



## Review Article

# Head and neck cancer treatment: An overview

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## ABSTRACT

The advanced head and neck cancers are most difficult for treatment. The newer approaches for the treatment being systemic chemotherapy combined with radiotherapy. Chemotherapy offers several advantages in metastatic head and neck cancers. The main choice for the systemic chemotherapy being platinum containing compounds (drugs), Taxanes, in recent years have shown to be promising and being included in the neo-adjuvant and concomitant therapy regimes. Further, targeted agents such as epidermal growth factor receptor inhibitors (EGFRs) have proven to be beneficial in concomitant and metastatic therapies.

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## 1. Introduction<sup>1-3</sup>

Head and neck cancers can be classified as squamous cell carcinomas of head and neck also abbreviated as SCCHN. Surgery or radiotherapy are the main choice of the treatments for SCCHN. With the advent of newer chemotherapeutic agents, the use of systemic agents is increasing. The overall treatment of patients with SCCHN depends upon the overall health status of the patient. At stage, I or II, a single modality therapy of surgery or radiotherapy is beneficial. Although surgery was initial treatment choice in 1980, the patients with advanced stage III or IV would also have surgery or radiation therapy, a choice that depends on the site of the disease and resect ability of cancers. Since poor results were obtained from this type of therapy especially with stage IV disease or unresectable cancers, in mid 1970s, systemic therapy was introduced. Systemic chemotherapy was usually administered with palliative intent to patients

with advanced stage IV disease, M1 cancers or recurrent disease beyond salvage local treatment.

## 2. Chemotherapy for SCCHN<sup>4-8</sup>

For patients with locally advanced head and neck cancers single chemotherapeutic agents such as methotrexate or cisplatin was introduced. It was evolved from the combined modality treatment for these patients. These agents were prescribed before local definitive treatment. Further combination of cisplatin and bleomycin administered and introduced as a single course before local therapy.

Further two or three courses of cisplatin and bleomycin were given. Also, with more clinical evaluation advancement methotrexate alone or combined with vinca alkaloids (vincristine or vinblastine) were added to the combination of cisplatin plus bleomycin.

In 1980, combination of cisplatin and 5-FU as continuous infusion was evaluated and became widely popular for SCCHN. Also, the concurrent chemotherapy with radiation therapy was evaluated and found useful for the patients

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with inoperable and /or unresectable head and neck cancers. Furthermore, in past century the clinical trials for the patients with SCCHN demonstrated progress in life states. The quality of life states improved with overall survival and especially when the larynx and preserved voice function in laryngeal and hypo pharyngeal cancers,<sup>9-13</sup>

The highest decrease rate in mortality rate has been found in head and neck cancers from 1990 to 1997. Most decline in mortality rate noted in patient with cancers of age of 65 years and both in men and women. Further new methods combined with the radiation therapy was targeted drug therapies help in better progress of diseases.<sup>14</sup>

### 3. Treatment

Types include induction chemotherapy or concomitant therapy.

#### 3.1. Induction chemotherapy<sup>15-20</sup>

It is mostly widely used in clinical practice and beneficial for the cases of metastasis and distant metastasis. Combination of Cisplatin (P) and 5-Fluorouracil (5-FU, F). PF is administered every 3 weeks is mostly used in induction regimen. It has been proven for increase in 5% five-year survival. A study was conducted a clinical trial wherein paclitaxel was also administered along with cisplatin and 5-FU. It was found that there was no significant difference in the survival rates. In another study docetaxel arm was used and showed benefit in survival but overall two-year survival was lower.<sup>21</sup> Further a study conducted by Posner et al. had demonstrated significant survival in with TPF arm as compared with the PF arm.<sup>22</sup>

#### 3.2. Concomitant therapy<sup>23-26</sup>

It improves loco-regional control rates and survival during radiotherapy with combination of chemotherapy. It improves organ conservation. The use of cisplatin in the concomitant therapy shows maximum benefit when used as first line treatment in radical setting. Cisplatin is thus an agent of choice for concomitant radiation therapy. Cisplatin potentiates repair of the sub-lethal damage by homologous and homologous repair mechanisms. The two cycles of cisplatin in low doses weekly or single agent carboplatin is used for improved patient compliance. Other agents include carboplatin and 5-FU and mitomycin-c. Further the intra-arterial cisplatin and concurrent radiation therapy in stage IV patients have been found to be useful and to neutralize the potential toxic effects of cisplatin sodium thiosulphate is used.

### 4. New Targeted Agents<sup>27-34</sup>

Epidermal Growth factor receptor (EGFR) over expression is associated with head and neck cancers. Cetuximab is a monoclonal antibody against EGFR and its clinical study

was reported by Bonner et al. A disease free survival with improved state of life and loco-region control was observed in the study. The study combined EGFR with radiotherapy.

Cetuximab use has shown higher mucosal and skin toxicity.

Lapatinib, a small molecule tyrosine kinase inhibitor associated with EGFR and EGFR Type 2 (HER 2) has shown activity against SCCHN. Mechanism of action of EGFR inhibitor is due to the fact of signal transduction pathways, which leads to the inhibition of cell proliferation. It has been also hypothesized that these agents have indirect effect on the inhibition of DNA repair, which is a reason for its efficacy in combination with the radiation induced DNA repair in normal tissue causing increased acute toxicity and radiation-induced carcinogenesis. Combination of chemotherapy with tyrosine kinase inhibitors is beneficial in head and neck cancers as they have different mechanism of action.

### 5. Conclusion

In head and neck cancers, clinical evidence as reported by some clinicians suggest benefits in neo-adjuvant, concomitant and the adjuvant (post-operative) settings, inspite of risk of higher treatment related toxicity. Also, novel agents combined with other therapies are beneficial.

### 6. Source of Funding

None.

### 7. Conflict of Interest

None.

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