Supplementary Materials

Appendix S1: Strategy of trials searching
Standard search

The standard search combined electronic searching (Medline Pub, Web of Science, CCT meta-register, clinicaltrials.gov), hand searching (review articles, meeting proceedings) and contacting experts in the field. All authors including many experts in NPC diagnosis and treatment were asked for help in identifying trials. This search was performed first in December 2016 for the preparation of the first draft of the protocol and then repeated in February 2017. Trials pre-selected on title and/or abstract were discussed for inclusion by at least two authors.

Electronic searching strategy referred to that in MAC-NPC[1].

For MEDLINE from PubMed:

((nasopharyngeal neoplasms/drug therapy[MAJR] OR nasopharyngeal neoplasms/radiotherapy[MAJR]) AND (clinical trial[Publication Type] AND (random* OR (Phase III)Fields: Title Word))) OR ((nasopharyngeal neoplasms/drug therapy[MAJR] OR nasopharyngeal neoplasms/radiotherapy[MAJR]) AND (clinical trial, phase III[Publication Type] OR randomized controlled trial[Publication Type]))

For Web of Science:

TS = (nasopharyn* OR cavum) AND TS = (chemotherapy OR chemoradiation OR chemoradiotherapy OR radiochemotherapy OR radio-chemotherapy OR pharmacotherapy) AND TS = (cancer* OR carcinoma* OR malignan* OR tumor* OR tumour* OR neoplasm) AND TS = (random*)

Document Types = (Abstract) Timespan = 2000-2017

Figure S1. Flow chart for the standard search.

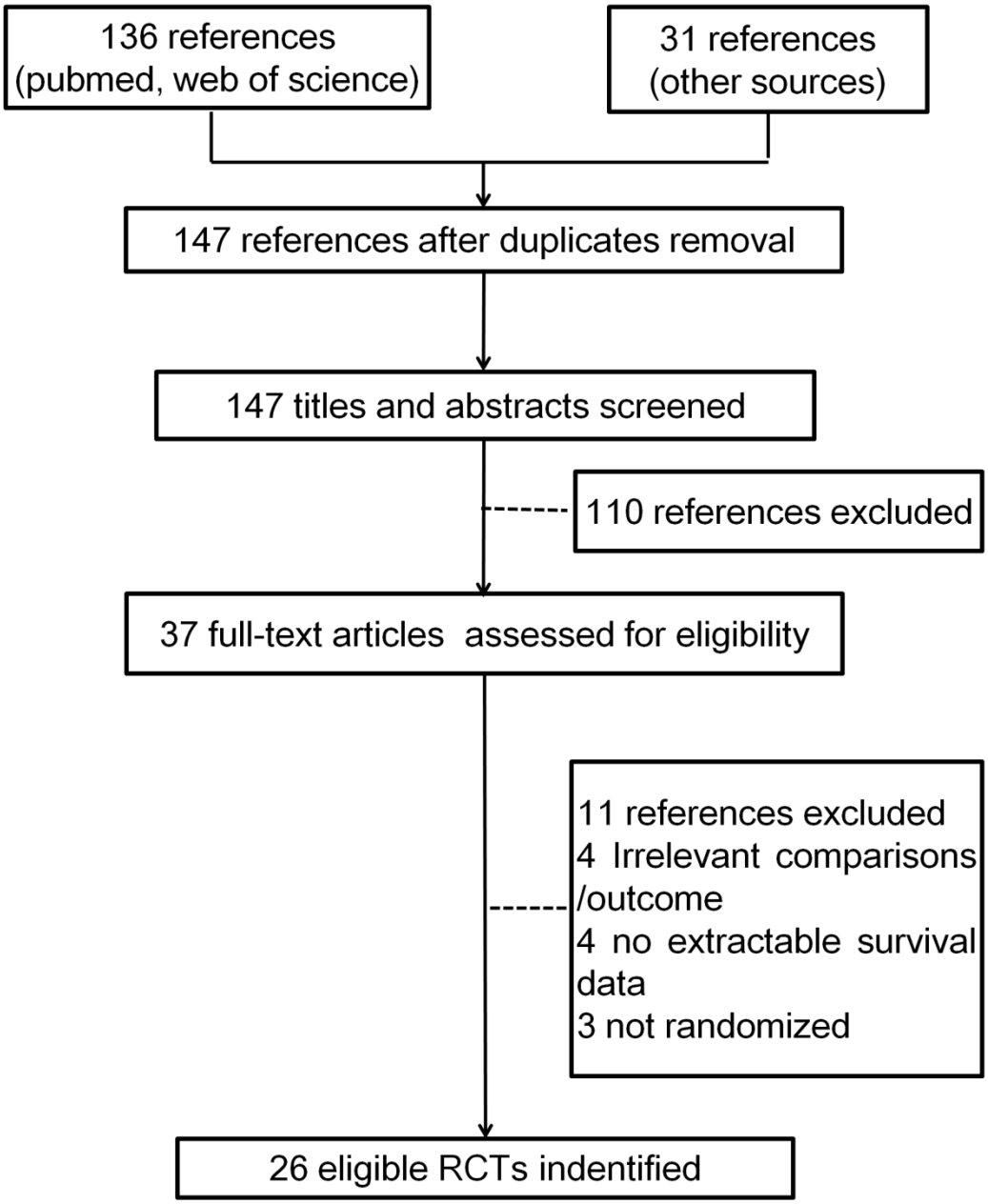

Table S1: Description of included trials.

Trial	Inclusion period	Inclusion Stage TNM classification	Histology, WHO classification	Radiotherapy, dose/duration	Chemotherapy		Patients randomized /analysed	Median follow-up, years
					Timing (treatment arm)	Dose number of cycles		
2D/3D RT ERA								
PWH-88[20]	1988-1991	II-IV (Ho)	3	T 66Gy/6.5weeks N-58Gy,N+65.5Gy	Induction (E) and Adjuvant (E)	IC: Cisplatin 100mg/m^2 2 cycles Fluorouracil 1,000 mg/m^2/d$_{2-4}$ 2 cycles AC: Cisplatin 100mg/m^2 4 cycles Fluorouracil 1,000 mg/m^2/d 4 cycles	82/77	2.9
AOCOA[21]	1989-1993	II-IV <10% (AJCC/UICC<1997)	2-3	T 66-74Gy/6.5-7.5weeks N-60-66Gy, N+66-76Gy	Induction (E)	IC: Cisplatin 60mg/m^2 2-3 cycles Epirubicin 100mg/m^2 2-3 cycles	334/334	5.4
VUMCA-89[22]	1989-1993	III-IV (AJCC/UICC<1997)	2-3	T 65-70Gy/6.5-7.5weeks N-50Gy, N+65Gy	Induction (E)	IC: Bleomycin 15mg 3 cyclcs Bleomycin 12mg/m^2/d$_{1-5}$ 3 cyclcs Epirubicin 70mg/m^2 3 cycles Cisplatin 100mg/m^2 3 cycles	339/339	7.0
INT-0099[23]	1989-1995	III-IV (AJCC/UICC<1997)	1-3	T 70Gy/7weeks N-50Gy, N+66-70Gy	Concomitant(E) and Adjuvant(E)	CC:Cisplatin 100mg/m^2 3 cycles AC: Cisplatin 80mg/m^2 3 cycles Fluorouracil 1000mg/m^2/d$_{1-4}$ 3cycles	193/193	16.8
Japan-91[24]	1991-1998	I-IV >10% (AJCC/UICC<1997)	1-3	T 66-68Gy/6.5-7.5we	Induction (E)	IC: Cisplatin 80mg/m^2 2 cycles	80/80	6.2

				eks N-50Gy, N+66-68Gy		Fluorouracil 800g/m^2/d_{2-5} 2 cycles		
TCOG-94[25]	1994-1999	III-IV (AJCC/UICC<1997)	1-3	T 70-72Gy/7-8weeks N-50Gy	Adjuvant(E)	AC: Cisplatin 20mg/m^2 9 cycles Fluorouracil 2200mg/m^2 9 cycles Leucovorin 120mg/m^2 9 cycles	158/158	15.0
PWHQEH-94[26]	1994-1999	II-IV <10% (AJCC/UICC1997)	1-3	T 66Gy/6.5weeks N-58Gy, N+65.5Gy	Concomitant(E)	CC: Cisplatin 40mg/m^2 weekly	350/350	14.1
QMH-95[27]	1995-1997	II-IV <10% (AJCC/UICC1997)	1-3	T 62.5-68Gy/7weeks N62.5-66Gy/7weeks (±boost 10Gy)	Concomitant(C,E) and Adjuvant(C,E)	CC: UFT 600mg/d 5-8weeks AC: Cisplatin 100mg/m^2 6 cycles Fluorouracil 1000mg/m^2/d_{1-3} 6 cycles Vincristine 2mg 6 cycles Bleomycin 30mg 6 cycles Methotrexate 150mg/m^2 6 cycles	222/222	14.0
VUMCA-95 (unpublished)	1995-2000	III-IV (AJCC/UICC<1997)	1-3	T 70Gy/7weeks N-50Gy, N+64-66Gy	Induction (C,E) and Concomitant(E)	IC: Bleomycin 10mg 3 cycles Bleomycin 12mg/m2/d_{1-5} 3 cycles Epirubicin 70mg/m^2 3 cycles Cisplatin 100mg/m^2 3 cycles CC: Hu 500-1000mg/d 7 cycles	509/509	5.8
SQNP01[28]	1997-2003	III-IV (AJCC/UICC1997)	2-3	T 70Gy/7weeks	Concomitant(E) and Adjuvant(E)	CC: Cisplatin 25mg/m^2/d_{1-4} 3 cycles AC: Cisplatin	221/221	11.9

						20mg/m^2/d_{1-4} 3 cycles Fluorouracil 1000mg/m^2/d_{1-4} 3 cycles		
NPC-9901[29]	1999-2004	III-IV (AJCC/UICC1997)	2-3	T≥66Gy/6.6weeks; N≥50Gy	Concomitant(E) and Adjuvant(E)	CC: Cisplatin 100mg/m^2 3 cycles AC: Cisplatin 80mg/m^2 3 cycles Fluorouracil 1000mg/m^2/d_{1-4} 3 cycles	348/348	10.4
NPC-9902[30]	1999-2004	III-IV (AJCC/UICC1997)	2-3	T 66Gy/5.5-6.6weeks	Concomitant(E) and Adjuvant(E)	CC: Cisplatin 100mg/m^2 3 cycles AC: Cisplatin 80mg/m2 3 cycles Fluorouracil 1000mg/m^2/d_{1-4} 3 cycles	189/189	10.6
Guangzhou2001[37]	2001-2003	III-IV (AJCC/UICC1997)	2-3	T 70-74Gy/6-7.5weeks N-50Gy, N+60-64Gy	Concomitant(E)	CC: Oxaliplatin 70mg/m^2 6 cycles	115/115	9.6
NPC008[31]	2002-2004	III-IV (AJCC/UICC1997)	2-3	T 66Gy/6.6weeks	Induction (E) and Concomitant(C, E)	IC: Docetaxel 75mg/m^2 2 cycles Cisplatin 75mg/m^2 2 cycles CC: Cisplatin 40mg/m^2 7 cycles	65/65	8.4
Guangzhou2002-02[32]	2002-2005	III-IV (Chinese 1992)	1--3	T 66-78Gy/6.6-7.8weeks N+60-70Gy	Induction (C,E) and Concomitant(E)	IC: Floxuridine 750mg/m^2/d 2 cycles Carboplatin AUC=6 2 cycles CC: Carboplatin AUC=6 3 cycles	408/408	7.4
Guangzhou2002-01[33]	2002-2005	III-IV (AJCC/UICC1997)	2-3	T 68-70Gy/6.8-7weeks N-50Gy,	Concomitant(E) and Adjuvant(E)	CC: Cisplatin 40mg/m^2 7 cycles AC: Cisplatin 80mg/m^2 3	316/316	6.2

				N+60-66Gy (±boost 10-14Gy)		cycles Fluororuracil 800mg/m^2/d$_{1-5}$ 3 cycles		
Guanghzou2003[34]	2003-2007	II (Chinese 1992)	2-3	T 68-70Gy/6.8-7weeks N-50Gy, N+60-62Gy LU TAI XIANG	Concomitant(E)	CC: Cisplatin 30mg/m^2 7 cycles	230/230	7.6
HeCOG[35]	2003-2008	II-IV >10% (AJCC/UICC2002)	1-3	T 66-70Gy/6.5-7weeks N-50Gy, N+66-70Gy	Induction (E) and Concomitant(C, E)	IC: Epirubicin 75mg/m^2 3 cycles Paclitaxel 175mg/m^2 3 cycles Cisplatin 75mg/m^2 3 cycles CC: Cisplatin 40mg/m^2 7 cycles	144/144	6.7
Italy-79[43]	1979-1983	I-IV >10% (modified HO and AJCC/UICC1978)	1-3	T 60-70Gy/8-10weeks N-50Gy, N+60-70Gy	Adjuvant(E)	AC: Vincristine 1.2 mg/m^2/d$_1$ 6 cycles Oral cyclophosphamide 200mg/m^2/d$_{1-4}$ 6 cycles Adriamycin 40mg/m^2/d$_1$ 6 cycles	229/229	3.6
Taiwan-93[42]	1993-1999	III-IV (AJCC/UICC1992)	1-3	T 70-74Gy/7-8weeks N-50-60Gy/5-6weeks, N+70-74Gy/7-8weeks	Concomitant(E)	CC: Cisplatin 20mg/m^2 2 cycles Fluororuracil 400mg/m^2 2 cycles	284/284	5.4
Guangzhou-93[40]	1993-1994	III-IV (Chinese1992)	1-3	T 68-72Gy N-50Gy, N+60-62Gy	Induction (E)	IC:Cisplatin 100mg/m^2/d$_1$ 3 cycles 2-3cycles Bleomycin 10mg/m^2/d$_{1,5}$ 2-3cycles Fluororuracil 800mg/m^2/ d$_{1-5}$ 2-3cycles	456/449	5.2

Shanghai 2004[39]	2004-2007	III-IV (AJCC/UICC2002)	2-3	T 70-76Gy N-50-60Gy (upper), 50-55Gy (lower) N+65-70Gy	Induction (E) Concomitant(C) and Adjuvant(E, C)	IC: Cisplatin 90mg/m^2 2 cycles Fluorouracil 1500g/m^2 2 cycles CC: Cisplatin 90mg/m^2 2 cycles Fluorouracil 1500g/m^2 2 cycles AC: Cisplatin 90mg/m^2 4 cycles Fluorouracil 1500g/m^2 4 cycles	338/338	5
IMRT and 2D/3D RT ERA								
Guangzhou 2006[36,38]	2006-2010	III-IV (AJCC/UICC2002)	2-3	T≥66Gy/6-7weeks N-50Gy, N+60-66Gy	Concomitant (C, E) and Adjuvant (E)	CC: Cisplatin 40mg/m^2 7 cycles AC: Cisplatin 80mg/m^2 3 cycles Fluorouracil 800mg/m^2/d$_{1-5}$ 3 cycles	508/508	5.7
Guangzhou 2008[46]	2008-2015	III-IV (AJCC/UICC2002)	2-3		Induction (E) and Concomitant (C, E)	IC: Cisplatin 80mg/m^2 2cycles Fluorouracil 800 mg/m^2/d$_{1-5}$ 2cycles CC: Cisplatin 80mg/m^2 3 cycles	476/476	4.2
IMRT ERA								
Singapore 2004[44]	2004-2012	III-IV (AJCC/UICC1997)	2-3	T N+ 69.96Gy N-60Gy	Induction (E) and Concomitant (C, E)	IC: paclitaxel 70mg/m^2 carboplatin AUC 2.5 gemcitabine 1000mg/m^2/ d$_{1,8}$ 3 cycles CC: Cisplatin 40mg/m^2 8 cycles	180/172	3.4
NPC-0501[41]	2006-2012	III-IV (AJCC/UICC2002)	2-3	T N+ ≥70Gy (66 Gy for T1-T2a tumors)	Induction (E), concomitant (E, C), and	IC: PF-Cisplatin 100mg/m^2 3cycles Fluorouracil 1000 mg/m^2	706/706	3.3

				N-≥50Gy	Adjuvant (C)	3cycles; PX- Cisplatin 100mg/m^2 3cycles oral capecitabine 2000 mg/m^2/daily 3cycles CC: Cisplatin 100mg/m^2 2-3 cycles AC: Cisplatin 80mg/m^2 ra3cycles Fluorouracil 1,000 mg/m^2/d 3cycles		
Guangzhou 2011[45]	2011-2013	III-IV (AJCC/UICC2009)	2-3	T N+ ≥66Gy N-≥50Gy	Induction (E) and Concomitant (C, E)	IC: Docetaxel 60 mg/m^2 3cycles, Cisplatin 60mg/m^2 3cycles Fluorouracil 600 mg/m^2 3cycles CC: Cisplatin 100mg/m^2 3 cycles	480/480	3.8

Note: The superscript number of each trial name corresponds to reference article in the manuscript. For example, PWH-88[20] means PWH-88 trial was from reference 20 named "A prospective randomized study of chemotherapy adjunctive to definitive radiotherapy in advanced nasopharyngeal carcinoma." According to the radiotherapy technique, all trials included were grouped into three categories including 2D/3D RT, 2D/3D RT and IMRT, and IMRT. In 2D/3D RT era, all treatments were in 2D/3D RT, except for three trials (NPC 9901, NPC 9902, and NPC008) in which IMRT was involved. However, due to the significantly lower rate of patients treated with IMRT compared with that of patients in 2D/3D RT, these three trials were also considered as 2D/3D RT. In 2D/3D RT and IMRT era, the rate of patients in IMRT was almost comparable to that of those in 2D/3D RT. Furthermore, all comparisons could be distinguished according to radiotherapy technique (2D/3D RT or IMRT) since we had raw data in these two trials (Guangzhou 2006 and Guangzhou 2008). In IMRT era, almost all patients (90%-100%) were treated

with IMRT.

TNM: Tumor Nodes Metastasis; WHO: World Health Organization; AJCC: American Joint Committee on Cancer; UICC: International Union Against Cancer; T: tumor; N-: negative neck lymph nodes; N+: positive neck lymph nodes; E: experimental arm; C: control arm; d: day; UFT: Uracil + Tegafur; Hu: hydroxyurea; AUC: area under the curve; IC: induction chemotherapy; AC: adjuvant chemotherapy; CC: concurrent chemoradiotherapy.

Table S2. Detailed Jadad Score components.

Study	Jadad score	Randomization	Double blinding	Drop-outs or withdrawals	Allocation concealment
PWH-88	4	2	0	1	2
AOCOA	5	2	0	1	2
VUMCA-89	5	2	0	1	2
INT-0099	4	1	0	1	2
Japan-91	5	2	0	1	2
TCOG-94	5	2	0	1	2
PWHQEH-94	5	2	0	1	2
QMH-95	4	1	0	1	2
SQNP01	5	2	0	1	2
NPC-9901	5	2	0	1	2
NPC-9902	4	1	0	1	2
Guangzhou2001	4	1	0	1	2
NPC008	5	2	0	1	2
Guangzhou2002-02	5	2	0	1	2
Guangzhou2002-01	5	2	0	1	2
Guangzhou 2003	5	2	0	1	2
HeCOG	5	2	0	1	2

Guangzhou 2006	5	2	0	1	2
Shanghai 2004	3	2	0	0	1
Guangzhou-93	3	1	0	1	1
NPC-0501	5	2	0	1	2
Taiwan-93	2	1	0	0	1
Italy-79	4	1	0	1	2
Singapore 2004	4	2	0	1	1
Guangzhou 2011	5	2	0	1	2
Guangzhou 2008	5	2	0	1	2

Table S3. League table presenting the results of the network meta-analysis when not distinguishing between radiotherapy techniques including four efficacy end points.

Overall survival						
CRT (7)	0.98 (0.79 to 1.23)	1.35 (0.82 to 2.22)	0.83 (0.66 to 1.03)	1.11 (0.86 to 1.43)	1.42 (1.17 to 1.73)	1.51 (1.07 to 2.14)
1.05 (0.88 to 1.26)	**CRT – AC (6)**	1.38 (0.87 to 2.17)	0.84 (0.66 to 1.07)	1.13 (0.88 to 1.45)	1.44 (1.22 to 1.71)	1.54 (1.10 to 2.15)
0.78 (0.51 to 1.19)	0.74 (0.50 to 1.10)	**IC – RT – AC (5)**	0.61 (0.37 to 1.01)	0.82 (0.49 to 1.36)	1.05 (0.66 to 1.68)	1.12 (0.64 to 1.94)
1.18 (0.98 to 1.42)	1.13 (0.93 to 1.37)	1.52 (0.99 to 2.33)	**IC – CRT (4)**	1.34 (1.07 to 1.69)	1.72 (1.36 to 2.16)	1.83 (1.26 to 2.65)
0.92 (0.75 to 1.11)	0.87 (0.72 to 1.05)	1.17 (0.77 to 1.80)	0.77 (0.66 to 0.91)	**IC – RT (3)**	1.28 (1.04 to 1.57)	1.36 (0.95 to 1.96)
0.73 (0.62 to 0.85)	0.69 (0.61 to 0.79)	0.94 (0.62 to 1.40)	0.62 (0.52 to 0.74)	0.8 (0.68 to 0.93)	**RT (2)**	1.07 (0.79 to 1.44)
0.68 (0.51 to 0.91)	0.65 (0.49 to 0.86)	0.88 (0.55 to 1.41)	0.58 (0.43 to 0.78)	0.75 (0.56 to 1.00)	0.94 (0.73 to 1.21)	**RT – AC (1)**
Progression-free survival						
CRT (7)	0.91 (0.77 to 1.08)	1.16 (0.79 to 1.70)	0.75 (0.64 to 0.88)	0.99 (0.83 to 1.19)	1.38 (1.19 to 1.60)	1.15 (0.84 to 1.58)
1.11 (0.94 to 1.30)	**CRT – AC (6)**	1.28 (0.90 to 1.82)	0.83 (0.70 to 0.99)	1.09 (0.91 to 1.30)	1.51 (1.33 to 1.73)	1.27 (0.92 to 1.73)
0.87 (0.60 to 1.26)	0.79 (0.56 to 1.11)	**IC – RT – AC (5)**	0.65 (0.44 to 0.96)	0.85 (0.58 to 1.26)	1.19 (0.82 to 1.71)	0.99 (0.62 to 1.58)
1.33 (1.14 to 1.54)	1.2 (1.02 to 1.41)	1.52 (1.05 to 2.21)	**IC – CRT (4)**	1.32 (1.12 to 1.54)	1.83 (1.55 to 2.15)	1.53 (1.10 to 2.13)
1.02 (0.86 to 1.20)	0.92 (0.77 to 1.09)	1.17 (0.80 to 1.69)	0.77 (0.66 to 0.89)	**IC – RT (3)**	1.39 (1.20 to 1.60)	1.16 (0.84 to 1.61)
0.73 (0.64 to 0.84)	0.66 (0.58 to 0.75)	0.84 (0.59 to 1.20)	0.55 (0.47 to 0.64)	0.72 (0.63 to 0.83)	**RT (2)**	0.84 (0.62 to 1.13)
0.87 (0.64 to 1.19)	0.79 (0.58 to 1.07)	1.00 (0.64 to 1.57)	0.66 (0.48 to 0.91)	0.86 (0.63 to 1.18)	1.19 (0.90 to 1.59)	**RT – AC (1)**
Distant Metastasis-free Survival						
CRT (7)	0.84 (0.62 to 1.14)	1.59 (0.89 to 2.84)	0.67 (0.51 to 0.89)	0.89 (0.65 to 1.22)	1.5 (1.17 to 1.92)	1.35 (0.80 to 2.27)
1.22 (0.95 to 1.55)	**CRT – AC (6)**	1.88 (1.12 to 3.18)	0.8 (0.55 to 1.16)	1.06 (0.75 to 1.49)	1.78 (1.41 to 2.24)	1.60 (0.96 to 2.66)
0.66 (0.4 to 1.08)	0.54 (0.35 to 0.85)	**IC – RT – AC (5)**	0.42 (0.23 to 0.79)	0.56 (0.31 to 1.02)	0.94 (0.55 to 1.62)	0.85 (0.42 to 1.73)
1.47 (1.17 to 1.85)	1.21 (0.9 to 1.63)	2.23 (1.32 to 3.78)	**IC – CRT (4)**	1.32 (0.97 to 1.8)	2.23 (1.62 to 3.06)	2.00 (1.14 to 3.51)
1.15 (0.89 to 1.48)	0.94 (0.72 to 1.24)	1.74 (1.04 to 2.9)	0.78 (0.61 to 0.99)	**IC – RT (3)**	1.68 (1.29 to 2.19)	1.51 (0.88 to 2.60)
0.7 (0.57 to 0.85)	0.58 (0.48 to 0.7)	1.06 (0.66 to 1.7)	0.48 (0.37 to 0.61)	0.61 (0.49 to 0.75)	**RT (2)**	0.90 (0.56 to 1.45)
0.79 (0.5 to 1.25)	0.65 (0.42 to 1.02)	1.2 (0.64 to 2.24)	0.54 (0.33 to 0.88)	0.69 (0.43 to 1.10)	1.13 (0.74 to 1.73)	**RT – AC (1)**
Loco Regional- free Survival						
CRT (7)	0.73 (0.53 to 1.01)	0.68 (0.39 to 1.21)	0.84 (0.63 to 1.11)	1.02 (0.76 to 1.37)	1.3 (1.00 to 1.69)	0.83 (0.47 to 1.46)
1.36 (0.99 to 1.87)	**CRT – AC (6)**	0.93 (0.57 to 1.52)	1.14 (0.80 to 1.64)	1.39 (1.00 to 1.93)	1.77 (1.39 to 2.26)	1.13 (0.64 to 1.98)
1.46 (0.83 to 2.59)	1.07 (0.66 to 1.75)	**IC – RT – AC (5)**	1.23 (0.68 to 2.22)	1.49 (0.84 to 2.65)	1.9 (1.12 to 3.23)	1.21 (0.58 to 2.53)
1.19 (0.90 to 1.59)	0.88 (0.61 to 1.26)	0.82 (0.45 to 1.48)	**IC – CRT (4)**	1.22 (0.96 to 1.55)	1.55 (1.16 to 2.08)	0.99 (0.55 to 1.79)
0.98 (0.73 to 1.32)	0.72 (0.52 to 1.00)	0.67 (0.38 to 1.19)	0.82 (0.65 to 1.05)	**IC – RT (3)**	1.28 (1.01 to 1.62)	0.81 (0.46 to 1.44)

0.77 (0.59 to 1.00)	0.56 (0.44 to 0.72)	0.53 (0.31 to 0.89)	0.64 (0.48 to 0.86)	0.78 (0.62 to 0.99)	**RT (2)**	0.64 (0.38 to 1.08)
1.21 (0.69 to 2.13)	0.89 (0.50 to 1.56)	0.83 (0.40 to 1.72)	1.01 (0.56 to 1.82)	1.23 (0.69 to 2.18)	1.57 (0.93 to 2.65)	**RT – AC (1)**

Note: The lower left triangles colored green were the results of fixed effects models, whereas the upper right triangles colored orange were the results of random effects models. As a convention the cells in the lower left triangles colored green contain the hazard ratio (HR, 95% confidence interval) in fixed effects models of the treatment with the higher number compared to the treatment with the lower number. The cells in the upper right triangles colored orange contain the hazard ratio (HR, 95% confidence interval) in random effects models of the treatment with the lower number compared to the treatment with the higher number.

IC: induction chemotherapy; AC: adjuvant chemotherapy; CRT: concurrent chemoraiotherapy; HR: hazard ratio; 95% CI: 95% confidence interval.

Table S4. Summary of network meta-analysis results for CRT, IC-CRT, and CRT-AC in the IMRT era according to the node stage.

Treatment Data	N0-N1				N2-N3			
	OS	PFS	DMFS	LRRFS	OS	PFS	DMFS	LRRFS
P value heterogeneity/inconsistency (Q test P value)	0.960	0.350	0.128	0.848	0.778	0.356	0.934	0.736
P value heterogeneity (within design)	0.960	0.350	0.128	0.848	0.778	0.356	0.934	0.736
P value inconsistency (between design)	------	------	------	-------	------	------	------	-------
CRT								
P-score, %	2.0	2.7	10.6	5.6	50.3	34.4	41.3	17.6
CRT-AC								
P-score, %	68.0	69.8	46.5	85.3	6.5	20.1	15.1	64.1
IC-CRT								
P-score, %	80.0	77.5	92.9	59.1	93.3	95.6	93.6	68.3
CRT-AC vs CRT								
HR (95%CI)	0.36 (0.12, 1.06)	0.49 (0.21, 1.14)	0.61 (0.19, 1.99)	0.32 (0.08, 1.26)	1.64 (0.79, 3.42)	1.16 (0.60, 2.23)	1.34 (0.62, 2.90)	0.58 (0.11, 3.11)
IC-CRT vs CRT								
HR (95%CI)	0.29 (0.11, 0.78)	0.46 (0.25, 0.82)	0.25 (0.08, 0.73)	0.56 (0.27, 1.17)	0.73 (0.45, 1.18)	0.66 (0.46, 0.96)	0.69 (0.43, 1.09)	0.64 (0.34, 1.22)
IC-CRT vs CRT-AC								
HR (95%CI)	0.81 (0.19, 3.52)	0.93 (0.33, 2.61)	0.41 (0.08, 2.02)	1.74 (0.37, 8.26)	0.44 (0.18, 1.07)	0.57 (0.27, 1.22)	0.51 (0.21, 1.26)	1.11 (0.18, 6.70)

IC: induction chemotherapy; AC: adjuvant chemotherapy; CRT: concurrent chemoraiotherapy; HR: hazard ratio; 95% CI: 95% confidence interval.

Table S5. Summary of network meta-analysis results for CRT, IC-CRT, and CRT-AC in the IMRT era according to the tumor stage.

Treatment Data	T1-T2				T3-T4			
	OS	PFS	DMFS	LRRFS	OS	PFS	DMFS	LRRFS
P value heterogeneity/inconsistency (Q test P value)	0.206	0.645	0.678	0.848	0.790	0.246	0.343	0.917
P value heterogeneity (within design)	0.206	0.645	0.678	0.848	0.790	0.246	0.343	0.917
P value inconsistency (between design)	------	------	------	-------	------	------	------	-------
CRT								
P-score, %	43.5	16.5	24.1	22.0	17.3	12.9	27.9	4.9
CRT-AC								
P-score, %	15.7	54.3	40.8	------	43.7	48.8	27.4	82.4
IC-CRT								
P-score, %	90.8	79.2	85.1	78.0	89.0	88.3	94.7	62.7
CRT-AC vs CRT								
HR (95%CI)	2.66 (0.24, 29.41)	0.63 (0.12, 3.38)	0.87 (0.15, 5.13)	-------	0.87 (0.47, 1.61)	0.83 (0.48, 1.44)	1.04 (0.52, 2.08)	0.45 (0.16, 1.30)
IC-CRT vs CRT								
HR (95%CI)	0.49 (0.18, 1.33)	0.47 (0.21, 1.06)	0.44 (0.18, 1.12)	0.58 (0.14, 2.39)	0.63 (0.41, 0.97)	0.65 (0.47, 0.90)	0.59 (0.37, 0.94)	0.63 (0.39, 1.01)
IC-CRT vs CRT-AC								
HR (95%CI)	0.19 (0.01, 2.50)	0.75 (0.12, 4.85)	0.51 (0.07, 3.77)	--------	0.73 (0.34, 1.54)	0.78 (0.41, 1.49)	0.57 (0.25, 1.31)	1.41 (0.44, 4.48)

IC: induction chemotherapy; AC: adjuvant chemotherapy; CRT: concurrent chemoraiotherapy; HR: hazard ratio; 95% CI: 95% confidence interval.

Table S6. League table presenting the results of the network meta-analysis for the 10 treatments after distinguishing between 2D/3D RT and IMRT including four efficacy end points.

Overall survival									
CRT (10)	0.9 (0.63 to 1.30)	0.89 (0.72 to 1.10)	0.97 (0.66 to 1.45)	1.23 (0.79 to 1.90)	1.05 (0.83 to 1.34)	0.6 (0.41 to 0.89)	1.20 (0.97 to 1.50)	1.38 (1.16 to 1.63)	1.46 (1.08 to 1.96)
1.11 (0.77 to 1.59)	**CRT (IMRT)[1] (9)**	0.98 (0.67 to 1.45)	1.08 (0.73 to 1.58)	1.36 (0.78 to 2.35)	1.17 (0.78 to 1.74)	0.67 (0.48 to 0.92)	1.33 (0.90 to 1.98)	1.52 (1.04 to 2.22)	1.61 (1.03 to 2.53)
1.13 (0.92 to 1.38)	1.02 (0.70 to 1.49)	**CRT-AC (8)**	1.09 (0.73 to 1.65)	1.38 (0.92 to 2.06)	1.18 (0.91 to 1.54)	0.68 (0.45 to 1.02)	1.35 (1.08 to 1.69)	1.55 (1.34 to 1.79)	1.64 (1.23 to 2.19)
1.03 (0.70 to 1.52)	0.93 (0.64 to 1.36)	0.91 (0.61 to 1.37)	**CRT-AC(IMRT)[1] (7)**	1.26 (0.71 to 2.22)	1.08 (0.70 to 1.67)	0.62 (0.46 to 0.84)	1.24 (0.81 to 1.89)	1.41 (0.94 to 2.12)	1.50 (0.93 to 2.41)
0.82 (0.53 to 1.26)	0.74 (0.43 to 1.27)	0.73 (0.49 to 1.08)	0.8 (0.46 to 1.39)	**IC-RT-AC (6)**	0.86 (0.54 to 1.37)	0.49 (0.28 to 0.86)	0.98 (0.63 to 1.53)	1.12 (0.74 to 1.69)	1.19 (0.73 to 1.93)
0.95 (0.75 to 1.20)	0.86 (0.58 to 1.27)	0.84 (0.65 to 1.08)	0.92 (0.60 to 1.41)	1.16 (0.73 to 1.83)	**IC-CRT (5)**	0.57 (0.38 to 0.87)	1.14 (0.95 to 1.38)	1.31 (1.04 to 1.64)	1.39 (0.99 to 1.94)
1.66 (1.14 to 2.44)	1.5 (1.09 to 2.08)	1.48 (0.99 to 2.20)	1.62 (1.20 to 2.18)	2.03 (1.17 to 3.53)	1.76 (1.16 to 2.66)	**IC-CRT(IMRT)[1](4)**	2.00 (1.32 to 3.03)	2.29 (1.53 to 3.41)	2.42 (1.52 to 3.87)
0.83 (0.67 to 1.03)	0.75 (0.51 to 1.11)	0.74 (0.60 to 0.91)	0.81 (0.53 to 1.23)	1.01 (0.66 to 1.57)	0.88 (0.73 to 1.05)	0.5 (0.33 to 0.75)	**IC-RT (3)**	1.14 (0.96 to 1.35)	1.21 (0.89 to 1.64)
0.73 (0.62 to 0.86)	0.66 (0.45 to 0.96)	0.65 (0.56 to 0.75)	0.71 (0.47 to 1.06)	0.89 (0.59 to 1.33)	0.77 (0.62 to 0.96)	0.44 (0.30 to 0.65)	0.88 (0.74 to 1.03)	**RT (2)**	1.06 (0.82 to 1.37)
0.69 (0.51 to 0.92)	0.62 (0.40 to 0.97)	0.61 (0.46 to 0.81)	0.67 (0.42 to 1.07)	0.84 (0.52 to 1.35)	0.73 (0.52 to 1.01)	0.41 (0.26 to 0.66)	0.83 (0.61 to 1.11)	0.94 (0.73 to 1.21)	**RT-AC (1)**
Progression-free survival									
CRT (10)	0.96 (0.73 to 1.28)	0.89 (0.74 to 1.07)	0.85 (0.62 to 1.18)	1.14 (0.78 to 1.67)	0.92 (0.74 to 1.13)	0.60 (0.44 to 0.82)	1.09 (0.90 to 1.31)	1.40 (1.21 to 1.63)	1.17 (0.85 to 1.59)
1.04 (0.78 to 1.38)	**CRT(IMRT)[1] (9)**	0.92 (0.68 to 1.25)	0.89 (0.65 to 1.20)	1.19 (0.76 to 1.86)	0.95 (0.69 to 1.30)	0.62 (0.49 to 0.80)	1.13 (0.83 to 1.54)	1.46 (1.09 to 1.96)	1.21 (0.81 to 1.81)
1.12 (0.93 to 1.35)	1.08 (0.80 to 1.46)	**CRT-AC (8)**	0.96 (0.68 to 1.35)	1.29 (0.91 to 1.81)	1.03 (0.82 to 1.29)	0.67 (0.49 to 0.93)	1.22 (1.01 to 1.48)	1.58 (1.38 to 1.80)	1.31 (0.96 to 1.78)
1.17 (0.85 to 1.63)	1.13 (0.83 to 1.53)	1.04 (0.74 to 1.47)	**CRT-AC(IMRT)[1] (7)**	1.34 (0.83 to 2.16)	1.07 (0.75 to 1.53)	0.7 (0.55 to 0.89)	1.27 (0.89 to 1.81)	1.65 (1.18 to 2.30)	1.37 (0.88 to 2.11)
0.87 (0.60 to 1.28)	0.84 (0.54 to 1.32)	0.78 (0.55 to 1.09)	0.75 (0.46 to 1.20)	**IC-RT-AC (6)**	0.8 (0.54 to 1.19)	0.52 (0.33 to 0.83)	0.95 (0.65 to 1.39)	1.23 (0.86 to 1.75)	1.02 (0.65 to 1.60)

1.09 (0.89 to 1.34)	1.05 (0.77 to 1.44)	0.97 (0.77 to 1.22)	0.93 (0.65 to 1.33)	1.25 (0.84 to 1.87)	**IC-CRT (5)**	0.66 (0.47 to 0.92)	1.19 (1.01 to 1.4)	1.53 (1.26 to 1.86)	1.27 (0.91 to 1.79)
1.67 (1.23 to 2.26)	1.6 (1.26 to 2.05)	1.48 (1.07 to 2.05)	1.42 (1.12 to 1.81)	1.91 (1.20 to 3.04)	1.52 (1.09 to 2.13)	**IC-CRT(IMRT)[1](4)**	1.81 (1.30 to 2.52)	2.34 (1.70 to 3.21)	1.94 (1.28 to 2.96)
0.92 (0.76 to 1.11)	0.89 (0.65 to 1.21)	0.82 (0.68 to 0.99)	0.79 (0.55 to 1.12)	1.05 (0.72 to 1.54)	0.84 (0.72 to 0.99)	0.55 (0.40 to 0.77)	**IC-RT (3)**	1.29 (1.12 to 1.49)	1.07 (0.78 to 1.47)
0.71 (0.61 to 0.83)	0.69 (0.51 to 0.92)	0.63 (0.55 to 0.73)	0.61 (0.43 to 0.85)	0.82 (0.57 to 1.16)	0.65 (0.54 to 0.79)	0.43 (0.31 to 0.59)	0.77 (0.67 to 0.89)	**RT (2)**	0.83 (0.62 to 1.11)
0.86 (0.63 to 1.17)	0.83 (0.55 to 1.24)	0.76 (0.56 to 1.04)	0.73 (0.47 to 1.13)	0.98 (0.63 to 1.54)	0.79 (0.56 to 1.10)	0.51 (0.34 to 0.78)	0.93 (0.68 to 1.28)	1.2 (0.90 to 1.60)	**RT-AC (1)**
Distant metastasis-free survival									
CRT (10)	0.81 (0.53 to 1.25)	0.83 (0.60 to 1.14)	0.84 (0.46 to 1.54)	1.57 (0.87 to 2.84)	0.74 (0.52 to 1.05)	0.48 (0.29 to 0.81)	0.93 (0.66 to 1.30)	1.51 (1.16 to 1.95)	1.35 (0.80 to 2.28)
1.22 (0.84 to 1.78)	**CRT(IMRT)[1] (9)**	1.02 (0.63 to 1.65)	1.03 (0.54 to 1.99)	1.93 (0.96 to 3.87)	0.91 (0.56 to 1.48)	0.59 (0.39 to 0.89)	1.14 (0.69 to 1.88)	1.85 (1.17 to 2.94)	1.65 (0.86 to 3.17)
1.23 (0.94 to 1.60)	1 (0.66 to 1.52)	**CRT-AC (8)**	1.01 (0.54 to 1.89)	1.9 (1.12 to 3.21)	0.89 (0.59 to 1.34)	0.58 (0.33 to 1.03)	1.12 (0.79 to 1.59)	1.81 (1.43 to 2.3)	1.62 (0.97 to 2.71)
1.2 (0.71 to 2.02)	0.98 (0.55 to 1.74)	0.98 (0.57 to 1.68)	**CRT-AC(IMRT)[1] (7)**	1.87 (0.84 to 4.17)	0.88 (0.45 to 1.72)	0.58 (0.28 to 1.20)	1.1 (0.57 to 2.13)	1.79 (0.96 to 3.33)	1.6 (0.74 to 3.46)
0.66 (0.40 to 1.10)	0.54 (0.30 to 0.99)	0.54 (0.34 to 0.85)	0.55 (0.27 to 1.10)	**IC-RT-AC (6)**	0.47 (0.25 to 0.90)	0.31 (0.14 to 0.66)	0.59 (0.32 to 1.08)	0.96 (0.56 to 1.65)	0.86 (0.42 to 1.75)
1.32 (0.98 to 1.77)	1.08 (0.70 to 1.64)	1.07 (0.77 to 1.50)	1.1 (0.62 to 1.96)	1.99 (1.15 to 3.44)	**IC-CRT (5)**	0.65 (0.37 to 1.14)	1.25 (0.91 to 1.73)	2.03 (1.42 to 2.90)	1.82 (1.01 to 3.27)
2.05 (1.31 to 3.23)	1.68 (1.18 to 2.38)	1.67 (1.02 to 2.74)	1.71 (0.90 to 3.26)	3.11 (1.61 to 5.99)	1.56 (0.96 to 2.54)	**IC-CRT(IMRT)[1](4)**	1.92 (1.08 to 3.42)	3.11 (1.80 to 5.39)	2.78 (1.36 to 5.70)
1.09 (0.83 to 1.43)	0.89 (0.58 to 1.36)	0.89 (0.67 to 1.18)	0.91 (0.52 to 1.60)	1.65 (0.98 to 2.76)	0.83 (0.64 to 1.07)	0.53 (0.32 to 0.87)	**IC-RT (3)**	1.62 (1.23 to 2.13)	1.45 (0.84 to 2.51)
0.69 (0.56 to 0.85)	0.56 (0.38 to 0.84)	0.56 (0.46 to 0.68)	0.58 (0.34 to 0.98)	1.05 (0.65 to 1.67)	0.52 (0.39 to 0.70)	0.34 (0.21 to 0.54)	0.63 (0.51 to 0.79)	**RT (2)**	0.89 (0.55 to 1.45)
0.79 (0.50 to 1.25)	0.64 (0.36 to 1.14)	0.64 (0.41 to 1.01)	0.66 (0.33 to 1.29)	1.19 (0.64 to 2.22)	0.6 (0.36 to 0.99)	0.38 (0.20 to 0.72)	0.72 (0.45 to 1.16)	1.14 (0.75 to 1.74)	**RT-AC (1)**
Loco regional-free survival									
CRT (10)	1.28 (0.78 to 2.11)	0.86 (0.62 to 1.21)	0.41 (0.16 to 1.05)	0.8 (0.45 to 1.43)	0.98 (0.68 to 1.40)	0.86 (0.47 to 1.56)	1.17 (0.83 to 1.64)	1.46 (1.10 to 1.94)	0.92 (0.52 to 1.63)
0.78 (0.47 to 1.29)	**CRT(IMRT)[1] (9)**	0.68 (0.40 to 1.14)	0.32 (0.12 to 0.86)	0.63 (0.31 to 1.27)	0.76 (0.45 to 1.31)	0.67 (0.42 to 1.08)	0.91 (0.53 to 1.56)	1.14 (0.68 to 1.92)	0.72 (0.35 to 1.48)
1.16 (0.83 to 1.61)	1.48 (0.87 to 2.51)	**CRT-AC (8)**	0.47 (0.18 to 1.21)	0.93 (0.57 to 1.51)	1.13 (0.77 to 1.67)	0.99 (0.53 to 1.87)	1.35 (0.96 to 1.89)	1.69 (1.33 to 2.16)	1.06 (0.60 to 1.87)

2.46 (0.96 to 6.31)	3.14 (1.16 to 8.51)	2.12 (0.83 to 5.43)	**CRT-AC(IMRT)[1] (7)**	1.96 (0.68 to 5.65)	2.4 (0.90 to 6.40)	2.11 (0.73 to 6.11)	2.87 (1.09 to 7.55)	3.59 (1.39 to 9.26)	2.26 (0.77 to 6.6)
1.25 (0.70 to 2.23)	1.6 (0.79 to 3.26)	1.08 (0.66 to 1.76)	0.51 (0.18 to 1.46)	**IC-RT-AC (6)**	1.22 (0.66 to 2.25)	1.07 (0.49 to 2.37)	1.46 (0.82 to 2.61)	1.83 (1.08 to 3.11)	1.15 (0.55 to 2.4)
1.02 (0.71 to 1.46)	1.31 (0.76 to 2.25)	0.88 (0.60 to 1.30)	0.42 (0.16 to 1.11)	0.82 (0.44 to 1.50)	**IC-CRT (5)**	0.88 (0.47 to 1.64)	1.19 (0.93 to 1.53)	1.49 (1.09 to 2.06)	0.94 (0.51 to 1.72)
1.17 (0.64 to 2.12)	1.49 (0.93 to 2.40)	1.01 (0.54 to 1.89)	0.47 (0.16 to 1.37)	0.93 (0.42 to 2.05)	1.14 (0.61 to 2.14)	**IC-CRT(IMRT)[1](4)**	1.36 (0.72 to 2.55)	1.7 (0.92 to 3.15)	1.07 (0.48 to 2.38)
0.86 (0.61 to 1.20)	1.1 (0.64 to 1.88)	0.74 (0.53 to 1.04)	0.35 (0.13 to 0.92)	0.69 (0.38 to 1.22)	0.84 (0.65 to 1.08)	0.74 (0.39 to 1.38)	**IC-RT (3)**	1.25 (0.98 to 1.60)	0.79 (0.44 to 1.40)
0.68 (0.52 to 0.91)	0.88 (0.52 to 1.47)	0.59 (0.46 to 0.75)	0.28 (0.11 to 0.72)	0.55 (0.32 to 0.93)	0.67 (0.49 to 0.92)	0.59 (0.32 to 1.09)	0.8 (0.62 to 1.02)	**RT (2)**	0.63 (0.37 to 1.06)
1.09 (0.61 to 1.93)	1.39 (0.68 to 2.87)	0.94 (0.53 to 1.65)	0.44 (0.15 to 1.30)	0.87 (0.42 to 1.82)	1.06 (0.58 to 1.95)	0.93 (0.42 to 2.07)	1.27 (0.71 to 2.26)	1.59 (0.94 to 2.69)	**RT-AC (1)**

Note: The lower left triangles colored green were the results of fixed effects models, whereas the upper right triangles colored orange were the results of random effects models. As a convention, the cells in the lower left triangles colored green contain the hazard ratios (HR, 95% confidence interval) in fixed effects models of the treatment with the higher number compared to the treatment with the lower number. The cells in the upper right triangles colored orange contain the hazard ratios (HR, 95% confidence interval) in random effects models of the treatment with the lower number compared to the treatment with the higher number. IMRT[1] suggests the radiotherapy technique of this regimen was intensity-modulated radiotherapy (IMRT), if not, the radiotherapy technique of this regimen was two-dimensional radiotherapy (2D-RT), or three-dimensional radiotherapy (3D-RT).

IC: induction chemotherapy; AC: adjuvant chemotherapy; CRT: concurrent chemoradiotherapy; HR: hazard ratio; 95% CI: 95% confidence interval.

Appendix S2: The comparison of chemoradiotherapy regimens in the 2D/3D RT era.

The three treatments that had the highest effect on OS were CRT-AC, CRT, and IC-CRT, with respective P-scores of 77.3%, 58.9%, and 51.3% (Table 3), respectively. The HRs (95% CIs) of CRT-AC compared with CRT or IC-CRT showed no significant differences, with respective values of 0.89 (0.72, 1.09) and 0.84 (0.65, 1.08) for OS (Supplementary Table 4). In addition, the three treatments that had the highest effect on PFS were CRT-AC, IC-CRT, and CRT with respective P-scores of 71.6%, 66.1%, and 47.5%, respectively. The HRs (95% CIs) of CRT-AC compared with CRT or IC-CRT also showed no significant differences, with respective values of 0.89 (0.74, 1.07) and 0.97 (0.77, 1.22) for PFS. The three best treatments for distant control were IC-CRT, CRT-AC, and IC-RT, with respective P-scores of 75.7%, 67.7%, and 50.7%. The three best treatments for locoregional control were IC-RT-AC, CRT-AC, RT-AC with respective P-scores of 69.4%, 66.0%, and 55.9% (Table 3)

Figure S2. Forest plot for distant metastasis-free survival (on the left) and local regional-free survival (on the right), showing results from direct comparisons. HR<1 is in favor of the first treatment mentioned in the title (ie, IC-CRT for the comparison IC-CRT vs RT). Only comparisons involving two trials or more are presented here. (IMRT)[1] suggests the radiotherapy technique of this regimen was intensity-modulated radiotherapy (IMRT), if not, the radiotherapy technique of this regimen was two-dimensional radiotherapy (2D-RT), or three-dimensional radiotherapy (3D-RT). The last two comparisons marked with (overall) suggested the radiotherapy techniques of treatments involved were not distinguished. IC, induction chemotherapy; AC, adjuvant chemotherapy; CRT, concurrent chemoradiotherapy; HR, hazard ratio; 95% CI, 95% confidence interval.

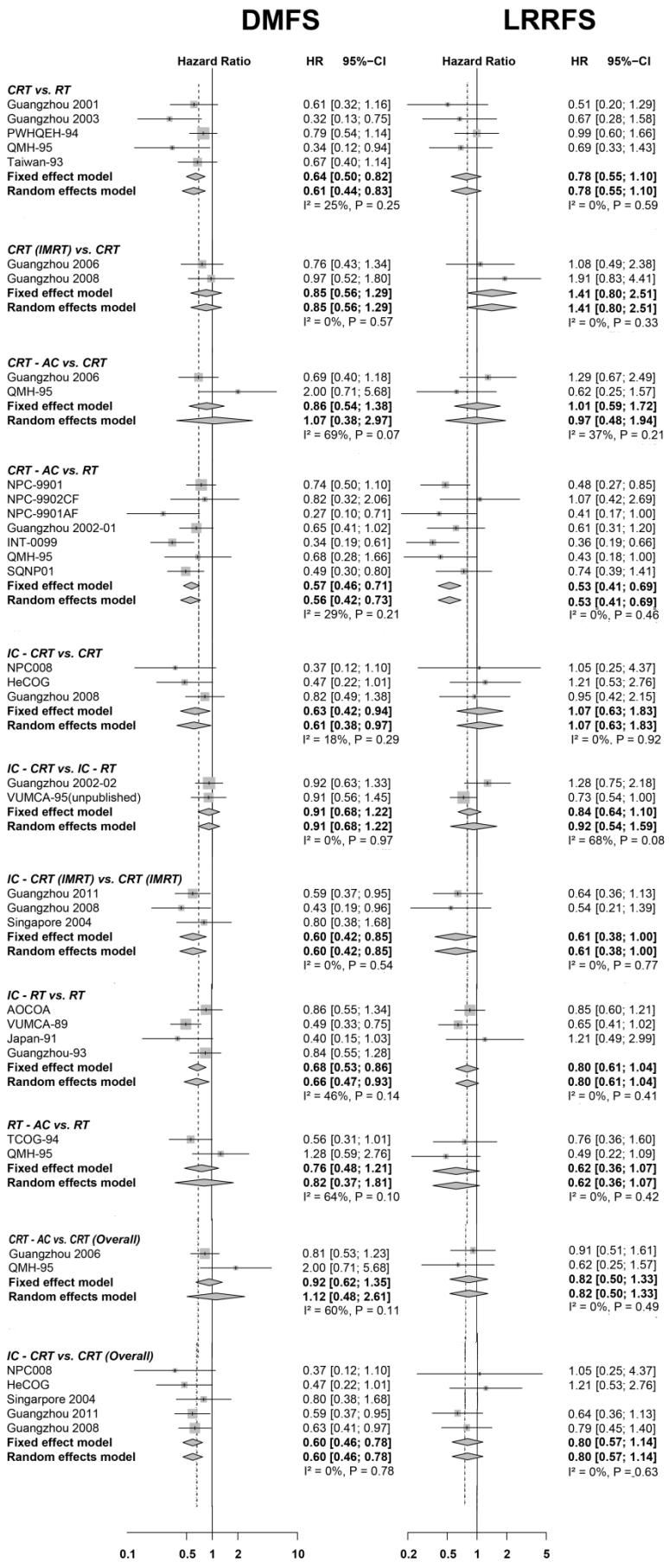
DMFS
LRRFS
Hazard Ratio
HR 95%−CI
Hazard Ratio
HR 95%−CI
CRT vs. RT
Guangzhou 2001 0.61 [0.32; 1.16] 0.51 [0.20; 1.29]
Guangzhou 2003 0.32 [0.13; 0.75] 0.67 [0.28; 1.58]
PWHQEH-94 0.79 [0.54; 1.14] 0.99 [0.60; 1.66]
QMH-95 0.34 [0.12; 0.94] 0.69 [0.33; 1.43]
Taiwan-93 0.67 [0.40; 1.14]
Fixed effect model 0.64 [0.50; 0.82] 0.78 [0.55; 1.10]
Random effects model 0.61 [0.44; 0.83] 0.78 [0.55; 1.10]
I² = 25%, P = 0.25 I² = 0%, P = 0.59
CRT (IMRT) vs. CRT
Guangzhou 2006 0.76 [0.43; 1.34] 1.08 [0.49; 2.38]
Guangzhou 2008 0.97 [0.52; 1.80] 1.91 [0.83; 4.41]
Fixed effect model 0.85 [0.56; 1.29] 1.41 [0.80; 2.51]
Random effects model 0.85 [0.56; 1.29] 1.41 [0.80; 2.51]
I² = 0%, P = 0.57 I² = 0%, P = 0.33
CRT - AC vs. CRT
Guangzhou 2006 0.69 [0.40; 1.18] 1.29 [0.67; 2.49]
QMH-95 2.00 [0.71; 5.68] 0.62 [0.25; 1.57]
Fixed effect model 0.86 [0.54; 1.38] 1.01 [0.59; 1.72]
Random effects model 1.07 [0.38; 2.97] 0.97 [0.48; 1.94]
I² = 69%, P = 0.07 I² = 37%, P = 0.21
CRT - AC vs. RT
NPC-9901 0.74 [0.50; 1.10] 0.48 [0.27; 0.85]
NPC-9902CF 0.82 [0.32; 2.06] 1.07 [0.42; 2.69]
NPC-9901AF 0.27 [0.10; 0.71] 0.41 [0.17; 1.00]
Guangzhou 2002-01 0.65 [0.41; 1.02] 0.61 [0.31; 1.20]
INT-0099 0.34 [0.19; 0.61] 0.36 [0.19; 0.66]
QMH-95 0.68 [0.28; 1.66] 0.43 [0.18; 1.00]
SQNP01 0.49 [0.30; 0.80] 0.74 [0.39; 1.41]
Fixed effect model 0.57 [0.46; 0.71] 0.53 [0.41; 0.69]
Random effects model 0.56 [0.42; 0.73] 0.53 [0.41; 0.69]
I² = 29%, P = 0.21 I² = 0%, P = 0.46
IC - CRT vs. CRT
NPC008 0.37 [0.12; 1.10] 1.05 [0.25; 4.37]
HeCOG 0.47 [0.22; 1.01] 1.21 [0.53; 2.76]
Guangzhou 2008 0.82 [0.49; 1.38] 0.95 [0.42; 2.15]
Fixed effect model 0.63 [0.42; 0.94] 1.07 [0.63; 1.83]
Random effects model 0.61 [0.38; 0.97] 1.07 [0.63; 1.83]
I² = 18%, P = 0.29 I² = 0%, P = 0.92
IC - CRT vs. IC - RT
Guangzhou 2002-02 0.92 [0.63; 1.33] 1.28 [0.75; 2.18]
VUMCA-95(unpublished) 0.91 [0.56; 1.45] 0.73 [0.54; 1.00]
Fixed effect model 0.91 [0.68; 1.22] 0.84 [0.64; 1.10]
Random effects model 0.91 [0.68; 1.22] 0.92 [0.54; 1.59]
I² = 0%, P = 0.97 I² = 68%, P = 0.08
IC - CRT (IMRT) vs. CRT (IMRT)
Guangzhou 2011 0.59 [0.37; 0.95] 0.64 [0.36; 1.13]
Guangzhou 2008 0.43 [0.19; 0.96] 0.54 [0.21; 1.39]
Singapore 2004 0.80 [0.38; 1.68]
Fixed effect model 0.60 [0.42; 0.85] 0.61 [0.38; 1.00]
Random effects model 0.60 [0.42; 0.85] 0.61 [0.38; 1.00]
I² = 0%, P = 0.54 I² = 0%, P = 0.77
IC - RT vs. RT
AOCOA 0.86 [0.55; 1.34] 0.85 [0.60; 1.21]
VUMCA-89 0.49 [0.33; 0.75] 0.65 [0.41; 1.02]
Japan-91 0.40 [0.15; 1.03] 1.21 [0.49; 2.99]
Guangzhou-93 0.84 [0.55; 1.28]
Fixed effect model 0.68 [0.53; 0.86] 0.80 [0.61; 1.04]
Random effects model 0.66 [0.47; 0.93] 0.80 [0.61; 1.04]
I² = 46%, P = 0.14 I² = 0%, P = 0.41
RT - AC vs. RT
TCOG-94 0.56 [0.31; 1.01] 0.76 [0.36; 1.60]
QMH-95 1.28 [0.59; 2.76] 0.49 [0.22; 1.09]
Fixed effect model 0.76 [0.48; 1.21] 0.62 [0.36; 1.07]
Random effects model 0.82 [0.37; 1.81] 0.62 [0.36; 1.07]
I² = 64%, P = 0.10 I² = 0%, P = 0.42
CRT - AC vs. CRT (Overall)
Guangzhou 2006 0.81 [0.53; 1.23] 0.91 [0.51; 1.61]
QMH-95 2.00 [0.71; 5.68] 0.62 [0.25; 1.57]
Fixed effect model 0.92 [0.62; 1.35] 0.82 [0.50; 1.33]
Random effects model 1.12 [0.48; 2.61] 0.82 [0.50; 1.33]
I² = 60%, P = 0.11 I² = 0%, P = 0.49
IC - CRT vs. CRT (Overall)
NPC008 0.37 [0.12; 1.10] 1.05 [0.25; 4.37]
HeCOG 0.47 [0.22; 1.01] 1.21 [0.53; 2.76]
Singarpore 2004 0.80 [0.38; 1.68]
Guangzhou 2011 0.59 [0.37; 0.95] 0.64 [0.36; 1.13]
Guangzhou 2008 0.63 [0.41; 0.97] 0.79 [0.45; 1.40]
Fixed effect model 0.60 [0.46; 0.78] 0.80 [0.57; 1.14]
Random effects model 0.60 [0.46; 0.78] 0.80 [0.57; 1.14]
I² = 0%, P = 0.78 I² = 0%, P = 0.63
0.1 0.5 1 2 10
0.2 0.5 1 2 5

Table S7. Summary of results of the sensitivity analyses for the seven treatments compared with RT alone when not distinguishing between radiotherapy techniques and the four efficacy end points.

Treatment Data	OS	PFS	DMFS	LRRFS
P value heterogeneity/inconsistency (Q test P value)	0.277	0.562	0.103	0.703
P value heterogeneity (within design)	0.260	0.364	0.164	0.557
P value inconsistency (between design)	0.388	0.774	0.161	0.714
RT				
P-score, %	18.9	4.2	14.4	3.2
IC-RT				
HR (95%CI)	0.89 (0.74, 1.08)	0.75 (0.64, 0.89)	0.56 (0.43, 0.72)	0.75 (0.59, 0.96)
P-score, %	40.6	50.8	74.7	43.4
RT-AC				
HR (95%CI)	1.07 (0.83, 1.37)	0.84 (0.63, 1.12)	0.88 (0.58, 1.34)	0.64 (0.38, 1.09)
P-score, %	11.6	32.4	27.4	62.4
IC-RT-AC				
HR (95%CI)	0.9 (0.60, 1.35)	0.82 (0.57, 1.17)	1.06 (0.66, 1.69)	0.53 (0.31, 0.90)
P-score, %	40.9	37.6	12.4	82.5
CRT				
HR (95%CI)	0.79 (0.66, 0.94)	0.77 (0.66, 0.90)	0.68 (0.54, 0.84)	0.81 (0.62, 1.07)
P-score, %	63.2	46.4	50.2	30.1
CRT-AC				
HR (95%CI)	0.66 (0.57, 0.75)	0.64 (0.56, 0.73)	0.57 (0.47, 0.69)	0.57 (0.45, 0.73)
P-score, %	93.9	84.5	72.5	80.9
IC-CRT				
HR (95%CI)	0.71 (0.56, 0.91)	0.59 (0.48, 0.73)	0.44 (0.33, 0.58)	0.73 (0.51, 1.06)
P-score, %	80.9	94.0	98.3	47.5

Note: This sensitivity analysis was conducted after the exclusion of four trials including Guangzhou-93 and Taiwan-93 trials whose HR values were computed based on the published survival curves, VUMCA-95 trial which was not published, NPC0501 whose adjusted HR value was chosen.

IC: induction chemotherapy; AC: adjuvant chemotherapy; CRT: concurrent chemoradiotherapy; HR: hazard ratio; 95% CI: 95% confidence interval.

Table S8. Summary of results of the sensitivity analyses for the 10 treatments compared with RT alone after distinguishing between 2D/3D RT and IMRT and the four efficacy end points.

Treatment Data	OS	PFS	DMFS	LRRFS
P value heterogeneity/inconsistency (Q test P value)	0.441	0.584	0.093	0.612
P value heterogeneity (within design)	0.191	0.244	0.118	0.534
P value inconsistency (between design)	0.807	0.894	0.209	0.566
RT				
P-score, %	15.2	3.0	10.2	8.5
IC-RT				
HR (95%CI)	0.93 (0.76, 1.13)	0.78 (0.66, 0.92)	0.56 (0.39, 0.79)	0.77 (0.60, 0.99)
P-score, %	27.2	34.7	56.6	39.2
RT-AC				
HR (95%CI)	1.07 (0.83, 1.37)	0.84 (0.63, 1.11)	0.89 (0.54, 1.47)	0.63 (0.37, 1.07)
P-score, %	10.1	26.4	19.1	59.5
IC-RT-AC				
HR (95%CI)	0.89 (0.59, 1.34)	0.82 (0.57, 1.17)	1.04 (0.59, 1.83)	0.55 (0.32, 0.94)
P-score, %	34.7	30.5	11.0	72.1
CRT				
HR (95%CI)	0.77 (0.64, 0.93)	0.74 (0.62, 0.88)	0.63 (0.47, 0.86)	0.72 (0.54, 0.96)
P-score, %	55.4	43.5	42.4	47.2
CRT in IMRT[1]				
HR (95%CI)	0.71 (0.48, 1.05)	0.72 (0.53, 0.98)	0.51 (0.31, 0.84)	0.94 (0.56, 1.60)
P-score, %	64.3	48.9	64.5	17.8
CRT-AC				
HR (95%CI)	0.65 (0.56, 0.75)	0.64 (0.56, 0.73)	0.54 (0.42, 0.70)	0.6 (0.47, 0.76)
P-score, %	79.4	72.4	59.8	69.4
CRT-AC in IMRT[1]				
HR (95%CI)	0.67 (0.41, 1.10)	0.57 (0.37, 0.88)	0.54 (0.28, 1.03)	0.29 (0.11, 0.75)
P-score, %	69.6	78.5	59.3	95.3
IC-CRT				
HR (95%CI)	0.8 (0.61, 1.05)	0.66 (0.52, 0.84)	0.44 (0.28, 0.67)	0.82 (0.54, 1.25)
P-score, %	49.0	65.8	79.8	31.7
IC-CRT in IMRT[1]				
HR (95%CI)	0.49 (0.31, 0.79)	0.46 (0.32, 0.67)	0.3 (0.17, 0.54)	0.64 (0.34, 1.20)
P-score, %	95.3	96.4	97.2	59.3

Note: This sensitivity analysis was conducted after the exclusion of four trials including Guangzhou-93 and Taiwan-93 trials whose HR values were computed based on the published survival curves, VUMCA-95 trial which was not published,

NPC0501 whose adjusted HR value was chosen. IMRT[1] suggests the radiotherapy technique of this regimen was intensity-modulated radiotherapy (IMRT), if not, the radiotherapy technique of this regimen was two-dimensional radiotherapy (2D-RT), or three-dimensional radiotherapy (3D-RT).
IC: induction chemotherapy; AC: adjuvant chemotherapy; CRT: concurrent chemoradiotherapy; HR: hazard ratio; 95% CI: 95% confidence interval.

Table S9. Summary of results of the second sensitivity analyses for the 10 treatments compared with RT alone after distinguishing between 2D/3D RT and IMRT and the four efficacy end points.

Treatment Data	OS	PFS	DMFS	LRRFS
P value heterogeneity/inconsistency (Q test P value)	0.421	0.402	0.389	0.347
P value heterogeneity (within design)	0.231	0.245	0.195	0.347
P value inconsistency (between design)	0.719	0.654	0.756	0.364
RT				
P-score, %	10.1	3.9	7.4	10.6
IC-RT				
HR (95%CI)	0.89 (0.75, 1.06)	0.79 (0.68, 0.92)	0.68 (0.54, 0.86)	0.73 (0.56, 0.96)
P-score, %	27.3	32.7	43.8	45.8
RT-AC				
HR (95%CI)	0.95 (0.65, 1.40)	0.85 (0.58, 1.24)	0.56 (0.31, 1.01)	0.76 (0.36, 1.60)
P-score, %	22.3	26.4	64.6	42.6
IC-RT-AC				
HR (95%CI)	0.9 (0.60, 1.34)	0.82 (0.57, 1.17)	1.05 (0.66, 1.68)	0.56 (0.33, 0.96)
P-score, %	29.8	30.6	8.5	71.1
CRT				
HR (95%CI)	0.73 (0.61, 0.89)	0.73 (0.62, 0.87)	0.76 (0.60, 0.95)	0.72 (0.51, 1.02)
P-score, %	57.7	45.0	30.6	48.6
CRT in IMRT[1]				
HR (95%CI)	0.66 (0.45, 0.97)	0.7 (0.52, 0.95)	0.61 (0.41, 0.92)	0.94 (0.55, 1.61)
P-score, %	69.7	53.1	57.9	19.5
CRT-AC				
HR (95%CI)	0.65 (0.56, 0.76)	0.64 (0.55, 0.73)	0.57 (0.46, 0.69)	0.61 (0.47, 0.79)
P-score, %	75.9	72.2	69.3	67.4
CRT-AC in IMRT[1]				
HR (95%CI)	0.71 (0.48, 1.07)	0.62 (0.44, 0.87)	0.61 (0.36, 1.05)	0.29 (0.11, 0.76)
P-score, %	59.0	72.0	56.9	95.3
IC-CRT				
HR (95%CI)	0.78 (0.58, 1.04)	0.66 (0.51, 0.85)	0.59 (0.42, 0.82)	0.78 (0.49, 1.25)
P-score, %	48.9	64.4	64.1	38.2
IC-CRT in IMRT[1]				
HR (95%CI)	0.44 (0.30, 0.66)	0.44 (0.32, 0.60)	0.37 (0.23, 0.59)	0.63 (0.33, 1.20)
P-score, %	99.4	99.6	96.9	61.0

Note: This sensitivity analysis was conducted after the exclusion of six trials (Japan-91, QMH-95, VUMCA-95, Guangzhou-2003, HeCOG, Italy-79), based on the more rigorous inclusion criteria: patients mainly with stage III or IV, non-metastatic

NPC according to the tumor node metastasis (TNM) system of the International Union Against Cancer and the American Joint Committee on Cancer (UICC/AJCC). Trials with early-stage patients were excluded if more than 10% of the participants had stage I/II cases. The regimens of chemotherapy had to be based on platinum agent. IMRT[1] suggests the radiotherapy technique of this regimen was intensity-modulated radiotherapy (IMRT), if not, the radiotherapy technique of this regimen was two-dimensional radiotherapy (2D-RT), or three-dimensional radiotherapy (3D-RT).
IC: induction chemotherapy; AC: adjuvant chemotherapy; CRT: concurrent chemoraiotherapy; HR: hazard ratio; 95% CI: 95% confidence interval.

Reference

1. Blanchard P, Lee A, Marguet S, Leclercq J, Ng WT, Ma J, et al. Chemotherapy and radiotherapy in nasopharyngeal carcinoma: an update of the MAC-NPC meta-analysis. The lancet oncology. 2015; 16: 645-55.