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RMAC study: A randomized study evaluating the efficacy of metronomic adjuvant chemotherapy in patients with recurrent head and neck cancers post salvage surgery, not eligible for re-irradiation

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Background

Adjuvant re-chemoradiation after salvage surgery improves disease-free survival in recurrent head and neck cancer. However, most patients are not eligible for re-irradiation and are kept under observation. We investigated the efficacy of metronomic adjuvant chemotherapy (MAC) in this group of patients in comparison with observation.

Methods

This is a randomized integrated phase II/III clinical trial. Adults with recurrent head and neck cancer, who underwent salvage surgery, and were not eligible for adjuvant re-irradiation were randomized in a 1:1 ratio to either MAC arm or observation. MAC consisted of oral methotrexate (at a dose of 15 mg per square meter of body surface area, weekly) and celecoxib (at a dose of 200 mg orally twice daily) for 6 months. The primary endpoint of phase II was disease-free survival (DFS), while that of phase III was overall survival (OS). For phase II, to detect an improvement in the hazard ratio (HR) with MAC, with a target HR of 0.67, type 1 error of 10% (1-sided) & type 2 error of 30%, 105 patients were required. For phase III, with a target HR of 0.77, type 1 error of 5% & type 2 error of 20%, 318 patients were required.

Results

We are reporting the results of the phase II part of the trial. The median DFS was 15.8 months (95% CI, 9.67-24.3) versus not reached (95% CI, 9.33-NA) in the MAC and observation arm, respectively (P=0.19). At a median follow up of 30.2 months (95% confidence interval (CI), 25.3 to 35.1) the 1-year and 2-year DFS was 59.4% (95% CI, 44.8 to 71.4) and 38.9% (95% CI, 25.1 to 52.5) in MAC arm, while the corresponding numbers were 62.3% (95% CI, 47.8 to 73.8) and 54.2% (95% CI, 39.8 to 66.5) in the observation arm (HR for progression, 1.42; 95% CI, 0.84 to 2.4; P=0.2). In the MAC arm the 1 year & 2- year OS was 78.7% (95% CI, 64.9 to 87.6) and 48% (95% CI, 34.1 to 62) respectively. In the observation arm the 1- year & 2- year OS was 79.2% (95% CI, 65.7 to 87.9) and 65.5% (95% CI, 50.9 to 76.7) (HR for death, 1.7, 95% CI, 0.94 to 3.08; P=0.08).

Conclusions

The adjuvant 6-month metronomic chemotherapy schedule was ineffective in improving outcomes in recurrent head and neck cancer patients post salvage surgery who are not eligible for re-radiation.

Clinical trial identification

Clinical Trials Registry- India (CTRI): CTRI/2016/04/006872.

Legal entity responsible for the study

Kumar Prabhash.

Funding

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Disclosure

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