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Letter to the editor

Methotrexate based oral chemotherapy for advanced oral cancer during COVID-19 pandemic: Another option in the therapeutic armamentarium



Dear Editor,

Oral cancer is the one of the common head and neck malignancy amongst males globally. Surgery remains the mainstay of treatment both in early and advanced stage disease and is associated with a significant improvement in overall survival [1]. COVID-19 pandemic has literally halted the elective cancer surgeries worldwide. Almost all the guidelines have suggested delaying the elective surgery whenever possible [2]. Many studies have suggested poor perioperative outcomes in Sars-Cov-2 positive patients who undergo surgery. This has posed a therapeutic and ethical dilemma to the surgeons as delaying the surgery for advanced oral cancer will prove to be a double whammy – inferior overall survival and poor quality of life. The role of neoadjuvant chemotherapy in advanced oral cancer is not yet fully established. A triple agent induction chemotherapy including Taxanes, platinum and 5-FU is the usual first line therapy but has a significant toxicity profile [3–5]. As true for surgery, it is recommended to avoid intravenous toxic chemotherapy during Covid-19 pandemic as well. This further leaves the oncologists dealing with the patients with advanced oral cancer in a tight spot. In the era of personalized medicine, where the repertoire of drugs directed against tumor cells has greatly increased, selecting an efficacious and apt drug regimen for an interim period till the time a definitive treatment can be administered to the patients remains a challenge not yet explicitly addressed.

Recent evidence – one publication in the journal *Oral Oncology* [6] and another conference presentation during ASCO 2020 virtual meeting [7] - supporting the role of Methotrexate based oral chemotherapy for the advanced oral cancer has turned out to be a silver lining amidst critical time of COVID-19 pandemic. In their experience of 23 patients with locally advanced T4a tumors treated with weekly oral Methotrexate and daily Celecoxib drugs, Sultania et al. [6] reported that the disease progressed in only three (13%) patients. Moreover, none of the patient had grade III or IV toxicity. A phase III trial, presented at ASCO 2020 [7], compared the overall survival of patients with relapsed-recurrent or metastatic upfront palliatively treated squamous cell carcinoma of head and neck with either Oral Metronomic Chemotherapy (oral Methotrexate 15 mg/m² weekly with Celecoxib 200 mg once daily, OMC) or intravenous Cisplatin (IVC) 75 mg/m², 3-weekly for 6 cycles. The trial highlighted that OMC led to a survival benefit of 11.67% (95% CI, -20.77 to -0.97) in six-months overall survival compared to IVC (62.26% vs. 50.89%). Moreover, OMC was better tolerated than IVC (18.9% vs. 30.2% grade 3 or above adverse events, $p = 0.01$). Though the trial addresses the patient population treated with a palliative intent, yet the benefit can be extrapolated in patients with non-metastatic advanced oral cancer who cannot be currently operated upon due to COVID19 pandemic and cannot be prescribed potentially toxic triple agent intravenous chemotherapy also.

“A bird in the hand is worth two in the bush” – adhering to this philosophy and considering the ease of prescription, home-based nature of therapy, proven effectiveness, and a likely improvement in survival, Oral Methotrexate and Celecoxib therapy may be the best bet in the management of patients with advanced oral cancer during the current crisis. Future Bayesian approach trials can only provide an affirmative answer to a best treatment regimen for the current scenario.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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