Preliminary Results of a Phase III Randomized Study Comparing Neoadjuvant Chemotherapy with Concurrent Chemotherapy in Locoregionally Advanced Nasopharyngeal Carcinoma

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Purpose/Objective(s): To compare neoadjuvant chemotherapy (NACT) with concurrent chemotherapy (CCRT) of the therapeutic gain, toxicities, and compliance for locoregionally advanced nasopharyngeal carcinoma (NPC).

Materials/Methods: Eligible patients were randomized to neoadjuvant chemotherapy (NACT) + radiotherapy (RT) + adjuvant chemotherapy (AC) arm or concurrent chemoradiotherapy (CCRT) + AC arm. Two arms received similar dosage and fractionation of conventional RT. A planned 70 Gy to primary lesion was delivered in 2.0 Gy per fraction, 5 fractions a week. Cisplatin 30 mg/m^2 and 5-Fluorouracil 500mg/m^2 administered for 3 days were administered every 28 days for two cycles as neoadjuvant chemotherapy. The same drugs with equal dose were administered on the first and 22nd days of the radiotherapy as concurrent chemotherapy. The 2–4 cycles of the same regimen were administered to both of two arms as AC 28 days later of the end of RT. The AC was administered every 28 days according to the patients' tolerance.

Results: A total of 338 Chinese NPC patients with 2002 AJCC Stage III to IV (M0) were recruited from September 2004 to April 2007. A total of 170 patients were randomized to the NACT arm and another 168 patients to the CCRT arm. A total of 333 (98.5%) patients finished the scheduled RT with a median dose of 72 Gy (range, 70–88 Gy). There were 8 patients dead since the last visit. No significant heterogeneity in 3-year disease-free survival (DFS) was observed between arms (76.0% vs. 77.6%; $p = 0.39$). The 3-year metastasis-free survival (MFS) rates were 82.2% vs. 91.1% ($p = 0.04$), favoring the CCRT arm. The 3-year relapse-free survival (RFS) rates were 92.0% vs. 83.1% ($p = 0.16$), slightly favoring the NACT arm. Similar results happened to the overall survival (OS) (95.7% vs. 93.1%; $p = 0.44$). Further subgroup analysis showed the 3-year MFS was 72.6% and 93.8% in NACT and CCRT arm, respectively, in the T3–4N0–1 population, and reached statistically significance (95% CI, 1.16–7.47; $p = 0.035$), but the same result was not achieved in T1–4N2–3 patients (85.3% vs. 89.4%; 95% CI, 0.60– 3.06; $p = 0.458$). Among the acute toxicities we observed, the rates of Grade 3/4 mucositis (52.4% vs. 35.9%; $p = 0.023$) and vomiting (13.7% vs. 4.7%; $p = 0.000$) were significantly higher in CCRT arm. There were 92.9%, 88.7% of patients finished two cycles of neoadjuvant/concurrent chemotherapy and 68.2%, 65.5% of patients finished four cycles of adjuvant chemotherapy in NACT and CCRT arm, respectively.

Conclusions: Our preliminary results show limited advantage of CCRT+AC over NACT+RT+AC only in T3–4N0–1 NPC patients in the MFS profile. But more acute toxicities were caused by CCRT arm and we observed a trend of better tolerance in NACT arm.

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