Head and neck Squamous Cell Carcinoma (HNSCC)

Akansha, Kevin, and Tri

Review: Head and neck squamous cell carcinoma (HNSCC)

Johnson et al.

What Is HNSCC?

- Sixth most common cancer worldwide
- Most common in adults
  - E.g median age at diagnosis of 66 years for HPV-negative HNSCC
- 30% expected increase by 2030
- Arises from squamous cells, found in outer layer of skin and mucous membranes
- Cancer develops in the mouth, nose, and throat (oral cavity)
- Like other cancers, can spread to other parts such as lymph nodes or lungs

Risk Factors

- Diverse range of risk factors:
  - Tobacco consumption, alcohol consumption, exposure to environmental pollutants and infection with viral agents (HPV and EBV)
- >35-fold higher risk of developing HNSCC for heavy users of tobacco and alcohol
- Smokeless tobacco, areca nut, betel quid associated with increased risk for HSNCC
- HPV-negative HNSCC or HPV-positive HNSCC

Risk Factors

HPV-negative HNSCC

- Triggered by substance use
- Tobacco consumption is the primary risk factor for development
- Tobacco associated with inflammation in exposed tissue, producing of cytokines, chemokines and growth factors and promoting proliferation, angiogenesis, and carcinogenesis.
- Alcohol synergizes with tobacco use to promote carcinogenesis

HPV-positive HNSCC

- Infection with HPV increases risk for HNSCC
- HPV infection is associated with most oropharyngeal cancers (>70%), less at other head and neck sites
- HPV-positive HNSCC exhibits distinct differences from HPV-negative HNSCC in gene expression, mutational and immune profiles, and more

Genomics

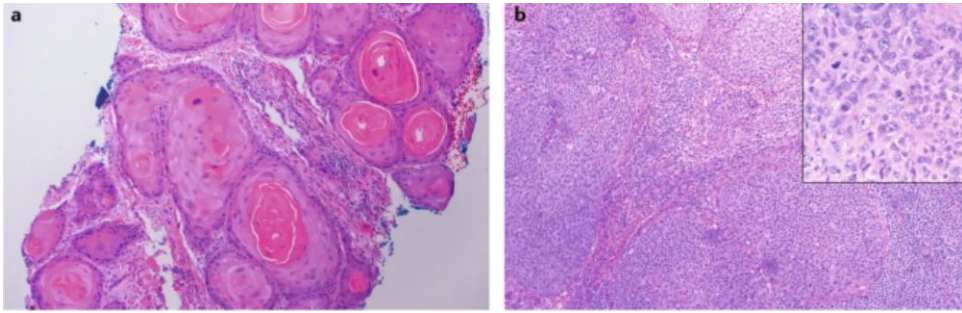
1) More driven by loss of tumor suppressors as opposed to mutations and oncogenes
    a) Loss of 9p21 region: tumor-suppressing genes CDKN2A and ARF (stabilize p53)
    b) Progression from hyperplasia → dysplasia → carcinoma : loss of regions coding for p53
    c) Dysplasia → carcinoma, carcinoma →metastasis: loss of 11q13, 13q21, 14q32, 6p, 8, 4q27, 10q23

Transcriptomics

1) p-EMT: partial epithelial-mesenchymal transition
2) Single-cell analyses of primary and metastatic tumors reveals cells w/ p-EMT are localized to leading edge of tumors
3) Predictor of metastasis, tumor grade, and pathological features

Diagnosis

- Histopathology
  - HNSCC must be established by biopsy of the primary tumour and/or neck mass
- Followed by staging evaluation:
  - complete head and neck examination with direct inspection of the oral cavity
  - CT or MRI to establish the extent of disease
  - chest CT to rule out distant metastatic disease



Prevention

Primary Prevention

- Avoidance of Tobacco, areca nut use, and other carcinogenic sources
- HPV vaccination
- Most cases of HNSCC would indeed be preventable with successful global elimination of tobacco use and implementation of HPV vaccination

Secondary Prevention

- Screening
    - Limited effect due to no validated tool existing for screening HPV-positive HNSCC

Treatment

- Highly curative approach, while optimizing preservation of function
- Use of a combination of surgery, radiation, immuno- and chemotherapy
- Continually developing treatment, as demonstrated in research paper
- Recommend treatment at high case facilities for improved survival rates

Pembrolizumab With or Without Chemotherapy in Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma: Updated Results of the Phase III KEYNOTE-048 Study

Harrington et al.

Pembrolizumab as first-line treatment for HNSCC

- Switch from EGFR-inhibitor cetuximab → programmed death 1 inhibitor pembrolizumab-chemotherapy drug clinical trial
- Updating results for phase III of clinical trial, with progression-free survival analysis

Purpose:

Analyzing the efficacy of Pembrolizumab and pembrolizumab chemotherapy for HNSCC

Methodology: Random allocation

- Eligible patients were age ≥ 18 years with previously untreated R/M squamous cell carcinoma
- Patients were randomly allocated 1:1:1
  - pembrolizumab alone
  - pembrolizumab plus platinum and 5-fluorouracil (pembrolizumab-chemotherapy)
  - cetuximab plus platinum and fluorouracil (cetuximab-chemotherapy).
- Primary endpoints were progression-free survival (PFS) and overall survival (OS). Secondary endpoints included objective response rate (ORR) and safety. Duration of response (DOR) was exploratory.

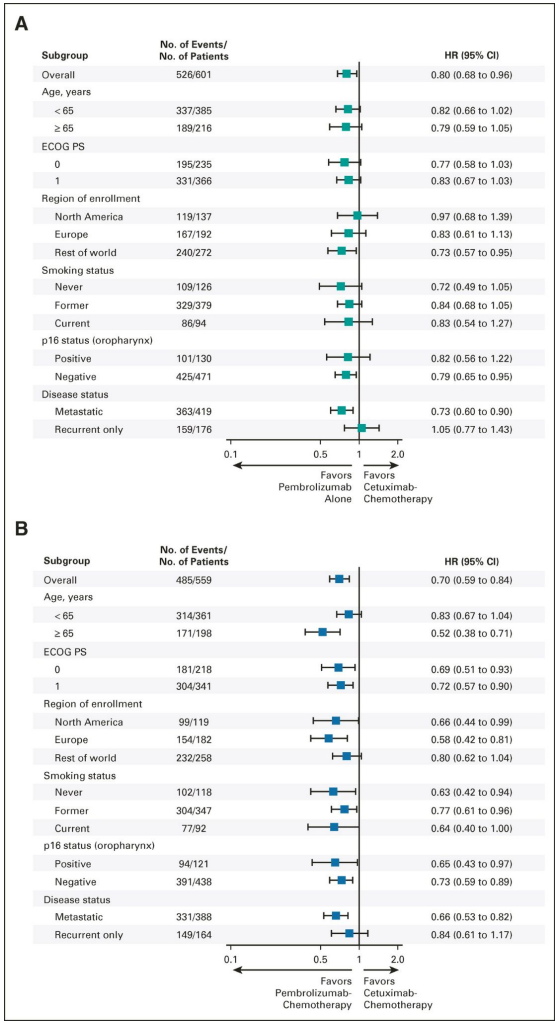


FIG 3: Subgroup Analysis of Overall Survival

1) Patients organized into subgroups. **“No. of events”** → “No. of deaths”
2) 95% confidence intervals for overall survival (months)
3) Group A: Pembrolizumab-alone vs cetuximab-chemotherapy
4) Group B: Pembrolizumab-chemotherapy vs cetuximab-chemotherapy
5) Appears that pembrolizumab overall is favored over cetuximab-chemotherapy as confidence intervals typically lean left

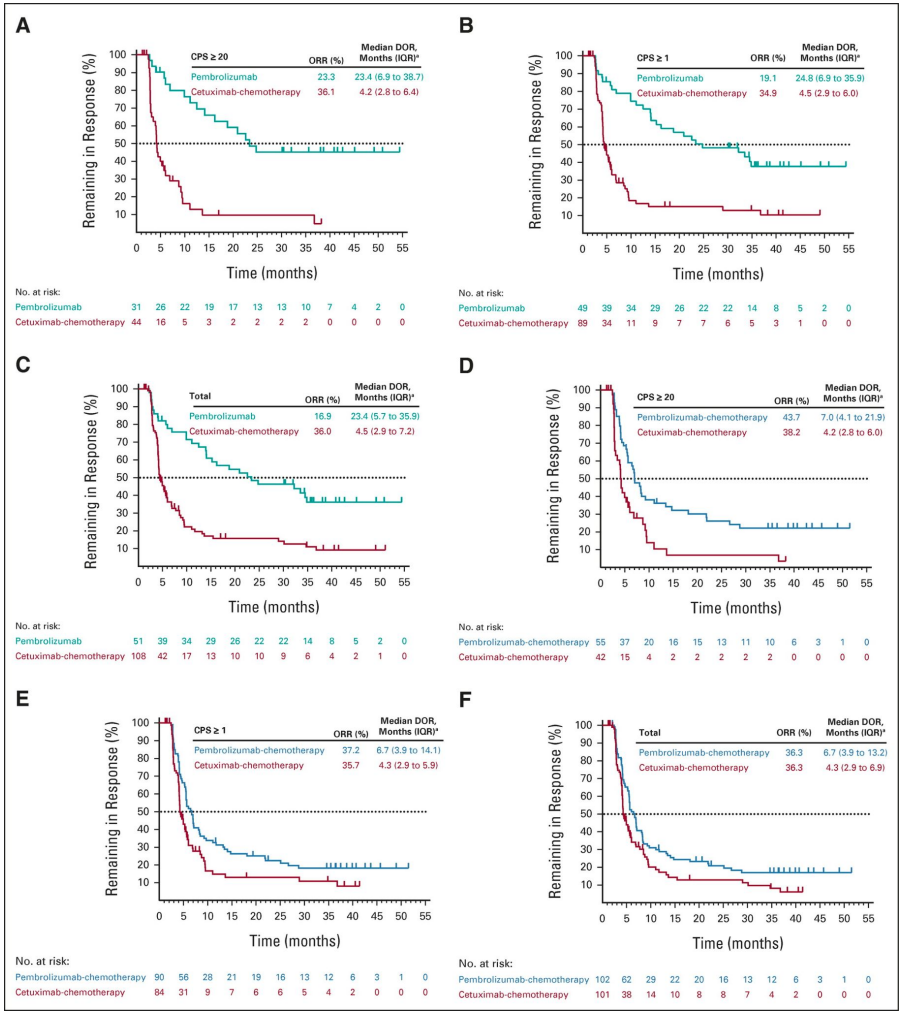


FIG 4: Kaplan-Meier for Duration of Response

1) A, B, C: pembrolizumab-alone vs. cetuximab-chemotherapy
2) D, E, F: pembrolizumab-chemotherapy vs cetuximab-chemotherapy
3) Pembrolizumab-chemotherapy and pembrolizumab-alone had higher ORR than cetuximab-chemotherapy

Results and Conclusions

Results

- Pembrolizumab alone prolonged OS vs. cetuximab-chemo (14.9 vs.10.3 months)
- PFS2 on taxane therapy was longer with pembrolizumab compared to non-taxane therapy

Conclusion

- With 4 years f/u, first-line pembrolizumab indicated better survival benefits vs. cetuximab-chemo in R/M HNSCC
- Pt react better in subsequent treatment after pembrolizumab-based therapy

Further Research

Research Directions:

- Further work into the potential risk of E-Cigarettes
- The oral microbiome, effect of oral health on oral cancers
- Further research into the effectiveness of pembrolizumab-only treatments vs. pembrolizumab-chemotherapy
- Effectiveness of current treatment on HPV-positive vs. HPV-negative cancers