Utilizing Clinical Pathways for Remission Maintenance in Ovarian Cancer

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Dr. Edwards has nothing to disclose.
Learning Objectives

• Identify the clinical and economic impact of current OC diagnostic and treatment limitations
• Recognize the advantages and disadvantages of existing clinical pathways for OC diagnosis and management
• Integrate updated guidelines and recent clinical data into OC clinical pathway development plans
• Employ strategies to improve the adoption of clinical pathways for the maintenance of OC remission that consider all available treatment options
The UPMC Strategic Framework

Smart Technology
Big Data

Good Science
Big Science

New Models of Care
Improved Outcomes - Cost Effective
Enterprise Analytics

Delivering real-time data to the bedside

Enterprise-Level Data Warehouse

Advanced data mining

Harmonize structured data (db Motion) and unstructured data (Nuance)

Aggregate data into central data warehouse: Cerner, Epic, Peoplesoft, HealthPlaNET, etc.

Clinical Data (Provider)

Financial

Population Data (Payer)

Genetics Genomics

- Deliver better outcomes/optimize cost
- Develop new models of care
- Enable the center for innovative science

Ask new questions

Make digital information usable

Ingest over 200 data sources
Specialty Care: New Models of Care
Pathways based solely on quality (and value)

- Providers
  - Treat the sick

- Clinician created
  - Care Pathway-Algorithms
  - Best Practices

- Payers
  - Maintain Health

- Cost
- Quality

- Patient Safety
  - Variation

- Appropriateness
How Pathways Are Use

• PATHWAYS ARE EMBEDDED IN DECISION SUPPORT INTEGRATED INTO THE PHYSICIAN/STAFF INTERFACE IN THE OUTPATIENT SETTING

• PATHWAY ADHERENCE IS COLLECTED WITH MULTIPLE COMPONENTS INCLUDING
  – PHYSICIAN DECLARATION
  – CONFIRMATION OF PATIENT EDUCATIONAL MATERIALS ABOUT THE INTERVENTION DELIVERED
  – CONFIRMATION THAT THE DECLARED INTERVENTION OCCURRED THROUGH BILLING AND PHARMACY

• METRICS OF THE PATHWAY INTERVENTION DRIVE PHYSICIAN INCENTIVE PAYMENT STRUCTURE
Key Points

• There is significant variability in direct cost per case within the same type of procedure.

• Open hysterectomies have the highest average direct cost per case, driven by a higher Med/Surg cost which is due to a longer LOS.

• Operating room cost is the main driver for minimally invasive procedures.

• Open hysterectomies have the worst quality outcomes, supporting the project goal of avoiding open procedures when possible.
Two Different Technical Approaches to Deploying Pathways

Oncology Pathways:

• Integrated Via Pathways application with Epic through a results interface, Best Practice Advisories, and result routing schemes
• Promote standardization of care
• Optimize communication of treatment intent
• Heighten awareness of clinical research

Surgical Pathway: Surgical Oncology

• Utilize Epic documentation flowsheets and Best Practice Advisories
• Enforce adoption of hysterectomy pathways to streamline the surgery and pre-operative ordering process
Who Develops the Pathways?

Committee Membership open to ALL Network providers.

Quarterly Med Onc Meetings
Semi-Annual Rad Onc Meetings
Annual Multidisciplinary Meetings

Academic & Community Co-Chairs
Provider clicks the Onc Pathways URL navigator section which launches Via Pathways Decision Support within the Office Visit navigator.
Pathway Determinants

01 Efficacy
If there is a clear choice, this is the pathway

02 Toxicity
If efficacy is comparable, choose the treatment with less toxicities to improve QOL and reduce hospitalization/ED visits

03 Cost
ONLY if efficacy and toxicities are comparable, choose the lowest cost treatment to the payer/patient
EPIC Integration with Pathways

• Basic Interfaces and Integration (available now):
  – EPIC demographics and scheduling to Pathways (ADT/SIU)
  – Active Directory single-sign-on
  – Pathways decision summary messages to EPIC (ORU)
  – Result Routing Schemes direct In Basket messages to Research and Clinical Staff
  – Pathways discrete regimen identifier passed to EPIC. Allows EPIC Beacon to queue up matching protocol for ordering using Best Practice Advisories
The Via Pathways Treatment Decision files as a result in the patient’s chart.

The result message is routed to the In Basket of the clinical staff.
Clinical Trial Eligibility Notification

- Clinical trial eligibility based on patient characteristics entered by the Oncologist during Via Pathways navigation
- If patient is eligible for clinical trial screening the trial will be presented for selection
- When selected, a BPA will fire in the patient’s chart stating “Pathways Clinical Trial Eligibility Notification Message has been sent to the CRC pool.”
- Result message will be sent to the In Basket of the research staff and will file in the patient’s chart.
**FY14 Pathway Adherence & Incentive Model**

Pathway Adherence Percentage = \( \frac{\text{Number of times physician adheres to pathway}}{\text{Number of hysterectomies performed}} \)

<table>
<thead>
<tr>
<th>Scenarios</th>
<th>Pathway Adherence?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician is directed out of Pathway after answering ‘Yes’ to the first question ‘Is hysterectomy the secondary procedure or cancer dx?’</td>
<td>✓</td>
</tr>
<tr>
<td>Physician completes Pathway and chooses ‘Refer to Specialist’ recommendation.</td>
<td>✓</td>
</tr>
<tr>
<td>Physician completes Pathway and performs recommended procedure.</td>
<td>✓</td>
</tr>
<tr>
<td>Physician clicks on Pathway but exits before completing.</td>
<td>✗</td>
</tr>
<tr>
<td>Physician performs a different type of hysterectomy than recommended.</td>
<td>✗</td>
</tr>
<tr>
<td>Physician performs hysterectomy without completing a pathway.</td>
<td>✗</td>
</tr>
</tbody>
</table>
22,000 Women diagnosed with ovarian cancer

Most common cancer in women

US women diagnosed annually

22,000

3rd Highest Mortality: Incidence Ratio
Clinical Burden of Ovarian Cancer

- 2017 US ovarian cancer estimates\(^1\):
  - 22,440 new diagnoses
  - 14,078 related deaths
- Ovarian cancer is a heterogeneous disease\(^2\)
  - Ovarian carcinomas represent majority of malignant tumors and are responsible for most ovarian cancer-related deaths\(^2\)
  - \(>70\%\) are HGSOCs
- No distinctive symptoms associated with early stages of the disease\(^2\)

Late diagnosis is a major factor contributing to the high mortality rate\(^2\)

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HGSOC = High-grade Serous Ovarian Cancer.

BRCA 1/2 Genetic Testing Guideline

**Recommendations**

**NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)**

Hereditary ovarian cancer testing criteria:
- Personal history of ovarian* cancer
  
  “[T]he National Comprehensive Cancer Network® (NCCN®) Panel recommends testing for patients with a personal history of ovarian carcinoma... diagnosed at any age” — Page BRCA1
- All patients with ovarian cancer should be referred for a genetic risk evaluation
  
  Primary treatment should not be delayed for a genetic risk evaluation — Page MS-17

**ASCO Expert Statement**

Cancers for which genetic counseling and testing should be considered, even in absence of family history:
- Epithelial ovarian, fallopian tube, or primary peritoneal cancer (most commonly, high-grade serous histology)

**SGO Clinical Practice Statement October 2014**

The Society of Gynecologic Oncology (SGO) encourages the medical community to offer genetic counseling and testing to all women with ovarian, fallopian tube and peritoneal carcinoma, regardless of age or family history

All of the above organizations recommend genetic counseling and genetic testing regardless of age or family history

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*Includes fallopian tube and primary peritoneal cancers. BRCA-related ovarian cancers are associated with epithelial nonmucinous histology.

Ovarian Cancer Stage at Diagnosis

Percent of Cases by Stage
- Localized: 15%
- Regional: 20%
- Distant: 60%
- Unstaged: 6%

5-Year Relative Survival by Stage at Diagnosis
- Localized: 93%
- Regional: 73%
- Distant: 29%
- Unstaged: 25%

Over two-thirds of women with advanced ovarian cancer will experience a disease recurrence.

Cost of Ovarian Cancer Care - Maintenance

- ADVANCED CANCER PATIENTS THE RULE
- MULTIPLE LINES UP TO 10TH LINE THERAPY NOT UNCOMMON
- PATIENT SURVIVAL WITH ACTIVE DISEASE THERAPY VERY EXTENDED
- TARGETED AND IMMUNOTHERAPY OPTIONS EXPANDING
- NO CLEAR DOMINANT MAINTENANCE STRATEGY CURRENTLY
- LIST OF CANDIDATE AGENTS FOR MAINTENANCE IS EXTENSIVE
Ovarian Cancer Cost of Care 2010 to 2020

- ALL CANCERS SURVIVORSHIP IS INCREASING!
- INCIDENCE OF OVARIAN CANCER IS PROJECTED TO DECREASE 4.71%
- POPULATION AGING WILL INCREASE CANCER DUE TO MORE WOMEN OVER 65
- INITIAL COST OF CARE IS 3\textsuperscript{RD} HIGHEST IN FIRST YEAR $99,715 PER CASE
- NATION-WIDE COST OF CARE WILL INCREASE FROM 5.12 TO 5.64 BILLION
- MOSTLY DUE SURVIVORSHIP EXTENSION
- PERSISTENT HIGH COST IN LAST YEAR OF LIFE
Therapies for Ovarian Cancer

Adjuvant Chemotherapy Unchanged for over 30 yrs!

Ovarian Cancer TREATMENTS
Ovarian Cancer: Staging

**STAGE I**
- Tumor limited to one or both ovaries
- Tumor may be found on ovarian surface
  - Possible capsule rupture
  - Malignant cells may be evident in peritoneal washings

**STAGE II**
- Tumor invades one or both ovaries, with extension into the pelvic region
  - Uterus
  - Fallopian tubes

**STAGE III**
- Tumor extends beyond pelvis
  - Abdominal (peritoneal) wall or abdomen
  - Nodes
  - Small bowel
  - Liver surface

**STAGE IV**
- Distant metastasis
  - Lung
- Liver invasion
Ovarian Cancer is a Heterogeneous Disease

**Genetic characteristics can be used to classify ovarian cancers as distinct clinical subtypes**

HRR = Homologous recombination repair.

Ovarian Cancer Maintenance History

• 24,000 CASES IN THE US EACH YEAR
• APPROXIMATELY 20,000 ARE ADVANCED STAGE
• WHILE RESPONSES EXCEED 80% FOR SURGERY AND CHEMOTHERAPY 2,000/24,000 WOMEN WILL DIE IN FIRST YEAR OF RESISTANT DISEASE

• FOLLOWING PRIMARY THERAPY 16,000 WOMEN WILL EXPERIENCE RECURRENCE AND 15,000 WILL DIE OF THEIR DISEASE AFTER EXTENDED SURVIVAL
Maintenance Therapy in Ovarian Cancer

**Definition**

- Prolonged treatment given after patient achieves response or remission after initial surgery and chemotherapy\(^1\)
- Treatment immediately following response to later lines of chemotherapy has also been investigated as maintenance therapy in randomized ovarian cancer trials\(^2,3\)

**Objectives**

1. To extend a clinically meaningful survival endpoint (OS, PFS)\(^1,4\)
2. To prolong the duration of remission\(^1\)
3. Not to substantially interfere with a patient’s quality of life due to toxicity associated with maintenance therapy\(^4\)

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Evidence Based Candidate Agents for Maintenance

- TAMOXIFEN - GOG standard
- CONTINUED BEVICIZUMAB OR PAACLITAXEL OR LIPOSOMAL DOXORUBICIN
- PARP (Poly-ADP Ribsoe) INHIBITORS
  - NIRAPARIB
  - OLAPARIB
  - RUCAPARIB
- OBSERVATION
- Rising CA 125 and no Index Disease
PARP Inhibitors

• PARP – family of proteins required for DNA repair (Base Excision Repair)
• PARP family - 17 proteins grouped into three subgroups and are activated by DNA strand breaks
• PARP inhibitors target tumors with genomic instability - HRD
• Oral agents from various pharmaceutical companies tested as treatment of active disease and as maintenance in tumors with BRCA germline mutations and recently non-mutated but susceptible ovarian cancer
FDA approved PARP with indication

- Olaparib Approved August 2017
  - Oral
  - Approved BRCA mutated therapy 2014
  - Approved maintenance for all ovarian cancer patients

- Niraparib Approved March 2017
  - Fast track approval
  - Active in mutated and non mutated cancers as maintenance

- Rucaparib Approved 2016
  - For previously treated recurrent ovarian cancer BRCA mutation
Niraparib (MK 4827)

- Maintenance trial oral agent - Current VIA choice
  - 553 patients randomized
  - Mutated tumor PFS 21.5 months vs 5.5 months placebo
  - Non-mutated PFS 9.3 months vs 3.9 mos placebo
  - Approved for partial and complete remission
  - Toxicity
    - Thromobcytopenia (severe 29 %)
    - Anemia
    - Fatigue
Olaparib—FDA approved maintenance 8/17

- Initial approval in 2014 for treatment of BRCA mutated
  - Capsule formulation being phased out
- Maintenance approval based on two trials after remission from platinum-base therapy in non-mutated patients
  - Capsule formulation utilized 300 mg BID
  - PFS 8.4 months versus 4.8 months placebo

Toxicity profile
- 20% anemia, fatigue, emesis

FDA August 2017
PARP Inhibitor Options in Ovarian Pathway

**Maintenance Therapy**
- If no prior PARP inhibitor, use Rucaparib 600 mg BID until disease progression or unacceptable toxicity.

**Third Line Therapy**
- If BRCA mutation present (germline or somatic):
  - Carboplatin AUC=6 + Paclitaxel 175 mg/m² q21 Days; re-evaluate every 3 cycles, treat until complete response, unacceptable toxicity, or disease progression.
- If neuropathy grade 2 or greater:
  - Carboplatin AUC=5 D1 + Gemcitabine 800 mg/m² D1, 8 q28 days; re-evaluate every 3 cycles, treat until complete response, unacceptable toxicity, or disease progression.

**Third Line Therapy**
- If recently progressed on Paclitaxel-based regimen:
  - Paclitaxel 80 mg/m² weekly + Bevacizumab 10 mg/kg q2 weeks, q28 days; re-evaluate every 3 cycles, treat until complete response, unacceptable toxicity, or disease progression.

**If patient refuses or is unlikely to benefit from further therapy:**
- PV37: End of Life Care/Hospice Care.

**If candidate for Phase I trial:**
- PV3: Referral to Phase I trial.

1. Consider as maintenance for recurrent disease after complete or partial response to platinum-based therapy.
Thank you

• QUESTIONS AND REFERENCES
  – ROBERT P. EDWARDS MD
  – MAGEE WOMENS HOSPITAL
  – 412-641-4212
Questions?