Cetuximab versus cisplatin in patients with HPV-positive, low risk oropharyngeal cancer, receiving radical radiotherapy


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Background: The incidence of Human papillomavirus-positive oropharyngeal cancer (HPV+ OPSCC) is rapidly rising. It is a distinct disease entity, affecting younger patients, with much better outcomes. However, standard treatment (cisplatin + radiotherapy) causes significant toxicity, which these young patients have to endure for decades. Cetuximab, an epidermal growth factor receptor inhibitor, has been proposed for treatment de-escalation to reduce toxicity of standard (cisplatin) treatment, but no randomised trials exist.

Methods: In this international, multi-centre, randomised, controlled trial, patients with low-risk HPV+ OPSCC were randomised to receive radiotherapy (70Gy in 35F) and either cisplatin (3 doses of 100 mg/m2) or cetuximab (400 mg/m2 loading dose followed by weekly 250 mg/m2). Outcomes were total number of severe (Grades 3-5) toxicity events, overall survival, and quality of life.

Results: We recruited 334 patients (166 in cisplatin arm and 168 in cetuximab arm) between November 2012 through October 2016 at 32 head and neck treatment centres in 3 countries: UK, Ireland and the Netherlands. Of patients randomised, 80% are male, mean age 57 years. The arms were well balanced. There were 10 recurrences and 6 deaths in cisplatin arm, compared to 29 recurrences and 20 deaths in cetuximab arm. There was a significant difference in the 2-year overall survival between cisplatin and cetuximab (97.5% vs 89.4% respectively, p = 0.001, HR = 4.99, 95% CI 1.70-14.67) and in 2-year recurrence rate (6.0% vs 16.1% respectively, p = 0.0087, HR = 3.39, 95% CI 1.61-7.19). There were no differences between the cisplatin and cetuximab arms in the reported mean number of overall (3.37 vs 5.45 events per patient respectively).
acute or late severe (grade 3-5) toxicity events per patient or all grade toxicity (overall 29.15 vs 30.05 event per patients respectively). There were significantly more serious adverse events (162 vs 95) in the cisplatin arm compared to the cetuximab arm.

**Conclusions:** There was significant detriment from the use of cetuximab instead of cisplatin in terms of tumour control, and no benefit in terms of reduced toxicity. Cisplatin and radiotherapy remains the standard of care in this setting.

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