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Letter to the editor

May we rely on induction chemotherapy again as a biological selection of radiosensitive head and neck cancer?

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With a better understanding of head and neck cancer (HNC) pathogenesis and the identification of good-prognosis subtypes, such as HPV-positive tumors, there is an urgent need to better identify patients who may avoid overtreatment and unnecessary toxic effects.

In this regard, the role of induction chemotherapy (IC) has evolved during last years. According to the MACH-NC study group, in locally advanced HNC concurrent chemotherapy improved overall survival compared to radiation alone, while there was no advantage with IC; however, questions remained about the possibility of better distant control with IC. Progressively, IC was widely accepted for organ preservation in sites that would otherwise be managed surgically, such as advanced laryngeal cancers. Since the landmark Veterans Administration Larynx Trial in laryngeal cancer, response to IC has been considered a way to biologically select which disease could be more sensitive to radiation therapy (RT), in turn achieving organ preservation without jeopardizing overall survival [1,2]. In the past, one single cycle of IC has been considered as a possible selection tool for curative chemoradiation, in the context of laryngeal cancer [3]. Similarly, in sinonasal undifferentiated cancer, response to IC demonstrated to be associated with better prognosis; moreover, it possibly identified patients benefitting or not of multimodal approach containing surgery [4].

Recently, the OPTIMA trial stratified HPV-positive oropharyngeal cancer patients by IC response in order to achieve deintensification of RT dose, with or without chemotherapy. Treatment de-intensification in these patients resulted in excellent pathological complete response and survival outcomes with reduced acute and late toxicity rates [5].

Due to its easy administration and flexibility, IC could be an elegant test for new therapeutic strategies [6]. However, the benefit of IC itself in improving prognosis over curative locoregional approaches in HNC remains elusive. Moreover, while lack of response to IC is a recognized negative predictor of a subsequent response to chemoradiation, obtaining a response to IC demonstrated to be prognostic of overall survival, but it was not a marker of favorable outcome after chemoradiation [7].

Also, IC is associated with toxicities, and not all patients could be eligible for this approach. This strategic approach can, in some patients, delay or reduce compliance of the following radical treatment, thus jeopardizing patient outcomes.

In 1992, after first laryngeal preservation trial publication, some Authors of the study group stated that “intensive efforts should be made to identify biologic tumor and patient characteristics that predict chemo-resistant or radioresistant tumors” as critical way to select patients for different treatments [8]. After more than 25 years, we are invoking treatment with IC again to biologically select patients who are responsive to RT.

Currently, there are no practical tools or available validated biomarkers to help identify patients who will benefit the most from a specific therapy. In the past years, efforts to define subgroups of patients by gene-expression profiling and to identify RT-predictive signatures have been made [8–10], but the predictive utility of these molecular classifications has not been prospectively identified, therefore making these speculations not yet clinically applicable. Identifying molecular aspects of the disease to tailor radiation doses and possibly the systemic treatment is an exciting field and research in this setting has already started [11].

Also, the definition of radiomic features represents a new frontier to predict radiation sensitivity and to apply tailored treatment approaches in HNC [12,13].

Even if IC has been shown to allow a selection of patients for further treatments, we support the concept to focus the scientific efforts to prospective trials of molecular and radiomic disease dissection to improve treatment efficacy and decrease toxicity rate.

Declaration of Competing Interest

None declared.

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Abbreviations: HNC, head and neck cancer; IC, induction chemotherapy; HPV, human papillomavirus; OS, overall survival; RT, radiation therapy

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