



Meta-Analysis of Chemotherapy in Head and Neck Cancer (MACH-NC): From 2009 to 2021, what's the update? A Mini Review



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Introduction

This mini review focusses on the 2021 update of the MAH-NC (Meta-analysis of chemotherapy in Head and Neck Cancer) [1]. Chemotherapy plays an important role in the treatment of locally advanced Head and Neck Squamous Cell Carcinomas (HNSCC). Chemotherapy can be given as concomitant, neoadjuvant and adjuvant setting. The first meta-analyses regarding chemotherapy in HNSCC was done in 2009 by Pignon et al. [2]. The current mini review aims to discuss the 2021 update of the same and aims to answer various questions regarding timing, regimen of chemotherapy used and its impact on Overall Survival (OS). In this analysis, a total of 107 trials including 19,805 patients with a median follow up of 6.5 years was included.

Effect of Induction Chemotherapy

Available data from 45 comparisons and 7054 patients. The Hazard Ratio (HR) of death was 0.96 in favor of induction chemotherapy with an absolute difference of 2.2% at 5 years. In terms of Event Free Survival (EFS), the HR was 0.96 with an absolute difference of 1.4% at 5 years. There was no significant difference of the effect of OS or EFS according to the type of induction chemotherapy. This included comparison of taxane+platinum+5FU (HR: 0.97) vs. platinum+5FU (HR: 0.90) vs. other regimens (HR: 1.00). There was no difference in EFS too. The benefit of induction chemotherapy on deaths related due to head and neck cancer and Loco Regional Failure (LRF) was not significant. There was no difference in terms of any specific patient characteristic like age, sex or tumor site. However, there was a decreasing effect of chemotherapy on OS in patients with poor performance status.

Take home message

Contrary to multiple trials, PF regimen showed a survival benefit superior to TPF regimen. Induction chemotherapy should only be considered in fit patients.

Effect of concomitant chemotherapy

Available data from 71 comparisons and 10,680 patients. Concomitant chemotherapy had HR of death 0.83 with an absolute benefit of 6.5% at 5 years and 3.6% at 10 years. Similar benefits were seen in terms of EFS as well. The benefit of chemotherapy on deaths related to head and neck cancer had an absolute benefit of 9.8% at 5 years. It also showed a significant decrease in Loco-Regional Failure (LRF) as well, but it was not significant in terms of . With respect to the type of chemotherapy regimen, EFS was significantly higher with poly-chemotherapy with platinum salt and lowest for mono-chemotherapy without platinum salt. The effect of chemotherapy showed a decreasing trend with increasing age, and it should be carefully weighted after the age of 70 years.

Take home message

Concomitant chemo-radiation is the mainstay of treatment in HNSCC as sole treatment or as adjuvant therapy after surgery. Concomitant chemotherapy demonstrated a greater survival advantage than induction chemotherapy.

Effect of adjuvant chemotherapy

Available data from 14 comparisons and 2915 patients. HR of death was 1.02 with an absolute benefit of 0.3% at 5 years. Similar results were obtained for EFS with benefit of 0.6% at 5 years. A

deleterious effect on 120-day mortality was observed which was not observed in the previous two arms. A decrease in LRF and DF was noted. There was a difference in EFS but not on OS for type of loco-regional treatment in comparison to surgery alone.

Take home message

Adjuvant chemotherapy did not have effect in OS or EFS despite of benefit in DFR and DF due to increased mortality.

Comparison of concomitant vs. induction vs. adjuvant

i. All endpoints showed benefit of concomitant chemotherapy i.e., OS, EFS and LRF

ii. The benefit of chemotherapy was greater in the concomitant group than in the induction and adjuvant groups both for OS and EFS.

iii. 120-day mortality was significantly higher in the adjuvant setting.

iv. The benefit on LRF was higher in concomitant and adjuvant group

v. The benefit on DF was higher in induction and adjuvant group

Conclusion

In conclusion, this meta-analysis clearly showed the benefit of concomitant chemotherapy along with radiotherapy in the treatment of head and neck squamous cell carcinoma. However, this does not apply in the selection of regimens which are in combination with immunotherapy.

References

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