How to treat recurrent/metastatic head and neck cancer: the economic issue in real-world practice

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Head and neck cancer (HNC) is the sixth most common type of cancer globally. Early stage (stage I–II) can be treated by surgery or radiotherapy only. Locally advanced stage (stage III–IVA) can be treated by surgery and radiotherapy with or without chemotherapy, or radiotherapy with or without chemotherapy with salvage surgery in reserve for residual or recurrent disease. In stage IVb inoperable disease, surgery is impossible and radiotherapy with or without chemotherapy should be considered. However, more than 50% of locally advanced HNC patients relapse locoregionally or at a distant site after primary therapy. Patients with distant metastatic and/or locoregionally recurrent diseases that are deemed to be incurable by surgery or radiotherapy are identified as recurrent/metastatic (R/M) HNC. For this group of patients, platinum-based chemotherapies are the first choice of treatment.

In 2008, Vermorken et al. published that the addition of anti-epithelial growth factor receptor (EGFR) monoclonal antibody to platinum-based chemotherapy was an effective regimen to prolong overall survival (OS) up to 10.1 months for R/M HNC. The major problem in real-world practice is the economic issue. Hannouf et al. developed a model to assess the cost-effectiveness of adding cetuximab to platinum-based chemotherapy for first-line R/M HNC, and an incremental cost-effectiveness ratio (ICER) exceeded $100,000 US dollars per QALY (quality adjusted life year) gained. Even in Taiwan with public health insurance famous around the world, most patients pay by themselves with an average of US$4800 dollars per month. This economic issue should be more concerning since newly developed drugs can improve the outcomes for R/M HNC but the costs are even higher. Just in 2016, the FDA approved two anti-PD1 immune checkpoint inhibitors, pembrolizumab and nivolumab, for R/M HNC progressing after platinum-based chemotherapy. Both anti-PD1 antibodies can prolong survival for R/M HNC patients who have been refractory to first-line therapy but the average cost would be more than US$10,000 per month. The condition is similar in most developing countries and this is difficult for HNC patients because most of them have lower socioeconomic status. Several alternative regimens have been tried to improve clinical outcome for R/M HNC without using novel target drugs. For example, some trials have been performed to examine a docetaxel, cisplatin and 5-fluorouracil (TPF) regimen in R/M HNC, since recent studies have shown that this triple combination therapy is a successful regimen with better outcomes than traditional cisplatin and 5-fluorouracil in an induction setting for locally advanced HNC. However, the toxicities for R/M HNC should be of more concern in the palliative setting because docetaxel is commonly associated with myelosuppression and the continuous 96-hour infusion of 5-FU is inconvenient. Modification with dosage reduction may be a safer way to use TPF in R/M HNC but the effectiveness should be carefully evaluated.

In a phase II study, which enrolled 19 locally advanced or R/M HNC patients, it showed that, under the triple regimen, the objective response rate (ORR) could reach up to 44%. In the Lin et al. study, which enrolled 55 Taiwanese R/M HNC patients treated with a dosage reduced docetaxel/cisplatin/5-FU (mTPF) regimen, the ORR and OS of this regimen were 56% and 10 months, respectively. Yossi et al. also showed that dosage reduced TPF was a useful regimen for Western countries in R/M HNC treatment, with ORR 39%. In the current study, Demirci et al. article enrolled 80 R/M HNC patients and showed that dosage reduced TPF (docetaxel 60 mg/m\(^2\) on day 1; cisplatin 60 mg/m\(^2\) on day 1; 5-FU 600 mg/m\(^2\) day 1 to 5; a cycle every 3 weeks for a total of 2–6 cycles) improved ORR and OS up to 46.3% and 11.5 months, respectively. Although the dosage reduction of TPF varied in different studies, all of these studies showed that dosage reduced TPF was an effective regimen as first-line R/M HNC treatment. In addition, although the most common grade 3–4 adverse events were neutropenia (22–55%), and anemia (10–13%), these adverse events seems to be manageable, even though granulocyte-colony stimulating factor (G-CSF) support is still suggested for patients who have ever suffered from grade 3–4 myelosuppression.

Because most HNC patients have lower socioeconomic status, how to maximize the cost-effectiveness of currently available therapeutic agents is a major issue for clinics. A dosage reduced TPF regimen has been considered as an alternative first-line regimen for R/M HNC in some real-world practice. More evidence to show the effectiveness and safety profile for TPF in palliative R/M HNC therapy will provide more help in a certain group of patients.

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