

**Table S1.** Overview of toxicities reported in other studies.

REF	CTCAE version	CCRT	CCRT + IMT	SCRT	Radical RT
<b>Pneumonitis <math>\geq 2</math></b>					
Our analysis	5.0	25.0%		17% (scrt/rt)	
<a href="#">Palma, IJROBP, 2013- Meta-analysis</a>	-	29.8%			
<a href="#">Liang, Ann Oncol, 2017</a>	-	18.9–33.3%			
<a href="#">Wang, Lung Cancer, 2012</a>	Nci ctc 2.0	25%			
<b>Pneumonitis grade 2</b>					
Our analysis	5.0	23%		14% (scrt/rt)	
<b>Phase II trials</b>					
<a href="#">Wang, Lung Cancer, 2012</a>	Nci ctc 2.0	18.1%			
<b>Phase III trials</b>					
<a href="#">RTOG 0617, Lancet Oncol, 2015</a>	3.0	4%			
<b>“Real world”</b>					
<a href="#">Naidoo, JCO, 2017.</a> Different types of cancers	4.0				
<b>Pneumonitis grade <math>\geq 3</math></b>					
Our analysis	5.0	2%		3% (scrt/rt)	
<b>Phase II trials</b>					
<a href="#">ETOP NICOLAS trial, Lung Cancer, 2019</a>			0%		
<a href="#">PET boost trial, Radiother Oncol, 2019</a>	3.0	0%		6.7%	
<a href="#">Wang, Lung Cancer, 2012</a>	Nci ctc 2.0	6.1%			
<b>Phase III Trials</b>					
<a href="#">Antonia, NEJM, 2017</a>	?	3.8% (1.3% Gr5)	4.2% (0.8% Gr5)		

<a href="#">RTOG-9410, J Natl Cancer Inst, 2011</a>			
Acute		2.1–3.6%	8.7%
Late		12.5–14.0%	14.8%
<a href="#">EORTC 08972-22973, Eur J Cancer, 2007</a>			
		18%	14%
<a href="#">NPC 95-01, J Clin Oncol, 2005</a>			
		5%	11%
<a href="#">RTOG 0617, Lancet Oncol, 2015</a>			
	3.0	4.7%	
<a href="#">ICOG0301, Lancet Oncol, 2012</a>			
		1.0%	3.1%
<b>“Real world”</b>			
<a href="#">Wiersma, Lung Cancer, 2013</a>			
	4.03	4.1%	
<a href="#">Phernambucq, Ann Oncol, 2010</a>			
		7.9%	
<a href="#">Naidoo, JCO, 2017</a> . Different types of cancers			
	4.0		
<a href="#">Dieleman, IJROBP, 2018</a>			
	4.0	1.3%	
<a href="#">Kim, Radiat Oncol J, 2019</a>			
	4.0	18.5%	14.3%
<a href="#">Jeremic, IJROBP, 2012</a>			
		12.1%	5.5%
<b>Esophagitis grade ≥2</b>			
Our analysis			
	5.0	40.0%	48% (scrt/rt)
<a href="#">Kim, Radiat Oncol J, 2019</a>			
	4.0	44.4%	17.9%
<a href="#">Wang, Lung Cancer, 2012</a> (Ph II)			
	Nci ctc 2.0	37.5%	
<b>Esophagitis grade 2</b>			
Our analysis			
	5.0	23%	37% (scrt/rt)
<a href="#">Palma, IJROBP, 2013- Meta-analysis</a>			
		32.2%	
<b>Phase III trials</b>			
<a href="#">RTOG 0617, Lancet Oncol, 2015</a>			
	3.0	23–24%	
<b>“Real world”</b>			
<b>Dysphagia/Esophagitis grade ≥3</b>			
Our analysis			
	5.0	17%	11% (scrt/rt)

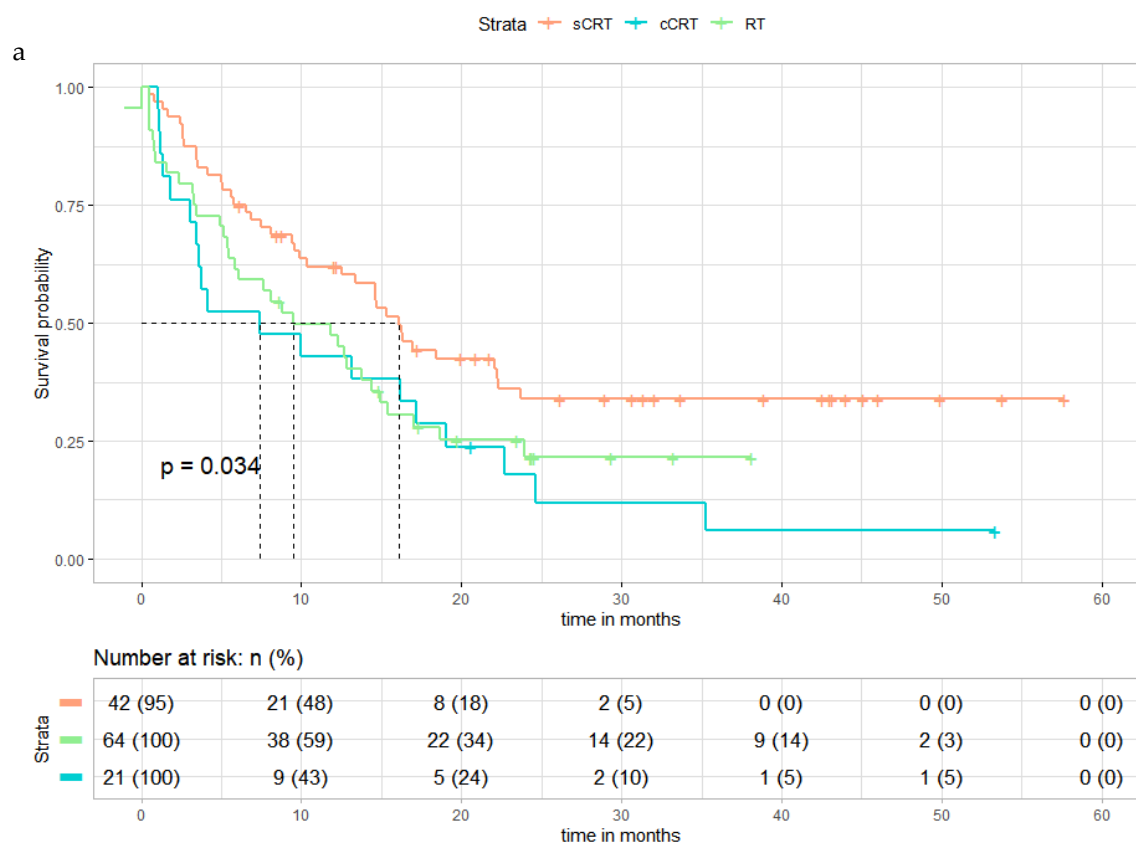
<a href="#">Palma, IJROBP, 2013- Meta-analysis</a>		18.0%	
<b>Phase II Trials</b>			
<a href="#">PET boost trial, Radiother Oncol, 2019</a>	3.0	14.3%	3.3%
<b>Phase III trials</b>			
<a href="#">EORTC 08972-22973, Eur J Cancer, 2007</a>		14%	5%
<a href="#">RTOG-9410, J Natl Cancer Inst, 2011</a>		22–45%	4%
<a href="#">NPC 95-01, J Clin Oncol, 2005</a>		32%	3%
<a href="#">Blanke, J Clin Oncol, 1995</a>		3%	
<a href="#">RTOG 0617, Lancet Oncol, 2015</a>	3.0	3–7%	
<a href="#">Liang, Ann Oncol, 2017</a>		6.3–20.0%	
<b>“Real world”</b>			
<a href="#">Wiersma, Lung Cancer, 2013</a>	4.03	33.9%	
<a href="#">Phernambucq, Ann Oncol, 2010</a>		28.1%	
<a href="#">Dieleman, IJROBP, 2018</a>	4.0	8.4%	
<a href="#">Jeremic, IJROBP, 2012</a>		10.6%	4.7%
<b>Cardiac events</b>			
Our analysis	5.0	8%	17% (scrt/rt)
<b>Phase II trials</b>			
<a href="#">PET boost trial, Radiother Oncol, 2019</a>	3.0	6.5% (≥3)	3.3% (≥3)
<b>Phase III trials</b>			
<a href="#">RTOG 0617, Lancet Oncol, 2015</a>	3.0	11%	
<b>“Real world”</b>			
<a href="#">Dess, JCO, 2017. St II-III</a>			
<a href="#">Dieleman, IJROBP, 2018</a>	4.0	2.6% (≥3)	
<a href="#">Jeremic, IJROBP, 2012</a>	-	0.2% (≥3)	0%

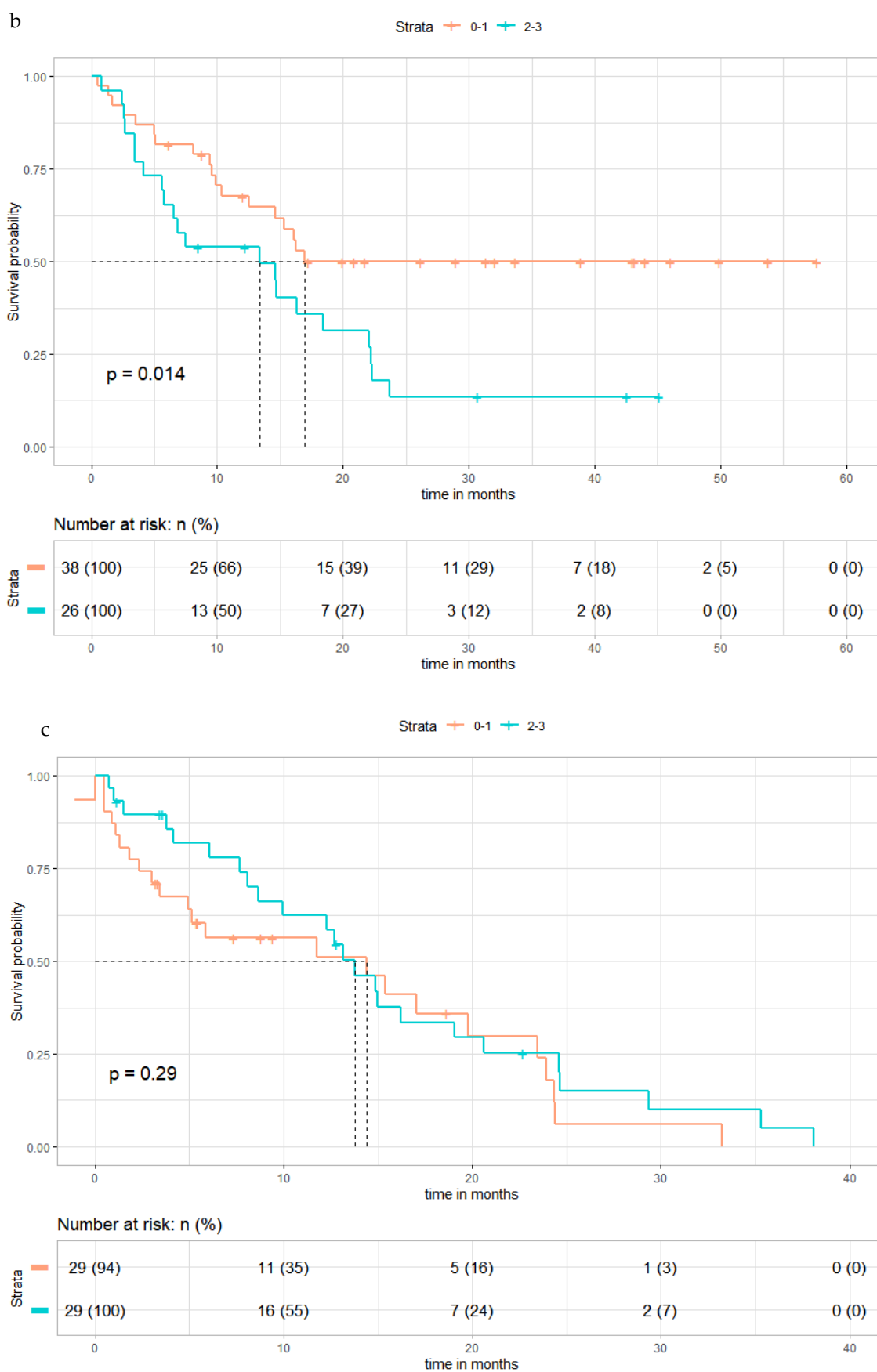
**Table S2.** Univariate analysis for progression free survival.

PTV per 100cc increase; Mean lung dose per 100 cGy increase; V25Gy/V40Gy/V60Gy heart per 10% increase; V5Gy contralateral lung per 10% increase;

	cCRT			sCRT/RT		
	HR	95% CI	p-value	HR	95% CI	P-value
V25Gy heart (%)	1.14	0.94–1.38	0.19	0.91	0.76–1.08	0.27
V40Gy heart (%)	1.20	0.97–1.49	0.10	0.87	0.70–1.08	0.20
V60Gy heart (%)	1.35	0.96–1.88	0.08	0.89	0.63–1.17	0.34
Mean heart dose (cGy)	1.02	0.99–1.11	0.12	0.98	0.95–1.00	0.27
V20Gy lungs (%)	1.19	0.70–2.04	0.52	1.20	0.87–1.64	0.27
V25Gy lungs (%)	1.17	0.67–2.06	0.59	1.20	0.85–1.69	0.30
V5Gy contralateral lung (%)	1.20	1.00–1.44	0.06	1.08	0.89–1.31	0.43
Mean lung dose (cGy)	1.03	0.94–1.11	0.49	1.02	0.97–1.11	0.40
V20Gy esophagus (cm <sup>3</sup> )	1.01	0.99–1.04	0.26	1.00	0.97–1.02	0.72
V40Gy esophagus (cm <sup>3</sup> )	1.02	0.99–1.05	0.14	1.00	0.97–1.02	0.77
V50Gy esophagus (cm <sup>3</sup> )	1.03	1.00–1.06	0.06	0.99	0.97–1.02	0.68
V60Gy esophagus (cm <sup>3</sup> )	1.03	0.99–1.07	0.21	0.99	0.96–1.03	0.71
N-stage 2	0.65	0.22–1.92	0.44	0.88	0.26–30.4	0.84
N-stage 3	0.86	0.27–2.72	0.80	1.01	0.28–3.59	0.99
Technique full VMAT	0.95	0.46–1.95	0.87	0.97	0.52–1.82	0.93
Age	1.02	0.98–1.06	0.25	1.02	0.99–1.04	0.23
Smoking history	1.01	1.00–1.02	0.15	1.01	1.00–1.02	0.16
PTV volume	1.18	1.11–1.35	0.01	0.98	0.91–1.11	0.57

Abbreviations: V25Gy/V40Gy/V60Gy heart: percentage of the heart that received at least 25/40/60Gy; V20Gy/V20Gy lungs: percentage of the total lung minus PTV that received at least 20/40/50Gy; V5Gy contralateral lung: percentage of the contralateral lung that received at least 5 Gy; V20Gy/V40Gy/V50Gy/V60Gy esophagus: volume (cm<sup>3</sup>) of the esophagus received at least 20/40/50/60 Gy; PTV: planning target volume; WHO: world health organization Radiotherapy; technique: full volumetric modulated arc therapy.





**Figure S1.** (a) Kaplan-Meier curves for progression free survival (PFS) for cCRT, sCRT and RT, (b) Kaplan-Meier PFS curves for patients with esophagitis grade 0–1 and grade 2–3, for cCRT only, (c) for sCRT/RT.