

Supplemental Appendix for:
Prognostic Value of the Cumulative Cisplatin Dose During Concurrent Chemoradiotherapy in Locoregionally-Advanced Nasopharyngeal Carcinoma: A Secondary Analysis of a Prospective Phase III Clinical Trial
Jun Ma et al.

Appendix S1.

The median cumulative cisplatin dose (CCD) for the entire cohort was 240 mg/m² (interquartile range, 200-280). To address whether low or high doses makes a difference, further analysis was conducted to compared the survival difference between patients receiving a CCD \leq 200 mg/m² (low CCD group) and those who received a CCD \geq 280 mg/m² (high CCD group). In total, 113 (37.9%) patients received a CCD \leq 200 mg/m² and 78 (26.2%) patients received a CCD \geq 280 mg/m².

The baseline characteristics of the 191 patients were listed in Table 1. The high CCD group had a higher percentage of patients receiving intensity-modulated radiotherapy (IMRT). Although, the high CCD group had more patients with N2-3 stage compared with that in low CCD group, the overall stage were well balanced between the two groups.

The 5-year overall survival (OS), disease-free survival (DFS), locoregional relapse-free survival (LRRFS) and distant metastasis-free survival (DMFS) rates for low CCD group vs. high CCD group were 76.2% vs. 82.4% ($P = 0.602$), 67.8% vs. 71.1% ($P = 0.713$), 86.8% vs. 90.2% ($P = 0.518$) and 79.7% vs. 76.5% ($P = 0.548$). After adjusting for various prognostic factors, multivariate analysis revealed CCD was still not an independent prognostic factor for patients with locoregionally advanced NPC (Table 2).

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Table S1. Basic characteristics of the 191 patients with locoregionally-advanced NPC receiving concurrent chemoradiotherapy

Characteristic	Cumulative cisplatin dose		<i>P</i> ^a
	≤ 240 mg/m ² No. (%)	≥ 280 mg/m ² No. (%)	
Sex			0.185
Male	77 (68.1)	60 (76.9)	
Female	36 (31.9)	18 (23.1)	
KPS			0.213
≥ 90	86 (76.1)	53 (67.9)	
< 90	27 (23.9)	25 (32.1)	
Age (years)			0.384
<45	45 (39.8)	36 (46.2)	
≥ 45	68 (60.2)	42 (53.8)	
T category ^b			0.087
T1	7 (6.2)	1 (1.3)	
T2	24 (21.2)	27 (34.6)	
T3	55 (48.7)	31 (39.7)	
T4	27 (23.9)	19 (24.4)	
N category ^b			0.003
N1	40 (35.4)	13 (16.7)	
N2	67 (59.3)	53 (67.9)	
N3	6 (5.3)	12 (15.4)	
Overall stage ^b			0.115
III	84 (74.3)	49 (62.8)	
IVA	23 (20.4)	19 (24.4)	
IVB	6 (5.3)	10 (12.8)	
Radiotherapy technique			< 0.001
2D/3DRT	65 (57.5)	66 (84.6)	
IMRT	48 (42.5)	12 (15.4)	

Abbreviation: KPS = Karnofsky performance score; 2DRT = 2-dimensional radiotherapy; 3DRT = 3-dimensional radiotherapy; IMRT = intensity-modulated radiotherapy; NPC = nasopharyngeal carcinoma.

^a*P*-values were calculated using chi-square test (or Fisher's exact test if indicated).

^b According to the 6th edition of the UICC/AJCC staging system.

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Jun Ma et al.

Table S2. Multivariate analysis of variables correlated with clinical outcomes in the 191 patients with locoregional advanced-stage NPC

Endpoints	HR	95% CI	<i>P</i> ^a
OS			
Sex, female vs. male	0.654	0.311-1.375	0.263
KPS, ≥ 90 vs. < 90	0.697	0.353-1.376	0.298
Age, ≥ 45 vs. < 45 years	1.759	0.917-3.372	0.089
T category, T3-4 vs. T1-2	1.164	0.546-2.478	0.694
N category, N2 vs. N1	1.101	0.539-2.247	0.792
N category, N3 vs. N1	2.736	1.044-7.173	0.041
Radiotherapy technique, 2D/3DRT vs. IMRT	0.657	0.323-1.336	0.247
Cumulative cisplatin dose, ≤ 200 vs. ≥ 280 mg/m ²	0.675	0.342-1.331	0.256
DFS			
Sex, female vs. male	0.683	0.366-1.273	0.230
KPS, ≥ 90 vs. < 90	0.845	0.470-1.519	0.573
Age, ≥ 45 vs. < 45 years	1.434	0.834-2.464	0.192
T category, T3-4 vs. T1-2	0.980	0.518-1.854	0.950
N category, N2 vs. N1	1.117	0.607-2.056	0.721
N category, N3 vs. N1	2.181	0.904-5.262	0.083
Radiotherapy technique, 2D/3DRT vs. IMRT	0.745	0.410-1.352	0.332
Cumulative cisplatin dose, ≤ 200 vs. ≥ 280 mg/m ²	0.787	0.450-1.375	0.401
LRRFS			
Sex, female vs. male	0.706	0.250-1.993	0.510
KPS, ≥ 90 vs. < 90	2.325	0.661-8.177	0.189
Age, ≥ 45 vs. < 45 years	0.788	0.308-2.020	0.620
T category, T3-4 vs. T1-2	1.008	0.333-3.045	0.989
N category, N2 vs. N1	0.741	0.269-2.039	0.562
N category, N3 vs. N1	2.508	0.707-8.903	0.155
Radiotherapy technique, 2D/3DRT vs. IMRT	0.490	0.163-1.474	0.204
Cumulative cisplatin dose, ≤ 200 vs. ≥ 280 mg/m ²	0.547	0.206-1.456	0.227
DMFS			
Sex, female vs. male	0.607	0.279-1.318	0.207
KPS, ≥ 90 vs. < 90	0.694	0.358-1.345	0.279
Age, ≥ 45 vs. < 45 years	1.635	0.847-3.156	0.143
T category, T3-4 vs. T1-2	1.033	0.478-2.230	0.934
N category, N2 vs. N1	1.073	0.522-2.202	0.849
N category, N3 vs. N1	1.639	0.543-4.941	0.381
Radiotherapy technique, 2D/3DRT vs. IMRT	0.918	0.466-1.810	0.805
Cumulative cisplatin dose, ≤ 200 vs. ≥ 280 mg/m ²	1.066	0.543-2.094	0.853

Abbreviations: NPC = nasopharyngeal carcinoma; OS = overall survival; DFS = disease-free survival; LRRFS = locoregional relapse-free survival; DMFS = distant metastasis-free survival; KPS = Karnofsky performance score; 2DRT = 2-dimensional radiotherapy; 3D = 3-dimensional radiotherapy; IMRT = intensity-modulated radiotherapy. HR = hazard ratio; CI = confidence interval.

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