Can Radiotherapy Cure Stage IV Cancer? The Future of Oligometastatic Cancer

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Disclosures

• FF has served on advisory boards for Astellas, Bayer, Blue Earth Diagnostics, Celgene, EMD Serono, Janssen, Myovant, Roivant, and Sanofi.
• FF has consulted for Clovis and Genentech.
• FF serves on the Scientific Advisory Board of SerImmune.
• FF is co-founder of PFS Genomics, a molecular diagnostic company in breast cancer
• JH has a pending patent, 62/809,014 “Systems and methods for predicting acute care visits during outpatient cancer therapy”
Roadmap

• What is radiotherapy?
• What is (oligo)metastatic cancer?
• Principles of treatment
• Radiation for oligometastasis
• Prostate cancer: a case study
• Studies on the horizon
Roadmap

• What is radiotherapy?
• What is (oligo)metastatic cancer?
• Principles of treatment
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What is radiotherapy?

- About half of cancer patients will receive radiotherapy\(^1\)
- Part of curative treatment for many cancers
- Can be in conjunction with surgery or chemotherapy

What is radiotherapy?

• About half of cancer patients will receive radiotherapy\(^1\)
• Part of curative treatment for many cancers
• Can be in conjunction with surgery or chemotherapy


Image source: Accuray
What is radiotherapy?

- About half of cancer patients will receive radiotherapy\(^1\)
- Part of curative treatment for many cancers
- Can be in conjunction with surgery or chemotherapy


Image source: NCI
What is radiotherapy?

- About half of cancer patients will receive radiotherapy\(^1\)
- Part of curative treatment for many cancers
- Can be in conjunction with surgery or chemotherapy

\(^1\) Delaney et al. *Clin Oncol.*, 2015.
Roadmap

• What is radiotherapy?
• **What is (oligo)metastatic cancer?**
• Principles of treatment
• Radiation for oligometastasis
• Prostate cancer: a case study
• Studies on the horizon
Molecular Basis of Metastasis
What is oligometastatic cancer?

• An intermediate state of cancer spread between localized disease and widespread metastases

• Proposed as a distinct clinical state by S Hellman and R Weichselbaum
EDITORIAL

Oligometastases

An attractive consequence of the presence of a clinically significant oligometastatic state is that some patients so affected should be amenable to a curative therapeutic strategy. The occasional success of surgical excision or
Based on Imaging...

- Changing imaging modalities
- Breast (PET not routine)
- Lack of benchmark gold standard
Imaging and detection are also getting better!
Why the Oligometastatic Space has Increased in Prostate Cancer: **The Advent of PET Imaging**

Axumin (fluciclovine F18) PET: Currently available at hundreds of imaging sites across the US FDA–approved for use in biochemical recurrence, reimbursed by Medicare and some private payers.
Using Advanced PET Imaging to Detect Extrapelvic Disease in Patients with PSA Recurrences

Fluciclovine F18 PET


Gallium 68 PSMA PET

Boreta L et al, Urology 2019; 129 (165-171)
PSMA vs Fluciclovine PET

Inter-reader variability (k)

<table>
<thead>
<tr>
<th></th>
<th>PSMA</th>
<th>Fluciclovine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.67</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Calais et al, Lancet Oncology 2019
PSMA PET Identifies Oligometastatic Disease at Low PSA Recurrences

- UCSF Experience using PSMA PET at time of recurrence
- 125 men with BCR after prostatectomy (PSA <2)
- 53% had a PSMA-avid lesion
- 38% had a lesion outside of the pelvis
- 30% had a lesion outside of a standard RT field

Boreta et al, *Urology* 2019
Are there different types of oligometasis?

• Extent
• Time
• Treatment
Types of oligometastasis

Synchronous oligometastatic disease

Metachronous oligorecurrence

Types of oligometastasis

The Evolution of Metastatic Disease

- Both the primary tumor and existing metastases can seed new metastases.

- The principal mode of spread is metastases to metastases.

- Thus, to cure oligometastatic disease, one may need to ablate both the primary and the metastases.
(Some) oligometastatic patients have indolent disease

Multivariate Analysis of Prognostic Factors in Metastatic Breast Cancer

Table 7. Regression Model Relating Survival to Pretreatment Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Regression Coefficient</th>
<th>Significance Level of Entry</th>
<th>Relative Risk</th>
<th>Ratio U/F</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDH</td>
<td>0.362</td>
<td>&lt;0.01</td>
<td>0.83</td>
<td>1.70</td>
</tr>
<tr>
<td>Performance status</td>
<td>0.281</td>
<td>&lt;0.01</td>
<td>0.81</td>
<td>1.41</td>
</tr>
<tr>
<td>Lung</td>
<td>0.470</td>
<td>&lt;0.01</td>
<td>0.88</td>
<td>1.42</td>
</tr>
<tr>
<td>Prior radiotherapy</td>
<td>0.302</td>
<td>&lt;0.01</td>
<td>0.76</td>
<td>1.40</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>0.188</td>
<td>&lt;0.01</td>
<td>0.83</td>
<td>1.45</td>
</tr>
<tr>
<td>Extent of disease</td>
<td>0.154</td>
<td>&lt;0.01</td>
<td>0.80</td>
<td>1.26</td>
</tr>
</tbody>
</table>

NOTE: Favorable risk was LDH ≤ 225; performance status 0–1; lung not involved; no prior radiotherapy; alkaline phosphatase ≤ 85; and extent of disease ≤ 5. Unfavorable risk was LDH > 450; performance status 3–4; lung involved; prior radiotherapy > 3; alkaline phosphatase > 350; and extent of disease > 20.

619 anthracycline treated patients, Minimum f/u 4 years

More limited progression

• Typically in the same organ
  • 89% of cumulative new metastases

• Typically few in number
  • 72% progress in 1-3 new metastases
Survival

Polymetastatic cluster (net down-regulation of miRs)
Oligometastatic cluster (net up-regulation of miRs)

Radiation (SBRT) treated oligometastases: Patterns of differentially expressed miRs correlate with phenotype and survival

Lussier et al. PLOS ONE. 2011.
Roadmap

• What is radiotherapy?
• What is (oligo)metastatic cancer?
• Principles of treatment
• Radiation for oligometastasis
• Prostate cancer: a case study
• Studies on the horizon
How do we treat metastases?

- Systemic therapy
- Surgery
- Radiation
  - Conventional radiation
  - Stereotactic radiation (SBRT/SABR)
- Ablation
Metastasectomy

- Associated with improved outcomes
- Series focus on specific sites of metastasis
Radiofrequency ablation

- Colorectal cancer
- Liver metastases only
- Systemic therapy
- With or without ablation

Roadmap

- What is radiotherapy?
- What is (oligo)metastatic cancer?
- Principles of treatment
- **Radiation for oligometastasis**
- Prostate cancer: a case study
- Studies on the horizon
Stereotactic body radiation therapy (SBRT)

- Used for lung, pancreas cancers
- Oligometastases
- Precise, image-guided, high dose radiation in few treatments

Pooling early studies

Stereotactic Body Radiotherapy for Multisite Extracranial Oligometastases
Final Report of a Dose Escalation Trial in Patients With 1 to 5 Sites of Metastatic Disease

Joseph K. Salama, MD; Michael D. Hasselle, MD; Steven J. Chmura, MD, PhD; Renuka Malik, MD; Neil Mehta, MD; Kamal M. Yenice, MD; Victoria M. Villaflor, MD; Walter M. Staedler, MD; Philip C. Hoffman, MD; Ezra E. W. Cohen, MD; Philip P. Connell, MD; Daniel J. Haraf, MD; Everett E. Vokes, MD; Samuel Hellman, MD; and Ralph R. Weichselbaum, MD

Concurrent sunitinib and stereotactic body radiotherapy for patients with oligometastases
Final report of a prospective clinical trial

Johnny Kao • Chien-Ting Chen • Charles C. L. Tong • Stuart H. Packer • Myron Schwartz • Shu-hsia Chen • Max W. Sung

Oligometastases Treated With Stereotactic Body Radiotherapy: Long-Term Follow-Up of Prospective Study

Michael T. Milano, M.D., Ph.D.,* Alan W. Katz, M.D., M.P.H.,* Hong Zhang, Ph.D., M.D.,* and Paul Okunieff, M.D.*;
Pooling early studies

Hong et al. PLOS ONE. 2018.
Pooling early studies

Hong et al. PLOS ONE. 2018.
Pooling early studies

Pooling early studies

<table>
<thead>
<tr>
<th>Strata</th>
<th>n</th>
<th>3-year OS</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1</td>
<td>92</td>
<td>75%</td>
<td>66-85%</td>
</tr>
<tr>
<td>Class 2</td>
<td>13</td>
<td>85%</td>
<td>75-95%</td>
</tr>
<tr>
<td>Class 3</td>
<td>189</td>
<td>55%</td>
<td>48-64%</td>
</tr>
<tr>
<td>Class 4</td>
<td>37</td>
<td>38%</td>
<td>24-60%</td>
</tr>
<tr>
<td>Class 5</td>
<td>30</td>
<td>13%</td>
<td>5-35%</td>
</tr>
</tbody>
</table>

Overall survival

Time (months)

Hong et al. PLOS ONE. 2018.
Pooling early studies

SABR-COMET

STEREOTACTIC ABLATIVE RADIOThERAPY FOR COMPREHENsIVE TREATMENT OF OLIGOMETASTATIC TUMORS (SABR-COMET): A RANDOMIZED PHASE II TRIAL

Patients with up to 5 metastatic lesions from any primary tumor site, meeting inclusion criteria

RANDOMIZATION
(1:2 ratio of randomization to Arm 1 vs. Arm 2)

ARM 1: STANDARD OF CARE
Palliative RT to any symptomatic sites
Further chemotherapy at discretion of medical oncologist

FOLLOW-UP

ARM 2: STANDARD OF CARE + SABR
SABR to all sites of known disease
Further chemotherapy at discretion of medical oncologist

FOLLOW-UP

http://clinicaltrials.gov/ct2/show/NCT01446744

SABR-COMET

Randomly assigned
(N = 99)

Allocated to control arm (n = 33)
  Received allocated intervention (n = 33)

Allocated to SABR arm (n = 66)
  Received allocated intervention (n = 64)
  Did not receive allocated intervention (n = 2)
    > 5 metastatic lesions at baseline (n = 2)

Lost to follow-up (n = 2)
  Withdrew from trial (n = 2)

Lost to follow-up (n = 3)
  Withdrew from trial (n = 3)

All patients analyzed (n = 33)

All patients analyzed (n = 66)

SABR-COMET

A

B

Overall Survival (%)

Progression-Free Survival (%)

Stratified log-rank test $P = .006$

Stratified log-rank test $P = .001$

Time (years)

Time (years)

No. at risk

Control 33 28 17 11 2 2 2
SABR 66 54 44 40 21 10 5

No. at risk

Control 33 6 4 2 1 1
SABR 66 32 23 20 6 3 2

**SABR-COMET**

### Table: Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control (n = 33)</th>
<th>SABR (n = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (IQR)</td>
<td>69 (64-75)</td>
<td>67 (65-74)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19 (58)</td>
<td>40 (62)</td>
</tr>
<tr>
<td>Female</td>
<td>14 (42)</td>
<td>26 (39)</td>
</tr>
<tr>
<td>Site of original primary tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>5 (15)</td>
<td>13 (20)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>9 (27)</td>
<td>9 (14)</td>
</tr>
<tr>
<td>Lung</td>
<td>6 (18)</td>
<td>12 (19)</td>
</tr>
<tr>
<td>Prostate</td>
<td>2 (6)</td>
<td>14 (21)</td>
</tr>
<tr>
<td>Other</td>
<td>11 (33)</td>
<td>18 (29)</td>
</tr>
<tr>
<td>Median time from diagnosis of primary tumor to system assignment, years (IQR)</td>
<td>2.3 (1.3-4.1)</td>
<td>2.4 (1.6-8.3)</td>
</tr>
</tbody>
</table>

### Table: No. of metastases

<table>
<thead>
<tr>
<th>No. of metastases</th>
<th>Control (n = 33)</th>
<th>SABR (n = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12 (36)</td>
<td>30 (46)</td>
</tr>
<tr>
<td>2</td>
<td>13 (40)</td>
<td>19 (29)</td>
</tr>
<tr>
<td>3</td>
<td>6 (18)</td>
<td>12 (19)</td>
</tr>
<tr>
<td>4</td>
<td>2 (6)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>5</td>
<td>0 (0)</td>
<td>3 (5)</td>
</tr>
</tbody>
</table>

### Table: Location of metastases (n = 191)

<table>
<thead>
<tr>
<th>Location of metastases</th>
<th>Control (n = 33)</th>
<th>SABR (n = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal</td>
<td>2 (6)</td>
<td>7 (11)</td>
</tr>
<tr>
<td>Bone</td>
<td>20 (61)</td>
<td>45 (69)</td>
</tr>
<tr>
<td>Liver</td>
<td>3 (9)</td>
<td>16 (25)</td>
</tr>
<tr>
<td>Lung</td>
<td>34 (53)</td>
<td>55 (83)</td>
</tr>
<tr>
<td>Other*</td>
<td>9 (28)</td>
<td>4 (6)</td>
</tr>
</tbody>
</table>

### Survival Analysis

- **Class 1**
  - n = 92
  - 3-year OS 75% (95% CI 66-85%)

- **Class 2**
  - n = 13
  - 3-year OS 85% (95% CI 67-100%)

- **Class 3**
  - n = 189
  - 3-year OS 55% (95% CI 48-64%)

- **Class 4**
  - n = 37
  - 3-year OS 38% (95% CI 24-60%)

- **Class 5**
  - n = 30
  - 3-year OS 13% (95% CI 5-35%)

---

Hong et al. *PLOS ONE.* 2018.
## Table 2: Summary of adverse events

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>All patients (n=99)</th>
<th>Control group (n=33)</th>
<th>Stereotactic ablative radiotherapy group (n=66)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse event grade ≥2</td>
<td>55 (56%)</td>
<td>15 (46%)</td>
<td>40 (61%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Related adverse event grade ≥2</td>
<td>22 (22%)</td>
<td>3 (9%)</td>
<td>19 (29%)</td>
<td>0.026</td>
</tr>
<tr>
<td>Adverse event associated with death (grade 5)</td>
<td>3 (3%)</td>
<td>0</td>
<td>3 (5%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Fatigue*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.45</td>
</tr>
<tr>
<td>Grade 2</td>
<td>6 (6%)</td>
<td>2 (6%)</td>
<td>4 (6%)</td>
<td>-</td>
</tr>
<tr>
<td>Grade 3</td>
<td>1 (1%)</td>
<td>1 (3%)</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Dyspnoea*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Grade 2</td>
<td>1 (1%)</td>
<td>0</td>
<td>1 (2%)</td>
<td>-</td>
</tr>
<tr>
<td>Grade 3</td>
<td>1 (1%)</td>
<td>0</td>
<td>1 (2%)</td>
<td>-</td>
</tr>
<tr>
<td>Pain (any type)*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.14</td>
</tr>
<tr>
<td>Grade 2</td>
<td>5 (5%)</td>
<td>0</td>
<td>5 (8%)</td>
<td>-</td>
</tr>
<tr>
<td>Grade 3</td>
<td>3 (3%)</td>
<td>0</td>
<td>3 (5%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Data are n (%). *Treatment related.
SABR-COMET

- No difference in quality of life:
  - Physical
  - Social
  - Emotional
  - Functional
  - Total

Roadmap

- What is radiotherapy?
- What is (oligo)metastatic cancer?
- Principles of treatment
- Radiation for oligometastasis
- Prostate cancer: a case study
- Studies on the horizon
Oligometastatic Disease Management

Stampede Arm H: A randomized phase 3 trial of RT vs no RT to the primary tumor in men with newly diagnosed metastatic PCa
- 2061 patients
- 40% with low metastatic burden

Parker et al, Lancet 2018
Radiation to the Primary Tumor Improves Survival for PCa Patients with Low Metastatic Burden

Low Metastatic Burden

Overall Survival

HR 0.68, 95% CI 0.52–0.90; p=0.007

Failure Free Survival

HR 0.59, 95% CI 0.49–0.72; p<0.0001

High Metastatic Burden

Overall Survival

HR 1.07, 95% CI 0.90–1.28; p=0.420

Failure Free Survival

HR 0.88, 95% CI 0.71–1.01; p=0.059

Parker et al, *Lancet* 2018
Oligometastatic Disease Management

- Prostate Directed Therapy
- Systemic Consolidative Therapy
- Metastasis Directed Therapy

Two randomized phase II studies:
- STOMP
- ORIOLE
The STOMP trial: Surveillance vs Metastasis-Directed Therapy for Oligometastatic Prostate Cancer

Primary endpoint:
- ADT-free survival

Stratification
- PSA doubling time
- Location of mets

Reason to start ADT
- Symptoms
- Local progression
- Polymetastatic progression

Ost et al, JCO 2017
STOMP: Metastasis-Directed Therapy Improves Biochemical Recurrence-Free Survival

Surveillance: 35% of pts had a PSA decline

Metastasis-Directed Therapy (MDT): 75% of pts had a PSA decline

Median ADT-free survival: 13 months in the surveillance arm vs 21 months in the MDT arm

Ost et al, JCO 2017
ORIOLE Trial: Observation vs Stereotactic Ablative Radiation for Oligometastatic PCa

Hazard Ratio: 0.30
95% CI: 0.11 - 0.81
p-value: 0.0023

Phillips R et al, *JAMA Onc* 2020
ORIOLE Trial: Patients who received SABR had variable coverage of occult PSMA radiotracer-avid lesions

Conventional imaging for eligibility and treatment planning (n = 36)

Blinded PSMA-PET obtained at baseline and Day 180 (n = 35)

Total consolidation (n = 19)

Subtotal consolidation (n = 16)

Phillips R et al, JAMA Onc 2020
ORIOLE Trial: Patients who received SABR had variable coverage of occult PSMA radiotracer-avid lesions

Hazard Ratio: 0.26
95% CI: 0.090 - 0.76
p-value: 0.0055

Phillips R et al, JAMA Onc 2020
A Tale of Two Patients

Patient 1

- Prostatectomy in 2007 for a Gleason 4+3 (with tertiary pattern 5) disease
- PSA recurrence treated with salvage RT + 4 months of ADT in 2013
- Now presents with oligometastatic disease in L pubic ramus with a slowly rising PSA to 1.3 in 2017
- No other detectable sites of disease
A Tale of Two Patients

The patient has had a single detectable site of metastasis, despite almost no treatment, over 4 years. No emergence of additional mets during this period.
A Tale of Two Patients

Patient 2

Also post-RP
Also treated with salvage RT + short term ADT for PSA recurrence

Emergence of multiple metastases over 1 month after SBRT

PSMA PET scan from 1/2017

PSMA PET scan from 2/2017
Not all Oligometastatic Disease is the Same!

Patient 1

Intensification of local therapy for the primary and metastases?

Patient 2

Intensification of systemic therapy?
Oligometastatic Disease Management

- Prostate Directed Therapy
- Systemic Consolidative Therapy
- Metastasis Directed Therapy
Intensification of systemic therapy for patients with high-risk localized disease (by conventional imaging)

<table>
<thead>
<tr>
<th>Source</th>
<th>N</th>
<th>Inclusion</th>
<th>Prostate Tx</th>
<th>Arms</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>GETUG 12 (Fizazi et al. 2015)</td>
<td>413</td>
<td>GS≥8, T3, PSA≥20, N+</td>
<td>Node neg: RP/RT Node pos: RT or none</td>
<td>3y ADT +/- 4c docetaxel</td>
<td>8y RFS 62% ADT+doce vs 50% ADT alone (HR 0.71, p=0.017)</td>
</tr>
<tr>
<td>RTOG 0521 (Sandler et al. 2015)</td>
<td>562</td>
<td>GS≥7, PSA ≥20, any T ≥T2 and GS≥8, PSA &lt;20</td>
<td>WPRT 46.8 Gy + Prostate boost 25.2-28.8 Gy</td>
<td>2y ADT +/- 6c docetaxel + prednisone</td>
<td>5y OS 93% ADT+doce vs 89% ADT alone (HR 0.70, 1-sided p=0.04)</td>
</tr>
<tr>
<td>STAMPEDE Docetaxel (James et al. 2016)</td>
<td>2962</td>
<td>New diagnosis high risk, N+ or M1 or high risk relapse (35% N0-1M0)</td>
<td>RT for N0M0 RT optional for N1M0</td>
<td>ADT +/- ZA ADT + Doc +/- ZA</td>
<td>Median OS 81mo ADT + doce vs 71mo ADT alone (HR 0.78, p=0.006)</td>
</tr>
<tr>
<td>STAMPEDE Abiraterone (James et al. 2017)</td>
<td>1917</td>
<td>New diagnosis high risk, N+ or M1 or high risk relapse (46% N0-1M0)</td>
<td>RT for N0M0 RT optional for N1M0</td>
<td>ADT +/- abiraterone</td>
<td>3y OS 83% ADT+abi vs 76% ADT alone (HR 0.63, p&lt;0.001)</td>
</tr>
</tbody>
</table>

One would predict that the subset of patients with oligometastatic disease are most likely to benefit
Roadmap

• What is radiotherapy?
• What is (oligo)metastatic cancer?
• Principles of treatment
• Radiation for oligometastasis
• Prostate cancer: a case study
• Studies on the horizon
NRG-BR002
(Phase II/III, 297 patients)

**PATIENT POPULATION**
Patients with locally controlled metastatic breast cancer with the following number of allowable metastases:
- ≤ 4 metastases seen on standard imaging within 60 days prior to registration when all metastatic disease is located within the following sites: peripheral lung, osseous (bone), spine
- ≤ 2 metastases seen on standard imaging within 60 days prior to registration when any one metastasis is located in one of the following sites: liver, central lung, mediastinal/cervical lymph node, abdominal/pelvic metastases (lymph node/adrenal gland) and at least 1 pathologically confirmed visualized on CT or PET/CT.

**STRATIFICATION**
- Number of metastases (1 vs. > 1)
- Hormone receptor status (ER and/or PR positive vs. ER and PR negative)
- HER2 status (Positive vs. Negative)
- First-line standard systemic chemotherapy (Yes vs. No)

**RANDOMIZATION**

**Arm 1**
Standard of care systemic therapy

**Arm 2**
- Standard of care systemic therapy
- Ablation of all metastases (SBRT or surgery ablation)
Studies on the horizon

SABR-COMET 3
(Phase III, 297 patients)

- Patients diagnosed with primary solid tumors and 1-3 oligometastases
- Pre-specify standard of care treatment
- 1:2 Randomization
  - Stratified by histology* and disease free interval**

Arm 1:
- Standard of Care

Arm 2:
- Standard of Care + SABR to all oligometastases

Primary Outcome: Overall Survival

Follow-up:
- Biomarker: baseline, 3M, at progression or 60M

CORE
(Phase II/III, 230 patients - phase II)

Patients with breast cancer with ≤3 oligometastases

Randomisation
1:1

SOC group
- May include chemotherapy, biological therapy, hormone therapy, palliative radiotherapy or observation at investigator’s discretion

SBRT + SOC group
- Dose and fractionation dependent on metastatic site
- SBRT to precede SOC

Follow-up:
- Patients are reviewed every 3 months during years 1 and 2, and 6 monthly thereafter up to 6 years.
- Follow up visits include a clinical exam, tumour imaging scans, and assessment of tumour marker CA 15-3 (where available)
Other questions on the horizon

- Who benefits from treatment?
- When should treatment be given?
- How do we synergize with advances in systemic therapy?
Thank you!

**UCSF**
- Thomas Hope
- Eric Small
- Rahul Aggarwal
- Lauren Boreta
- Melody Xu
- Susan Wu
- Adam Gadzinski

**Duke University**
- Joseph Salama, MD

**Johns Hopkins**
- Phuoc Tran

**Gent University**
- Piet Ost

**Peter MacCallum**
- Michael Hoffman