Prognostic Factors in Head and Neck Cancer

Thursday, February 18, 2016, 7:00 am MT
Moderator: Christine Gourin, MD, Johns Hopkins University

- Molecular Profile of HPV-positive Oropharyngeal Squamous Cell Carcinoma Stratified by Smoking Status
  J. P. Zevallos, University of North Carolina Hospitals, Chapel Hill, NC

- Detection of Recurrence in HPV Associated Oropharynx Squamous Cell Carcinoma
  J. M. Frakes, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

- Does Age Matter? Survival Outcomes with the Addition of Concurrent Chemotherapy for Elderly Head and Neck Cancer Patients Undergoing Definitive Radiation Using the National Cancer Data Base
  S. D. Karam, University of Colorado Denver, Aurora, CO
Molecular Profile of HPV-positive Oropharyngeal Squamous Cell Carcinoma Stratified by Smoking Status

J. P. Zevallos¹,²,⁴, E. Yim², P. Brennan³, A. Y. Liu⁴, J. M. Taylor², M. Weissler¹, D. Anantharaman³, B. Abedi-Ardekani³, A. F. Olshan⁴, and D. N. Hayes⁵

¹University of North Carolina Hospitals, Chapel Hill, NC, ²Department of Otolaryngology/Head and Neck Surgery, University of North Carolina at Chapel Hill, Chapel Hill, NC, ³International Agency for Research on Cancer, Lyon, France, ⁴Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, ⁵University of North Carolina School of Medicine, Chapel Hill, NC
• HPV-positive oropharyngeal cancer (OPSCC) has an excellent prognosis compared to HPV-negative OPSCC

• Mutations and other genetic characteristics of HPV-positive oropharyngeal cancer in smokers have not been well defined

• How does dual exposure to HPV and tobacco manifest on the molecular level, and how could we use this information to guide treatment?

• Purpose: to compare the genomic characteristics of HPV-positive OPSCC in smokers and non-smokers using targeted next generation DNA sequencing

CHANCE study HPV-positive OPSCC 5 year survival:
Never smokers 82%
Ever smokers 60%
Results: Mutations

<table>
<thead>
<tr>
<th>GENE</th>
<th>Overall % mutated</th>
<th>Never smoker % mutated</th>
<th>Ever smoker % mutated</th>
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<tbody>
<tr>
<td>NOTCH1</td>
<td>14</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>FAT1</td>
<td>12</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>CASP8</td>
<td>6</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>AJUBA</td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>CDKN2A</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>TP53</td>
<td>5</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>FGFR2</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>FGFR3</td>
<td>8</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>PIK3CA</td>
<td>38</td>
<td>50</td>
<td>34</td>
</tr>
<tr>
<td>PTEN</td>
<td>8</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>PIK3R1</td>
<td>2</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>MLL2</td>
<td>24</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>MLL3</td>
<td>41</td>
<td>44</td>
<td>40</td>
</tr>
<tr>
<td>HLA-A</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>KRAS</td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>HRAS</td>
<td>2</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>
Results: Pathways in HPV-positive smokers
Results: HPV type and read depth

- HPV DNA detected in 66/66 cases
  - HPV 16 95%
  - HPV 18 0%
  - HPV 35 3%
  - HPV 58 1%

- Mean number of HPV reads/sample = 838,520

Number of HPV reads inversely related to smoking and survival status
Conclusions

- Distinct differences in genomic characteristics of HPV-positive heavy smokers vs. light smokers/non-smokers
  
  - HPV-positive smokers acquire mutations in tobacco-related genes but maintain HPV-positive signature (PI3K pathway as initiating event?)
  
  - Lower number of HPV reads associated with smoking and poor survival may suggest accumulation of tobacco-associated mutations, less dependency on E6/E7 and HPV-mediated oncogenesis
  
  - Important implications for personalizing treatment, decision-making on HPV-positive OPSCC treatment de-intensification and targeted therapies
  
  - Larger studies focused on defining high-risk HPV-positive OPSCC through DNA and RNA sequencing are currently underway at the University of North Carolina
Detection of Recurrence in HPV Associated Oropharynx Squamous Cell Carcinoma


H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL
Background

• Several retrospective and prospective trials have shown increased survival and decreased toxicity in patients with HPV+ OPSCC

• As the number of oropharyngeal cancer patients and survivors grows, so does the need to determine general time to recurrence and the most effective modes of recurrence detection, in order to guide optimal follow-up care
Method

• 246 patients with either HPV+ or p16+ OPSCC who received definitive radiotherapy, most of whom received concurrent chemotherapy (85%)

• Median follow up was 36 months

• All patients had 3 month post treatment PET/CT and physical exams every 3 months in the 1st year following treatment, every 4 months in the 2nd year, and every 6 months in years 3 through 5
• 100% of local failures were detected by physical exam, including direct visualization (n=2) or flexible laryngoscopy (n=4).

• 89% of regional failures were found due to symptoms or 3 month post treatment imaging.

• Patients with ≥5 nodes or level 4 lymph nodes present were more likely to suffer regional failure.

• 71% of distant metastases were found due to symptoms or 3 month post treatment imaging.

• Increased risk with LN > 6 cm, bilateral LN, ≥5 LN, or level 4 LNs.

**Grade ≥ 3 late toxicity occurred in 9% of patients, with resolution in the majority for an overall toxicity of 2%**
Conclusions

• The majority of recurrences and toxicities can be detected by post treatment imaging at three months and physical exam during the first six months following treatment.

• Minimizing tests that do not compromise outcomes will not only help decrease anxiety/stress for our patients but also ease the financial burden of cancer care.

• Outcomes are excellent with low rates of permanent toxicity when treatment delivered by a specialized multidisciplinary team.
Does Age Matter? Survival Outcomes with the Addition of Concurrent Chemotherapy for Elderly Head and Neck Cancer Patients Undergoing Definitive Radiation Using the National Cancer Data Base

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Background

• Chemoradiation (CRT)
  • Improves survival in locally advanced head and neck cancer
  • Decreased survival benefit with age, specifically ≥71, seen on seminal meta-analysis
  • Only 4% of patients on meta-analysis were >70 years of age
  • Under-represented elderly patient population on clinical trials

• Purpose
  • Evaluate whether the addition of chemotherapy to radiation alone confers a survival benefit in head and neck cancer patients ≥71 years
Method

• The National Cancer Database (NCDB)
  • 1998-2011
  • 23% >70

• Patients
  • ≥71 years, receiving RT +/- CT
  • Oropharynx, larynx, hypopharynx
  • Stage III and IV (T1-2, N(+) or T3-4, N0-3)
  • CRT: CT starts 14 days before or 14 days after RT

• Overall Survival Analysis
  • Cox regression: Univariate (UVA), multivariate (MVA)
  • Propensity score-matching (PSM)
  • Recursive partitioning analyses (RPA)
<table>
<thead>
<tr>
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<th>RT alone (n=1,504)</th>
<th>CRT (n=2,538)</th>
</tr>
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<tbody>
<tr>
<td>5-year overall survival (OS)</td>
<td>15.2%</td>
<td>30.3%, HR 0.59, 95% CI 0.55-0.63, p&lt;0.001</td>
</tr>
<tr>
<td>PSM, 5-year OS</td>
<td>18.1%</td>
<td>26.4%, HR 0.73, 95% CI 0.66-0.80, p&lt;0.001</td>
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</tbody>
</table>
Results

• On RPA, CRT was associated with **improved survival** in:
  - Patients ≤ 81 years old
  - Low co-morbidity (CD) score
  - Either T1-2/N2-3 or T3-4/N0-3

• On RPA, **no survival benefit** in:
  - Age > 81 years old
  - Ages 71-80 with T1-T2/ N1, CD 0-1
  - Ages 71-80 with T3-4/N1+, CD1+
Conclusions

- CRT confers longer OS over RT in subgroup of elderly patients:
  - Age ≤ 81 years
  - With T1-2, N2-3 or
  - T3-4, any N disease; and
  - Low co-morbidity scores
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Q & A

Online attendees: Please use the chat function in Adobe Connect to submit questions.
Additional questions and interview requests:

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ASTRO’s Press Office in Scottsdale
Town Hall Room, JW Marriott Camelback Resort & Spa
February 18-19, 8am-4pm MT
480-905-7935
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Slides, photos, and audio will be available following the briefing at www.astro.org/HNpress.