 44 patients enrolled in the trial, 37 had evaluable NCF assessment at 6 months after HA-PCI (2 had no CHT, 2 had no BL TMT B assessment, 1 died and 2 have pending NCF results). At the time of analysis, 13 patients (35%; 90% CI: 22-50%) showed no NCF decline. The median follow-up was 12 months with a 1-year OS rate of 84% (95% CI: 65-93%). Four patients died due to SCLC, 1 due to respiratory failure, 1 due to hemorrhage, and 1 for unknown reason. The most common acute adverse events grade ≥ 3 were anemia (21%), febrile neutropenia (19%) and fatigue (14%).

Conclusions: The rate of patients with no NCF decline 6 months after HA-PCI in LD SCLC does not seem to be better, but rather similar to that observed in patients receiving sequential PCI. Early HA-PCI appears feasible. OS was promising in this selected population. Updated and additional results will be presented.

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