

## **Chemotherapy and radiotherapy in nasopharyngeal carcinoma: an update of the MAC-NPC meta-analysis.**

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### **Abstract**

#### **BACKGROUND:**

A previous individual patient data meta-analysis by the Meta-Analysis of Chemotherapy in Nasopharynx Carcinoma (MAC-NPC) collaborative group to assess the addition of chemotherapy to radiotherapy showed that it improves overall survival in nasopharyngeal carcinoma. This benefit was restricted to patients receiving concomitant chemotherapy and radiotherapy. The aim of this study was to update the meta-analysis, include recent trials, and to analyse separately the benefit of concomitant plus adjuvant chemotherapy.

#### **METHODS:**

We searched PubMed, Web of Science, Cochrane Controlled Trials meta-register, ClinicalTrials.gov, and meeting proceedings to identify published or unpublished randomised trials assessing radiotherapy with or without chemotherapy in patients with non-metastatic nasopharyngeal carcinoma and obtained updated data for previously analysed studies. The primary endpoint of interest was overall survival. All trial results were combined and analysed using a fixed-effects model. The statistical analysis plan was pre-specified in a protocol. All data were analysed on an intention-to-treat basis.

#### **FINDINGS:**

We analysed data from 19 trials and 4806 patients. Median follow-up was 7.7 years (IQR 6.2-11.9). We found that the addition of chemotherapy to radiotherapy significantly improved overall survival (hazard ratio [HR] 0.79, 95% CI 0.73-0.86,  $p < 0.0001$ ; absolute benefit at 5 years 6.3%, 95% CI 3.5-9.1). The interaction between treatment effect (benefit of chemotherapy) on overall survival and the timing of chemotherapy was significant ( $p = 0.01$ ) in favour of concomitant plus adjuvant chemotherapy (HR 0.65, 0.56-0.76) and concomitant without adjuvant chemotherapy (0.80, 0.70-0.93) but not adjuvant chemotherapy alone (0.87, 0.68-1.12) or induction chemotherapy alone (0.96, 0.80-1.16). The benefit of the addition of chemotherapy was consistent for all endpoints analysed (all  $p < 0.0001$ ): progression-free survival (HR 0.75, 95% CI 0.69-0.81), locoregional control (0.73, 0.64-0.83), distant control (0.67, 0.59-0.75), and cancer mortality (0.76, 0.69-0.84).

#### **INTERPRETATION:**

Our results confirm that the addition of concomitant chemotherapy to radiotherapy significantly improves survival in patients with locoregionally advanced nasopharyngeal carcinoma. To our knowledge, this is the first analysis that examines the effect of concomitant chemotherapy with and without adjuvant chemotherapy as distinct groups. Further studies on the specific benefits of adjuvant chemotherapy after concomitant chemoradiotherapy are needed.