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Editorial

Oral Metronomic Therapy in Oral Cancer

T R Gururaja Rao*

Professor, Former Principal in Dayananda Sagar College of Dental Sciences, Bangalore, India

***Corresponding Author:** T R Gururaja Rao, Professor, Former Principal in Dayananda Sagar College of Dental Sciences, Bangalore, India.

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Metronomic chemotherapy is an emerging therapeutic option in clinical oncology and it may prove useful at least in metastatic head and neck cancer patients. To develop rational therapeutic strategies, it is important to identify molecular targets that are linked to the pathogenesis of head and neck cancer. The oral metronomic therapy involves the frequent, continuous, low-dose oral administration of chemotherapy without long breaks. It treats cancer primarily by inhibiting tumor angiogenesis and enhancing the immune response. It offers a low-cost, less toxic alternative for metastatic, advanced, or palliative, particularly in head and neck cancers.

Key aspects of oral metronomic chemotherapy:

- **Mechanism:** Unlike maximum tolerated dose (MTD) chemotherapy that kills cancer cells directly, the targets the endothelial cells of the tumor vasculature, stopping blood vessel growth, and enhances the immune system to tackle cancer.
- **Benefits:** It has a favorable toxicity profile with significantly fewer side effects such as nausea or hair loss. It is also economically viable for long-term use.
- **Common applications:** This therapy is utilized for palliative care in advanced/recurrent cancers, particularly head and neck squamous cell carcinoma (HNSCC). It has shown efficacy as a Maintenance or second-line treatment in some settings.
- **Common drugs:** Typical drugs used include low-dose methotrexate, celecoxib, and sometimes erlotinib.
- **Effectiveness:** Studies show that it can improve overall survival and quality of life compared to traditional, higher-dose chemotherapy in certain advanced cancer cases.

In a few studies as it was done to reduce toxicity oral metronomic chemotherapy, consisting of low-dose methotrexate once per week and celecoxib once per day, is one such alternative. This combination has shown promising results in a randomised phase 2 trial 15 involving patients with recurrent, relapsed, or newly diagnosed locally advanced head and neck cancer, who had orocutaneous fistula or extensive disease precluding any localised therapy and a poor prognosis. These patients showed improved progression-free survival (hazard ratio [HR] 0.63 [95% CI 0.42 - 0.91]) and overall survival (0.61 [0.40 - 0.95]) compared with patients given single-agent intravenous cisplatin. These results have been replicated in large prospective and retrospective studies. In the previous phase 2 trial, the low incidence of grade 3 and above adverse events (18.9% in the oral metronomic chemotherapy group vs 31.4% in the single-agent intravenous cisplatin group) and the low cost of therapy (less than US$15 per month), are other attractive features of the metronomic regimen.