



The new front line in advanced nasopharyngeal cancer

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In reference to the article by Zhang *et al.* (1), we would like to congratulate the authors for reporting the first randomized controlled trial in the recurrent/metastatic nasopharyngeal cancer (NPC) setting. This study compares two widely used cisplatin containing doublet chemotherapy regimens and covers a great gap in the management of patients with metastatic or recurrent NPC. The results from this study with progression free survival (PFS) being the primary endpoint established the superiority of gemcitabine over infusional 5FU as the companion to the cisplatin backbone.

The combination of cisplatin and infusional 5FU, developed by Wayne State University for the treatment of head and neck squamous cell carcinoma (2), showed similar activity and efficacy in NPC and was widely adopted as the standard regime in NPC for many years. However, the need for in-patient administration as well as complications associated with central venous access devices has prompted the search for outpatient and bolus administration of platinum-based doublet regimens with comparable toxicities. Gemcitabine is a desirable agent, because it may be administered as a short intravenous infusion in the outpatient setting and avoids the inconveniences of infusional 5FU. Furthermore, it has also demonstrated activity and efficacy as a single agent or in combination with platinum in metastatic or recurrent NPC, with overall response rate reported in the range of 28–73% (3–5).

In this study, the authors reported an improvement in median PFS, amongst other clinical endpoints, with cisplatin/gemcitabine (7.0 versus 5.6 months, $P < 0.0001$),

and preliminary analysis suggested this might translate into meaning improvement in overall survival (29.1 versus 20.9 months, $P = 0.0025$). Furthermore, the convenience of administration of cisplatin/gemcitabine in the outpatient setting makes it advantageous in terms of logistics and patient convenience.

Finally, it is worth mentioning that the cisplatin/gemcitabine group experienced more grade 3 and above hematologic toxicities than those treated with cisplatin/5FU (neutropenia 23% versus 13%, $P = 0.0251$; thrombocytopenia 13% versus 2%, $P = 0.0007$). In contrast, patients in the cisplatin/5FU group experienced a greater incidence of grade 3 and above mucositis (15% versus 0%, $P < 0.0001$). Nevertheless, the incidence of serious adverse events attributed to treatment was low and similar between the two groups (4% versus 6%). The proportions of other nonhematologic toxicities were otherwise identical in the two treatment groups.

Beyond doubt, this study provides needed data about the optimal chemotherapy regime in the first line treatment of recurrence/metastatic NPC. Current research is focused not only on developing novel agents such as immunotherapy, but also on identifying potential predictors of treatment benefit, with earlier integration of molecular markers into NPC trials. Further prospective clinical trials, evaluating different treatment strategies are warranted to improve patients' outcome and minimize toxicity of treatment.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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