The State of Cancer Care: Reflections from the 2017 ASCO Annual Meeting

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Overview

• Opening remarks by Dr. Margaret Tempero
• Highlights from the 2017 ASCO Annual Meeting
  • Selected Plenary Sessions
    • OlympiAD Study – Dr. Mark Robson
    • LATITUDE Study – Dr. Karim Fazazi
    • Patient reported outcomes for symptom monitoring – Dr. Ethan Basch
  • Selected Late Breaking Abstracts
    • STREAM Study – Dr. Viviane Hess
    • CALM Study – Dr. Gary Rodin
    • BCMA CAR-T cells in patients with relapse refractory MM – Dr. Wanhong Zhao
• Conclusions and Final Thoughts
• Questions/Comments
OlympiAD: Phase III trial of olaparib monotherapy versus chemotherapy for patients with HER2-negative metastatic breast cancer and a germline BRCA mutation

Mark Robson,1 Seock-Ah Im,2 Elibeta Senkus,3 Binghe Xu,4 Susan M Domchek,5 Norikazu Masuda,6 Suzette Delaloge,7 Wei Li,# Nadine Tung,# Anne Armstrong,9 Wenting Wu,11 Carsten Goessel,# Sarah Runewicz,11 Pierfranco Conte13

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ClinicalTrials.gov identifier: NCT02000622. This study was sponsored by AstraZeneca.

Phase II studies of olaparib in breast cancer

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Tutt et al (n=54)</th>
<th>Gelmon et al (n=26, 10 gBRCAm)</th>
<th>Kaufman et al (n=62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locally advanced/metastatic BRCA4m BC</td>
<td>Advanced metastatic or recurrent BC, triple negative or known BRCA4m</td>
<td>Advanced BRCA4m BC that progressed despite 2-3 previous lines of chemotherapy for advanced/metastatic BC</td>
<td></td>
</tr>
<tr>
<td>Prior lines of therapy for advanced disease</td>
<td>3 (median, including adjuvant)</td>
<td>3 (median, including adjuvant)</td>
<td>4.6 (mean, metastatic only)</td>
</tr>
<tr>
<td>ORR</td>
<td>41%</td>
<td>0% (50% unconfirmed in BRCA4m)</td>
<td>13%</td>
</tr>
<tr>
<td>Median DoR</td>
<td>144 days</td>
<td>–</td>
<td>204 days</td>
</tr>
</tbody>
</table>

BC, breast cancer; DoR, duration of response; ORR, objective response rate

OlympiAD study design

- HER2-negative metastatic BC
  - ER+ and/or PR+ or TNBC
  - Deleterious or suspected deleterious gBRCAm
  - Prior anthracycline and taxane
  - ≥2 prior chemotherapy lines in metastatic setting
  - HR+ disease progressed on ≥1 endocrine therapy, or not suitable
  - If prior platinum use
    - No evidence of progression during treatment in the advanced setting
    - ≥12 months since (neo)adjuvant treatment

Primary endpoint: progression-free survival by BICR

Secondary endpoints:
- Time to second progression or death
- Overall survival
- Objective response rate
- Safety and tolerability
- Global HRQoL (EORTC-QLQ-C30)

Olaparib
300 mg tablets bd

2:1 randomization

Chemotherapy treatment of physician’s choice (TPC)
- Capecitabine
- Eribulin
- Vinorelbine

Olaparib
300 mg bd

Chemotherapy
TPC

Progression/deaths, n (%)
Median PFS, months

163 (79.5)
7.0

71 (73.2)
4.2

HR 0.58
95% CI 0.43 to 0.80, P<0.0009

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Time to second progression or death (PFS2) by investigator assessment

- **Olaparib 300 mg bd**
  - 104 (50.7%%) deaths
  - Median PFS2: 13.2 months
- **Chemotherapy TPC**
  - 53 (54.6%%) deaths
  - Median PFS2: 9.3 months

**HR 0.57**
95% CI 0.40 to 0.83; P=0.0033

Overall survival (interim analysis; 46% data maturity)

- **Olaparib 300 mg bd**
  - 94 (45.5%%) deaths
  - Median OS: 19.3 months
- **Chemotherapy TPC**
  - 46 (47.4%%) deaths
  - Median OS: 19.6 months

**HR 0.90**
95% CI 0.63 to 1.29; P=0.5665

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Adverse events (any grade) in ≥15% of patients

- Nausea: 58%
- Anemia: 40%
- Vomiting: 30%
- Fatigue: 29%
- Neutropenia: 27%
- Diarrhea: 21%
- Headache: 20%
- Cough: 17%
- Decreased white blood cells: 16%
- Decreased appetite: 16%
- Pyrexia: 14%
- Increased ALT: 11%
- Increased AST: 9%
- Hand-foot syndrome: 3%

Adverse events (%) with Olaparib 300 mg bid (N=205) and Chemotherapy TPC (N=91)

Grade ≥3 adverse events in ≥2% patients in either arm

- Anemia: 16%
- Neutropenia: 9%
- Decreased white blood cells: 3%
- Fatigue: 3%
- Leukopenia: 2%
- Decreased platelet count: 2%
- Increased AST: 2%
- Dyspnea: 1%
- Headache: 1%
- Hand-foot syndrome: 0%

Adverse events (%) with Olaparib 300 mg bid (N=205) and Chemotherapy TPC (N=91)
Conclusions

- Olaparib tablet monotherapy provided a statistically significant and clinically meaningful PFS benefit versus standard-of-care chemotherapy for patients with HER2-negative metastatic breast cancer and a gBRCAm.
- Olaparib was generally well tolerated with <5% discontinuing treatment for toxicity and a lower rate of Grade ≥3 AEs compared with chemotherapy.
- OlympiAD is the first Phase III study in metastatic breast cancer patients demonstrating benefit for a PARP inhibitor over an active comparator.

LATITUDE: A phase 3, double-blind, randomized trial of androgen deprivation therapy with abiraterone acetate plus prednisone or placebos in newly diagnosed high-risk metastatic hormone-naïve prostate cancer patients

Karim Fizazi,1 NamPhuong Tran,2 Luis Fein,3 Nobuaki Matsubara,4 Alfredo Rodriguez-Antolin,5 Boris Y. Alekseev,6 Mustafa Özgüroğlu,7 Dingwei Ye,8 Susan Feyerabend,9 Andrew Protheroe,10 Peter De Porre,11 Thian Kheoh,12 Youn C. Park,13 Mary B. Todd,14 Kim N. Chi,15 on behalf of the LATITUDE Investigators

1Gustave Roussy, University of Paris Sud, Villejuif, France, 2Janssen Research & Development, Los Angeles, CA, 3Instituto de Oncología de Rosario, Rosario, Argentina, 4National Cancer Center Hospital East, Chiba, Japan, 512th Octubre University Hospital, Madrid, Spain, 6A. I. Favorsky Moscow Cancer Research Institute, Moscow, Russian Federation, 7Cerrahpaşa Medical Faculty, Istanbul University, Istanbul, Turkey, 8Fudan University Shanghai Cancer Center, China, 9Studieprospekt Kliniken, Nürnberg, Germany, 10Oxford University Hospitals/ Foundation NHS Trust, Oxford, UK, 11Janssen Research & Development, Leuven (Belgium), 12Janssen Research & Development, San Diego, CA, 13Janssen Research & Development, Raritan, NJ, 14Janssen Global Services, Raritan, NJ, 15BC Cancer Agency, Vancouver, BC, Canada
ADT + docetaxel: a new standard of care for men with mCNPC and high metastatic burden (2015)

<table>
<thead>
<tr>
<th>Overall Survival</th>
<th>ADT + DOC</th>
<th>ADT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (mos)</td>
<td>Median (mos)</td>
</tr>
<tr>
<td>GETUG-15(^1)</td>
<td>62.1</td>
<td>48.6</td>
</tr>
<tr>
<td>CHAARTED(^2)</td>
<td>57.6</td>
<td>47.2</td>
</tr>
<tr>
<td>STAMPEDE(^3)</td>
<td>60</td>
<td>45</td>
</tr>
</tbody>
</table>

Objective

To evaluate the addition of AA + P to ADT on clinical benefit in men with newly diagnosed, high-risk, mCNPC

High-risk defined as meeting at least 2 of 3 high-risk criteria:
- Gleason score of ≥ 8
- Presence of ≥ 3 lesions on bone scan
- Presence of measurable visceral lesion
Overall study design of LATITUDE

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- Conducted at 235 sites in 34 countries in Europe, Asia-Pacific, Latin America, and Canada
- Designed and fully enrolled prior to publication of CHARnTED/STaMPEDE results

Statistically significant 38% risk reduction of death

Hazard ratio, 0.62 (95% CI, 0.51-0.76)
P<0.0001

OS rate at 3 years:
- ADT + AA + P: 66%
- ADT + placebos: 49%

Median follow-up: 30.4 months

No. of events: 406 (48% of 853)
ADT + AA + P: 160
ADT + placebos: 237

No. at risk

<table>
<thead>
<tr>
<th>Months</th>
<th>ADT + AA + P</th>
<th>ADT + placebos</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>597</td>
<td>802</td>
</tr>
<tr>
<td>6</td>
<td>555</td>
<td>564</td>
</tr>
<tr>
<td>12</td>
<td>519</td>
<td>554</td>
</tr>
<tr>
<td>18</td>
<td>479</td>
<td>504</td>
</tr>
<tr>
<td>24</td>
<td>368</td>
<td>432</td>
</tr>
<tr>
<td>30</td>
<td>233</td>
<td>332</td>
</tr>
<tr>
<td>36</td>
<td>93</td>
<td>172</td>
</tr>
<tr>
<td>42</td>
<td>9</td>
<td>57</td>
</tr>
<tr>
<td>48</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Presented By Karim Fizazi at 2017 ASCO Annual Meeting
OS benefit consistently favorable across subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>ADT + AA + P Median (mo)</th>
<th>ADT + placebos Median (mo)</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>NR</td>
<td>34.7</td>
<td>0.63 (0.51 - 0.79)</td>
</tr>
<tr>
<td>ECOG 0</td>
<td>NR</td>
<td>35.2</td>
<td>0.64 (0.48 - 0.86)</td>
</tr>
<tr>
<td>ECOG 2</td>
<td>NR</td>
<td>31.3</td>
<td>0.61 (0.46 - 0.79)</td>
</tr>
<tr>
<td>Logistic disease</td>
<td>Yes</td>
<td>32.3</td>
<td>0.51 (0.33 - 0.79)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>35.1</td>
<td>0.55 (0.37 - 0.83)</td>
</tr>
<tr>
<td>Creatin score</td>
<td>&lt; 1.5</td>
<td>NR</td>
<td>0.62 (0.43 - 0.91)</td>
</tr>
<tr>
<td></td>
<td>&gt; 1.5</td>
<td>NR</td>
<td>0.63 (0.37 - 0.82)</td>
</tr>
<tr>
<td>Bone metastasis</td>
<td>&lt; 40</td>
<td>NR</td>
<td>0.65 (0.45 - 0.96)</td>
</tr>
<tr>
<td></td>
<td>&gt; 40</td>
<td>NR</td>
<td>0.60 (0.41 - 0.85)</td>
</tr>
<tr>
<td>Region</td>
<td>Asia</td>
<td>NR</td>
<td>0.72 (0.52 - 0.98)</td>
</tr>
<tr>
<td></td>
<td>Europe</td>
<td>NR</td>
<td>0.80 (0.59 - 1.05)</td>
</tr>
<tr>
<td></td>
<td>Rest of world</td>
<td>NR</td>
<td>0.70 (0.45 - 1.00)</td>
</tr>
</tbody>
</table>

Statistically significant 53% risk reduction of radiographic progression or death

Hazard ratio, 0.47 (95% CI, 0.39 - 0.55)
P < 0.0001
Statistically significant improvement in all secondary end points

<table>
<thead>
<tr>
<th>Secondary End Points</th>
<th>ADT + AA + P (n = 597) Median (months)</th>
<th>ADT + placebo (n = 592) Median (months)</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to PSA progression</td>
<td>33.2</td>
<td>7.4</td>
<td>0.30 (0.26-0.35)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time to pain progression</td>
<td>NR</td>
<td>16.6</td>
<td>0.70 (0.58-0.83)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time to next symptomatic skeletal event</td>
<td>NR</td>
<td>NR</td>
<td>0.70 (0.54-0.92)</td>
<td>0.0086</td>
</tr>
<tr>
<td>Time to chemotherapy</td>
<td>NR</td>
<td>38.9</td>
<td>0.44 (0.35-0.56)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time to subsequent prostate cancer therapy</td>
<td>NR</td>
<td>21.6</td>
<td>0.42 (0.35-0.50)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

NR = not reached.

Statistically significant 70% risk reduction of time to PSA progression

Hazard ratio, 0.30 (95% CI, 0.26-0.35)
P<0.0001
Statistically significant 30% risk reduction of time to pain progression

Hazard ratio, 0.70 (95% CI, 0.58-0.83)
P<0.0001
ADT + AA + P, not reached

ADT + placebos, 16.6 mo

Statistically significant 58% risk reduction of time to subsequent PC therapy

Hazard ratio, 0.42 (95% CI, 0.35-0.50)
P<0.0001
ADT + AA + P, not reached

ADT + placebos, 21.6 mo
Adverse events of special interest

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>ADT + AA + P (n = 597)</th>
<th>ADT + placebos (n = 602)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 3</td>
<td>Grade 4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>10</td>
<td>0.8</td>
</tr>
<tr>
<td>ALT increased</td>
<td>5</td>
<td>0.3</td>
</tr>
<tr>
<td>AST increased</td>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>Bone pain</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac disorder</td>
<td>3</td>
<td>0.6</td>
</tr>
<tr>
<td>Anemia</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>Back pain</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Spinal cord compression</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions

- In the phase 3 LATITUDE, addition of AA + P to ADT led to:
  - Significantly improved OS with a 38% reduction in the risk of death
  - Significantly prolonged rPFS (53% reduction) and all secondary end points
- The overall safety profile of ADT + AA + P was consistent with prior studies in patients with mCRPC
Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment (NCT00578006)

Ethan Basch, Allison Deal, Amylou Dueck, Antonia Bennett, Thomas Atkinson, Howard Scher, Mark Kris, Clifford Hudis, Paul Sabbatini, Dorothy Dulko, Lauren Rogak, Allison Barz, Deborah Schrag

From: Lineberger Comprehensive Cancer Center, University of North Carolina; Memorial Sloan Kettering Cancer Center; Mayo Clinic; Dana-Farber Cancer Institute

Standard Approach to Symptom Monitoring

- Limited Time
- Forget to Discuss
- Reluctance to Contact
- Problems Connecting

REACTIVE APPROACH
Alternative: Systematic Symptom Monitoring

Presented By Ethan Basch at 2017 ASCO Annual Meeting

Study Design

Presented By Ethan Basch at 2017 ASCO Annual Meeting
### Patient Self-Reporting Interface

**Example: Pain**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>I have not had pain.</td>
</tr>
<tr>
<td>Grade 1 (Mild)</td>
<td>I have had mild pain, but it does not interfere with my normal functioning.</td>
</tr>
<tr>
<td>Grade 2 (Moderate)</td>
<td>I have had moderate pain, and my pain or my use of pain medications interferes with my normal functioning. But I am still able to carry out my normal daily activities.</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>I have had severe pain, and my pain or my use of pain medications severely interferes with my normal daily activities.</td>
</tr>
<tr>
<td>Grade 4 (Disabling)</td>
<td>My pain has been disabling.</td>
</tr>
</tbody>
</table>

### Statistics

- **Primary outcome:** QOL, measured by EQ-5D
  - 80% power to detect an effect size of 0.40 for change from baseline to 6 months between arms (t-test, two-sided alpha 0.05)
  - *Analysis previously reported* (J Clin Oncol 2016;34:557-565)
- **Overall survival**
  - Ascertained from National Death Index
  - Estimated using Kaplan-Meier method
  - Compared between arms using a log-rank test and Cox proportional hazards regression adjusting for age, sex, race, education level, level of prior computer/email experience, cancer type
Patient Participation

- Patients self-reported symptoms 73% of the time when prompted to do so
- Nurses took action in response to alerts 77% of the time
  - Counselling, supportive medications, referrals to ER, chemotherapy dose modifications, imaging

Quality of Life

- Assessed at 6 months, compared to baseline
- Compared to standard care, 31% more patients in the self-reporting arm experienced QOL benefits ($P<0.001$)

*Basch: J Clin Oncol 2016;34:557-565*
Proportion of Patients Visiting Emergency Room

- Compared to standard care, 7% fewer patients in the self-reporting arm visited the ER, with durable effects throughout the study \((P=0.02)\)

Overall Survival

- Compared to standard care, median survival was 5 months longer among patients in the self-reporting arm \((31.2 \text{ vs. } 26.0 \text{ months})\) \((P=0.03)\)
- Remained significant in multivariable analysis: Adjusted hazard ratio 0.832 \((95\% \text{ CI; } 0.696, 0.995)\)
Conclusions

- Systematic symptom monitoring with patient self-reporting improves overall survival
- This approach should be considered for inclusion as a part of standard symptom management
- Future efforts should focus on implementation strategies for integrating self-reporting into electronic health records and into workflow of oncology practice
STREAM Intervention

www.stress-aktiv-mindern.ch

- 8-week program (8 modules)
  1-2 hours per week
- Based on established stress management programs\(^1\)
- Therapist-guided: once weekly written contact with psychologist


Study design
Endpoints and Statistics

Efficacy endpoints

Primary endpoint: Quality of life FACIT-F total score at T2
Secondary endpoints: Distress (Distress Thermometer) and mood (HADS score) at T2

Efficacy analyses:

Analyses of Covariance (ANCOVAs)* in intention-to-treat population, significance level two-sided α 0.05

Sample Size

60 participants/arm, Δ 9 points FACIT-F score at T2, power 0.80, two-sided α 0.05

*ANCOVA with post-scores T2 as dependent variable, pre-scores T1 as covariate, group allocation (intervention vs control) as independent variable, adjusted for baseline distress (DT ≥ 5 vs <5)

Results

Patient flow

Total assessed for eligibility (n=236)
Written informed consent and completion of baseline questionnaires (n=129)
Randomised to intervention (n=66)
Allocated to intervention (n=66)
No further treatment (n=66)
No further follow-up (n=66)
2-month follow-up (n=66)
Primary assessment (n=66)

Included (n=108)
Intervention (n=55)
Withdrawal (n=53)

Excluded (n=128)
Intervention (n=66)
Withdrawal (n=62)

Presented By Viviane Hess at 2017 ASCO Annual Meeting
### Results

**Baseline characteristics**

<table>
<thead>
<tr>
<th></th>
<th>All (n=129)</th>
<th>Control group (n=64)</th>
<th>Intervention group (n=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (median), years (IQR)</strong></td>
<td>52 (46-58)</td>
<td>53 (46-58)</td>
<td>51 (46-57)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>109 (84.5%)</td>
<td>56 (87.5%)</td>
<td>53 (81.5%)</td>
</tr>
<tr>
<td>male</td>
<td>20 (15.5%)</td>
<td>8 (12.5%)</td>
<td>12 (18.5%)</td>
</tr>
<tr>
<td><strong>Tumor origin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>breast</td>
<td>92 (71.3%)</td>
<td>47 (73.4%)</td>
<td>45 (69.2%)</td>
</tr>
<tr>
<td>gynecological tract</td>
<td>7 (5.4%)</td>
<td>5 (7.8%)</td>
<td>2 (3.1%)</td>
</tr>
<tr>
<td>lung</td>
<td>5 (3.9%)</td>
<td>3 (4.7%)</td>
<td>2 (3.1%)</td>
</tr>
<tr>
<td>ONS/head and neck</td>
<td>4 (3.1%)</td>
<td>1 (1.6%)</td>
<td>3 (4.6%)</td>
</tr>
<tr>
<td>lymphoma</td>
<td>11 (8.5%)</td>
<td>4 (6.2%)</td>
<td>7 (10.8%)</td>
</tr>
<tr>
<td>skin/soft tissue</td>
<td>1 (0.8%)</td>
<td>1 (1.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>gastrointestinal tract</td>
<td>7 (5.4%)</td>
<td>2 (3.1%)</td>
<td>5 (7.7%)</td>
</tr>
<tr>
<td>urogenital tract</td>
<td>2 (2%)</td>
<td>1 (1.6%)</td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td><strong>Disease stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized disease</td>
<td>111 (86.0%)</td>
<td>55 (85.9%)</td>
<td>56 (86.2%)</td>
</tr>
<tr>
<td>Metastatic disease</td>
<td>18 (14.0%)</td>
<td>9 (14.1%)</td>
<td>9 (13.8%)</td>
</tr>
</tbody>
</table>

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Presented By Viviane Hess at 2017 ASCO Annual Meeting
Results

**Intervention**

<table>
<thead>
<tr>
<th>Intervention group (n=65)</th>
<th>Median duration, weeks (IQR)</th>
<th>Adherence</th>
<th>Usability</th>
<th>Therapeutic alliance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11.7 weeks (9.1 to 18.6)</td>
<td>6 out of 8 modules</td>
<td>SUS score, module 1, mean (IQR)</td>
<td>WAI-SR score, mean (IQR)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>52 (80.0%)</td>
<td>87.5 (81.2 to 95.0)</td>
<td>3.77 (3.38 to 4.14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>All 8 modules</td>
<td>SUS score, module 8, mean (IQR)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>49 (75.4%)</td>
<td>90.0 (82.5 to 95.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Therapists’ time per patient/week**

<table>
<thead>
<tr>
<th>minutes, mean (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.3 (IQR 9.5-17.9)</td>
</tr>
</tbody>
</table>

Results

**Efficacy outcomes**

*ANCOVAs T2-T1*

<table>
<thead>
<tr>
<th>Distress</th>
<th>Quality of life</th>
<th>Mood</th>
</tr>
</thead>
<tbody>
<tr>
<td>DT</td>
<td>FACIT-F</td>
<td>HADS</td>
</tr>
<tr>
<td>Treatment effect, mean [95%CI]</td>
<td>Treatment effect, mean [95%CI]</td>
<td>Treatment effect, mean [95%CI]</td>
</tr>
<tr>
<td>-0.85</td>
<td>8.59</td>
<td>-1.28</td>
</tr>
<tr>
<td>(-1.60; -0.10)</td>
<td>(2.45 to 14.73)</td>
<td>(-3.02; 0.45)</td>
</tr>
<tr>
<td>p = 0.03</td>
<td>p = 0.007</td>
<td>p = 0.15</td>
</tr>
</tbody>
</table>

Presented By Viviane Hess at 2017 ASCO Annual Meeting
Results
2-month Follow-up

Follow-up intervention group
FACIT-F, DT and HADS score did not change significantly between T2 and T3

Follow-up control group
51/64 patients underwent intervention after T2

<table>
<thead>
<tr>
<th></th>
<th>Mean change (95%CI)*</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of life (FACIT-F)</td>
<td>10.95 (6.18 to 15.71)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Distress thermometer (DT)</td>
<td>-1.25 (-1.95 to -0.55)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hospital Anxiety and Depression Scale (HADS)</td>
<td>-2.83 (-4.29 to -1.36)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

*paired t-test on ITT population (n=64) T2-T3

STREAM: Conclusions

- Therapist-guided online stress management program for newly diagnosed cancer patients is feasible during treatment with a low drop out rate
- Cancer patients can be reached via online recruitment
- Majority of participants were female, breast cancer patients in the curative setting
- 75% of patients had high levels of distress at baseline
- Therapist-guided online stress management program STREAM significantly improved quality of life including fatigue and lowered distress
Managing Cancer And Living Meaningfully (CALM): A Randomized Controlled Trial of a Psychological Intervention for Patients with Advanced Cancer

Gary Rodin MD, FRCPC
Head, Department of Supportive Care
Princess Margaret Cancer Centre

Co-Principal Investigators:
Sarah Hales MD, PhD, FRCPC
Psychiatrist, Department of Supportive Care
Princess Margaret Cancer Centre

Chris Lo PhD
Research Psychologist, Department of Supportive Care
Princess Margaret Cancer Centre

Funding: Canadian Institutes of Health Research

Managing Cancer And Living Meaningfully (CALM)

- A novel, brief supportive-expressive psychotherapy intervention
  - 3-6 individual sessions over 3-6 months with a specially trained cancer clinician
  - Relational support and reflective space

- Attention to four broad domains:
  - Symptom management & communication with healthcare providers
  - Changes in self and relationships with close others
  - Spirituality and sense of meaning and purpose
  - Future-oriented concerns, hope and mortality
Rationale for CALM

- Predictable and often overwhelming challenges
- Motivation for help heightened due to the perceived shortness of time
- Systematic and routine psychological interventions for patients with advanced disease are not implemented in most cancer centers
- Evidence has not been available to demonstrate the effectiveness of such interventions

Methods

- Unblinded RCT with two trial conditions:
  - CALM plus Usual Care (UC) or UC

- Participants:
  - Patients with advanced cancer recruited from ambulatory oncology clinics at a comprehensive cancer center

- Inclusion criteria:
  - ≥18 years of age
  - Fluent in English
  - No cognitive impairment
  - Confirmed diagnosis of advanced or metastatic cancer
Outcomes

- **Primary outcome:**
  - Severity of depressive symptoms (*Patient Health Questionnaire*-9) (PHQ-9)

- **Secondary outcomes included:**
  - Quality of life (*Quality of Life at the End-of-Life Cancer Scale*) (QUAL-EC)
  - Emotional support from healthcare providers (*Clinical Evaluation Questionnaire*) (CEQ)
  - Death anxiety (*Death and Dying Distress Scale*) (DADDS)
  - Generalized anxiety (*Generalized Anxiety Disorder*-7) (GAD-7)
  - Spiritual well-being (*Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being Scale*) (FACIT-Sp)

### Primary Outcome

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>UC Mean (SD)</th>
<th>CALM Mean (SD)</th>
<th>$\Delta_{M1,M2}^*$</th>
<th>CI (lower, upper)</th>
<th>p-value</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>7.41 (4.75)</td>
<td>7.45 (4.96)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3 months</td>
<td>7.01 (4.82)</td>
<td>5.97 (4.83)</td>
<td>1.09</td>
<td>0.04, 2.13</td>
<td>0.04</td>
<td>0.23</td>
</tr>
<tr>
<td>6 months</td>
<td>6.66 (4.96)</td>
<td>5.35 (3.99)</td>
<td>1.33</td>
<td>0.27, 2.38</td>
<td>0.01</td>
<td>0.30</td>
</tr>
</tbody>
</table>

*$\Delta_{M1,M2}$ is the regression-estimated mean difference between groups controlled for baseline*
Clinical Importance

- The proportion of depressed individuals with a clinically meaningful reduction* in depressive symptoms:
  - 52% CALM vs. 33% UC at 3 months
  - 64% CALM vs. 35% UC at 6 months

- CALM participants were also:
  - Less likely to develop depressive symptoms of at least subthreshold severity at 3 months:
    - 13% CALM vs. 30% UC

* Minimal clinically important difference (MCID) ≥ 5 point reduction on PHQ-9

Secondary Outcomes

- Secondary outcomes which favored CALM at 3 and 6 months included:
  - Greater end-of-life preparation
  - Greater opportunity to talk about future-oriented concerns and feel less frightened
  - Greater ability to express and manage feelings

- Additional outcomes favoring CALM at 6 months included:
  - Better ability to talk and feel understood about how cancer has affected their life
  - Better ability to explore ways of communicating with the healthcare team & family
  - Better ability to deal with changes in relationships as a result of cancer
  - Greater clarification of values and beliefs

- All effects were strengthened at 6 months
Conclusions

- CALM is an effective intervention that alleviates depressive symptoms in individuals with advanced or metastatic cancer and helps them to address the multiple and predictable challenges they face.

- A global network is now being established to train health professionals in the delivery of this intervention and to evaluate its effectiveness in diverse clinical and cultural settings.

Durable remissions with BCMA specific chimeric antigen receptor (CAR)-modified T cells in patients with refractory/relapsed multiple myeloma

Wanhong Zhao (alternative presenter)

Frank (Xiaohu) Fan 1, Wanhong Zhao 2, Jie Liu 1, Ali He 2, Yinxia Chen 1, Xingmei Cao 2, Nan Yang 2, Baiyan Wang 2, Pengyu Zhang 2, Yilin Zhang 2, Fangxia Wang 2, Bo Lei 2, Lufang Gu 2, Xugeng Wang 2, Quichuan Zhuang 2 and Wanggang Zhang 2

1Nanjing Legend Biotech Inc., Nanjing, China
2Hematology Division, The Second Affiliated Hospital of Xi’an Jiaotong University, Xi’an, China
Legend LCAR-B38M Treatment Scheme

Clinical trials.gov/NCT03090659

- Screening & enrollment
- Conditioning Chemotherapy
- LCAR-B38M Infusion
- First Tumor Assessment

Day -5 Day 0 Day 2 Day 6 Day 30

Manufacturing (No Bridging Therapy Allowed)
Investigational Product Hospitalization Period
Follow up post-treatment and assessment

Clinical efficacy of LCAR-B38M product

Related Ig (mg/dL)

Days post CART infusion

Pt11 (IgA)
Pt10 (IgG)
Pt12 (IgA)
Pt111 (IgA)
Pt12 (IgA)
Pt14 (IgG)
Pt15 (IgG)
Pt16 (IgA)
Pt17 (IgG)
Pt18 (IgA)
Pt19 (IgA)

Normal upper limit of IgG
Normal upper limit of IgA

Presented By Wanhong Zhao at 2017 ASCO Annual Meeting
Clinical efficacy of LCAR-B38M product

Legend’s first CR case in MM CAR-T clinical trial

- Patient #2 follow-up (two months after CAR-T therapy)

✓ All Hematology indexes recovered as normal;
✓ Tumor cells in bone marrow disappeared completely;
✓ Abnormal immunoglobulin disappeared.
Clinical efficacy of LCAR-B38M product

- The 6th MM patient had widely spread extramedullary lesion of metastases found all over the body before our treatment, but all lesions have disappeared after the treatment.

Efficacy follow-up of LCAR-B38M CAR-T cells

Typical outcome of treated patients in efficacy follow-up

- Patient: 6
- CRS: MRD negative
- PR: Serum immunofixation turn negative, Urine immunofixation turn negative
- VGPR: >90% reduction of aberrant MM Ig
- sCR: >50% reduction of aberrant MM Ig
- Time since LCAR- B38M CAR- T Treatment, Months
Efficacy follow-up of LCAR-B38M CAR-T cells

- Patients treated before Jan 30, 2017
- Total
- Best efficacy

<table>
<thead>
<tr>
<th>PR</th>
<th>VGPR</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

- Objective response rate (ORR): 100%

Safety: Major adverse events is cytokine release syndrome (CRS)

- Adverse Event, n (%)
  - Grade ≥3 adverse event: 2 (5.7%)
  - Serious adverse event: 0 (0)
  - Fatal events excluding disease progression: 0 (0)

- Cytokine release syndrome (CRS):

- Days post CART infusion:
  - Days 0 to 30
  - Days 31 to 60
  - Days 61 to 90
  - Days 91 to 180

Presented By Wanhong Zhao at 2017 ASCO Annual Meeting
Conclusions

- LCAR-B38M CAR-T technology exert quick and reproducible therapeutic effects in refractory and relapsed multiple myeloma patients.

- >12 months follow-up of early patients shows durable and stringent complete remission which raises hopes of cure.

- LCAR-B38M technology not only demonstrate outstanding efficacy, but also suggest a great safety profile.

- US clinical trial is under way and the technology will be fully validated under "American (FDA) standard".

Questions?