Supplementary Methods

1. Pre-treatment examination

The following examinations were routinely implemented within the two-to-four weeks prior to the first-cycle of induction chemotherapy (IC-1): complete medical history, physical examination, blood and biochemistry tests, nasoendoscopy, neck and nasopharyngeal magnetic resonance imaging, chest radiography, abdominal ultrasonography and whole-body bone scan; ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography was performed for 187/545 patients (34.3%) at initial evaluation. Moreover, the tumor-related biomarkers plasma, i.e., Epstein-Barr virus (EBV) DNA titer, IgA antibodies against viral capsid antigen (VCA-IgA) and early antigen (EA-IgA), were quantified before treatment. A real-time quantitative polymerase-chain-reaction assay was employed to detect plasma EBV DNA, by targeting the *Bam*HI-W region of the EBV genome using the amplification primers 5'-GCCAGAGGTAAGTGGACTTT-3' and 5'-TACCACCTCCTCTTCTTGCT-3'; the dual fluorescence-labelled oligomer 5'-(FAM) CACACCCAGGCACACACTACACAT (TAMRA)-3' served as a probe [1]. The GenBank sequence database was used to obtain all sequence data.

2. Induction chemotherapy regimens

Induction chemotherapy (IC) regimens comprised cisplatin–5-fluorouracil (PF; 80 mg/m^2 and 4,000 mg/m^2, respectively), docetaxel–cisplatin (TP; 75 mg/m^2 and 75 mg/m^2, respectively), and docetaxel–cisplatin–5-fluorouracil (TPF; 60 mg/m^2, 60 mg/m^2 and 3,000 mg/m^2, respectively) every 3 weeks for 2-4 cycles. All chemotherapeutic drugs were administered on day 1 of each 21-day cycle, except for 5-

fluorouracil which was given via continuous intravenous infusion on days 1-5.

3. Concurrent chemotherapy

The timing of initiation of concurrent chemoradiotherapy is on day 21 after completion of IC. Concurrent chemotherapy was cisplatin (30-40 mg/m^2) weekly, or cisplatin (80-100 mg/m^2) every 3 weeks concurrently with intensity-modulated radiotherapy (IMRT). The prescribed doses of IMRT were 66-72 Gy/28-33 fractions to the planning target volume (PTV) of the primary gross tumor volume, 64-70 Gy/28-33 fractions to the PTV of the gross tumor volume of the involved lymph nodes, 60-63 Gy/28-33 fractions to the PTV of the high-risk clinical target volume, and 54-56 Gy/28-33 fractions to the PTV of the low-risk clinical target volume. Target volumes were delineated slice-by-slice on treatment planning computed tomography scans using an individualized delineation protocol in accordance with the International Commission on Radiation Units and Measurements reports 50 and 62. If patients suffered relapse/metastatic disease during follow-up, palliative treatment (e.g., chemotherapy, intracavitary brachytherapy, and salvage surgery) was provided, as appropriate.

4. Follow-up

Follow-up was measured from the day of diagnosis to day of last visit or death. Each patient attended follow-up appointments at least every 3 months during the first 2 years, then every 6 months thereafter or until death. If a patient had suspected residual or recurrent local disease, a biopsy was required to confirm malignancy. The regulations for stopping treatment and dose modifications/reductions have been described previously [2].

5. Clinicopathologic covariates for multivariate analysis

Clinicopathologic covariates were age at diagnosis, sex, family history of cancer, comorbidity, cigarette smoking, World Health Organization histologic type, VCA-IgA, EA-IgA, EBV DNA titer, neutrophil-to-lymphocyte ratio (absolute neutrophil count/absolute lymphocyte count; average within 4 weeks prior to IC-1), clinical stage, T category, N category (8th edition of the Union for International Cancer Control/American Joint Committee on Cancer staging system), and chemotherapy regimen.

References

1. Shao JY, Zhang Y, Li YH, Gao HY, Feng HX, Wu QL, et al. Comparison of Epstein-Barr virus DNA level in plasma, peripheral blood cell and tumor tissue in nasopharyngeal carcinoma. Anticancer Res. 2004;24:4059-66.
2. Sun Y, Li WF, Chen NY, Zhang N, Hu GQ, Xie FY, et al. Induction chemotherapy plus concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: a phase 3, multicentre, randomised controlled trial. Lancet Oncol. 2016;17: 1509-20.