

Supplementary Tables

SUPPLEMENTARY TABLE 1. Univariate and Multivariate Analysis for All-Cause Mortality in Surgical Patients

| Variable | Univariate | Multivariate | <i>P</i> -value |
|--|-----------------|-----------------------|-----------------|
| | <i>P</i> -value | Hazard ratio (95% CI) | |
| Age (continuous) | 0.615 | | |
| Sex (male vs. female) | 0.289 | | |
| Race (caucasian vs. others) | 0.422 | | |
| ECOG performance status (0 vs. 1–2) | 0.779 | | |
| Histology (squamous cell carcinoma vs. adenocarcinoma) | 0.797 | | |
| Histologic grade (G3 vs. Gx/G1/G2) | <0.001 | 2.36 (1.60-3.48) | <0.001 |
| Tumor location (distal/GEJ vs. upper/middle) | 0.215 | | |
| Primary tumor length (continuous) | 0.083 | | |
| Clinical T stage (T1b-2 vs. T3-4) | 0.372 | | |
| Clinical N stage (N0 vs. N+) | 0.084 | | |
| Induction chemotherapy (yes vs. no) | 0.903 | | |
| Baseline PET SUVmax (continuous) | 0.392 | | |
| Total radiation dose (50.4 Gy vs >50.4 Gy) | 0.151 | | |
| Chemotherapy groups (Platinum/5FU vs. Taxane/5FU) | 0.853 | | |
| Chemotherapy groups (Carbo/Paclitaxel vs. Taxane/5FU) | 0.951 | | |
| Chemotherapy groups (Doce/5FU/Platinum vs. Taxane/5FU) | 0.326 | | |
| Chemotherapy groups (Other/Unk vs. Taxane/5FU) | 0.950 | | |

Abbreviations: ECOG, Eastern Cooperative Oncology Group; GEJ, gastroesophageal junction; PET, position emission tomography; SUV, standard uptake value.

Taxane=Docetaxel, Paclitaxel; 5FU=continuous infusion 5FU or Xeloda; Platinum=carboplatin, cisplatin or oxaliplatin; Carbo=Carboplatin; Doce=Docetaxel; Other=Irinotecan-based, cetuximab, experimental agents; Unk=unknown

SUPPLEMENTARY TABLE 2. Univariate and Multivariate Analysis for All-Cause Mortality in Non-Surgical Patients

| Variable | Univariate | Multivariate | |
|--|------------|-----------------------|---------|
| | P-value | Hazard ratio (95% CI) | P-value |
| Age (continuous) | 0.623 | | |
| Sex (male vs. female) | 0.041 | | |
| Race (caucasian vs. others) | 0.542 | | |
| ECOG performance status (0 vs. 1–2) | 0.557 | | |
| Histology (squamous cell carcinoma vs. adenocarcinoma) | 0.172 | | |
| Histologic grade (G3 vs. Gx/G1/G2) | 0.581 | | |
| Tumor location (distal/GEJ vs. upper/middle) | 0.071 | 1.43 (1.05-1.96) | 0.025 |
| Primary tumor length (continuous) | 0.009 | | |
| Clinical T stage (T1b-2 vs. T3-4) | 0.033 | | |
| Clinical N stage (N+ vs. N0) | <0.001 | 2.09 (1.48-2.94) | <0.001 |
| Induction chemotherapy (yes vs. no) | 0.903 | | |
| Baseline PET SUVmax (continuous) | <0.001 | 1.07 (1.03-1.11) | 0.001 |
| Total radiation dose (50.4 Gy vs >50.4 Gy) | 0.097 | | |
| Chemotherapy groups (Platinum/5FU vs. Taxane/5FU) | 0.378 | | |
| Chemotherapy groups (Carbo/Paclitaxel vs. Taxane/5FU) | 0.884 | | |
| Chemotherapy groups (Doce/5FU/Platinum vs. Taxane/5FU) | 0.131 | | |
| Chemotherapy groups (Other/Unk vs. Taxane/5FU) | 0.451 | | |

Abbreviations: ECOG, Eastern Cooperative Oncology Group; GEJ, gastroesophageal junction; PET, position emission tomography; SUV, standard uptake value.

Taxane=Docetaxel, Paclitaxel; 5FU=continuous infusion 5FU or Xeloda; Platinum=carboplatin, cisplatin or oxaliplatin; Carbo=Carboplatin; Doce=Docetaxel; Other=Irinotecan-based, cetuximab, experimental agents; Unk=unknown

SUPPLEMENTARY TABLE 3. Chi-Square analysis of the relationship of chemotherapy type and toxicities

| | N | Gr 0-2 | Gr 3-4 | Chi-square p-value |
|-----------------------------|-----|--------|--------|-----------------------|
| Dysphagia Toxicity | | | | |
| Taxane/5FU | 303 | 271 | 32 | 0.135 |
| Platinum/5FU | 196 | 186 | 10 | |
| Carbo/Paclitaxel | 14 | 14 | 0 | |
| Doce/5FU/Platinum | 24 | 23 | 1 | |
| Other/Unk | 50 | 47 | 3 | |
| Esophagitis Toxicity | | | | |
| Taxane/5FU | 303 | 251 | 52 | 0.015 |
| Platinum/5FU | 196 | 179 | 17 | |
| Carbo/Paclitaxel | 14 | 13 | 1 | |
| Doce/5FU/Platinum | 24 | 23 | 1 | |
| Other/Unk | 50 | 47 | 3 | |
| Pneumonitis Toxicity | | | | |
| Taxane/5FU | 303 | 296 | 7 | 0.367 |
| Platinum/5FU | 196 | 195 | 1 | |
| Carbo/Paclitaxel | 14 | 14 | 0 | |
| Doce/5FU/Platinum | 24 | 24 | 0 | |
| Other/Unk | 50 | 50 | 0 | |
| Cardiac Toxicity* | | | | |
| Taxane/5FU | 303 | 299 | 4 | 0.413 |
| Platinum/5FU | 196 | 190 | 6 | |
| Carbo/Paclitaxel | 14 | 14 | 0 | |
| Doce/5FU/Platinum | 24 | 24 | 0 | |
| Other/Unk | 50 | 50 | 0 | |

Taxane=Docetaxel, Paclitaxel; 5FU=continuous infusion 5FU or Xeloda; Platinum=carboplatin, cisplatin or oxaliplatin; Carbo=Carboplatin; Doce=Docetaxel; Other=Irinotecan-based, cetuximab, experimental agents; Unk=unknown

* such as atrial fibrillation or heart failure

SUPPLEMENTARY TABLE 4. Univariate and Multivariate Analysis for Predictors of Grade 3-4 Esophagitis

| Variable | Univariate | Multivariate | P-value |
|--|------------|-----------------------|---------|
| | P-value | Hazard ratio (95% CI) | |
| Age (continuous) | 0.811 | | |
| Sex (male vs. female) | 0.326 | | |
| Race (caucasian vs. others) | 0.584 | | |
| ECOG performance status (0 vs. 1–2) | 0.150 | | |
| Histology (squamous cell carcinoma vs. adenocarcinoma) | 0.009 | 2.23 (1.26-3.95) | 0.006 |
| Histologic grade (G3 vs. Gx/G1/G2) | 0.692 | | |
| Tumor location (distal/GEJ vs. upper/middle) | 0.135 | | |
| Primary tumor length (continuous) | 0.243 | | |
| Clinical T stage (T1b-2 vs. T3-4) | 0.774 | | |
| Clinical N stage (N0 vs. N+) | 0.024 | 1.85 (1.03-3.32) | 0.04 |
| Induction chemotherapy (yes vs. no) | 0.132 | | |
| Baseline PET SUVmax (continuous) | 0.847 | | |
| Total radiation dose (50.4 Gy vs >50.4 Gy) | 0.379 | | |
| Chemotherapy groups (Platinum/5FU vs. Taxane/5FU) | 0.008 | 0.45 (0.25-0.80) | 0.007 |
| Chemotherapy groups (Carbo/Paclitaxel vs. Taxane/5FU) | 0.345 | | |
| Chemotherapy groups (Doce/5FU/Platinum vs. Taxane/5FU) | 0.131 | | |
| Chemotherapy groups (Other/Unk vs. Taxane/5FU) | 0.005 | | |

Abbreviations: ECOG, Eastern Cooperative Oncology Group; GEJ, gastroesophageal junction; PET, position emission tomography; SUV, standard uptake value.

Taxane=Docetaxel, Paclitaxel; 5FU=continuous infusion 5FU or Xeloda; Platinum=carboplatin, cisplatin or oxaliplatin; Carbo=Carboplatin; Doce=Docetaxel; Other=Irinotecan-based, cetuximab, experimental agents; Unk=unknown

SUPPLEMENTARY TABLE 5. Comparison clinical characteristics and pathology results of the present study with CROSS

| Characteristic | Present study | % | CROSS | %* | χ^2 (P-value) |
|-------------------------------------|---------------|------|-------|----|--------------------|
| Age (y) | | | | | --- |
| Median | 60 | | 60 | | |
| Range | 21-83 | | 36-79 | | |
| Sex | | | | | 0.000 |
| Male | 244 | 87.8 | 134 | 75 | |
| Female | 34 | 12.2 | 44 | 25 | |
| Tumor histology | | | | | 0.000 |
| Adeno | 249 | 89.6 | 134 | 75 | |
| Squamous | 16 | 5.8 | 41 | 23 | |
| Other | 13 | 4.6 | 3 | 2 | |
| Tumor Length(cm) | | | | | --- |
| Median | 5 | | 4 | | |
| Interquartile | 3-7 | | 3-6 | | |
| Tumor location | | | | | 0.000 |
| Proximal third | 1 | 0.4 | 4 | 2 | |
| Middle third | 8 | 2.9 | 25 | 14 | |
| Distal third | 155 | 55.7 | 104 | 58 | |
| Esophagogastric junction | 114 | 41.0 | 39 | 22 | |
| Missing data | 0 | 0 | 3 | 3 | |
| Clinical T stage[†] | | | | | 0.365 |
| cT1 | 1 | 0.4 | 1 | 1 | |
| cT2 | 34 | 12.2 | 26 | 15 | |
| cT3 | 238 | 85.6 | 150 | 84 | |
| cT4 | 4 | 1.4 | 0 | 0 | |
| Could not be determined | 1 | 0.4 | 1 | 1 | |
| Clinical N stage[†] | | | | | 0.537 |
| N0 | 101 | 36.3 | 59 | 33 | |
| N1 | 176 | 63.3 | 116 | 65 | |
| Could not be determined | 1 | 0.4 | 3 | 2 | |
| Karnofsky Performance Status | | | | | 0.000 |
| 100 | 25 | 9.0 | 144 | 81 | |
| 80-90 | 244 | 87.8 | 34 | 19 | |
| 70 | 9 | 3.2 | 0 | 0 | |
| pT-stage[§] | | | | | 0.001 |
| pTis | 0 | 0 | 1 | 1 | |
| pT0 | 74 | 26.6 | 62 | 39 | |
| pT1 | 47 | 16.9 | 15 | 10 | |
| pT2 | 31 | 11.2 | 32 | 20 | |
| pT3 | 122 | 43.9 | 49 | 30 | |
| pT4 | 4 | 1.4 | 1 | 1 | |
| Unknown | 0 | 0 | 1 | 1 | |
| pN-stage[§] | | | | | 0.442 |
| pN0 | 182 | 65.4 | 111 | 69 | |

| | | | | | |
|--|-----------|------|----------|----|-------|
| pN1 | 96 | 34.6 | 50 | 31 | |
| No. of LNs resected-Median (p25-p75) | 20(14-26) | | 15(9-21) | | --- |
| No. of positive LNs-Median (p25-p75) | 0(0-1) | | 0(0-1) | | |
| Radicality of resection[#] | | | | | 0.141 |
| R0 resection | 265 | 95.3 | 148 | 92 | |
| R1 resection | 13 | 4.7 | 13 | 8 | |
| Tumor regression grade | | | | | 0.046 |
| Grade 1 | 73 | 26.3 | 47 | 29 | |
| Grade 2 | 82 | 29.5 | 52 | 32 | |
| Grade 3 | 86 | 30.9 | 32 | 20 | |
| Grade 4 | 32 | 11.5 | 29 | 18 | |
| Missing | 5 | 1.8 | 1 | 1 | |

Abbreviations: * Percentages may not total 100 because of rounding; LNs= Lymph Nodes; p25-p75: interquartile range; [§]pT and pN-stage according to the sixth edition of AJCC TNM-classification; [#]R0-resection was defined as no vital tumor cells within 1 mm of all resection margins. Tumor regression grade was defined as: Grade 1: no evidence of vital residual tumor cells in both primary tumor and resected lymph nodes. Grade 2: pT0N1 or >0% but <10% vital residual tumor cells in the primary tumor, Grade 3: 10-50% vital residual tumor cells in the primary tumor, Grade 4: >50% vital residual tumor cells in the primary tumor

SUPPLEMENTARY TABLE 6. Studies comparing IMRT and 3D-CRT for esophageal cancer.

| Study | Details | IMRT | 3D-CRT | p value |
|----------------|------------------------------|-------------|-------------|---------|
| Freilich J (9) | No. of patients | 138 | 94 | |
| | Radiation dose | Varies | Varies | - |
| | Median survival | 32 months | 29 months | 0.74 |
| | Median relapse free survival | 25 months | 20 months | 0.66 |
| | Grade ≥ 3 toxicity (%) | 24.6 | 37.2 | 0.04 |
| | Hospitalization (%) | 26.7 | 31.9 | 0.17 |
| | Feeding tube (%) | 9.5 | 8.5 | 0.83 |
| | Mean weight loss SD (%) | 9 (7.4) | 6.1 (4.3) | 0.012 |
| Lin SH (16) | No. of patients | 263 | 413 | |
| | Radiation dose | 50.4Gy/28f | 50.4Gy/28f | - |
| | 5-yr survival | 44% | 34% | <0.01 |
| | Median survival | 43.2 months | 25.2 months | <0.01 |
| | Cancer-specific deaths | N* | N* | 0.86 |
| | Pulmonary deaths | N* | N* | 0.39 |
| | Cardiac related deaths | N* | N* | 0.049 |
| Lin XD (18) | No. of patients | 30 | 30 | |
| | Radiation dose | 60Gy/30f | 60Gy/30f | - |
| | 3-yr survival | 66.7 | 63.3 | >0.05 |
| | Lung V20 | 21.2±5.1 | 24.9 ±5.9 | <0.05 |
| | Lung V30 | 15.3 ±3.8 | 17.5 ±3.9 | <0.05 |
| | Grade 3+4 esophagitis | 10.0% | 6.7% | >0.05 |
| | Grade 3+4 pneumonitis | 0.0% | 3.3% | >0.05 |

* The details were not shown in the text.