Content available at: https://www.ipinnovative.com/open-access-journals

Current Trends in Pharmacy and Pharmaceutical Chemistry

Journal homepage: https://www.ctppc.org/

Review Article

Head and neck cancer treatment: An overview

A.G. Nerkar[1,2,3,*]

[1] *Dept. of Medicinal Chemistry and Pharmacology, Parul Institute of Pharmacy & Research, Parul University, Vadodara, Gujarat, India*
[2] *Founder and Director, Ateos Foundation of Science Education and Research, Pune, Maharashtra, India*
[3] *Founder and Director, Carolene Therapeutics, Pvt. Ltd., Aurangabad, Maharashtra, India*

ARTICLE INFO

Article history:
Received 08-09-2021
Accepted 30-09-2021
Available online 16-11-2021

Keywords:
SCCHN
Cisplatin
EGFR

ABSTRACT

The advance 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 (EGFRIs) have proven to be beneficial in concomitant and metastatic therapies.

1. Introduction [1–3]

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 [4–8]

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

* *Corresponding author*.
E-mail address: dragnerkar@gmail.com (A. G. Nerkar).

https://doi.org/10.18231/j.ctppc.2021.012

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,[9–13]

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.[14]

3. Treatment

Types include induction chemotherapy or concomitant therapy.

3.1. Induction chemotherapy[15–20]

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 placlitaxel 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.[21] Further a study conducted by Posner et al. had demonstrated significant survival in with TPF arm as compared with the PF arm.[22]

3.2. Concomitant therapy[23–26]

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[27–34]

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 tyro sine 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.

References

1. Vokes EE, Weichselbaum RR, Lippman SM, Hong WK. Head and neck cancer. *New Engl J Med*. 1993;328(3):184–94.
2. Forastiere A, Koch W, Trotti A, Sidransky D. Head and neck cancer. *New Engl J Med*. 2001;345(26):1890–900.
3. Mao L, Hong WK, Papadimitrakopoulou VA. Focus on head and neck cancer. *Cancer cell*. 2004;5(4):311–7. doi:10.1016/s1535-6108(04)00090-x.
4. Argiris A, Karamouzis MV, Raben D, Ferris RL. Head and neck cancer. *Lancet*. 2008;371(9625):1695–709. doi:10.1016/S0140-6736(08)60728-X.
5. Chow LQ. Head and neck cancer. *New Engl J Med*. 2020;382(1):60–72. doi:10.1056/NEJMra1715715.
6. Clavel M, Vermorken JB, Cognetti F, Cappelaere P, Mulder D, Schornagel PH, et al. Randomized comparison of cisplatin, methotrexate, bleomycin and vincristine (CABO) versus cisplatin and 5-fluorouracil (CF) versus cisplatin (C) in recurrent or metastatic squamous cell carcinoma of the head and neck: A phase III study of the EORTC Head and Neck Cancer Cooperative Group. *Ann Oncol*. 1994;5(6):521–7.
7. Hong WK, Bhutani R, Shapshay SM, Strong S. Induction chemotherapy in advanced squamous head and neck carcinoma with high-dose cis-platinum and bleomycin infusion. *Cancer*. 1980;44(1):19–25. doi:10.1002/1097-0142(197907)44:1<19::aid-cncr2820440104>3.0.co;2-r.

8. Jacobs C, Lyman G, García EV, Sridhar KS, Knight W, Hochster H, et al. A phase III randomized study comparing cisplatin and fluorouracil as single agents and in combination for advanced squamous cell carcinoma of the head and neck. *J Clin Oncol* . 1980;10(2):257–63. doi:10.1200/JCO.1992.10.2.257.
9. Sarraf MA. Treatment of locally advanced head and neck cancer: historical and critical review. *Cancer Control*. 2002;9(5):387–99. doi:10.1177/107327480200900504.
10. Rooney M, Kish J, Jacobs J, Kinzie J, Weaver A, Crissman J, et al. Improved complete response rate and survival in advanced head and neck cancer after three-course induction therapy with 120-hour 5-FU infusion and cisplatin. *Cancer*. 1985;55(5):1123–31. doi:10.1002/1097-0142(19850301)55:5<1123::aid-cncr2820550530>3.0.co;2-8.
11. Shapshay SM, Hong WK, Incze JS, Sismanis A, Bhutani R, Vaughn CW. Prognostic indicators in induction cis-platinum bleomycin chemotherapy for advanced head and neck cancer. *Am J Surg*. 1980;140(4):543–51. doi:10.1016/0002-9610(80)90208-1.
12. Perry DJ, Weltz MD, Brown AW, Henderson RL, Neglia WJ, Berenberg JL. Vinblastine, bleomycin and cisplatin for recurrent or metastatic squamous cell carcinoma of the head and neck. *Cancer*. 1982;50(11):2257–60. doi:10.1002/1097-0142(19821201)50:11<2257::aid-cncr2820501104>3.0.co;2-0.
13. Kish JA, Weaver A, Jacobs J, Cummings G, Sarraf A. Cisplatin and 5-fluorouracil infusion in patients with recurrent and disseminated epidermoid cancer of the head and neck. *Cancer*. 1984;53(9):1819–43. doi:10.1002/1097-0142(19840501)53:9<1819::aid-cncr2820530903>3.0.co;2-r.
14. Blanchard P, Bourhis J, Lacas B, Posner MR, Vermorken JB, Hernandez JJ, et al. Taxane-cisplatin-fluorouracil as induction chemotherapy in locally advanced head and neck cancers: an individual patient data meta-analysis of the meta-analysis of chemotherapy in head and neck cancer group. *J Clin Oncol*. 2013;31(23):2854–60. doi:10.1200/JCO.2012.47.7802.
15. Pointreau Y, Atean I, Calais FJ, Lefebvre G. Induction chemotherapy in head and neck cancer: a new paradigm. *Anticancer Drugs*. 2011;22(7):613–33. doi:10.1097/CAD.0b013e3283425871.
16. Hitt R, Pousa AL, Trufero JM, Escrig V, Carles J, Rizo A, et al. Phase III study comparing cisplatin plus fluorouracil to paclitaxel, cisplatin, and fluorouracil induction chemotherapy followed by chemoradiotherapy in locally advanced head and neck cancer. *J Clin Oncol*. 2005;23(34):8636–45. doi:10.1200/JCO.2004.00.1990.
17. Adelstein DJ. Induction chemotherapy in head and neck cancer. *Hematol Oncol Clin North Am*. 1999;13(4):689–98. doi:10.1016/s0889-8588(05)70086-1.
18. Vokes EE, Kies M, Haraf DJ, Mick R, Moran WJ, Kozloff M, et al. Induction chemotherapy followed by concomitant chemoradiotherapy for advanced head and neck cancer: impact on the natural history of the disease. *J Clin Oncol*. 1995;13(4):876–83. doi:10.1200/JCO.1995.13.4.876.
19. Hanna GJ, Haddad RI, Lorch JH. Induction chemotherapy for locoregionally advanced head and neck cancer: past, present, future? *Oncologist* . 2013;18(3):288–93. doi:10.1634/theoncologist.2012-0286.
20. Silver HJ, Dietrich MS, Murphy BA. Changes in body mass, energy balance, physical function, and inflammatory state in patients with locally advanced head and neck cancer treated with concurrent chemoradiation after low-dose induction chemotherapy. *Head Neck*. 2007;29(10):893–900. doi:10.1002/hed.20607.
21. Lorch JH, Goloubeva O, Haddad RI, Cullen K, Sarlis N, Tishler R, et al. Long term results of TAX324, a randomized phase III trial of sequential therapy with TPF versus PF in locally advanced squamous cell cancer of the head and neck. *Lancet Oncol*. 2011;12(2):153–62. doi:10.1016/S1470-2045(10)70279-5.
22. Posner MR, Hershock DM, Blajman CR, Mickiewicz E, Winquist E, Gorbounova V, et al. Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer. *New England Journal of Medicine*. 2007;357(17):1705–1720.
23. Bhide SA, Ahmed M, Barbachano Y, Newbold K, Harrington KJ, Nutting CM. Sequential induction chemotherapy followed by radical chemo-radiation in the treatment of locoregionally advanced head-and-neck cancer. *Br J Cancer*. 2008;99(1):57–62. doi:10.1038/sj.bjc.6604444.
24. Argiris A, Haraf DJ, Athanasiadis I, Kozloff M, Mittal B, Pelzer H, et al. Induction chemotherapy followed by concurrent chemoradiation for advanced head and neck cancer: improved disease control and survival. *J National CompreheKies MS*. 1998;16(8):393–403.
25. Shirinian MH, Weber RS, Lippman SM, Dimery IW, Earley CL, Garden AS, et al. Laryngeal preservation by induction chemotherapy plus radiotherapy in locally advanced head and neck cancer: the MD Anderson Cancer Center experience. *Head & neck*. 1994;16(1):39–44. doi:10.1002/hed.2880160109.
26. Lefebvre JL. Laryngeal preservation in head and neck cancer: multidisciplinary approach. *Lancet Oncol*. 2006;7(9):747–55. doi:10.1016/S1470-2045(06)70860-9.
27. Department of Veterans Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *New Engl J Med*. 1991;324(24):1685–90. doi:10.1056/NEJM199106133242402.
28. Shirinian MH, Weber RS, Lippman SM, Dimery IW, Earley CL, Garden AS, et al. Laryngeal preservation by induction chemotherapy plus radiotherapy in locally advanced head and neck cancer: the MD Anderson Cancer Center experience. *Head & neck*. 1994;16(1):39–44.
29. Kies MS, Holsinger FC, Lee JJ, William JR, Glisson WN, Lin BS, et al. Induction chemotherapy and cetuximab for locally advanced squamous cell carcinoma of the head and neck: results from a phase II prospective trial. *J Clin Oncol*. 2010;28(1):8–14. doi:10.1200/JCO.2009.23.0425.
30. Rampino M, Bacigalupo A, Russi E, Schena M, Lastrucci L, Iotti C, et al. Efficacy and feasibility of induction chemotherapy and radiotherapy plus cetuximab in head and neck cancer. *Anticancer Res*. 2012;32(1):195–9.
31. Geoffrois L, Martin L, Raucourt D, Sun D, Tao XS, Maingon Y, et al. Induction chemotherapy followed by cetuximab radiotherapy is not superior to concurrent chemoradiotherapy for head and neck carcinomas: results of the GORTEC 2007-02 phase III randomized trial. *J Clin Oncol*. 2018;36(31):3077–83. doi:10.1200/JCO.2017.76.2591.
32. Souza D, Davis JA, Zhang DW, Khattri Y, Seiwert A, Aktolga TY, et al. A phase II study of lapatinib in recurrent/metastatic squamous cell carcinoma of the head and neck. *Clin Cancer Res*. 2012;18(8):2336–79. doi:10.1158/1078-0432.CCR-11-2825.
33. Harrington KJ, El-Hariry IA, Holford CS, Lusinchi A, Nutting CM, Rosine D, et al. Phase I study of lapatinib in combination with chemoradiation in patients with locally advanced squamous cell carcinoma of the head and neck. *J Clini Oncol*. 2009;27(7):1100–7. doi:10.1200/JCO.2008.17.5349.
34. Campo D, Hitt JM, Sebastian R, Carracedo P, Lokanatha C, Bourhis D, et al. Effects of lapatinib monotherapy: results of a randomised phase II study in therapy-naive patients with locally advanced squamous cell carcinoma of the head and neck. *Br J Cancer*. 2011;105(5):618–45. doi:10.1038/bjc.2011.237.

Author biography

A.G. Nerkar, Professor

Cite this article: Nerkar AG. Head and neck cancer treatment: An overview. *Curr Trends Pharm Pharm Chem* 2021;3(4):47-49.