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The effect of prophylactic cranial irradiation (PCI) for young stage III NSCLC patients: Subgroup analyses of the NVALT-11/DLCRG-02 study

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 $\textbf{Background:} \ The \ NVALT-11/DLCRG-02 \ phase \ III \ study \ compared \ PCI \ to \ observation$ after chemo-radiotherapy (RT) for stage III NSCLC and showed a significant decrease in the cumulative incidence of symptomatic brain metastases (BM) in the PCI arm at two years (7% vs 27% [HR 0.23]). We here performed exploratory subgroup analyses. Methods: Two year cumulative incidence rates were calculated and competing risk regression, with death of any cause as competing risk, was used to examine the time to symptomatic BM in the following subgroups: age, gender, performance status, disease stage and tumour type, prior surgery, chemotherapy cycles, thoracic RT dose and total concurrent chemo-RT treatment time. For continuous variables, the median was used as a cut-off value. The effect of PCI was only examined if the initial result was significant.

Results: In total, 174 patients were analysed. The symptomatic BM incidence was significantly lower in the subgroup of older (>61 years) versus younger (= <61 years) patients (7% vs 26% [HR 0.25]). Stratified by age, PCI only significantly reduced the symptomatic BM incidence in younger patients (9% vs 42% [HR 0.18])(Table).

Subgroup			Hazard ratio	95% CI
Age (>61 years vs ≤ 61	All		0.25	0.10 - 0.6
years)	≤61 PCl vs	observation	0.18	0.06 - 0.5
	>61 PCI vs	observation	0.47	0.09 - 2.5
Female vs Male			1.31	0.92 - 1.8
WHO performance status		0	-	-
		1	0.86	0.41 - 1.8
		2	2.12	0.59 - 7.6
Squamous vs non-squamous			0.76	0.34 - 1.6
Stage IIIb vs IIIa			0.97	0.47 - 1.9
Prior vs no prior surgery			1.21	0.45 - 3.2
Chemotherapy cycles (>3 vs \leq 3)			0.97	0.42 - 2.2
Thoracic RT dose (>60 Gy vs \leq 60 Gy)			1.15	0.57 - 2.3
Total concurrent chemo-RT time			1.43	0.70 - 2.9

Conclusions: The symptomatic BM incidence was significantly lower in older (>61 years) compared to younger (= <61 years) patients, likely due to higher numbers of adenocarcinoma in the younger patients group. The effect of PCI was only significant in younger patients. This study was randomized based on treatment allocation and subgroups might be too small to detect significant differences. Therefore, our results are hypothesis generating and should be prospectively tested.

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