AGENDA

<table>
<thead>
<tr>
<th>Time</th>
<th>Presentation</th>
<th>Presenters/Co-presenters</th>
</tr>
</thead>
<tbody>
<tr>
<td>4:30-4:45 pm</td>
<td>Introduction &amp; Reminders</td>
<td>ECHO Team</td>
</tr>
<tr>
<td>4:45-5:00 pm</td>
<td>Gynecologic/Onco-podiatric Oncology Care</td>
<td>Drs. Lauren Rye &amp; Jennifer Kampa</td>
</tr>
<tr>
<td></td>
<td>Based on Mutation Status</td>
<td>With expert panel discussion by Dr. Anne O'Dea</td>
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<tr>
<td>5:05-5:25 pm</td>
<td>Case Presentation #1:</td>
<td>Case Presenter:</td>
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<tr>
<td></td>
<td></td>
<td>NCC, Dr. O'Dea &amp; Larson</td>
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<tr>
<td></td>
<td>Case Presentation #2:</td>
<td>Sarita Regional/Trinity Women Cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Center, Dr. O'Dea</td>
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<tr>
<td></td>
<td>Case Presentation #3:</td>
<td></td>
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<tr>
<td></td>
<td>Case Presentation #4:</td>
<td></td>
</tr>
<tr>
<td>5:25-5:30 pm</td>
<td>Homework, Wrap-up, and Announcements</td>
<td>ECHO Team</td>
</tr>
</tbody>
</table>

Continuing education credit statements:

- Physician: The University of Kansas Medical Center Office of Continuing Medical Education is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.
- The University of Kansas Medical Center Office of Continuing Medical Education designates this live activity for a maximum of 1.00 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.
- ACHC/CHN: The University of Kansas Medical Center Jett Health Education Center that is approved as a provider of CHN by the American NAM, Board of Nursing. This continuing education activity is approved for 1.2 contact hours applicable for ACHC, or ESN, or ESN CHN. Completed forms must be submitted to the University of Kansas Medical Center. The Provider Provider number: ESN 55-627. Mary Beth Warren, MS, RN, Coordinator.
- Nursing: Participation cannot exceed 25% of the offering to receive credit.
Funding Sources

The series is funded by the Association of Community Cancer Centers and the Pfizer Independent Grants for Learning and Education, as well as internal support through KU Cancer Center and the Midwest Cancer Alliance.

Continuing education credit or certificate of attendance

ACTIVITY IDENTIFICATION CODE: 3534  
DEADLINE TO ENTER CODE AND COMPLETE EVALUATION: 9/9/19

• Using your mobile phone, you can text the activity identification code to (828) 216-8314;
OR
• Accessing www.ceds.com from a mobile device or PC and entering the activity identification code;
OR
• Downloading the ceds mobile app (iOS, Android) and using the activity identification code to sign-in to events.
Check-In

- Participant Locations (use chat box to list names of attendees at your site)
  - Cancer Center of Kansas
  - KDHE, Susan G. Komen, or other agencies
  - Lawrence Memorial Hospital
  - North Kansas City Hospital
  - Olathe Medical Center
  - Salina Regional/Tommie Walker Cancer Center
  - Truman Medical Center
  - University of Kansas Health System
    - Has Med
    - KU Cancer Center
    - St. Francis
    - University of New Mexico
Recording
We will be recording this Breast Cancer Genetics ECHO for educational and quality improvement purposes.

By participating in this ECHO clinic you are consenting to be recorded.

Some Helpful Tips
- Test both audio & video
- Mute microphone when not speaking
  - Bottom left of your screen
  - Remember to unmute before speaking
- Your participation is important!
  - Speak clearly
  - Short and to the point comments are best
  - Use chat function
- Position webcam effectively
  - Show your face
  - Have a good light source from the front
  - Avoid being backlit

Polling Questions

![Polling Question]

Share Group Response
Personalizing Oncology Care Based on Mutation Status

- Germline vs. somatic testing
- Review of NCCN guidelines for single indication testing
- Approved therapies in patients with MBC and pathogenic mutations
- Case Studies

Somatic vs Germline Mutation

- Somatic mutation: a change in the DNA of a cell that is not inherited, not inherited
- Germline mutation: a change in the DNA of a cell that can be inherited, inherited

Prevalence of BRCA1/2 Mutations

- 215,000 new cases of invasive breast cancer in 2017
- Her2+: ~17,000 patients
- 5-10% BRCA1/2
- 6,000 patients
- Not Her2+: ~18,000 patients
- 2-5% BRCA1/2
- 7,500 patients
Poly (ADP-ribose) polymerase inhibitor

- Single strand breaks → required by PARP
- Single strand breaks + double strand break
  PARP Inhibitor
- Double strand break → required by homologous recombination (HR)
- Double strand break → cell death
  BRCA deficiency

FDA Approved PARP Inhibitors

Olaparib
- Indicated in patients with deleterious or suspected deleterious germline BRCA1 or BRCA2 mutations who have been treated with chemotherapy in the neoadjuvant or adjuvant setting. Patients with human epidermal growth factor receptor 2 (HER2) negative, HER2-negative breast cancer and who are positive for both germline and somatic mutations in BRCA1 or BRCA2 are eligible.
- Select patients for therapy based on an FDA-approved companion diagnostic test
- 300 mg twice daily

OlympiAD: Phase III trial of olaparib in gBRCA mutation associated breast cancer

- HER2-negative mBC
  - Eri, anastrozole, or trastuzumab
- Deleterious or suspected deleterious gBRCA mutation
- Prior anthracyclines and taxanes
- ≤2 prior chemotherapy lines in metastatic setting
- HR+ disease progression on ≥1 ET, or not suitable for ET
- If prior endocrine use:
  - No evidence of progression during treatment in the advanced setting
  - ≤12 mo since last documented response
- Primary endpoint: PFS by blinded independent review
Olaparib associated with a 42% increase in median PFS as compared to treatment of physician's choice

Overall survival: ITT

Overall survival in prespecified subgroups
### OlympiAD: Adverse Events

<table>
<thead>
<tr>
<th>Grade ≥ 3 AEs in ≥ 10% of Patients</th>
<th>Grade ≥ 3 AEs in ≥ 2% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Nausea</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Dose delay</td>
<td>Dose delay</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Diarrhea</td>
</tr>
</tbody>
</table>

### EMBRACA: Phase III trial of talazoparib in gBRCA mutation-associated BC

- Locally advanced or metastatic HER2-negative breast cancer
- Germline BRCA1 or BRCA2 mutation
- No more than 3 prior cytotoxic chemotherapy regimens for locally advanced or metastatic disease
- Prior treatment with a taxane and/or anthracycline unless medically contraindicated

### Summary (OlympiAD and EMBRACA)

<table>
<thead>
<tr>
<th>Event</th>
<th>OlympiAD</th>
<th>EMBRACA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (95% CI)</td>
<td>0.59 (0.40-0.88)</td>
<td>0.54 (0.40-0.76)</td>
</tr>
<tr>
<td>OS (95% CI)</td>
<td>0.51 (0.28-0.95)</td>
<td>0.70 (0.54-0.90)</td>
</tr>
<tr>
<td>GMR</td>
<td>39.9% (19.9%-79.1%)</td>
<td>66.6% (22.2%-96.5%)</td>
</tr>
<tr>
<td>Dose reduction (95% CI)</td>
<td>0.64 (0.31-0.97)</td>
<td>0.55 (0.37-0.82)</td>
</tr>
<tr>
<td>AEs at Grade 3</td>
<td>36.1%</td>
<td>39.2%</td>
</tr>
<tr>
<td>AEs at Grade ≥ 3</td>
<td>26.3%</td>
<td>30.9%</td>
</tr>
<tr>
<td>Thrombocytopenia at Grade 3</td>
<td>2.6%</td>
<td>14.7%</td>
</tr>
<tr>
<td>Neutropenia (any grade)</td>
<td>54.9%</td>
<td>48.5%</td>
</tr>
<tr>
<td>AEs (any grade)</td>
<td>3.4%</td>
<td>35.2%</td>
</tr>
</tbody>
</table>
Future Directions
Breast Cancer Treatment & Genetic Testing

- PARP:
  - Current Clinical Trials
  - Pathogenic mutations outside BRCA1/2
  - Neoadjuvant
  - Platinum based therapy

Case Studies

Wrap Up
- Thank you for your participation!
- Make sure to sign in your name in the chat box.
- Review organizational process for screening, evaluation, education & consent, and testing.
- Focus on Homework: Complete the workflow analysis worksheet
- See you next month: October 9, 2019 at 4:30PM