**10-Year Outcome on the Efficacy and Late Toxicities Attributed to the Addition of Concurrent-Adjuvant Chemotherapy for Stage III-IVB Nasopharyngeal Carcinoma (Combined Analyses of the NPC-9901 and NPC-9902 Trials)**

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**Purpose/Objective(s):** Concurrent-adjuvant chemoradiotherapy (CRT) became a recommended treatment for locoregionally advanced nasopha- ryngeal carcinoma (NPC) since the first report of significant survival benefit by the Intergroup-0099 Study. However, data on late toxicities are lacking. Previous reports from confirmatory trials (NPC-9901 and NPC- 9902 Trials on N2-3 and T3-4N0-1 disease, respectively) concurred that this regimen could improve tumor control, but did not achieve significant gain in overall survival (OS) up to 5 years. Validation of the long-term therapeutic ratio is needed.

**Materials/Methods:** All patients had histologically confirmed non-keratinizing carcinoma of the nasopharynx and stage III-IVB disease by AJCC classification (fifth edition). Focusing on patients irradiated with conven- tional-fractionation, the current study evaluated 218 patients randomly assigned to radiotherapy-alone (RT) and 223 patients to CRT using cisplatin in concurrence with RT, followed by adjuvant cisplatin plus fluorouracil.

**Results:** Only 4% patients were lost to follow-up; the median follow-up was 13.9 years.

Regarding late toxicity, there was no significant difference in the latency to manifestation, damage at specific sites, and overall severity between the two groups. The mortality rate due to treatment toxicity was 4.0% vs 3.2%, incidental / unknown cause was 14.8% vs 12.8%. The increase in toxicities and non-cancer deaths observed in early years diminished with long follow-up, ultimately resulting in significant gain in OS. Further analyses on actual treatment showed that those with ≥2 concurrent cycles had significantly better locoregional control (86% vs 74%, P = 0.001) and those with ≥ 2 adjuvant cycles had better distant control (73% vs 64%, P = 0.019) than those with 0-1 cycles.

**Conclusion:** Long-term results confirmed that adding concurrent cisplatin plus adjuvant cisplatin-fluorouracil to conventional-fractionated RT could significantly improve OS without excessive late toxicities for patients with locoregionally advanced NPC. However, better compliance and/or more potent therapy is needed for improving distant control.