TARGETING CANCER: TECHNOLOGY & BIOLOGY

ASTRO 56TH ANNUAL MEETING

Welcome
56th Annual Meeting
American Society for Radiation Oncology

“Palliative Care, Quality of Life and Patient-Reported Outcomes”
News Briefing

Moderator: Tracy Balboni, MD, MPH

Monday, Sept. 15, 2014
11 a.m. (PT)
Randomized Phase II Trial of Best Supportive Care, Manuka Honey Liquid, and Manuka Honey Lozenges for Prevention of Radiation Esophagitis during Chemotherapy and Radiotherapy for Lung Cancer

Lawrence B. Berk, MD, PhD; Snehal Deshmukh, MS; Shannon Fogh, MD; Kevin Roof, MD; Sherif Yacoub, MD, PhD; Thomas Gergel, MD; Kevin Stephans, MD; Andreas Rimner, MD; Albert DeNittis, MD, MS; John Pablo, MD; Justin Rineer, MD; Arnab Chakravarti, MD; Deborah Bruner, PhD, RN

Supported by RTOG grant U10 CA21661, and CCOP grant U10 CA37422 from the National Cancer Institute (NCI)
Background

• Folk literature on using honey to heal wounds.

• Four published randomized clinical trials showing efficacy of honey for prevention of radiation oropharyngeal mucositis.
  ▪ The trials used local honeys.
    ○ Biswal et al., 2003
      – 40 patients,
      – Malaysia,
      – Tea Plant honey
    ○ Motallebnejad et al., 2008
      – 40 patients
      – Iran
      – honey from Thymus and Astragale in the Alborz mountains in northern Iran
    ○ Rashad et al., 2009
      – 40 patients,
      – Egypt
      – clover plant Trifolium alexandrenum
    ○ Khanal et al., 2010;
      – 40 patients
      – Nepal
      – honey extracted from beehives of the Western Ghats forests
Methodology

• Chose to evaluate esophagitis during combined chemotherapy and radiation therapy for lung cancer.

• Randomized to:
  - No attempt at preventing the mucositis, just treating as needed
  - 10 cc Manuka honey 4 times a day from start of treatment
  - A Manuka honey lozenge (from 10 cc of honey) 4 times a day from start

• Primary endpoint was the patient’s own reporting of pain in the esophagus on a 0-10 scale at 4 weeks into treatment.

• Also looked at other time points and other related endpoints.
Results

• Enrolled 163 patients in the three arms.

• No difference between honey and no prevention at 4 weeks.

• No difference between honey and no prevention in the other endpoints except one, and that could be due to chance.
Conclusion

• Testing natural products introduces many unknown and uncontrollable variables and issues when compared to standard drug protocols.

• In this trial Manuka honey had no significant effect on preventing pain due to radiation esophagitis.

• To confirm results, a trial with a honey active in other trials is needed.
The Impact of Radiation Therapy on Lymphedema Risk and the Agreement between Subjective and Objective Lymphedema Measures: NSABP B-32 Secondary Data Analysis

S. A. McCloskey¹, H. Bandos²,³, T.B. Julian³, J. Kopec², N. Wolmark², S.J. Anderson²,³, D. Krag², E.P. Mamounas²,⁴, P.A. Ganz¹,²

¹University of California Los Angeles, Los Angeles, CA, ²National Surgical Adjuvant Breast and Bowel Project (NSABP), Pittsburgh, PA, ³Department of Biostatistics, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, ⁴MD Anderson Cancer Center Orlando, Orlando, FL, ⁵Allegheny Cancer Center at Allegheny General Hospital
Background

- Lymphedema is a known consequence of loco-regional breast cancer therapies
- Lymphedema impacts arm function, body image, and quality of life
- We performed a secondary data analysis of NSABP B-32 clinical trial data to assess the impact of RT on lymphedema risk
NSABP B-32 Secondary Data Analysis: Comparison Groups

<table>
<thead>
<tr>
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<th>Sentinel Node Biopsy → Axillary Lymph Node Dissection</th>
<th>Sentinel Node Biopsy</th>
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<tbody>
<tr>
<td></td>
<td>Radiation</td>
<td>No Radiation</td>
</tr>
<tr>
<td>Objective metric (n=3894)</td>
<td>1591 (83%)</td>
<td>331 (17%)</td>
</tr>
<tr>
<td>Subjective metric (n=730)</td>
<td>272 (78%)</td>
<td>75 (22%)</td>
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</table>

- 93% underwent breast conserving surgery
- 97% received breast or chest wall only radiation (non regional nodal radiation)
Why would breast/chest wall radiation impact lymphedema risk?

Collateral Damage to Level 1/2 Axilla
No impact of RT on measured lymphedema...

Among Women Undergoing Sentinel Node Biopsy

No impact of RT on patient reported lymphedema…
Among Women Undergoing Axillary Lymph Node Dissection

No impact of RT on measured lymphedema...

No impact of RT on patient reported lymphedema...

% RAVD>10%

% Bothersome Lymphedema

ALND
ALND+RT
Conclusions

• There is no evidence to suggest a detrimental impact of non regional nodal breast or chest wall RT on risk of lymphedema beyond surgery

• We found an interesting lack of agreement between patient reported bothersome lymphedema and measured lymphedema

• Further analyses are in progress to better understand optimal evaluation of lymphedema
Welcome
Comparison of Patient-Reported Outcomes with Single Fraction (SF) versus Multiple Fraction (MF) Palliative Radiotherapy for Bone Metastases

J. Conway¹,², I. Olivotto¹,², S. Miller¹,³, R. Halperin¹,⁴, D. Hoegler¹,⁴, E. Yurkowski⁷, Q. Gentles⁶, W. Beckham⁵, J. Stephen⁶, H. Daudt⁵, J. French², R. Olson¹,³,⁴

¹University of British Columbia; BC Cancer Agency; ²Vancouver Centre, ³Centre for the North ⁴Centre for the Southern Interior ⁵Vancouver Island Centre ⁶Fraser Valley Centre; ⁷University of Northern British Columbia
Background

• Considerable variation in fractionation for all bone mets (BM), despite evidence for equivalent efficacy for single fraction (SF) versus multiple fraction (MF) radiotherapy (RT)
  ▪ < 10% use of SFRT in the United States
  ▪ 30 – 60% in Canada and Europe

• Why the variability?
  — $ likely driving some variation
    ▪ But, variability in Canada, despite no influence of $
  — Trials often excluded patients with BM “complicated” by fracture or neurological compromise

• Why is this important?
  — SFRT is less costly, more convenient, and associated with better quality of life.
Methods

• We prospectively collected 648 patients’ self-reported:
  ▪ Pain levels
  ▪ Physical function
  ▪ Symptom frustration

• Collected in all patient who received RT for BM
  ▪ At all six BC Cancer Agency centres
  ▪ Including those with complicated bone metastases
Results

**Figure 1: All Painful BM (n=605)**

Partial Pain Response (improved by ≥1 point)

- SFRT: 73%
- MFRT: 73%

Complete Pain Response (follow-up score = 0)

- SFRT: 19%
- MFRT: 22%

p = 0.93

**Figure 2: Improvement ≥1-Point in Function and Degree of Symptom Distress**

All BM with Functional Complaints (n=453)

- SFRT: 71%
- MFRT: 77%

p = 0.20

All BM with Symptom Frustration (n=528)

- SFRT: 77%
- MFRT: 80%

p = 0.46
Results

After controlling for gender, site of primary, site of metastasis, re-treatment, or complicated BM:

• No difference in Partial Pain response by SFRT vs. MFRT
  ▪ Odds Ratio: 1.00 (95% CI 0.68 – 1.48; 0 = 0.99)

• No difference in Complete Pain Response by SFRT vs. MFRT
  ▪ Odds Ratio: 0.82 (0.53 – 1.27; p = 0.38)
Conclusion

• This prospective study supports trial evidence that SFRT = MFRT in the clinical practice setting (not just clinical trial)

• Improvements in pain, function, and degree of symptom distress were similar between SFRT and MFRT

• Indicates SFRT should be the standard management policy for uncomplicated BM

• No evidence that SF was inferior to MF in complicated BM, though this study is limited by small sample size in this subset (to date)
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Welcome
A randomized phase III study in advanced esophageal cancer (OC) to compare the quality of life (QoL) and palliation of dysphagia in patients treated with radiotherapy (RT) or chemoradiotherapy (CRT)

TROG 03.01 NCIC CTG ES.2.


The study was carried out in Australia, New Zealand, Canada and the UK and was supported by the Australian Government (NHMRC, Cancer Australia) and the NCI Canada and was independent of pharmaceutical industry support
Background

• Why did we need to look at palliative treatment for Esophageal cancer?
  ▪ Rapid advances in the treatment of some cancers have lead to more cures.
  ▪ Other cancers have defied our best curative therapies and this leads to either futile toxic treatments or no active treatment at all.
  ▪ We needed better information on which patients could not be cured and how we could help them.
Analysis

• 90% of patients with advanced esophageal cancer have swallowing problems.
  ▪ Many patients have the cancer bypassed by a stent or a tube. This can be painful and eventually block swallowing.

• Quality of life assessment measures the relief of symptoms and the effects – good and bad – of treatment.

• This trial measured:
  ▪ Swallowing improvement
  ▪ Overall quality of life
  ▪ How long the benefit lasted
Results

- RT alone improved swallowing in 67.89% of patients compared to 73.87% of those receiving RT + chemo, this was not a significant difference (p=0.34).

- However, chemo caused increased toxicity with more nausea (p<0.01) and vomiting (p<0.01).

- Quality of life Eating domain was improved in 74% with RT alone and 68% when chemo was added.
Results – Overall Survival

- No significant, or even possibly extrapolated difference between the curves.
- 21 patients (approx. 10%) still alive at 2 years
  - All thought to be incurable with advanced disease, responded to simple treatment.
Conclusion

- RT alone remains an excellent tool for palliation of patients with advanced OC and should remain the standard of care.

- The trial better defines people who are not curable, as well as patients who still have hope of cure with active cancer treatment, even a simple 2 week course of RT.

- Chemotherapy, however, statistically increased toxicity, but not symptom benefit or survival.

- All patients with esophageal cancer should receive the opinion of a radiation oncologist regarding the best treatment for their disease.
ICORG 05-03: Prospective Randomised Non-inferiority Phase III Trial Comparing 2 Radiation Schedules in Malignant Spinal Cord Compression (not proceeding with surgical decompression)

P. Thirion; L. Sullivan; A. Clayton-Lea; C. Small; O. Mc Ardle; P. Kelly; I. Parker; J. O’Sullivan; D. Hacking; C. Collins; M. Pomeroy; M. Moriarty

All Ireland Cooperative Oncology Research Group
Background & Methodology

• Malignant Spinal Cord Compression (MSCC)
  • occurs in patients with advanced cancer, usually with bone involvement
  • is related to (nerve) spine compression by secondary deposit(s)
  • exposes to pain, paralysis, or incontinence
  • Is usually treated by decompressive surgery and radiotherapy

• Trial Objective:
  ▪ To compare prospectively 2 fractionation radiotherapy schedules (20 Gy / 5# vs. 10 Gy / 1#) in patients with malignant spinal cord compression not proceeding with surgical decompression.

• Trial design:
  ▪ ICH-GCP compliant prospective randomised non-inferiority phase III trial
  ▪ Power: 80%, significance level : 5%, +0.4 non-inferiority margin in mobility change at 5 weeks
  ▪ Sample size: 76 evaluable patients (alive at 5 weeks), requiring an
Methodology (2)

• Eligibility Criteria:
  - Pathologically proven metastatic cancer (excluding haematological/germ cell malignancies)
  - MRI documented treatment naïve symptomatic MSCC.

• Two arms:
  - Control arm: EBRT: 20 Gy / 5 #
  - Experimental arm: EBRT: 10 Gy / 1 #
  - Radiotherapy technique according to institutional practice, no central QA

• End-points:
  - Primary:
    - Change in mobility status at 5 weeks (Modified Tomita 3 points scale)
  - Secondary end-points:
    - Change in bladder control status at 5 weeks (In-house 3 points scale)
    - Acute & long-term toxicity (RTOG scale)
    - Overall survival
Results (1)
Patient Population Characteristics

- Accrual period: 2006-2014, 5 participating centres, showing the challenge of research in the area of palliative radiotherapy
- Main patient characteristics similar in both treatment arms

<table>
<thead>
<tr>
<th>Main Patient Characteristics</th>
<th>Eligible patients (116)</th>
<th>Evaluable patients (76)</th>
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<tbody>
<tr>
<td></td>
<td>Control arm (38)</td>
<td>Experimental arm (38)</td>
</tr>
<tr>
<td>Age (Median, min-max)</td>
<td>68.7 (29.7 – 87.4)</td>
<td>68.7 (33.3 – 87.4)</td>
</tr>
<tr>
<td>KPS (Median, min-max)</td>
<td>60 (30-100)</td>
<td>70 (40 – 100)</td>
</tr>
<tr>
<td>Gender ratio (♀/♂)</td>
<td>36.2% / 63.8%</td>
<td>47.4% / 52.6%</td>
</tr>
<tr>
<td>Primary (Prostate / Breast/ Lung)</td>
<td>24.3% / 20% / 19.1%</td>
<td>28.9% / 28.9% / 5.3%</td>
</tr>
<tr>
<td>Cervical / Thoracic / Lumbar / Sacrum / X levels</td>
<td>4.3% / 67% / 23.5% / 2.6% / 2.6%</td>
<td>2.6% / 65.7% / 21.1% / 5.3% / 5.3%</td>
</tr>
<tr>
<td>Baseline Mobility Status (Unaided / Walking with aid / Bed-bound)</td>
<td>41.7% / 25.3% / 33%</td>
<td>47.4% / 28.9% / 23.7%</td>
</tr>
<tr>
<td>Baseline Bladder Function Status (Continent / Incontinent / Catheterised)</td>
<td>73% / 6.1% / 20%</td>
<td>68.4% / 10.5% / 21.1%</td>
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Results (2)

• Primary end-point:
  - No difference in change in mobility at 5 weeks between the 2 arms.
  - Only 10% of patients experienced an improvement, 58-68% of patients experiencing a stabilization.

• Secondary functional end-points:
  - No difference between treatment arms in bladder control change at 5 weeks, Neurological Deterioration-Free Survival (duration of functional stabilisation and improvement) and Overall Survival (median overall survival= 4 months).

• Toxicity (favourable):
  - Acute: 1 non-neurological G3 event (in experimental arm), no G4-5 toxicity.
  - Long-term: 2 non-neurological G3 events (1 in each arm), no G4-5 toxicity.
Conclusions

• ICORG 05-03 results:
  ▪ Patient with MSCC treated by external beam radiation therapy alone have a poor vital and functional prognosis.
  ▪ Radiotherapy alone provides only short term functional stabilisation.
  ▪ 10 Gy -single fractionation radiation schedule provides similar outcome than 20 Gy / 5 fractions.

• In clinical daily practice:
  ▪ Patient should be proposed Direct Decompressive Surgery followed by Radiotherapy when appropriate (current standard of care).
  ▪ If patient not considered for surgery, a 10 Gy-single fraction schedule is a reasonable standard.

• Further clinical research is warranted and should be supported to improve the outcome of patients diagnosed with MSCC.
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