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Head & Neck Cancer, Neurologic tumor

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Moderator：Yoshitaka Honma（Department of Head and Neck, Esophageal Medical Oncology, National Cancer Center Hospital）
Moderator：Yoshitaka Narita（Department of Neurosurgery and Neuro-Oncology, National Cancer Center Hospital）
Discussant：Yoshitaka Narita（Department of Neurosurgery and Neuro-Oncology, National Cancer Center Hospital）
Discussant：Tomoya Yokota（Division of Gastrointestinal Oncology, Shizuoka Cancer Center）

FR5-1
Burden of Human Papillomavirus-driven Head and Neck Cancers in Japan（THE BROADEN STUDY）and HPV attributability based on p16INK4a, HPV-DNA and HPV E6*I mRNA

Nobuhiko Oridate（Department of Otolaryngology-Head and Neck Surgery, School of Medicine, Yokohama City University）

FR5-2
First-Line Pembrolizumab for Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma：5-Year Update of the Japanese Subgroup of KEYNOTE-048

Yasushi Shimizu（Hokkaido University Hospital）

FR5-3
A multicenter exploratory phase II study of neoadjuvant bevacizumab for newly diagnosed malignant glioma

Toshihide Tanaka（Neurosurgery, Hospital, The Jikei University）

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FR5-1

Burden of Human Papillomavirus-driven Head and Neck Cancers in Japan (THE BROADEN STUDY) and HPV attributability based on p16INK4a, HPV-DNA and HPV E6*I mRNA

Nobuhiko Oridate [1], Yuki Saito [2], Ken-Ichi Nibu [3], Edith Morais [4], Ya-Ting Chen [5], Jacqueline C. Spitzer [6], Kayo Sato [7], Itori Saito [7], Ichiro Tazaki [7]

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Introduction

HPV, smoking, and alcohol consumption are known key contributors for head and neck cancers (HNC). Despite decreasing rates of smoking and alcohol consumption, HNC incidence has increased, particularly for oropharyngeal cancers (OPC). This study aimed to assess HPV attributability in HNC at two time periods in Japan.

Methods

BROADEN is a non-interventional, cross-sectional, multi-center study of HNC patients diagnosed in 2008-09 and 2018-19. FFPE tumor samples were collected from patients in a consecutive-retrospective manner, using stringent ICD coding to avoid site misclassification. Tumors were centrally tested for presence of HPV-related biomarkers. HPV attributability required at least two positive tests (SPF_{10} HPV-DNA PCR, $p16^{ink4a}$ immunohistochemistry, or E6*I HPV-mRNA test) for OPC, and HPV PCR DNA plus mRNA positivity for non-OPC.

Results

Nineteen oncology centers participated, enrolling 1,108 patients with 950 valid and 158 invalid FFPE tumor samples (valid samples included 473 OPC and 477 non-OPC; 435 for 2008-09 and 515 for 2018-19). HPV attributability in OPC increased from 44.9 % in 2008-09 to 52.1 % in 2018-19. HPV attributability in oral cavity was 0 % in both 2008-09/2018-19. HPV was tested in 471 OPC tumors and 231 samples were HPV attributable. In total, 211 samples were positive on all three HPV tests, seven positive on DNA and mRNA (two had $p16^{INK4a}$ tests unavailable), five positive on DNA and $p16^{INK4a}$, and eight positive on $p16^{INK4a}$ and mRNA. Among OPC cases, 5.9 % of $p16^{INK4a}$ positive samples (14/238) were non-HPV attributable (false positive) and 2.1 % of $p16^{INK4a}$ negative samples (5/233) were HPV attributable (false negative).

Conclusions

Results of this study demonstrate the impact of HPV on OPC in Japan, with the increase of HPV attributability over time. Although good concordance was observed between HPV attributability and $p16^{INK4a}$ positivity in OPC, the presence of $p16^{INK4a}$ false-positive cases (5.9 %) contain potential clinical problems.

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FR5-2

First-Line Pembrolizumab for Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma：5-Year Update of the Japanese Subgroup of KEYNOTE-048

Yasushi Shimizu [1], Shunji Takahashi [2], Nobuhiko Oridate [3], Kaoru Tanaka [4], Yasushi Fujimoto [5], Koji Matsumoto [6], Tomoya Yokota [7], Tomoko Yamazaki [8], Masanobu Takahashi [9], Tsutomu Ueda [10], Nobuhiro Hanai [11], Hironori Yamaguchi [12], Hiroki Hara [13], Tomokazu Yoshizaki [14], Ryuji Yasumatsu [15], Masahiro Nakayama [16], Kiyoto Shiga [17], Takashi Fujii [18], Kenji Mitsugi [19], Kenichi Takahashi [20], Nijiro Nohata [20], Burak Gumuscu [21], Nati Lerman [21], Makoto Tahara [22]

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Background: Previously reported results (2020) from the phase 3 KEYNOTE-048 trial (NCT02358031) showed OS with pembrolizumab (pembro) monotherapy was better than EXTREME in the CPS ≧ 20 subgroup and was similar in the total and CPS ≧ 1 subgroups in Japanese pts with recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). OS with pembro+chemotherapy (chemo) was similar to OS with EXTREME in all subgroups. We report 5-y OS and PFS estimates for the Japanese subgroup of KEYNOTE-048.

Methods: Pts with incurable R/M HNSCC of the oropharynx, oral cavity, hypopharynx, or larynx were randomly assigned 1:1:1 to receive pembro 200 mg Q3W, pembro+chemo, or EXTREME. Primary end points were OS and PFS. Efficacy was assessed in the PD-L1 CPS ≧ 1, PD-L1 CPS ≧ 20, and total populations.

Results: In Japan, 67 pts were enrolled (pembro, 23; pembro+chemo, 25; EXTREME, 19). As of February 21, 2022, median follow-up (range) was 71.3 mo (61.2-80.3) for pembro vs EXTREME and 70.1 mo (61.2-81.5) for pembro+chemo vs EXTREME. The 5-y OS rate for pembro vs EXTREME was 23.8 % vs 12.5 % in CPS ≧ 1, 35.7 % vs 12.5 % in CPS ≧ 20, and 30.4 % vs 10.5 % in the total population. The 5-y OS rate for pembro+chemo vs EXTREME was 10.5 % vs 14.3 % in CPS ≧ 1, 20.0 % vs 14.3 % in CPS ≧ 20, and 8.0 % vs 12.5 % in the total population. The 5-y PFS rate for the total population was 4.3 % vs 5.3 % for pembro vs EXTREME and NR vs 6.3 % for pembro+chemo vs EXTREME. In the pembro, pembro+chemo, and EXTREME groups 17 (73.9 %), 11 (44.0 %), and 14 (73.6 %) pts, respectively, received subsequent anticancer therapy; 9 pts (47.3 %) in the EXTREME group received a subsequent PD-1/L1 inhibitor. No new safety signals were observed.

Conclusions: First-line pembro and pembro+chemo continued to show long-term clinical benefit and manageable safety in Japanese pts with R/M HNSCC with extended follow-up of 5 y. Results from this study further support pembro and pembro + chemo as first-line treatment for Japanese pts with R/M HNSCC.

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FR5-3

A multicenter exploratory phase II study of neoadjuvant bevacizumab for newly diagnosed malignant glioma

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Purpose: We conducted the multicenter study for neoadjuvant bevacizumab (neoBev) for newly diagnosed glioblastoma (nGB) .In this study, median overall survival (mOS) related to radiological response, of which reliability as prediction of OS were explored. Patients: A total of 15 patients with nGB were enrolled, given ring enhancement and edema on MRI. Two weeks after neoBev, the tumor volumes on T1CE and FLAIR were assessed. Three to four weeks after neoBev, surgery was performed. Clinical outcome including mOS were analyzed. Results: The average volume decrease rates on T1CE and FLAIR were -37 % and -54 %, respectively. The decrease rate on T1CE was not correlated with that on FLAIR. Based on MRI, good (GR) and poor (PR) responder on T1CE were defined as more or less of average volume reduction rate, respectively. mOS of GR and PR on T1CE were 19.8 months and 12.9 months, respectively. In contrast, mOS of GR and PR on FLAIR were 16.0 months and 17.0 months, respectively. Conclusion: mOS in the present cohort was not significantly prolonged. Early tumor volume regression on T1CE but not FLAIR after neoBev therapy has a significant prognostic indicator for mOS in nGB.

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