WELCOME
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Domiciliary Humidification Reduces Symptom Burden and Hospital Admissions Associated With Mucositis During Radiotherapy for Head and Neck Cancer: Trans Tasman Radiation Oncology Group (TROG) 07.03 RadioHUM Randomised Phase III Trial Results
A. Macann, Auckland City Hospital, Auckland, NZ

Human Papillomavirus (HPV) and Overall Survival (OS) After Progression of Oropharyngeal Squamous Cell Carcinoma (OPSCC)
C. Fakhry, Johns Hopkins Medical Institutions, Baltimore

Mutant-Allele Tumor Heterogeneity (MATH) Adds to Human Papillomavirus (HPV) Status in Predicting Outcome in Head and Neck Squamous Cell Carcinoma (HNSCC)
J. W. Rocco, Massachusetts General Hospital, Boston

Distant Metastatic Failure Patterns in Squamous Cell Cancer of the Oropharynx (SCCOP) Treated with Chemoradiation: the Impact of Human Papillomavirus (HPV)
S. Trosman, Cleveland Clinic
Domiciliary Humidification Reduces Symptom Burden and Hospital Admissions Associated With Mucositis During Radiotherapy for Head and Neck Cancer: Trans Tasman Radiation Oncology Group (TROG) 07.03 RadioHUM Randomised Phase III Trial Results

A. Macann, Auckland City Hospital, Auckland, NZ
Background

• The RadioHUM study run by TROG investigated the management of side effects from radiotherapy to the mouth and throat region.

  o This treatment causes severe inflammation and ulceration in the mouth and throat (mucositis), resulting in pain and problems with maintaining nutrition.

  o In some patients the side effects of radiotherapy are severe enough that patients need to be admitted to hospital.
Background (cont.)

- The trial included 210 patients from New Zealand and Australia.
- Fisher & Paykel Healthcare humidifiers were provided for patient use in the home during radiotherapy treatment.
  - A plastic nasal interface delivered the humidified air through the nose and could be worn while sleeping or during the day.
- The rationale for using the humidifier is based on the fact that moisturizing wounds generally enables them to heal faster.
Findings

• The need for hospitalization was reduced and the amount of time spent as an inpatient almost halved for patients using humidifiers.
  o On average, patients using humidifiers spent 57% as many days hospitalized as a control group in the study that didn’t have humidifiers (control 4.1 days; humidification 2.3 days).
  o At 3 months after radiotherapy the return of eating patterns to close to normal was also significantly higher in the group using humidifiers. (Nutritional Mode: control 4.8; humidification 5.2).
Findings (cont.)

• Many patients didn’t use the humidifier as much as was hoped.
  o Only 43% of the patients adhered to the program for appropriate use of the humidifier and met a benchmark for compliance.

• When patients were compliant in using the humidifier, there were trends for patients themselves to report a reduction in symptom burden when using humidification.
  o In patients who met the humidification compliance benchmark, a clinician assessment of symptom burden using CTCAE version 3.0 functional mucositis scores (area under the curve) was also reduced (control 8.63; humidification 6.74).
  o The proportion of compliant humidification patients who never needed a feeding tube was also increased (control 0.73; humidification 0.85).
Outcomes

• The RadioHUM study has provided efficacy signals consistent with a role for humidification in reducing symptom burden during radiotherapy for patients with head and neck cancer.
  - These efficacy signals were seen across clinician reported outcomes, patient reported outcomes, and independent outcomes like hospitalization rates.

• Although patients in the study did not use the humidifiers as much as was hoped, we obtained feedback about why some patients did not like using the humidifier.

• Our next step is to work at increasing the proportion of patients who use the humidifier effectively.
Human Papillomavirus (HPV) and Overall Survival (OS) After Progression of Oropharyngeal Squamous Cell Carcinoma (OPSCC)

C. Fakhry, Johns Hopkins Medical Institutions, Baltimore
Background

• Human papillomavirus (HPV) – a sexually transmitted infection – is now responsible for the majority of oropharyngeal squamous cell cancers (OPCs).

• HPV-positive vs. HPV-negative OPCs have better survival after treatment.

• Question: Does HPV-positivity have an impact on survival when patient has recurrence of cancer?
RTOG 0129

Arm 1
Standard fractionation (70 Gy/ 37 fx) x 7 wks
Cisplatin 100mg/m² (D 1, 22, 43)

Arm 2
Accelerated fractionation with concomitant boost (AFX-CB) {72 Gy/ 42 fx x 6 wks}
Cisplatin 100mg/m² (D 1, 22)

RTOG 0522

Arm 1
AFX-CB (70 Gy/ 35 fx) x 6 wks or IMRT
Cisplatin 100 mg/m² (D 1, 22)

Arm 2
AFX-CB (70 Gy/ 35 fx) x 6 wks or IMRT
Cisplatin 100 mg/m² (D 1, 22)
Cetuximab 400 mg/m² (pre-), 200 mg/m² (weekly)
Results

• 181 patients with recurrent disease (105 HPV-positive and 76 HPV-negative)

• Median time to disease recurrence: 8.2 vs. 7.3 months, p=0.67
Overall Survival After Disease Progression

Survival (%)

Years after Progression

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>p16-positive</th>
<th>p16-negative</th>
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</thead>
<tbody>
<tr>
<td>0 years</td>
<td>105</td>
<td>76</td>
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<tr>
<td>1 year</td>
<td>61</td>
<td>27</td>
</tr>
<tr>
<td>2 years</td>
<td>51</td>
<td>19</td>
</tr>
</tbody>
</table>

p16-positive 54.6%
p16-negative 27.6%
p<0.001
Overall Survival and Surgical Salvage

**Survival (%)**

Years after Progression

![](image1.png)

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>p16-positive</th>
<th>p16-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>29</td>
<td>20</td>
</tr>
<tr>
<td>No Surgery</td>
<td>76</td>
<td>56</td>
</tr>
</tbody>
</table>

**Surgery**

- p16-positive: 72.4%
- p16-negative: 45.0%
- p = 0.004

**No Surgery**

- p16-positive: 47.4%
- p16-negative: 20.9%
- p = 0.003
Conclusions

• HPV-positive OPC patients have longer survival than HPV-negative OPC patients.
• OPC patients who undergo surgical salvage live longer.
Mutant-Allele Tumor Heterogeneity (MATH) Adds to Human Papillomavirus (HPV) Status in Predicting Outcome in Head and Neck Squamous Cell Carcinoma (HNSCC)

J. W. Rocco, Massachusetts General Hospital, Boston
Hypothesis

- **Intratumor Heterogeneity** results in tumor cell subpopulations that are able to survive, proliferate, spread and resist therapy - resulting in treatment failure.
Representative MATH Scores

Low

Medium

High

HN_62469-Tumor
MATH 19 ± 3

HN_62601-Tumor
MATH 34 ± 4

HN_62417-Tumor
MATH 54 ± 5

Relative occurrence

0.0 0.2 0.4 0.6 0.8

± MAD
Median

± MAD
Median

± MAD
Median
MATH and HPV status improves patient outcome prognostication

- MATH was still significantly related to outcome when HPV status was taken into account.
- A substantial portion of the relation of MATH to outcome does not arise from its relationship to HPV status.
- MATH improves patient outcome prognostication beyond that provided by HPV status alone.
Summary

- MATH provides a quantitative way to measure intratumor heterogeneity based on NGS of the primary tumor.
- High MATH scores are associated with decreased overall survival.
- MATH is particularly effective in predicting outcome in patients treated with chemoradiation.
- MATH, in conjunction with HPV status, is likely an effective prognostic marker of patient outcome.
- MATH could readily be incorporated into clinical trial design assessing de-intensification strategies, or identifying patients for alternative strategies.
Conclusions

• The TCGA HNSCC data set, with four times as many patients, allowed us to validate and significantly extend our previous finding that high intra-tumor heterogeneity as measured by MATH is related to shorter overall survival in patients with HNSCC.

• Use of identical criteria allowed us to replicate our earlier results regarding both MATH and overall survival and the elevated HR found for patients with high MATH tumors being treated with chemoradiation.

• The larger number of HPV+ patients in this data set allowed us to determine that MATH was significantly related to outcome in analyses that took HPV status into account, indicating that MATH can provide additional and important prognostic information in HPV+ tumors that may well impact on treatment decisions in the near future.
Distant Metastatic Failure Patterns in Squamous Cell Cancer of the Oropharynx (SCCOP) Treated with Chemoradiation: the Impact of Human Papillomavirus (HPV)

S. Trosman, Cleveland Clinic
Human Papillomavirus (HPV)

- DNA virus shown to be tumorigenic in certain epithelial tissues (cervical, anogenital)
- High rate of detection in squamous cell carcinoma of the oropharynx (SCCOP)
  - Non-smokers, non-drinkers
  - Poorly differentiated, basaloid morphology, fewer p53 mutations
  - 60% reduction in risk of death from cancer
  - Increased sensitivity to chemoradiation
  - Similar rate of distal metastases
Our Study

- Retrospective review of 285 patients with Stage III-IV SCCOP treated with chemoradiation from 2002 to 2013
- 35 total patients identified that failed with distant metastases (DM)
  - 27/245 HPV+ patients (11%)
  - 8/40 HPV- patients (20%)
Results

Sites of Metastatic Disease in HPV+ and HPV- SCCOP

- Peritoneum
- Pleura
- Brain
- Intra-abdominal lymph nodes
- Liver
- Bone
- Lung

HPV- vs HPV+
Results

Timing of Distant Metastatic Failure

\[ p = 0.03 \]
Conclusions

• Distant metastases in HPV+ SCCOP occur later, involve more subsites, and involve sites atypical for smoking-related head and neck cancer.

• Patients may need more inclusive follow-up for longer periods of time.

• The role of imaging, such as PET/CT, may need to be expanded.

• HPV+ SCCOP is a unique disease process with a different etiology, histopathology, and clinical behavior than HPV-disease.
Q & A

Please use the Q & A function at the bottom of your screen.
For additional information or to arrange and interview with today’s authors, please contact:

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