

REPLY TO LETTER TO THE EDITOR**Reply to “Do not de-escalate oncology care in oropharyngeal cancer routinely”**

Dr. Petr Szturz and Dr. Jan B. Vermorken have made important remarks about our study “De-escalation of post-treatment surveillance in oropharyngeal cancer.” They raise potential concerns about de-intensifying routine follow-up of oropharyngeal squamous cell carcinoma (OPSCC).

We suggest that follow-up of HPV-associated OPSCC could be de-intensified 2 years after treatment, since the majority of recurrences and toxicities present within 2 years.^{1,2} We encourage rapid access consultation whenever new symptoms arise. Our article did not support treatment de-escalation outside randomized, controlled studies.

The prognosis of HPV+ OPSCC is excellent, with 3-year local and regional control over 90%.^{3,4} Dr. Szturz and Dr. Vermorken refer to a study in which, after 3 years of follow-up, the proportion of HPV+ OPSCC patients presenting with distant metastases was only 1.5% (7 of 457).⁵ The number of routine imaging studies needed to detect one late, asymptomatic distant failure of HPV + OPSCC is high. Exposing all HPV+ patients to prolonged follow-up, and repeated imaging, is not likely to produce significant survival benefits for the minority of patients with poor prognosis.

Although atypical sites of distant metastases have been reported in the literature, the most common sites are the lungs, liver, and bone, irrespective of HPV status.^{1,6,7} In a study by Fakhry et al median time to disease progression was also similar in HPV+ and in HPV– OPSCC, supporting close surveillance within the first 2 years in both groups.¹

Whether early detection of distant metastasis in asymptomatic HPV+ OPSCC patients is beneficial in terms of life quality, psychosocial well-being, or survival is yet controversial. In decelerating progression of incurable disease, the potential survival advantage and treatment toxicity should be carefully assessed in randomized, controlled studies.⁸

We agree that careful monitoring of treatment toxicity is important. Intense follow-up during the first 2 years detects the majority of side-effects, and a multidisciplinary team should be available throughout follow-up for early intervention. Traditional, clinical outpatient examinations could be partly replaced by modern methods, such as web-based screening tools, in detecting late side-effects. In the future, carefully planned treatment de-escalation protocols hopefully decrease permanent morbidity.

Intense follow-up may be justified in patients with reduced life management skills, or with lower capacity for self-assessment. Reducing routine follow-up for fit, asymptomatic patients improves availability for those who need more guidance, or quick assessment because of new symptoms. In a strict, protocol directed follow-up patients may unnecessarily wait for a scheduled appointment, even when a rapid check-up is required.

The extent to which patient preferences should guide cancer follow-up and imaging, or medical decision making in general, is an interesting issue from the perspective of health economics.⁹ Dr. Szturz and Dr. Vermorken refer to a cross-sectional study by Mueller et al. In that study, the majority of head and neck cancer patients favored fewer visits than the current standard.¹⁰

We would like to thank Dr. Szturz and Dr. Vermorken for their valuable comments, and editors of the Head and Neck journal for the opportunity to respond to their letter.

Taru Ilmarinen MD, PhD 

Harri T. Keski-Säntti MD, PhD

Mari L. Markkanen-Leppänen MD, PhD

Aaro Haapaniemi MD, PhD

Laura Tapiovaara MD, PhD 

Timo Atula MD, PhD

Leif Bäck MD, PhD 

Department of Otorhinolaryngology – Head and Neck Surgery, Helsinki University Hospital, Helsinki, Finland

Correspondence

Taru Ilmarinen, Department of Otorhinolaryngology – Head and Neck Surgery, Helsinki University Hospital, Helsinki, Finland.

Email: taru.t.ilmarinen@hus.fi

ORCID

Taru Ilmarinen  <https://orcid.org/0000-0001-8674-6417>

Laura Tapiovaara  <https://orcid.org/0000-0002-9747-6624>

Leif Bäck  <https://orcid.org/0000-0001-8383-7671>

REFERENCES

1. Fakhry C, Zhang Q, Nguyen-Tan PF, et al. Human papillomavirus and overall survival after progression of oropharyngeal squamous cell carcinoma. *J Clin Oncol*. 2014;32:3365-3373.
2. Frakes JM, Naghavi AO, Demetriou SK, et al. Determining optimal follow-up in the management of human papillomavirus-positive oropharyngeal cancer. *Cancer*. 2016;122:634-641.
3. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med*. 2010;363:24-35.
4. O'Sullivan B, Huang SH, Perez-Ordonez B, et al. Outcomes of HPV-related oropharyngeal cancer patients treated by radiotherapy alone using altered fractionation. *Radiother Oncol*. 2012;103:49-56.
5. Huang SH, Perez-Ordonez B, Weinreb I, et al. Natural course of distant metastases following radiotherapy or chemoradiotherapy in HPV-related oropharyngeal cancer. *Oral Oncol*. 2013;49:79-85.
6. Trosman SJ, Koyfman SA, Ward MC, et al. Effect of human papillomavirus on patterns of distant metastatic failure in oropharyngeal squamous cell carcinoma treated with chemoradiotherapy. *JAMA Otolaryngol Head Neck Surg*. 2015;141:457-462.
7. Gronhoj C, Jakobsen KK, Jensen DH, et al. Pattern of and survival following loco-regional and distant recurrence in patients with HPV+ and HPV- oropharyngeal squamous cell carcinoma: a population-based study. *Oral Oncol*. 2018;83:127-133.
8. Cohen EEW, Bell RB, Bifulco CB, et al. The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of squamous cell carcinoma of the head and neck (HNSCC). *J Immunother Cancer*. 2019;7:184-019-0662-5.
9. Masroor F, Corpman D, Carpenter DM, et al. Association of NCCN-recommended posttreatment surveillance with outcomes in patients with HPV-associated oropharyngeal squamous cell carcinoma. *JAMA Otolaryngol Head Neck Surg*. 2019; doi: 10.1001/jamaoto.2019.1934.
10. Mueller SA, Riggauer J, Elicin O, Blaser D, Trelle S, Giger R. Patients' preferences concerning follow-up after curative head and neck cancer treatment: a cross-sectional pilot study. *Head Neck*. 2019;41:2174-2181.