NEWS BRIEFING
The briefing will begin shortly.
Initial report of a randomized trial comparing conventional- vs conventional plus fluciclovine \textsuperscript{(18}F\textsubscript{)} PET/CT imaging-guided post-prostatectomy radiotherapy for prostate cancer (LBA-1)

*Dr. Ashesh Jani, Winship Cancer Institute of Emory University*

CCTG SC.24/TROG 17.06: A randomized phase II/III study comparing 24Gy in 2 stereotactic body radiotherapy (SBRT) fractions versus 20Gy in 5 conventional palliative radiotherapy (CRT) fractions for patients with painful spinal metastases (LBA-2)

*Dr. Arjun Sahgal, Sunnybrook Cancer Center of University of Toronto*

Phase III randomized trial of postoperative adjuvant conventional radiation (3DCRT) versus image guided intensity modulated radiotherapy (IG-IMRT) in cervical cancer (PARCER): Final analysis (Abstract 2)

*Dr. Supriya Chopra, Tata Memorial Centre*

Stereotactic ablative fractionated radiotherapy versus radiosurgery for oligometastatic neoplasia to the lung: A randomized phase II trial (Abstract 5)

*Dr. Shankar Siva, Peter MacCallum Cancer Centre*

Stereotactic radiosurgery versus whole-brain radiation therapy for patients with 4-15 brain metastases: A phase III randomized controlled trial (Abstract 41)

*Dr. Jing Li, The University of Texas MD Anderson Cancer Center*
Initial Report of a Randomized Trial Comparing Conventional- vs Conventional plus Fluciclovine (^{18}F) PET/CT Imaging-Guided Post-Prostatectomy Radiotherapy for Prostate Cancer

Ashesh B. Jani, MD, FASTRO

Winship Cancer Institute of Emory University
Disclosures

Funding Source: NIH – RO1 CA169188 (PI’s: Dr. Ashesh B. Jani / Dr. David Schuster)

• Dr. Ashesh B. Jani:
  • Employee: Emory University / The Emory Clinic
  • Advisory Board: Blue Earth Diagnostics, Ltd. (last in 3/2018)

• Dr. Mark Goodman:
  • Royalties: Nihon MediPhysics Co, Ltd.

• Dr. David Schuster:
  • Consultant: Syncona; AIM Specialty Health; Global Medical Solutions Taiwan; Progenics Pharmaceuticals, Inc.
  • Research Grants: Blue Earth Diagnostics, Ltd; Nihon MediPhysics Co, Ltd.; Telix Pharmaceuticals (US) Inc.; Advanced Accelerator Applications; FUJIFILM Pharmaceuticals U.S.A., Inc; Amgen

• Emory University:
  • Blue Earth Diagnostics, Ltd. (Cassette Arrangement)
Background

• The decision to offer radiation after prostatectomy for patients with recurrent prostate cancer is complex
  • High failure rates
  • More accurate radiation therapy decisions and treatment planning needed
  • Limitations of conventional imaging
Background

- The decision to offer radiation after prostatectomy for patients with recurrent prostate cancer is complex
  - High failure rates
  - More accurate radiation therapy decisions and treatment planning needed
  - Limitations of conventional imaging

MOLECULAR IMAGING
EMPIRE-1 Trial

Emory Molecular Prostate Imaging for Radiotherapy Enhancement

NIH RO1 CA169188
Jani & Schuster
ClinicalTrials.gov: NCT01666808

EMPIRE-1 Trial

Patient consent / enrollment / eligibility:
Adenocarcinoma of prostate, post RRP
Detectable PSA
Negative Bone Scan
CT or MR of abd/pelvis showing no extra-pelvic metastases
Radiotherapy Decision Attestation Sheet completed by provider

Stratify:
Pathologic Risk Factors [(one or more of: ECE, SV invasion, +margins, or node+) vs none]
Pre-radiotherapy PSA level (≤2.0 ng/mL vs > 2.0 ng/mL)
Androgen deprivation therapy intent (yes vs no)

Randomize

Arm A:
Radiotherapy planning based on standard imaging

Arm B:
Treatment decisions and planning volumes based on standard imaging recorded.
FACBC scan done
Radiotherapy decisions and planning based on FACBC scan.

Fluciclovine (18F) Findings/Treatment decision:

1. Extra-pelvic uptake:
   Abort XRT
2. Pelvic nodal uptake:
   Prostate bed
   (64.8-70.2/1.8Gy)
   + Pelvis
   (40.5-50.4/1.8Gy)
3. Prostate-bed only uptake:
   Prostate bed
   (64.8-70.2/1.8Gy)
4. No uptake:
   Prostate bed
   (64.8-70.2/1.8Gy)
Failure-Free Survival

- Three years after treatment, failure-free survival rates were higher in the PET arm.
- FFS benefit remained four years after treatment.
- Median follow-up:
  - Overall: 2.48 Y
  - Failure-free pts: 3.06 Y

*PRIMARY ENDPOINT

3Y-FFS: 63.0% vs 75.5%
P=0.003 (Z test)

4Y-FFS: 51.2% vs 75.5%
P < 0.001 (Z test)
Provider-Reported Toxicity (CTCAE v.5.0)

No significant differences in maximum:
  • Acute GU
  • Acute GI
  • Late GU
  • Late GI

Suggests treatment to PET-directed volumes was tolerable.

Patient-reported toxicity (AUA & EPIC-CP) analysis pending

<table>
<thead>
<tr>
<th>Acute GU (max)</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm A/1 (no PET)</td>
<td>7 (8.64%)</td>
<td>53 (65.43%)</td>
<td>18 (22.22%)</td>
<td>3 (3.70%)</td>
<td>0.255</td>
</tr>
<tr>
<td>Arm B/2 (PET)</td>
<td>3 (3.95%)</td>
<td>55 (72.37%)</td>
<td>18 (23.68%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acute GI (max)</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm A/1 (no PET)</td>
<td>23 (28.40%)</td>
<td>47 (58.02%)</td>
<td>11 (13.58%)</td>
<td>0 (0.00%)</td>
<td>0.436</td>
</tr>
<tr>
<td>Arm B/2 (PET)</td>
<td>18 (23.68%)</td>
<td>42 (55.26%)</td>
<td>16 (21.05%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Late GU (max)</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm A/1 (no PET)</td>
<td>6 (7.50%)</td>
<td>32 (40.00%)</td>
<td>37 (46.25%)</td>
<td>5 (6.25%)</td>
<td>0.678</td>
</tr>
<tr>
<td>Arm B/2 (PET)</td>
<td>10 (13.33%)</td>
<td>29 (38.67%)</td>
<td>31 (41.33%)</td>
<td>5 (6.67%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Late GI (max)</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm A/1 (no PET)</td>
<td>47 (58.75%)</td>
<td>23 (28.75%)</td>
<td>10 (12.50%)</td>
<td>0 (0.00%)</td>
<td>0.580</td>
</tr>
<tr>
<td>Arm B/2 (PET)</td>
<td>49 (65.33%)</td>
<td>20 (26.67%)</td>
<td>6 (8.00%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions/Summary

- Randomized trial of imaging tests with primary cancer control endpoint are important but uncommon

- First trial of PET over conventional imaging alone for post-prostatectomy radiation therapy (Note: single institution study where radiotracer was invented)

- **Inclusion of fluciclovine (\(^{18}\text{F}\)) resulted in significant improvement in failure rate at 3Y**

- Integration of novel PET radiotracers into XRT decisions and planning warrant further study
**PET Findings / Treatment decision:**

1. Extra-pelvic uptake: Abort XRT
2. Pelvic nodal uptake: Prostate bed + Pelvis XRT (Boost sites of uptake)
3. Prostate-bed only uptake: Prostate bed XRT (Boost sites of uptake)
4. No uptake: Prostate bed XRT (no boost)

---

**Boost:**
- Pelvic nodes: 54-56 Gy
- Prostate bed: 70-76 Gy
CCTG SC.24/TROG 17.06: A Randomized Phase II/III Study Comparing 24gy in 2 Stereotactic Body Radiotherapy (SBRT) Fractions Versus 20gy In 5 Conventional Palliative Radiotherapy (CRT) Fractions for Patients with Painful Spinal Metastases

Arjun Sahgal, MD
Sunnybrook Odette Cancer Centre, University of Toronto
Disclosures

• Employer: University of Toronto
• Research grants: Elekta, BrainLAB, Varian
• Consulting services: Elekta, Merck, Abbvie, Roche
• Honoraria and Travel Support: Elekta, Medtronic, BrainLAB, Varian, Accuray
• Advisory Board: Varian, VieCURE, ISRS, AOSPINE Tumour Knowledge forum co-chair

• Full author list: Arjun Sahgal (PI), Sten Myrehaug, Shankar Siva, Giuseppina L. Masucci, Mathew Foote, Michael Brundage, Jim Butler, Edward Chow, Michael G. Fehlings, Zsolt Gabos, Jeffrey Greenspoon, Marc Kerba, Young Lee, Mitchell Liu, Pejman J. Maralani, Isabelle Thibault, Rebecca K. Wong, Maaike Hum, Keyue Ding, Wendy R. Parulekar
Overview

• **Purpose**: For patients with painful spinal metastases, determine if complete pain response rate can be improved with spine SBRT vs. CRT

• SBRT fractionation scheme of 24 Gy in 2 fractions* compared with standard of care CRT regimen of 20 Gy in 5 fractions

• Phase 2/3 randomized controlled trial
Trial Design

**Primary Endpoint**
Complete Pain Response (CR) rate at 3 months

**Secondary Endpoints**
- CR at 6 months
- Radiation Site Specific (RSS) Progression-Free Survival (RSS PFS) at 3 and 6 months
  - Quality of Life (QOL)
  - Change in the total SINS at 3 and 6 months
  - Overall Survival (OS)

---

**Painful Spine Metastases**
(Up to 3 contiguous segments)

1:1 randomization

**SBRT**
- 24 Gy in 2 fractions
- N=114

**CRT**
- 20 Gy in 5 fractions
- N=115
Trial Participants

- Initial Phase 2 RCT converted to a Phase 3 RCT without interruption of accrual
- Accrual period: January 2016 – September 2019

<table>
<thead>
<tr>
<th>Category</th>
<th>SBRT</th>
<th>CRT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients randomized</td>
<td>114</td>
<td>115</td>
<td>229</td>
</tr>
<tr>
<td>Did not receive study treatment</td>
<td>4</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Not evaluable at 3 months</td>
<td>16</td>
<td>22</td>
<td>38</td>
</tr>
<tr>
<td>Intent to treat (ITT) analyses</td>
<td>114</td>
<td>115</td>
<td>229</td>
</tr>
<tr>
<td>Safety/QA Analyses (as-treated)</td>
<td>110</td>
<td>115</td>
<td>225</td>
</tr>
</tbody>
</table>
### Results: Pain Response Rates

<table>
<thead>
<tr>
<th></th>
<th>SBRT (N=114)</th>
<th>CRT (N=115)</th>
<th>SBRT (N=114)</th>
<th>CRT (N=115)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complete response</strong></td>
<td><strong>35%</strong></td>
<td><strong>14%</strong></td>
<td><strong>16%</strong></td>
<td><strong>32%</strong></td>
</tr>
<tr>
<td><strong>Partial response</strong></td>
<td><strong>18%</strong></td>
<td><strong>25%</strong></td>
<td><strong>16%</strong></td>
<td><strong>9%</strong></td>
</tr>
<tr>
<td><strong>Stable disease</strong></td>
<td><strong>24%</strong></td>
<td><strong>30%</strong></td>
<td><strong>27%</strong></td>
<td><strong>23%</strong></td>
</tr>
<tr>
<td><strong>Progressive disease</strong></td>
<td><strong>6%</strong></td>
<td><strong>12%</strong></td>
<td><strong>7%</strong></td>
<td><strong>4%</strong></td>
</tr>
<tr>
<td><strong>Indeterminant</strong></td>
<td><strong>18%</strong></td>
<td><strong>19%</strong></td>
<td><strong>34%</strong></td>
<td><strong>32%</strong></td>
</tr>
<tr>
<td><strong>Mean change in total SINS (SD)</strong></td>
<td><strong>-0.94 (1.69)</strong></td>
<td><strong>-0.49 (1.61)</strong></td>
<td><strong>-0.74 (1.99)</strong></td>
<td><strong>-0.73 (1.86)</strong></td>
</tr>
</tbody>
</table>
## Multivariable Analyses for CR at 3 and 6 months

<table>
<thead>
<tr>
<th>Variable</th>
<th>3 Month Assessment</th>
<th>6 Month Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>95%CI</td>
</tr>
<tr>
<td>SBRT</td>
<td>3.47</td>
<td>1.77-6.80</td>
</tr>
<tr>
<td>CRT</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Age ≥ 65</td>
<td>1.58</td>
<td>0.82-3.06</td>
</tr>
<tr>
<td>Age &lt; 65</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.33</td>
<td>0.54-3.26</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>ECOG 2</td>
<td>0.74</td>
<td>0.19-2.89</td>
</tr>
<tr>
<td>ECOG 0 or 1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pain Score at Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 to 10</td>
<td>0.92</td>
<td>0.39-2.20</td>
</tr>
<tr>
<td>5 to 7</td>
<td>0.74</td>
<td>0.36-1.54</td>
</tr>
<tr>
<td>2 to 4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Primary Cancer:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GU (excluding RCC)</td>
<td>1.22</td>
<td>0.32-4.65</td>
</tr>
<tr>
<td>Lung</td>
<td>1.49</td>
<td>0.54-4.08</td>
</tr>
<tr>
<td>Other</td>
<td>0.58</td>
<td>0.09-3.77</td>
</tr>
<tr>
<td>Breast</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total baseline SINS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 to 12</td>
<td>1.12</td>
<td>0.58-2.15</td>
</tr>
<tr>
<td>≤ 6</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

• This is the first Phase 3 randomized trial to show that dose escalation with modern radiation therapy techniques improves pain outcomes for patients with spinal bone metastases

• Spine SBRT is superior to CRT and achieved a 21% absolute increase in the CR to pain at 3 months, which was durable at 6 months and statistically significant

• A regimen of 24 Gy in 2 SBRT fractions was safe, non-destabilizing and associated with better patient financial perception
Phase III Randomized Trial of Postoperative Adjuvant Conventional Radiation (3DCRT) versus Image Guided Intensity Modulated Radiotherapy (IG-IMRT) in Cervical Cancer (PARCER): Final Analysis

Supriya Chopra, MD
Tata Memorial Centre
Disclosures

Research Funding PARCER Trial

• Department of Science and Technology, India
• Department of Atomic Energy, Clinical Trials Centre, India.

• Other Research Funding: Varian International, Terry Fox Foundation, Terry Fox International, Department of Atomic Energy Clinical Trials Centre, India

• Full author list: S. Chopra,¹ T. Dora,² S. Gupta,¹ S. Kannan,¹ R. Engineer,³ S. Menachery,¹ R. Phurailatpam,¹ U.M. Mahantshetty,⁴ J. Swamidas,¹ J. Ghosh,¹ A. Maheshwari,⁴ S. TS,⁴ R. Kerkar,⁴ K. Deodhar,⁴ P. Popat,⁵ and S.K. Shrivastava⁴; ¹ACTREC, Tata Memorial Centre, Homi Bhabha National Institute, Navi Mumbai, India, ²Homi Bhabha Cancer Hospital, Tata Memorial Centre, Sangrur, India, ³Tata Memorial Hospital, Mumbai, India, ⁴Tata Memorial Hospital, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India, ⁵Homi Bhabha National Institute, Mumbai, India
Background

• Postoperative Radiation indicated for Cervix and Endometrial Cancers.

• Increase in GI symptom burden and toxicity in long term survivors after adjuvant radiation

• Phase II Studies
  • RTOG 0418/ RTCMIENDOMETRE demonstrated 27-28% acute GI toxicity with IMRT
  • No comparator arm

• Phase III Trial
  • NRG 1203: Improvement in patient reported outcomes at wk 5 and year 1 with IMRT as compared to 3DCRT.
  • No difference at 3 years with IMRT.

• Lack of Clarity on Long Term Impact of Postoperative IMRT
Hypothesis

*IG-IMRT will improve late GI toxicity free survival in patients undergoing adjuvant RT for cervix cancer.*

Conducted across 3 clinical sites of Tata Memorial Centre

NCT01279135/CTRI2012/120349
## Study Eligibility

<table>
<thead>
<tr>
<th><strong>Inclusion Criteria</strong></th>
<th><strong>Exclusion Criteria</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cervical Cancer</td>
<td>• Positive Para aortic nodes or indication for extended field RT.</td>
</tr>
<tr>
<td>• Age &gt;18 years</td>
<td>• History of multiple previous abdominal surgeries/radiation</td>
</tr>
<tr>
<td>• Type III Hysterectomy with intermediate or high risk features</td>
<td>• Any medical condition predisposing to bowel toxicity</td>
</tr>
<tr>
<td>• Type I/II hysterectomy necessitating adjuvant CRT</td>
<td></td>
</tr>
</tbody>
</table>
**Study Inclusion**

Central review of Target Delineation.

**Randomization**

**3DCRT**

**IMRT**

**Trial Schema: PARCER**

Baseline QOL/CTCAE

Weekly CTCAE

QOL CTCAE version 3.0

Scheduled Follow up, Clinical evaluation, Quality of Life, CTCAE, Every 3 monthly for 2 years. Every 6 monthly year 2-5. Yearly thereafter. Censoring at last follow up or relapse.
Primary Endpoint

Grade ≥ II GI Toxicity Free Survival

Number at risk (number censored)

<table>
<thead>
<tr>
<th></th>
<th>3DCRT</th>
<th>IGIMRT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>141 (19)</td>
<td>142 (14)</td>
</tr>
<tr>
<td>12</td>
<td>101 (19)</td>
<td>112 (28)</td>
</tr>
<tr>
<td>24</td>
<td>60 (10)</td>
<td>76 (13)</td>
</tr>
<tr>
<td>36</td>
<td>44 (3)</td>
<td>61 (11)</td>
</tr>
<tr>
<td>48</td>
<td>39 (12)</td>
<td>49 (12)</td>
</tr>
<tr>
<td>60</td>
<td>27 (9)</td>
<td>35 (12)</td>
</tr>
<tr>
<td>72</td>
<td>17 (5)</td>
<td>23 (12)</td>
</tr>
<tr>
<td>84</td>
<td>12 (8)</td>
<td>11 (9)</td>
</tr>
<tr>
<td>96</td>
<td>2 (2)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>108</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>120</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Time since random assignment (months)

p log rank = 0.009, HR 0.47 (95% CI 0.30-0.74)

Adjusted for stratification factors- RT type and Sx type

78% vs. 57%
Pelvic Relapse Free Survival

\[ p_{\text{log rank}} = 0.84, \text{ HR } 0.91 \text{ (95\% CI } 0.39-2.15) \]

<table>
<thead>
<tr>
<th>Time since random assignment (months)</th>
<th>Number at risk (No. censored)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3DCRT</td>
</tr>
<tr>
<td></td>
<td>141 (13) 124 (21) 100 (17) 80 (17) 63 (20) 43 (11) 32 (9) 23 (15) 8 (7) 1 (0)</td>
</tr>
</tbody>
</table>

2020 AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO) ANNUAL MEETING
### Planned Subgroup Analysis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Events/Patients</th>
<th>Hazard Ratio (95% CI)</th>
<th>P (Interaction)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of RT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT+RT</td>
<td>41/107</td>
<td>0.40 (0.23, 0.69)</td>
<td>0.204</td>
</tr>
<tr>
<td>RT Alone</td>
<td>13/ 34</td>
<td>0.78 (0.33, 1.84)</td>
<td></td>
</tr>
<tr>
<td><strong>Type of Surgery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wertheim's</td>
<td>29/71</td>
<td>0.61 (0.34, 1.08)</td>
<td>0.165</td>
</tr>
<tr>
<td>Simple .</td>
<td>25/70</td>
<td>0.32 (0.15, 0.69)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>54/141</td>
<td>0.47 (0.30, 0.74)</td>
<td></td>
</tr>
</tbody>
</table>

Favors IGIMRT | Favors 3DCRT
Conclusions

• IG-IMRT is superior to 3DCRT in reducing Late GI toxicity in women undergoing postoperative pelvic RT.

• Greater Benefit of IG-IMRT in those receiving radio-sensitizing concurrent chemotherapy.

• No difference in tumour control rates in the pelvis with use of IG-IMRT

• IG-IMRT should represent the new standard of care for postoperative pelvic RT in women with gynecological cancers.
Stereotactic Ablative Fractionated Radiotherapy versus Radiosurgery for Oligometastatic Neoplasia to the Lung: A Randomized Phase II Trial

Shankar Siva, MD
Peter MacCallum Cancer Centre
Disclosures

• Research funding: Varian Industries, Merck-Sharp-Dohme, Astra Zeneca, Bayer Pharmaceuticals
• Speaker Honoraria: Astra Zeneca, Bristol Meyer Squibb, Reflexion
• Travel support: Astra Zeneca

• Full author list:
The lung is the second most common place for cancer to spread

Most patients are treated with lifelong anti-cancer drug therapy only, with little prospect for long term cancer control

Some patients have limited spread to the lungs, and may be suitable for surgery (invasive) or Stereotactic body radiotherapy (SBRT, non-invasive)

In this study, we evaluated two schedules of SBRT, single session and multi-session, for patients with limited secondary spread to the lung
TROG 13.01 SAFRON II: Trial Summary

Key Inclusion: ≤3 secondaries to the lung from any non-blood malignancy, tumor size ≤ 5cm, peripheral lung location, all primary and extrathoracic disease treated

- Primary Endpoint: Severe side effects at 1 year
- Total sample size = 90 patients over 3 years (13 centers Australia and NZ), recruited 2015-2018
Side effects (any grade) and difference between arms

Higher swallowing symptoms and skin rash with multi-session SBRT

Single session: multi session
Primary Endpoint – high grade side effects within 1 year

• ARM 1 (single fraction) - There were two patients with grade 3 (medical intervention) events, both lasted < 3 months in duration, with no grade 4 (life threatening) or 5 (fatal) events.

• ARM 2 (four fraction) – There was one patient with a grade 5 event (pneumonitis within 3 months of SBRT, underlying ILD), with no grade 3 or 4 events.

• Grade 3+ toxicities related to treatment within 1 year
  • ARM 1 = 5% [80% CI: 1-14]
  • ARM 2 = 3% [80% CI: 0.3% - 10%]
Oncological Outcomes – Local Control

Freedom from local failure % (95% CI) at 12 months by arm

Single Fraction = 93% (79, 98)
Multi Fraction = 95% (81, 99)
Oncological Outcomes – Recurrence, Survival

Kaplan-Meier estimates % (95% CI) at 12 months by arm

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Single Fraction</th>
<th>Multi Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival</td>
<td>95 (83, 99)</td>
<td>93 (80, 98)</td>
</tr>
<tr>
<td>Disease free survival</td>
<td>59 (43, 72)</td>
<td>60 (44, 73)</td>
</tr>
</tbody>
</table>
Conclusions

• Both single fraction (28Gy) and four fraction (48Gy) SBRT have acceptable toxicity for patients with 1-3 secondary cancer deposits in the lung

• Oncological outcomes from both approaches appear similar to 1-year
IMPACT - WHAT DOES THIS MEAN?

- Single session SBRT is convenient, non-invasive safe and appears effective to date for lung secondaries
- Maybe considered a one-stop, ‘knockout punch’
- These findings may have implications for treatment selection in resource-constrained environments (such as the pandemic)
Stereotactic Radiosurgery Versus Whole-brain Radiation Therapy For Patients With 4-15 Brain Metastases: A Phase III Randomized Controlled Trial

Jing Li, MD, PhD
University of Texas MD Anderson Cancer Center
Disclosures

- Employer: University of Texas – MD Anderson Cancer Center
- Research funding from BMS
- Research funding from Medtronic
- Honorarium from Novocure and Monteris
- MD Anderson internal research grants

- Full author list: J. Li, E.B. Ludmir, Y. Wang, N. Guha-Thakurta, M.F. McAleer, S.H. Settle, Jr, D.N. Yeboa, A.J. Ghia, S.L. McGovern, C. Chung, K.D. Woodhouse, T.M. Briere, C.M. Sullaway, D.D. Liu, G. Rao, E.L. Chang, A. Mahajan, E.P. Sulman, P.D. Brown, and J.S. Wefel; 1Department of Radiation Oncology, Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, 2Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, 3The University of Texas MD Anderson Cancer Center, Houston, TX, 4Anchorage Radiation Therapy Center, Anchorage, AK, United States, 5University of Texas MD Anderson Cancer Center, Houston, TX, 6Department of Radiation Oncology, University of Southern California Keck School of Medicine, Los Angeles, CA, 7Department of Radiation Oncology, Mayo Clinic, Rochester, MN, 8New York University, Department of Radiation Oncology, New York City, NY
Background

- Up to 30% of cancer patients develop brain metastases
  - Rising incidence due to prolonged survival and better imaging surveillance
  - Historically poor overall survival (~1-4 months)
    - Main treatment modalities: radiation and surgery
    - Whole brain radiation (WBRT) associated with significant cognitive side effects
- In patients with 1-3 (or 4) brain metastases
  - Two Phase III randomized trials established stereotactic radiosurgery (SRS) as the standard care, replacing WBRT, due to better preservation of patients’ cognitive function, without compromising overall survival (Chang EL, Lancet Onc 2009; Brown PD, JAMA 2016)
- Purpose of the current study
  - To investigate if SRS could replace WBRT in patients with 4-15 brain metastases in a phase III randomized trial
Key Eligibility Criteria:

- Adult patient with 4-15 untreated brain mets confirmed by neuroradiology (up to 20 lesions allowed at the time of treatment)
- All lesions amenable to SRS treatment
- KPS \( \geq 70 \)
- No LMD (radiographic or cytological)
- No prior WBRT
- Prior SRS to 1-3 brain mets with > 6 weeks intervals allowed
- Excluded prior surgical resection of brain mets
- Excluded histology: melanoma, small cell carcinoma, lymphoma/leukemia, or germ cell histology
- Systemic therapy allowed at the discretion of treating oncologist

Stratification factors:

- **Histology** (breast vs. other)
- **Age** (18-59 vs. 60 and over)
- **Number of lesions** (4-7 vs. 8-15)
- **KPS** (70-80 vs. 90-100)
- **Extra-cranial disease status** (progressive disease prior to enrollment vs. no progression)
- **Baseline HVLT** (<\(= 17 \) vs. \(> 28 \))
- **Radiotherapy** (Prior SRS vs. no prior SRS)

Neurocognitive function tests:

- **Memory**: HVLT_R_TR, HVLT_R_DR, HVLT_R Recognition
- **Executive function**: COWA, and Trail Making test Part B (TMTB)
- **Attention Span**: WAIS-III Digit Span
- **Psychomotor Speed**: WAIS-III Digit Symbol, Trail Making test Part A (TMTA)
- **Motor dexterity**: Grooved Pegboard

Primary Endpoints

- Memory function at 4 mo (HVLT_R_TR)
- Local control at 4 mo
Memory Function at 4 Months
-- Primary Endpoint

• HVLT_R_TR: change of Z-score from baseline

• At 4 months
  o **SRS**: Increased by 0.21 (SD 1.15) (n=18)
  o **WBRT**: Decreased by 0.74 (SD 1.31) (n=13)
  o $p=0.041$

• At 1 month and 6 months
  o Clinically meaningful and statistically significant benefit with SRS was also observed at 1 month ($p=0.033$) and 6 months ($p=0.012$)
Global Cognitive Function Measure
(Clinical Trial Battery Composite Score)

- Composite score
  - Mean Z-score from HVLT_R_TR, HVLT_R_DR, and HVLT_R Rec, COWA, TMTA, and TMTB
  - Change from baseline
- Better cognitive composite scores in SRS arm
  - Statistically significant at months 1, 4 and 6

<table>
<thead>
<tr>
<th>Follow up Time Point</th>
<th>SRS median [IQR]</th>
<th>WBRT median [IQR]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-mo (median [IQR])</td>
<td>-0.12 [-0.38, 0.47]</td>
<td>-0.71 [-1.26, -0.28]</td>
<td>0.024</td>
</tr>
<tr>
<td>4-mo (median [IQR])</td>
<td>0.28 [-0.03, 0.60]</td>
<td>-0.57 [-0.88, -0.17]</td>
<td>0.004</td>
</tr>
<tr>
<td>6-mo (median [IQR])</td>
<td>0.31 [-0.23, 0.70]</td>
<td>-0.16 [-0.84, -0.01]</td>
<td>0.027</td>
</tr>
<tr>
<td>9-mo (median [IQR])</td>
<td>0.64 [-0.16, 1.00]</td>
<td>-0.08 [-0.32, -0.01]</td>
<td>0.153</td>
</tr>
<tr>
<td>12-mo (median [IQR])</td>
<td>0.25 [-0.09, 1.03]</td>
<td>-0.12 [-0.14, 0.27]</td>
<td>0.823</td>
</tr>
</tbody>
</table>
Overall Survival

- **Overall survival by intention-to-treat**
  - 69 out of 72 pts evaluable for OS
    - 35 for SRS and 34 for WBRT
    - Estimate median OS

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Events (death)</th>
<th>Median (month)</th>
<th>95% CI (month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRS</td>
<td>35*</td>
<td>30</td>
<td>7.8</td>
<td>6.1 – 14.6</td>
</tr>
<tr>
<td>WBRT</td>
<td>34**</td>
<td>26</td>
<td>8.9</td>
<td>6.4 – 26.4</td>
</tr>
</tbody>
</table>

*Include 6 patients who had more than 20 lesions at time of SRS planning and received WBRT off protocol

**Include 4 patients received SRS and 2 patients received HA-WBRT off protocol

Estimating Overall Survival Curves with the Kaplan-Meier Method by intention-to-treat: $P=0.59$
Other Results

• Local Control at 4 mo
  • 95% (SRS) vs 87% (WBRT), p-value 0.79

• Distant brain control
  • 60% (SRS) vs 80% (WBRT), p-value 0.37

• **Time to systemic therapy**
  • 1.7 weeks (SRS) vs 4.1 weeks (WBRT), **p-value 0.001**

• Toxicities
  • ≥ Grade 3 toxicities 8% (SRS) vs 15% (WBRT)
  • Radiation necrosis: 17% at patient level and 4% at lesion level
Summary

Despite early termination of the trial due to NRG CC001 and use of memantine in 2/3 WBRT patients, in patients with 4-15 brain mets:

• SRS was associated with reduced risk of neurocognitive deterioration compared to WBRT, as demonstrated by a constellation of neurocognitive tests, individually or by composite scores
  • The differences between the two arms were large and clinically meaningful
• No difference in overall survival rates
• SRS was associated with shorter time to systemic therapy
Conclusion

The results from this phase III randomized trial strongly supports the use of SRS in patients with 4-15 brain metastases to better preserve cognitive function and to minimize interruption of systemic therapy, without compromising overall survival.
You can submit questions to via the “Questions” pane, or use the "Raise hand" option if you would like to ask your question directly (we will unmute your microphone).