

Patients with HPV-positive oropharynx cancer should receive chemoradiation

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Prof Hisham Mehanna, Chair, Head and Neck Surgery, Institute of Cancer and Genomic Sciences, University of Birmingham, UK, study author. Credit: © European Society for Medical Oncology

Patients with human papilloma virus (HPV)-positive throat cancer should receive chemoradiotherapy rather than cetuximab with radiotherapy, according to late-breaking research reported at the ESMO 2018 Congress in Munich.

"Many [patients](#) have been receiving [cetuximab](#) with [radiotherapy](#) on the assumption that it was as effective as chemotherapy with radiotherapy and caused less side effects but there has been no head-to-head comparison of the two treatments," said study author Prof Hisham Mehanna, Chair, Head and Neck Surgery, Institute of Cancer and Genomic Sciences, University of Birmingham, UK.

Throat [cancer](#) is rapidly becoming more common in Western countries. For example in the UK, incidence was unchanged in 1970 to 1995, then doubled in 1996 to 2006, and doubled again in 2006 to 2010. The rise has been attributed to HPV, a sexually transmitted infection. Most throat cancer was previously caused by smoking and alcohol and affected 65-70 year-old working class men. Today HPV is the main cause and patients are around 55, middle class, working, and have young children.

HPV-positive throat cancer responds well to a combination of [cisplatin](#) chemotherapy and radiotherapy, and patients can survive for 30-40 years, but the treatment causes lifelong side effects including [dry mouth](#), difficulty swallowing, and loss of taste. Patients deemed unable to tolerate chemotherapy, for example because of poor kidney function or older age, receive cetuximab, an epidermal growth factor receptor (EGFR) inhibitor, and radiotherapy.

This study compared side effects and survival with the two treatments in 334 patients with HPV-positive throat cancer enrolled from 32 centres in the UK, Ireland, and the Netherlands. Patients were randomly allocated to radiotherapy and either cisplatin or cetuximab. Eight in ten patients were male and the average age was 57 years.

During the two-year study there were ten recurrences and six deaths with cisplatin compared to 29 recurrences and 20 deaths with cetuximab. Patients on cisplatin had a significantly higher two-year overall survival rate (97.5%) than those on cetuximab (89.4%; $p=0.001$, hazard ratio [HR] 4.99, 95% confidence interval [CI] 1.70-14.67). Cancer was over three times more likely to recur in two years with cetuximab compared to cisplatin, with recurrence rates of 16.1% versus 6.0%, respectively ($p=0.0007$, HR 3.39, 95% CI 1.61-7.19).

There were no differences between groups in the overall number of side effects, or of acute or late severe (grade 3-5) toxic events including dry mouth and difficulty swallowing. There were significantly more serious adverse events such as renal and haematological problems with cisplatin than with cetuximab.

Mehanna said: "Cetuximab did not cause less toxicity and resulted in worse overall survival and more cancer recurrence than cisplatin. This was a surprise—we thought it would lead to the same survival rates but better toxicity. Patients with throat cancer who are HPV positive should be given cisplatin, and not cetuximab, where possible."

Commenting on the study for ESMO, Dr. Branislav Bystricky, Head, Medical and Radiation Oncology Department, University Hospital Trencin, Slovakia, said: "It was believed that cetuximab causes less side effects and was therefore a good option for HPV-positive throat cancer patients who are young and expected to survive for several decades, as well as those less able to tolerate chemotherapy. This study shows that the best treatment choice for patients with HPV-positive [throat cancer](#) is cisplatin and radiotherapy. This combination gives 'double' the benefit since it is more effective in terms of survival and does not worsen all grade toxicity compared to cetuximab with radiotherapy."

Bystricky noted that the results were in agreement with interim findings

of the US National Cancer Institute's RTOG 1016 trial, which is scheduled to report this month. He said: "We now have two studies showing that these patients should not be given cetuximab. Future research should examine whether genotyping for the KRAS-variant can select a group of patients that will benefit from cetuximab treatment with radiotherapy."

More information: Abstract LBA9_PR 'Cetuximab versus cisplatin in patients with HPV-positive, low risk oropharyngeal cancer, receiving radical radiotherapy' will be presented by Hisham Mehanna during the Presidential Symposium 3 on Monday, 22 October, 16:30 to 18:00 (CEST) in Room 18 - Hall A2. *Annals of Oncology*, Volume 29 Supplement 8 October 2018

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