



**ORIGINAL RESEARCH PAPER**

**Oral Pathology**

**NEO ADJUVANT THERAPIES IN ORAL CANCER -A REVIEW**

**KEY WORDS:** Neo-adjuvant, surgery, stem cell, therapy

<b>Dr.Arunkumar. R*</b>	Intern, Department of oral pathology, Adhiparasakthi dental college and hospital, Melmaruvathur *Corresponding Author
<b>Dr. Devi. M</b>	Prof, Department of oral pathology, Adhiparasakthi dental college and hospital, Melmaruvathur
<b>Dr. A. Beeula</b>	Senior lecturer, Department of oral pathology, Adhiparasakthi dental college and hospital, Melmaruvathur
<b>Dr. Shamala. S</b>	Prof and Head, Department of oral pathology, Adhiparasakthi dental college and hospital, Melmaruvathur

**ABSTRACT**

One of the most prevalent cancers in the world today is Squamous cell carcinoma of Head and Neck (HNSCC), which is distinguished by a physiologically heterogeneous group of tumors, non-specific biomarkers, and a dismal prognosis. Although the traditional surgical therapy methods have made positive strides, they result in long-term deformity, a shift in one's sense of self, and physically debilitating effects, whereas chemo and radiation therapy result in serious toxicities that have a detrimental influence on patients' quality of life. In order to enhance individual health outcomes and survival, neo-adjuvant therapeutic approaches were developed. Thus the current article reviews the various neo-adjuvant therapies and their significance in contrast to conventional surgery.

**INTRODUCTION**

Oral cancer is the sixth most common cancer worldwide, which continues to pose a severe public health issue. Alcohol and tobacco use are the major etiological factors linked to oral cancer development. Efforts to lessen the burden of this condition focus on prevention and early identification of oral cancer. For patients with oral cancer, particularly in advanced stages of the disease, surgery is the mainstay of therapy. Prior to the primary surgical therapy, neo-adjuvant therapy is provided to boost the effectiveness in the course of treatment beyond what can be achieved with surgery alone. Neo-adjuvant therapies are administered in advance of the primary surgical therapy in order to shrink tumours and eradicate cancer cells that have metastasized. Nanotechnology in cancer therapeutics, Chemo-embolisation, Ablation therapy, Neo-adjuvant Chemotherapy, Chrono-Chemotherapy, Stem cell therapy are neo-adjuvant therapies that can be provided in early stage malignancies.

**EARLY DIAGNOSIS OF ORAL CANCER**

There are two methods for identifying early stage of oral cancer:

- Screening programs to find asymptomatic patients with suspicious oral lesions
- Specialized diagnostic tools to identify the asymptomatic oral lesions

**NEO ADJUVANT THERAPIES IN ORAL CANCER**

The great majority of operable oral malignancies are best treated primarily with surgery. With comparable control rates to surgery, neo-adjuvant therapy is an alternative for treating early-stage oral malignancies. Also in cases of recurrent lesions, neo-adjuvant therapies can be used, and they do not cause any significant cosmetic or functional impairment. Furthermore, lesions must be shallow, easily accessible, in order to be treated with neo-adjuvant therapy. (3)

**Nanotechnology in cancer therapeutics** - Nano technological targeted cancer chemotherapy has been offered as a solution to the issues associated with chemotherapy for cancer. It delivery entails for selective as well as effective localization on target cells in therapeutic concentration while reducing its concentration at non-target sites, thereby maximizing therapeutic index, effective bio distribution of the drug, toxicity reduction, which is significant factor in cancer chemotherapy. (7)

**Chemo-embolization** - Chemo-embolization aims to boost the regional advantage by decreasing blood flow with the use of embolising agents and microcapsule, which leads to hypoxia necrosis, increased tumour residency time. In the head and neck area, other than the difficulty of producing embolising agents, there are several barriers to use this technique to temporarily stop all blood flow in the head and neck region. Anastomoses pose a risk of local necrosis to the nerve ganglions and eyes. Due to these factors, chemo-embolization for head and neck squamous cell carcinoma (SCC) has been rare to date. (8)

**Ablation cancer therapy** - Ablation is a treatment method that eliminates tumours without removing them. It is typically recommended for small tumours less than 3 cm in size when surgery is not an option. For larger tumours, embolization and ablation are combined. Due to the possibility of killing part of the normal tissue surrounding the tumour, this method may not be recommended for treating tumours that are close to major blood arteries. (1) Thermal ablation has the advantage of treating tumours with a specific volume in locations where surgery is challenging. Unfortunately, large tumours like colon cancer primary, soft tissue sarcomas, head and neck nodules, and superficial skin disorders won't benefit much from this type of treatment. (9)

**Chrono-chemotherapy** - The delivery of medications in a time-specific manner is a novel strategy to increase the effectiveness of chemotherapeutic medicines. It is becoming clear that the time of chemotherapy delivery is just as important as the dosage. Because circadian clock cycles have an impact on human body physiology, the timing of drug delivery affects drug toxicity and therapeutic effectiveness. (10) The World Health Organization has just lately acknowledged docetaxel, doxorubicin, fluorouracil, and paclitaxel as anticancer chemotherapy medicines that target circadian clock genes (Bcl2, Top2a, Tmys, and Bcl2 respectively). They can therefore be used in Chrono-chemotherapy to treat oral cancer. (10)

**Neo-adjuvant chemotherapy**- The optimal cancer chemotherapy should prevent normal cells from undergoing the desired therapeutic response while delivering the right amount of medication at the site of action with right controlled rate and for a long period of time. (1)

Drug resistance, which happens when tumour cells that were initially suppressed by an anti-cancer medication start to grow resistant to the agent, which is a dangerous effect of chemotherapy. The primary causes of this are decreased medication uptake and increased drug efflux.

Rooney et al., 1985, states that locally and in the combined prevention, systemic chemotherapy regimens using cisplatin and 5-fluorouracil seem to be very effective.

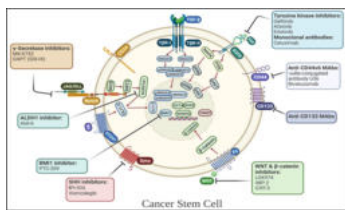
Jaulerry et al., 1992, states that cisplatin and 5-fluorouracil regimens prevents metastatic spread.

Stell and Rawson, 1990; Munro et al., 1995, states that the benefits of induction chemotherapy are still debatable, as it is linked to substantial toxicity and morbidity that might affect the survival.

The involvement of anatomical landmarks on imaging and clinical examination determines resectability in oral tumours largely. Absolute contraindications to surgery include the tumour's extension to the muscles of pre-vertebras, skull base, and carotid artery invasion.

Patil et al., states that the presence of other anatomical landmarks can restrict the scope of operation and make it challenging to establish clear margins. Technically, such tumors can be classified as unresectable. In these patients, it seems sense that size reduction caused by neo-adjuvant chemotherapy could lead to a successful surgical resection. (11)

**Stem cell therapy** - Epigenetic alterations cause normal stem cells, precursor/progenitor cells, or cancer stem cells (CSCs) to develop. They play a part in the growth, metastasis, and recurrence of cancer, which suggests that they may be effective in treating solid tumours. (1) Growing evidence suggests that the development and spread of tumours are caused by a group of cancer stem cells, which are the only cells able to sustain long-term self-renewal and produce the phenotypic ally varied tumour cell population. Modern cancer therapies may be failing because they have less of an impact on CSCs that may be dormant but are still essential and still have the ability to fully repopulate the tumor.(8) Therefore, the effects of the presence of CSCs must be taken into account in neo-adjuvant treatment options for the elimination of cancer. (12)



**Figure 1: Cancer Stem cell directed therapy in HNSCC (Oral Cancer Stem Cells:Therapeutic Implications and Challenges- Linah A. Shahoumi)**

**CONCLUSION**

The majority of the aforementioned medications and therapies have shown minimal rates of patient response, but they have novel mechanisms of action, boost the anti-tumour effects of conventional chemotherapeutic drugs and radiotherapy, and have toxicity profiles that differ from those of conventional therapy. They can be used as neo-adjuvant therapies in advance to traditional therapies. Thus various neo-adjuvant therapies can be better understood in order to develop therapeutic strategies that successfully halt tumour development and progression.

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