Oral Scientific Sessions

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Prospective Randomized Phase 2 Study of Concurrent Chemoradiation Therapy (CCRT) Versus Chemotherapy Alone in Stage IV Esophageal Squamous Cell Carcinoma (ESCC)

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Purpose/Objective(s): Stage IV ESCC carries a poor prognosis with a median survival of 6-9 months. The standard treatment has traditionally been chemotherapy. Palliative radiation therapy was used for symptom relief. The optimal treatment for stage IV ESCC has not yet been established. The aim of this study was to compare the efficacy and safety of CCRT versus chemotherapy alone in patients with stage IV ESCC.

Materials/Methods: Patients with stage IV ESCC were randomly assigned to the CCRT group and the chemotherapy group. Both groups of patients received at least 2 cycles of chemotherapy with cisplatin and docetaxel every 3 weeks. Patients in CCRT group received 50-60 Gy/ 25-30 fractions/ 5-6 weeks of concurrent radiation therapy to the esophageal primary tumor. The primary end point was overall survival (OS). The secondary end points were progression-free survival (PFS), object response rate (ORR) of primary tumor and toxicity.

Results: Between August 2013 and October 2015, 60 patients were enrolled and divided into the CCRT group (n = 30) and the chemotherapy group (n = 30). The 60 patients were comprised of 48 male and 12 female patients, with a median age of 56 years (range 36 - 70 years). The baseline clinical characteristics of the 2 groups were similar. Patients in the CCRT group received a mean 54.7 Gy of radiation therapy and a mean 3.6 cycles of chemotherapy, whereas patients in the chemotherapy group received a mean 3.8 cycles. The ORR of the primary tumor was higher in the CCRT group than in the chemotherapy group (83.3% vs. 46.7%, $P = 0.001$). At a median follow-up of 18 months, median PFS (9.3 vs. 4.7 months, $P = 0.021$) and median OS (18.3 vs. 10.2 months, $P = 0.001$) were significantly longer in the CCRT than that in the chemotherapy group. Overall survival rates at 1and 2 years were 73.3% and 43.3% respectively, in the CCRT group, and 46.6%and 26.7% respectively in chemotherapy group ($P = 0.030$) Although $\geq$ grade 3 neutropenia was significantly more frequent in the CCRT group than that in the chemotherapy group (33.3% vs. 20.0%, $P < 0.05$), the rates of other toxicities did not differ.

Conclusion: Concurrent chemoradiation therapy was well tolerated and associated with longer PFS and OS than chemotherapy alone in patients with stage IV ESCC. Controlled randomized, multi-center trials are required to determine whether CCRT is a primary treatment option for patients with stage IV ESCC.

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Vortex Trial: A Randomized Controlled Multicenter Phase 3 Trial of Volume of Postoperative Radiation Therapy Given to Adult Patients With Extremity Soft Tissue Sarcoma (STS)

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Purpose/Objective(s): To assess whether reducing the volume of tissue irradiated postoperatively improves limb function in patients with extremity soft tissue sarcoma (STS) without impairing local control.

Materials/Methods: Eligible patients had proven extremity STS for whom tumor resection and postoperative radiation therapy were indicated. No adjuvant chemotherapy was permitted. Patients were registered preoperatively for tumor and normal tissue collection and baseline TESS questionnaire. Patients eligible for radiation therapy after surgery were consented and randomized to either of the trial arms in a 1:1 ratio (stratified by surgical margin, tumor grade and treatment center). Patients were treated either in the Control arm (C): 50 Gy in 25 fractions to CTV1 (GTV + 5cm cranio-caudally and 2cm axially) followed by 16 Gy in 8 fractions to CTV2 (GTV + 2 cm c-c and axially) or the Research arm (R): 66 Gy in 33 fractions to CTV2 alone. Co-primary outcome measures were differences in limb function at 2 years (TESS score) and time to local recurrence. The trial required 210 patients to detect a difference in mean TESS of 10 (SD 20) with a two-sided alpha of 5% and power of 95%.Secondary outcomes were late soft tissue and bone toxicity, disease-free and overall survival, and level of disability. Toxicity outcomes were assessed using the chi square test, survival outcomes by Kaplan-Meier and Cox regression modelling.

Results: Two hundred sixteen patients were randomized, 108 in each arm. Tumor/normal tissues were collected from 206 randomized and 301 registered patients. Baseline characteristics were balanced between the trial arms with exception of location and TESS. There were 176 lower limb tumors; C; 96, R; 80 and 40 upper limb; C; 12, R; 28. Median baseline TESS was 92 (22-100) for C and 97 (10-100) for R. Mean change in TESS at 2 years was -5.0 (SD 18) in C and -4.9 (SD 18) in R ($P = 0.97$). In both arms the TESS scores dropped postoperatively followed by recovery over subsequent months. Median follow-up was 4.8yr (C and R). The 5-year local recurrence free survival (LRFS) rates were; for C: 86% (95% CI = 75-93) and for R: 84% (95% CI = 74-90) HR = 1.5 (95% CI = 0.7-3.3). For C the 5-year overall survival was 72% (95% CI = 61-81) and for R 67% (95% CI = 56-76; HR = 1.2 (95% CI = 0.7-2.0). There were no statistical differences between the arms in late radiation toxicity grade 2+ at 2 years: skin (C 34%, vs R 37%; $P = 0.77$), subcutaneous (C 47%, vs R 41%; $P = 0.39$), bone (C 11%, vs R 15%; $P = 0.48$) and joint (C 18% vs R 18%; $P = 0.91$).

Conclusion: There was no difference in limb function at 2 years between control and research arms. Because of the small number of events it was not possible to state whether or not the research arm was inferior for LRFS. Currently we are not able to recommend the smaller volumes used in the research arm as standard of care.

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