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LETTER TO THE EDITOR

# Induction Chemotherapy as a Bridge to CCRT in Resource-constrained Settings: A Step Forward Needing Stronger Evidence

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*Dear Editor*

We read with interest the study by Talukdhar and colleagues, which compared induction chemotherapy (ICT) followed by concurrent chemoradiotherapy (CCRT) with CCRT alone in inoperable locally advanced head and neck cancer (LAHNC) [1]. The authors report a significantly higher complete response (CR) rate in the ICT arm (58.57% vs 32.85%, p=0.002), with comparable toxicity profiles. While the study addresses a clinically relevant question in a resource-constrained setting, we wish to raise several methodological concerns that temper the strength of these conclusions.

*Non-randomized design and selection bias*

The authors acknowledge that purposive allocation rather than randomization was used to assign patients to the two arms. Despite applying uniform inclusion/exclusion criteria, this approach is inherently susceptible to allocation bias. It is unclear whether baseline disease characteristics such as primary site distribution, nodal burden, and performance status were statistically comparable between the arms. The study reports that baseline characteristics were "similar" but does not provide a formal statistical comparison. Without this, differential response rates cannot be confidently attributed to the intervention alone.

*Radiotherapy technique*

Perhaps more consequential is the use of two-dimensional (2D) radiotherapy planning for all patients. Modern management of LAHNC employs intensity-modulated radiotherapy (IMRT), which reduces salivary gland and mucosal doses, improves locoregional control, and mitigates the severity of xerostomia and mucositis [2]. The reported toxicity rates while statistically comparable between arms may reflect the intrinsic toxicity burden of 2D planning rather than the ICT regimen itself, limiting the generalizability of these findings to contemporary practice. Notably, the xerostomia rates in both arms appear considerable, which is expected under conventional techniques.

*Response evaluation timing and survival outcomes*

The authors evaluate treatment response at 3 months post-CCRT, citing that this extended assessment window may explain their higher CR rates compared to the DeCIDE trial and others. However, CR at 3 months, while a meaningful early endpoint, is only a surrogate for long-term locoregional control and overall survival. As the authors themselves note, neither progression-free survival nor overall survival data were collected due to the short study period. Complete response without durable control is of limited clinical consequence, particularly in LAHNC where patterns of failure including distant metastasis determine ultimate prognosis.

*ICT regimen*

The ICT protocol used cisplatin plus 5-fluorouracil (PF) differs from the docetaxel, cisplatin, and 5-fluorouracil (TPF) triplet that has largely superseded doublet regimens in the literature and is associated with superior outcomes in randomized trials [3]. The choice of PF may have underestimated the potential benefit of ICT in this population.

Despite these limitations, the study makes a practically important point for the South Asian context: in settings with significant waiting periods before CCRT initiation, ICT may prevent disease progression and potentially improve the proportion of patients who eventually achieve locoregional control. This "bridging" rationale is pragmatically sound, even if the survival benefit remains unproven. We would encourage the authors to pursue prospective randomized follow-up, incorporating IMRT,

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TPF-based induction, and survival as primary endpoints, to build on this preliminary but promising signal.

## References

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