Esophageal cancer

CHEMORADIOThERAPy WITH OR WITHOUT Cetuximab

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TRIAL SUMMARY: Long-term SCOPE 1 results

SCOPE 1 was one of the largest phase 2/3 trials to explore the impact of adding cetuximab to conventional definitive chemoradiotherapy (dCRT) in the treatment of localized esophageal cancer. It demonstrated worse survival and greater toxicity associated with the addition of cetuximab (C). At the 2016 ASCO GI Symposium, SCOPE 1 authors presented long-term results of this study. Patients were randomly assigned to chemotherapy with cisplatin 60 mg/m² on day 1 and capecitabine 625 mg/m² daily for 3 weeks, for 4 cycles, with or without C 400 mg/m² on day 1 followed by 250 mg/m² weekly. Radiation therapy was delivered in doses of 50 Gy in 25 fractions, given concurrently with cycles 3 and 4. A total of 258 patients (129 on dCRT and 129 on dCRT+C) from 36 centres were recruited between February 2008 and February 2012. Median follow-up was 46.7 months (36.0–49.0) for all surviving patients. In dCRT and dCRT+C arms, 65.1% and 69.8% of patients, respectively, had died. Esophageal cancer was the cause of death in 82.1% in the dCRT group and 86.7% in the dCRT+C group (p=0.41).

Results: Median overall survival (OS) was 34.5 (95% CI: 24.7, 42.3) months in the dCRT and 24.7 (95% CI: 18.6, 31.3) months in the dCRT+C group (HR=1.25; p=0.137); corresponding 3-year OS was 47.2% and 37.6%. Median PFS was 24.1 (95% CI: 15.3,29.9) months and 15.9 (95% CI: 10.7, 20.8) months, respectively (HR=1.28, p=0.114). There was some evidence that local PFS (within the radiation therapy field) was lower in those receiving dCRT+C (HR=1.38, p=0.051). On multivariate analysis, stage I-II (vs stage III), full-dose radiation therapy and higher cisplatin intensity (>75% vs <75%) were associated with improved OS and PFS. Patterns of recurrence were similar in both arms: local recurrence in 35%; distant-only recurrence in 51% of dCRT, and 44% of dCRT+C; both local and distant recurrence in 14% of dCRT and 21% of dCRT+C. In the dCRT arm 81.6% of patients relapsed within the radiation field vs 83.3% in dCRT+C arm (p=0.8). The mature analysis of these data demonstrated unprecedented survival in the dCRT arm, comparable to surgical trials. The OS inferiority of dCRT+C is no longer statistically significant. The lower PFS within the radiation field in the dCRT+C arm was consistent with the lower number of patients receiving full-dose radiation therapy in the dCRT+C arm.

IN BRIEF

Already known
• Cetuximab added to conventional definitive chemoradiotherapy (dCRT) to treat localized esophageal cancer showed worse survival and more toxicity.

What this study showed
• Long-term results from the study showed unprecedented survival in the dCRT arm, comparable to surgical trials.

Next steps
• Patients who are not candidates for curative surgery of localized esophageal cancer might expect good results with definitive chemoradiation.
COMMENTS: The SCOPE 1 trial was one of the largest studies evaluating definitive radiation therapy in the treatment of localized esophageal cancer. It demonstrated worse OS and increased toxicity in the experimental arm, where cetuximab was added to definitive chemoradiation. Long-term outcomes of this trial were presented at the 2016 ASCO GI Cancers Symposium in San Francisco. Out of 258 patients recruited from 36 centers, 129 received definitive chemoradiation and 129 received definitive chemoradiation with cetuximab. The median followup was 46.7 months; 65.1% of patients in control arm and 69.8% in investigational arm have died. Esophageal cancer was the cause of death in 82.1% and 86.7% of cases, respectively. Reported median OS was 34.5 months (95% CI: 24.7, 42.3) in the control arm and 24.7 months (95% CI: 18.6, 31.3) in the investigational arm. Three-year OS and median PFS were 47.2% vs 37.6% and 24.1 vs 15.9 months, respectively. Interestingly, local PFS within the radiation field was lower in the investigational arm (HR=1.38, p=0.051). On multivariate analysis, in stage I–II vs III–IV disease, full-dose radiation therapy and higher cisplatin dose intensity (≥75% vs <75%) were associated with improved OS and PFS. This followup analysis showed OS and PFS in patients treated with definitive chemoradiation comparable to that reported in surgical trials (e.g. 3-year median survival of 31% in the OE02 trial). Therefore, patients with localized esophageal cancer who are not candidates for curative surgery could still be treated with definitive chemoradiation and expect results comparable with surgery.