Poly ADP-Ribose Polymerase (PARP) Inhibitors for Ovarian Cancer

Public Meeting – September 14, 2017

ICER

INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Welcome and Introduction

- **Why are we here today?**
  - Innovation promising substantial benefits to patients and their families

    - "[Two thirds] of women are diagnosed in advanced stage where there is no hope of cure, remissions become increasingly shorter, and then the cancer becomes a chronic disease. Chronic, in the case of [ovarian cancer], means that you live on an increasingly limited menu of chemo and clinical trials along with their host of side effects, praying that each one will hold you for a long time while knowing that the cancer ultimately becomes resistant and you'll need to find something new."

      -- Ovarian Cancer Survivor

    - The approval of Lynparza marked the first new treatment for ovarian cancer in six years. The investment made in this personalized approach to cancer was extraordinary: a decade of research, and the participation of thousands of cancer patients enrolling in PARP inhibitor clinical trials to advance science for themselves, but also for their families."

      -- Facing Our Risk of Cancer Empowered (FORCE)

Welcome and Introduction

- **Why are we here today?**
  - Treatments with new mechanisms of action often raise questions about appropriate use and price
  - Increasing health care costs affect individuals, state and federal budgets
  - Patients can have difficulty accessing drugs through insurance barriers and/or out-of-pocket costs
  - Benefit of objective evaluation and public discussion of the evidence on effectiveness and value

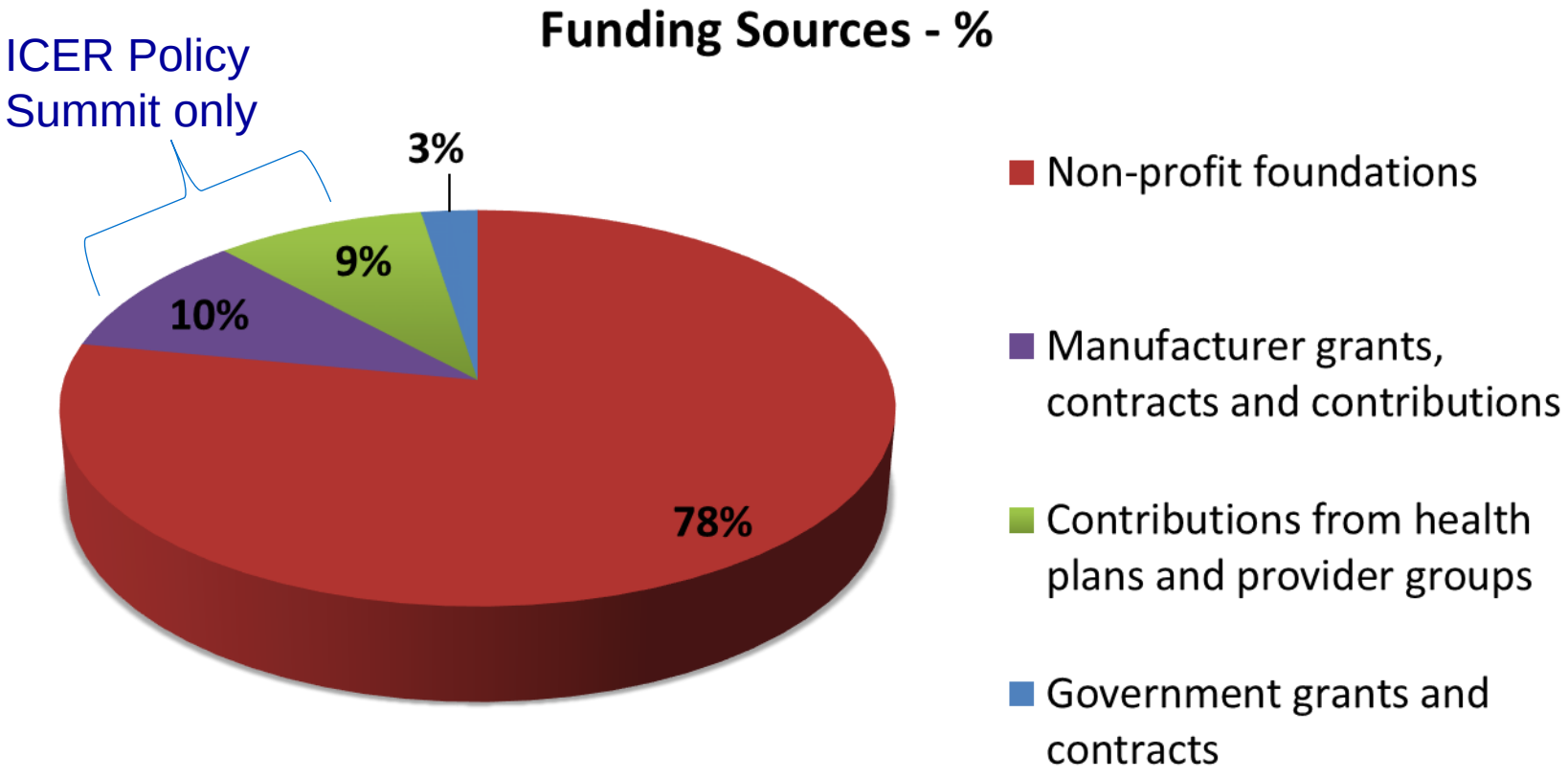
Welcome and Introduction

- Midwest Comparative Effectiveness Public Advisory Council (CEPAC)

- The Institute for Clinical and Economic Review (ICER)

Sources of Funding, 2017

ICER Policy Summit only

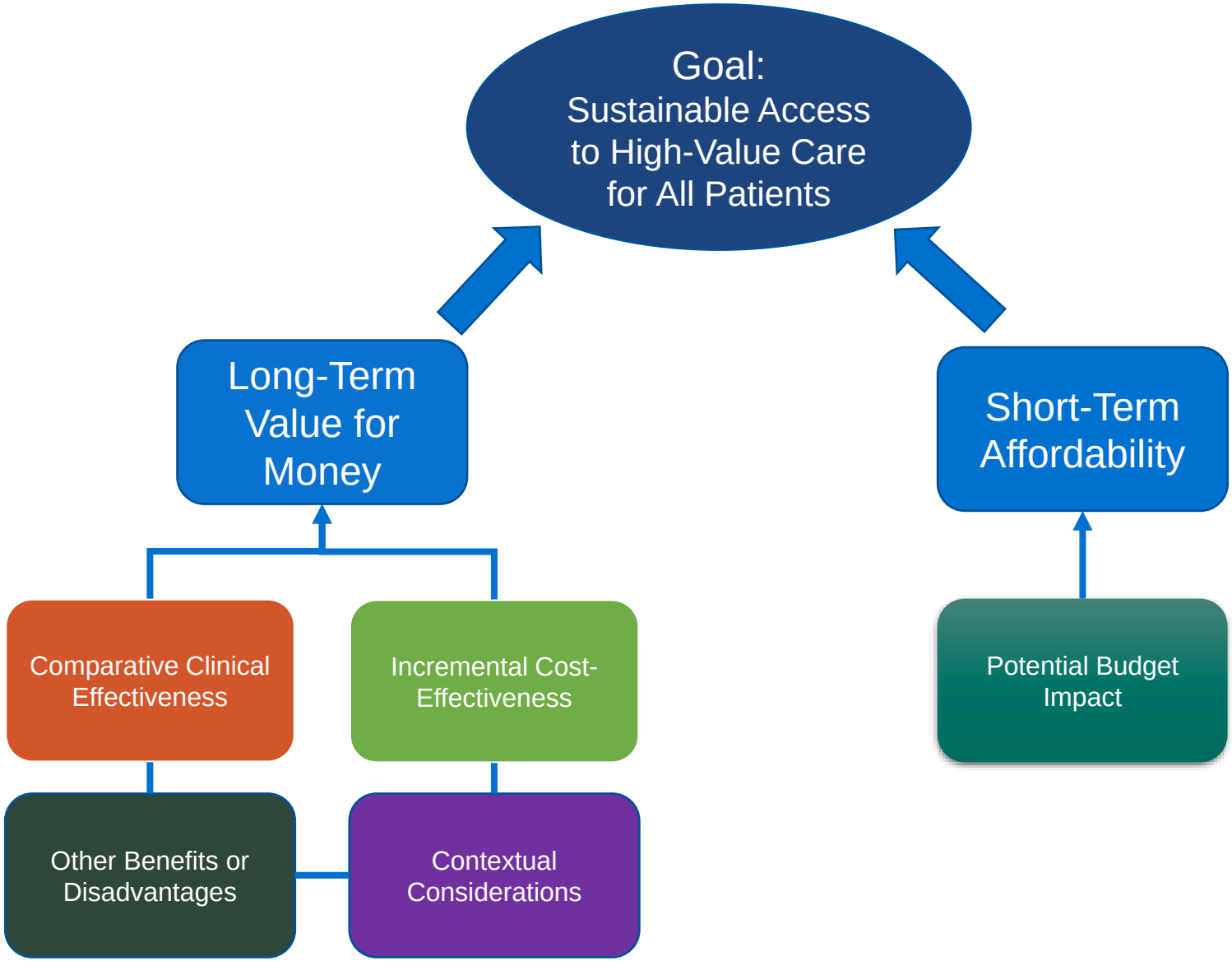


Welcome and Introduction

How was the ICER report on treatments for ovarian cancer developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Colorado cost-effectiveness modeling
- Public comment and revision
- Clinical expert report reviewers
  - Gini Fleming, MD
  - Andrea Wahner Hendrickson, MD

- How is the evidence report structured to support CEPAC voting and policy discussion?


Goal:
Sustainable Access to High-Value Care for All Patients
Long-Term Value for Money
Short-Term Affordability
Comparative Clinical Effectiveness
Incremental Cost-Effectiveness
Potential Budget Impact
Other Benefits or Disadvantages
Contextual Considerations

Agenda

10:00am: Welcome and Opening Remarks

10:15 am: Presentation of the Evidence

Evidence Review: Lipika Samal, MD

Comparative Value: R. Brett McQueen, PhD, University of Colorado

11:15 am: Manufacturer Public Comment and Discussion

11:45 pm: Public Comments and Discussion

12:15 pm: Lunch

1:00 pm: Midwest CEPAC Deliberation and Votes

2:30 pm: Policy Roundtable

3:30 pm: Reflections and Wrap Up

4:00 pm: Meeting Adjourned

Evidence Review

Lipika Samal, MD
Harvard Medical School

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Disclosures

None

Key ICER review team members

- Dan Ollendorf
- Geri Cramer
- Patricia Synnott
- Aqsa Mugal

Topic in Context

- Ovarian cancer is the most common cause of gynecologic cancer death and fifth-leading cause of cancer death in women
- Recurrence is common and the prognosis is poor after three lines of therapy
- Poly ADP-ribose polymerase (PARP) Inhibitors offer new mechanism of action
  - Oral agents initially indicated for patients with genetic mutations affecting DNA repair, such as *BRCA1* or *BRCA2* mutations

Key Terms

► **Germline BRCA mutation (gBRCAm)** – inherited deleterious mutation in either a *BRCA1* or *BRCA2* tumor suppressor gene

► **Somatic BRCA mutation (sBRCAm)** – deleterious or suspected deleterious alteration in the *BRCA1* or *BRCA2* genes that is acquired

► **Homologous Recombination Deficiency (HRD)** –An inability to efficiently repair damaged DNA.

PARP Inhibitors Overview

PARP inhibitor	Indication	Date of FDA Approval	WAC per Month (USD)*
Olaparib (Lynparza™, AstraZeneca)[19]	1) Patients with germline BRCA-mutated recurrent disease (≥3 prior lines of chemotherapy) 2) Maintenance treatment for platinum sensitive recurrent disease	1) December 19, 2014 2) August 17, 2017	$13,679
Rucaparib (Rubraca®, Clovis Oncology)[19]	Patients with germline and/or somatic BRCA-mutated recurrent disease (≥2 prior lines of chemotherapy)	December 19, 2016	$13,940
Niraparib (Zejula™, Tesaro, Inc.)[20]	Maintenance treatment for platinum sensitive recurrent disease	March 27, 2017	$14,965

*Price reflects the wholesale acquisition price listed on Red Book Online (Greenwood Village, CO: Truven Health Analytics. http://www.micromedexsolutions.com/. Accessed August 22, 2017), and is based on indicated dose

Insights from Patient Groups

- Recurrent ovarian cancer a difficult diagnosis:
  - Low likelihood of cure
  - Non-specific nature of symptoms
  - Substantial toxicity of cytotoxic chemotherapies
- Psychosocial support from nurses, clinicians, family and other caregivers essential
- Financial toxicity from costs of initial surgery and multiple lines of therapy is substantial

Populations of Interest

- **Population 1: "Recurrent, BRCA-mutated disease"**
  - Deleterious BRCA mutation
  - Relapsed after multiple lines of chemotherapy
- **Population 2: "Maintenance therapy for platinum-sensitive disease"**
  - ≥ 2 prior platinum-based chemotherapy regimens
  - Complete or partial response to the most recent regimen

Interventions & Comparators: Recurrent, BRCA-mutated disease

- **Interventions**
  - Olaparib: *4th-line or later treatment*
  - Rucaparib: *3rd-line or later treatment*
- **Comparators**
  - Bevacizumab + standard chemotherapy for recurrent disease
  - Pegylated liposomal doxorubicin + carboplatin (PLD+C)

Interventions & Comparators: Maintenance therapy for platinum-sensitive disease

- **Interventions**
  - Olaparib
  - Niraparib
- **Comparators**
  - Placebo (i.e., surveillance only)
  - Bevacizumab

Results

- 15 reports of 6 studies
  - Grey literature from conference proceedings, FDA materials, and data submitted by the manufacturers included
  - Recurrent population: limited to single-arm trials
  - Maintenance population: 3 peer-reviewed studies that included a control arm

No Direct or Indirect Comparisons

- No current head-to-head studies of PARP inhibitors
- Differences in study populations precluded even formal indirect comparisons:
  - Different patient populations
    - e.g. BRCA mutation type, number of prior chemotherapies, platinum sensitivity
  - Evaluation protocols for tumor assessment
    - e.g. different intervals between scheduled measurements of response, assessment by investigator versus blinded independent central review

Olaparib: Recurrent, BRCA-mutated Disease

- Subgroup analysis of one single-arm trial
- Median OS 17 months
  - ~6-9 months with standard relapse therapies
- Median PFS 7 months
  - ~4-6 months with standard relapse therapies
- Health-related quality of life was not reported

Olaparib: Maintenance Therapy for Platinum-Sensitive Disease

- Two RCTs of olaparib vs. placebo
  - Phase 2: Study 19
  - Phase 3: SOLO2
- Key differences between studies
  - Dosing/formulation
  - BRCA mutation status
- No OS benefit shown in Study 19
  - Data are still immature in Phase 3 SOLO2 study

Olaparib: Maintenance Therapy for Platinum-Sensitive Disease

- Study 19: median PFS 8 months for olaparib vs. 5 months for placebo
  - Subgroup analyses of PFS
    - BRCAm: 11 months vs. 4 months
    - Non-BRCAm: 7 months vs. 5.5 months
- SOLO2: median PFS 19 months vs. 5.5 months
- No significant differences in quality of life

Niraparib: Maintenance Therapy for Platinum-Sensitive Disease

- One RCT of niraparib vs. placebo
- No OS benefit shown (data still immature)
- Median PFS:
  - Germline BRCAm: 21 vs. 6 months
  - Non-germline BRCAm: 9 vs. 4 months
    - HRD with somatic BRCA mutation: 21 vs. 11 months
    - Vs. benefit of 3-5 months without BRCAm or HRD
- No significant differences in quality of life

Rucaparib: Recurrent, BRCA-mutated Disease

- Subgroup analyses from 2 single-arm Phase 2 trials
- OS data are not yet available
- Median PFS: 10 months
  - ~6 months with standard relapse therapies
- Quality of life data not reported

Harms

- Common side effects: nausea, vomiting, anemia, thrombocytopenia, and neutropenia
- Dose reduction due to toxicity common (ranged from 22-67% across trials vs. 3% with placebo)
- FDA warnings for myelodysplastic syndrome and acute myeloid leukemia (≤2% of patients)
- PARP inhibitors seem to be better tolerated than alternative relapse therapies, some of which include black box warnings

Controversies and Uncertainties

- No survival data demonstrating benefit over historical treatment options
- Suitability of PFS to evaluate clinical benefit in maintenance setting
- No comparative data in recurrent, BRCA-mutated ovarian cancer population

Other Benefits & Contextual Considerations

- Novel mechanism of action offering possible improvement over standard relapse therapies
- Low-grade adverse effects relative to cytotoxic chemotherapy
- Simplicity of oral regimen

Public Comments

- Most appropriate comparison is head-to-head between PARP inhibitors
- ICER review minimizes benefits of progression-free survival to patients

Summary

- Single-arm data only for recurrent, BRCA-mutated disease
- PFS benefit over historical comparators and placebo
  - Maintenance therapy benefits greatest in gBRCAm and HRD
- Data on overall survival extremely limited
- Toxicity profile favorable vs. standard chemo

Evidence Ratings

Population/PARP inhibitor	ICER Evidence Rating
Recurrent, BRCA-mutated disease	
Olaparib	P/I
Rucaparib	P/I
Niraparib	I
Maintenance therapy in platinum-sensitive disease	
Olaparib	C+
Niraparib	C+
Rucaparib	I

Long-Term Cost Effectiveness

Lead: R. Brett McQueen, PhD

Collaborators:

- Jonathan D. Campbell, PhD
- Melanie D. Whittington, PhD
- Chong Kim, MS
- Mausam Patidar, MS

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Disclosures

- Collaborators:
  - Varun Kumar, ICER
  - Rick Chapman, ICER
  - Dan Ollendorf, ICER
  - Patricia Synnott, ICER
  - Geri Cramer, ICER

- Financial support provided to the University of Colorado from the Institute for Clinical and Economic Review (ICER).

- The University of Colorado researchers report no industry funding related to ovarian cancer

Objective

To model the costs and outcomes for three PARP inhibitors (olaparib, rucaparib, and niraparib) in the treatment of adult women with ovarian cancer

Methods in Brief

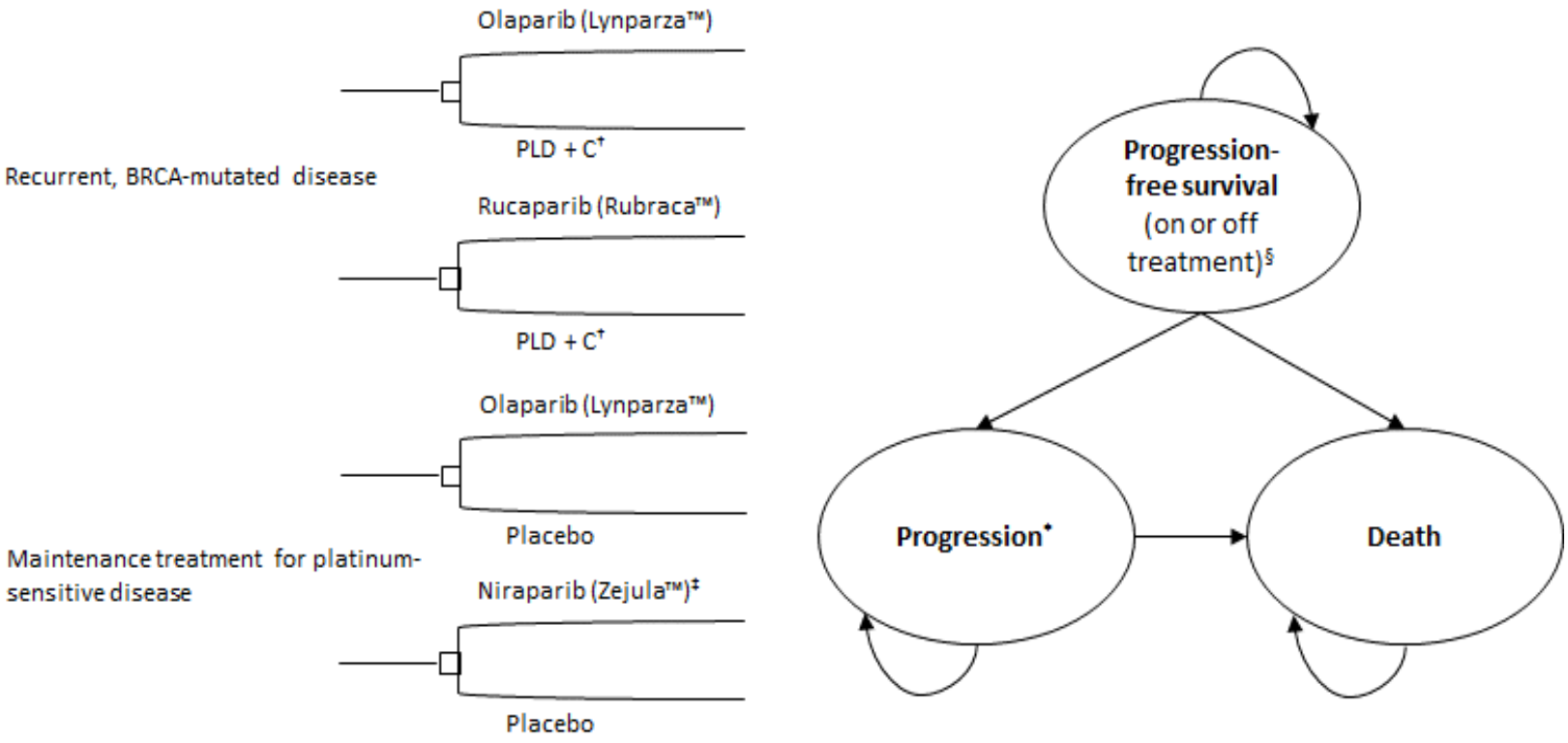
Interventions and Comparators

- Treatment of recurrent, BRCA-mutated disease:
  - *Olaparib (germline-BRCA only, 4th-line or later treatment) vs. pegylated liposomal doxorubicin in combination with carboplatin (PLD+C)*
  - *Rucaparib (any deleterious BRCA mutation, 3rd-line or later treatment) vs. PLD+C*
- Maintenance treatment for platinum-sensitive disease:
  - *Olaparib (gBRCA only) vs. placebo (i.e., surveillance only)*
  - *Niraparib (gBRCA) vs. placebo*
  - *Niraparib (non-gBRCA) vs. placebo*

Methods Overview

- Model: Semi-Markov model with time-dependency
- Setting: United States
- Perspective: Health Care Sector (direct medical care and drug costs)
- Time Horizon: 15 years
- Discount Rate: 3% per year (costs and outcomes)
- Cycle Length: 1 month
- Primary Outcome: Cost per quality-adjusted life year (QALY) gained
- Secondary Outcome: Cost per life year (LY) gained

Model Schematic



§ Separate utility and cost inputs were incorporated for on or off treatment

*The semi-Markov approach allows for modeling of progression defined by multiple subsequent lines of treatment (data dependent)

†Pegylated liposomal doxorubicin + carboplatin

‡Nirparib was evaluated for both gBRCAmut and non-gBRCAmut subpopulations whereas olaparib was evaluated within a gBRCAmut sub-cohort only

Key Assumptions

- Parametric curve functions were fit separately for each population/treatment setting to extrapolate data beyond trial horizon (to 15 years).
- Assumed same likelihoods of overall survival for rucaparib and niraparib from olaparib evidence for both treatment populations.
- Assumed proportionate gain in overall survival from gain in progression-free survival from best comparative available evidence (i.e., olaparib vs. placebo in maintenance population only).
- Subsequent treatment reflected onset of symptomatic disease progression (where estimated in trial evidence).

Parameters: Drug Cost

Drug Cost Parameters	WAC per unit	WAC per month	Net price per unit	Net price per month	Reference
Olaparib 100/150mg†	$112.35	$13,679	$101.12	$12,311	Assumed 10% off WAC
Niraparib 100mg†	$163.89	$14,965	$147.50	$13,469	Assumed 10% off WAC
Rucaparib 200/250/300mg†	$114.50	$13,940	$103.05	$12,546	Assumed 10% off WAC
PLD + C per mg	$55.51	$3,610	$49.95	$3,249	Assumed 10% off WAC

Price reflects the wholesale acquisition price listed on Red Book Online (Greenwood Village, CO: Truven Health Analytics. http://www.micromedexsolutions.com/. Accessed August 23, 2017)

†Range in dose modeled based on observed trial dose modifications cited in FDA labels or clinical reviews

Parameters: Grade 3 or 4 Adverse Events

	Olaparib (BRCA-mutated)	Olaparib (maintenance)	Rucaparib	Niraparib	PLD + C
Abdominal pain	8%	0%	3%	2%	*
Anemia	18%	4%	25%	25%	7.9%
Fatigue	8%	6%	11%	8%	7%
Hand-foot syndrome	*	*	*	*	24%
Hypertension	*	*	*	9%	*
Thrombocytopenia	3%	6%	5%	35%	15.9%
Leukopenia	*	*	*	7%	*
Nausea	3%	2%	5%	3%	5%
Neutropenia	7%	8%	5%	21%	35.2%
Proteinuria	*	*	*	*	*
Rash	*	0%	0.3%	0.5%	4.2%
Stomatitis	*	*	*	0.5%	8%
Vomiting	4%	4%	4%	2%	8%

Adverse events were included in the model only if they were grade 3 or 4 and experienced by more than 5% of the population.
*Not reported

Model Results

Base-Case Results: Olaparib

Intervention	Intervention Costs*	Non-Intervention Costs§	Total Costs	LYG	QALYs
Recurrent BRCA-mutated population					
Olaparib	$115,100	$43,032	$158,133	2.11	1.26
PLD + C (4th line or later use)	$20,040	$41,229	$61,269	0.91	0.59
Incremental cost per outcome				$80,258/LYG	$146,210/QALY
Maintenance therapy for platinum-sensitive disease					
Olaparib – gBRCAm	$194,475	$53,158	$247,633	3.75	2.67
Placebo (Olaparib) – gBRCAm	$9,050	$46,474	$55,519	3.09	2.08
Incremental cost per outcome				$288,538/LYG	$324,116/QALY

*Intervention costs include cost of PARP or comparator (exception placebo) and subsequent chemotherapy costs
§Non-intervention costs include supportive care costs (office visit, CT scan, blood test), adverse event costs, and end of life costs
QALY: Quality-Adjusted Life Year
LYG: Life-Year Gained

Threshold Results: Olaparib

	WAC per unit	WAC per month	Unit Price to Achieve $50,000 per QALY	Unit Price to Achieve $100,000 per QALY	Unit Price to Achieve $150,000 per QALY	Discount from WAC to Reach Thresholds
Olaparib (recurrent BRCA-mutated)	$112.35	$13,679	$43.31	$73.35	$103.39	8% - 61%
Olaparib (maintenance for platinum-sensitive)	$112.35	$13,679	$14.44	$30.24	$46.06	59% - 87%

Base-Case Results: Niraparib

Intervention	Intervention Costs*	Non-Intervention Costs§	Total Costs	LYG	QALYs
Maintenance therapy for platinum-sensitive disease					
Niraparib – gBRCAm	$181,077	$62,348	$243,461	3.86	2.77
Placebo (Niraparib) – gBRCAm	$5,027	$46,474	$51,502	3.09	2.12
Incremental cost per outcome				$245,092/LYG	$291,454/QALY
Niraparib – non-gBRCAm	$122,106	$53,203	$175,310	2.59	1.84
Placebo (Niraparib) – non-gBRCAm	$5,200	$43,144	$48,344	2.59	1.77
Incremental cost per outcome				Not estimable	$1,907,822/QALY

Threshold Results: Niraparib

	WAC per unit	WAC per month	Unit Price to Achieve $50,000 per QALY	Unit Price to Achieve $100,000 per QALY	Unit Price to Achieve $150,000 per QALY	Discount from WAC Unit Price to reach WTP thresholds
Niraparib – gBRCA (maintenance for platinum-sensitive)	$163.89	$14,965	$16.07	$43.28	$70.50	57% - 90%

Base-Case Results: Rucaparib

Intervention	Intervention Costs*	Non-Intervention Costs§	Total Costs	LYG	QALYs
Recurrent BRCA-mutated population					
Rucaparib	$202,103	$45,031	$247,135	2.11	1.41
PLD + C (3rd line or later use)	$23,144	$43,868	$67,012	1.28	0.80
Incremental cost per outcome				$217,738/LYG	$294,593/QALY

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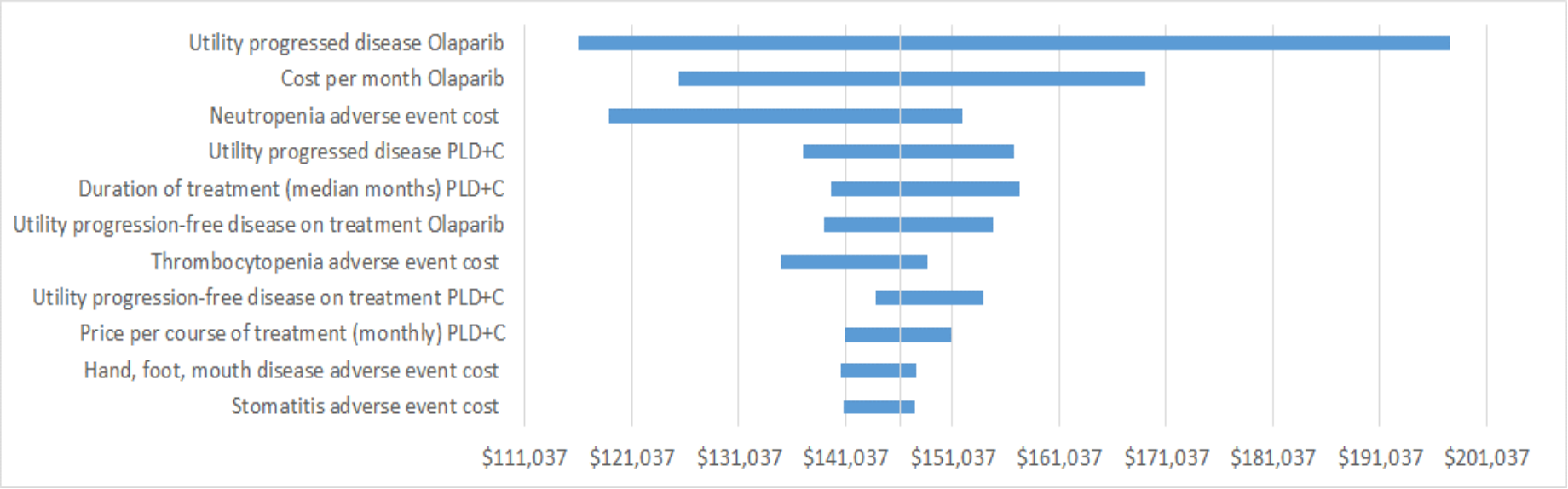
Threshold Results: Rucaparib

	WAC per unit	WAC per month	Unit Price to Achieve $50,000 per QALY	Unit Price to Achieve $100,000 per QALY	Unit Price to Achieve $150,000 per QALY	Discount from WAC Unit Price to reach WTP thresholds
Rucaparib (recurrent BRCA-mutated)	$114.50	$13,940	$26.09	$41.82	$57.55	50% - 77%

Tornado Diagram for olaparib vs. PLD+C (4th line or later use)



Probabilistic Sensitivity Analysis Results

Intervention	% Cost-Effective at $50,000/QALY	% Cost-Effective at $100,000/QALY	% Cost-Effective at $150,000/QALY
Recurrent BRCA-mutated population			
Olaparib vs PLD + C (4th line)	0.10%	1.70%	52.50%
Rucaparib vs PLD + C (3rd line)	0.00%	0.00%	0.00%
Maintenance therapy for platinum-sensitive disease			
Olaparib (gBRCA) vs Olaparib Control (gBRCA)	0.00%	0.00%	0.00%
Niraparib (gBRCA) vs Niraparib Control (gBRCA)	0.00%	0.00%	0.20%
Niraparib (non-gBRCA) vs Niraparib Control (non-gBRCA)	0.00%	0.00%	0.00%

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Scenario Analysis Results

- Combining gBRCA and non-gBRCA data in maintenance population comparisons resulted in higher cost-effectiveness estimates than in base case
- Sensitivity analysis for olaparib PFS resulted in lower cost-effectiveness estimates than in base case but of similar magnitude
- Use of partitioned survival method produced similar results (within 10% of base-case findings).

Limitations

- Limited comparative evidence on the relationship between progression-free survival and overall survival
- Evidence to generate life-year and QALY estimates in PLD+C derived from mixed BRCA- and non-BRCA-mutated populations
- Additional costs from infusion fees or provider mark-ups for PLD+C not included
  - Model results relatively insensitive to changes in these costs
- Limited comparative evidence (i.e., single-arm data only) and model structure to generate uncertainty estimates around transition probabilities

Conclusions

- PARP inhibitors are likely to provide gains in quality-adjusted and overall survival over alternative therapies, but are not currently priced in alignment with these benefits
  - Exception: olaparib in recurrent, BRCA-mutated ovarian cancer

Public Comments Summary

- Enhanced transparency on modeling calculations (e.g., present functional forms considered for survival analysis)
- Equivalency between progression-free survival and overall survival

Appendix Slides

Parameters: Transition Probabilities

- Parametric survival curves fit to PFS and OS Kaplan-Meier data utilizing the approach described by Guyot and colleagues
- Extracted data points from digitized copies of published survival curves
- Estimated the underlying individual patient data using extracted values, number of surviving patients at each time interval, and maximum likelihood functions
- Base-case parametric function selected based on best model fit using AIC values and visual comparison

Evidence to Generate Transition Probabilities

Recurrent BRCA-mutated population			
Transition probabilities	Olaparib	PLD+C	Notes
Progression-free to progressive	Kaufman et al. 2015 J Clin Oncol Figure 1	Pujade-Lauraine et al. and Hanker et al. Figure 2A 3rd relapse	Evidence not split into multiple lines of therapy. PLD+C evidence from combination of BRCA-mutated and non-BRCA-mutated population.
Overall Survival	Kaufman et al. 2015 J Clin Oncol Figure 2	Pujade-Lauraine et al. and Hanker et al. Figure 2B 3rd relapse	
	Rucaparib	PLD+C	Notes
Progression-free to progressive	Konecny et al. 2017 presentation Slide 14	Pujade-Lauraine et al. and Hanker et al. Figure 2A 2nd relapse	Evidence not split into multiple lines of therapy. Overall survival from olaparib recurrent BRCA-mutated evidence. PLD+C evidence from combination of BRCA-mutated and non-BRCA-mutated population.
Overall Survival	Kaufman et al. 2015 J Clin Oncol Figure 2	Pujade-Lauraine et al. and Hanker et al. Figure 2B 2nd relapse	

Evidence to Generate Transition Probabilities

Maintenance therapy for platinum-sensitive disease		
Transition probabilities	Olaparib and Placebo arms	Notes
Progression-free to progressive	Pujade-Lauraine et al. 2017 presentation SOLO2 PFS IA curve	Evidence split into multiple lines of therapy for olaparib only.
Overall Survival	Ledermann 2016 Figure 2B	
Progression-free to discontinuation	Single HTA submission olaparib maintenance Figure 5	
Progressive subsequent therapy 1 to subsequent therapy 2	Single HTA submission olaparib maintenance Figure 13	
	Niraparib gBRCAm and Placebo arms	Notes
Progression-free to progressive	Mirza et al. NEJM Figure 2A	Evidence not split into multiple lines of therapy. Overall survival and discontinuation rates from olaparib applied.
Overall Survival	Ledermann 2016 Figure 2B	
Progression-free to discontinuation	Single HTA submission olaparib maintenance Figure 5	
	Niraparib non-gBRCAm and Placebo arms	Notes
Progression-free to progressive	Mirza et al. NEJM Figure 2C	Evidence not split into multiple lines of therapy. Discontinuation rates from olaparib applied. Overall survival from olaparib placebo arm was applied to both arms of niraparib OS non-gBRCAm as there was no statistically significant difference between OS.
Overall Survival	Ledermann 2016 Figure 2C	
Progression-free to discontinuation	Single HTA submission olaparib maintenance Figure 5	

Parameters: Utilities (1)

Recurrent BRCA-mutated population	Base Case	Lower Range	Upper Range	Std. Error	Distribution	Source/Notes
Progression-free disease (on treatment) [Olaparib]	0.77	0.72	0.82	0.024	Beta	Olaparib NICE HTA Submission
Progression-free disease (on treatment) [Rucaparib]	0.77	0.72	0.82	0.024	Beta	Olaparib NICE HTA Submission
Progression-free disease (on treatment) [PLD+C]	0.7977	0.7572	0.8382	0.024	Beta	Havrilesky et al. 2009
Progressed disease	0.50	0.37	0.63	0.065	Beta	Mehta et al. 2014

Parameters: Utilities (2)

Maintenance therapy for platinum-sensitive disease	Base Case	Lower Range	Upper Range	Std.Error	Distribution	Source/Notes
Progression-free disease (on treatment) [Olaparib]	0.77	0.73	0.808	0.024	Beta	Olaparib NICE HTA Submission
Progression-free disease (on treatment) [Niraparib]	0.77	0.73	0.808	0.024	Beta	Olaparib NICE HTA Submission
Progression-free (off treatment) [Olaparib]	0.71	0.66	0.76	0.024	Beta	Olaparib NICE HTA Submission
Progression-free (off treatment) [Niraparib]	0.71	0.66	0.76	0.024	Beta	Olaparib NICE HTA Submission
Progressed disease [Niraparib]	0.68	0.55	0.80	0.065	Beta	Olaparib NICE HTA Submission assumed avg of 1st & 2nd subsequent trtmt
First subsequent therapy [Olaparib]	0.72	0.58	0.84	0.065	Beta	Olaparib NICE HTA Submission
Second subsequent therapy [Olaparib]	0.65	0.52	0.77	0.065	Beta	Olaparib NICE HTA Submission

Adverse Event Disutilities

Adverse Event (ICD-9-CM)	Base Case Disutility	SE	Lower	Upper	Distribution	Source
Anemia (285.9)	-0.022	0.0171	-0.002	-0.066	Beta	Tesaro data on file(non-gBRCAm overall)
Fatigue (780.71)	-0.0204	0.0161	-0.002	-0.062	Beta	Olaparib NICE HTA Submission for any grade 3/4vs. no grade ¾
Hypertension (401)	-0.0204	0.0161	-0.002	-0.062	Beta	Olaparib NICE HTA Submission for any grade 3/4vs. no grade ¾
Thrombocytopenia (287.5)	-0.015	0.0116	-0.001	-0.045	Beta	Tesaro data on file (non-gBRCAm overall)
Leukopenia (288.5)	-0.0204	0.0161	-0.002	-0.062	Beta	Olaparib NICE HTA Submission for any grade 3/4vs. no grade ¾
Nausea (787.01)	-0.0204	0.0161	-0.002	-0.062	Beta	Olaparib NICE HTA Submission for any grade 3/4vs. no grade ¾
Neutropenia (288)	-0.014	0.0137	-0.0004	-0.051	Beta	Tesaro data on file (non-gBRCAm overall)
Hand, foot, and mouth disease (074.3)	-0.0204	0.0161	-0.002	-0.062	Beta	Olaparib NICE HTA Submission for any grade 3/4vs. no grade ¾
Stomatitis (528)	-0.0204	0.0161	-0.002	-0.062	Beta	Olaparib NICE HTA Submission for any grade 3/4vs. no grade ¾
Rash (782.1)	-0.0204	0.0161	-0.002	-0.062	Beta	Olaparib NICE HTA Submission for any grade 3/4vs. no grade ¾

*Adverse event disutilities were applied for 3 cycles in the model

Parameters: Adverse Event Costs

Grade 3/4 Adverse Events (ICD-9-CM)	Base-Case	SE	Lower	Upper	Distribution
Anemia (285.3)	$7,533	$10,958	$5	$38,830	Gamma
Fatigue (780.71)	*	*	*	*	*
Hypertension (401)	$6,903	$7,256	$125	$26,587	Gamma
Thrombocytopenia (287.5)	$10,607	$16,207	$3	$57,183	Gamma
Leukopenia (288.5)	$8,705	$12,202	$10	$43,381	Gamma
Nausea (787.01)	$7,007	$9,370	$14	$33,455	Gamma
Neutropenia (288)	$13,633	$22,203	$1	$77,893	Gamma
Hand, Foot, and Mouth Disease (074.3)	$4,032	$5,463	$7	$19,482	Gamma
Stomatitis (528)	$10,796	$15,551	$8	$55,154	Gamma
Rash (782.1)	$5,359	$7,306	$8	$26,040	Gamma
*Not estimated in HCUPnet, assumed to be $0					

Threshold Survival Results: Rucaparib

Intervention	LYG	QALYs
PLD + C (3rd line or later use)	1.28	0.80
Rucaparib (recurrent BRCA-mutated)	4.41	2.72

Public Comment: Manufacturer Representatives

Public Comment

Lisa Schlager, FORCE

Conflicts of interest:
Receipt or potential receipt of anything of monetary value, including but not limited to, salary or other payments for services such as consulting fees or honoraria in excess of $5,000

If yes please describe the relationship below:

FORCE receives program funding from industry partners. These grants provide general support for our national outreach, education and support initiatives for the hereditary cancer community.

Donor list includes:

Clovis, Tesaro, AstraZeneca

Seana Roubinek, Survivor and Advocate

Conflicts of interest:
Any relationship that could be considered a financial conflict of interest

If yes please describe the relationship below:

I am a Patient Ambassador for Snow Companies, Inc. The program is sponsored by Tesaro (a pharmaceutical company) but I am nota brand ambassador.
I have the opportunity to speak to different groups of people and tell my story about my journey through ovarian cancer. Any honoraria that I am eligible to earn goes directly to charity.

Chad Ramsey, VP Policy, OCRFA

Conflicts of interest:

Receipt or potential receipt of anything of monetary value, including but not limited to, salary or other payments for services such as consulting fees or honoraria in excess of $5,000

If yes please describe the relationship below:

In the past year, OCRFA has received programmatic support at the $5000+ level from the following:

- Amerisource Bergen
- AdvaMedDx
- Astra Zeneca
- BIO
- Clovis Oncology
- Gail Baird Foundation
- Genentech
- ImmunoGen
- Janssen Oncology
- Merck
- Morphotek
- Myriad
- PhRMA
- TESARO

Jill Holdren, Patient

Conflicts of interest:

None to disclose

Break for Lunch

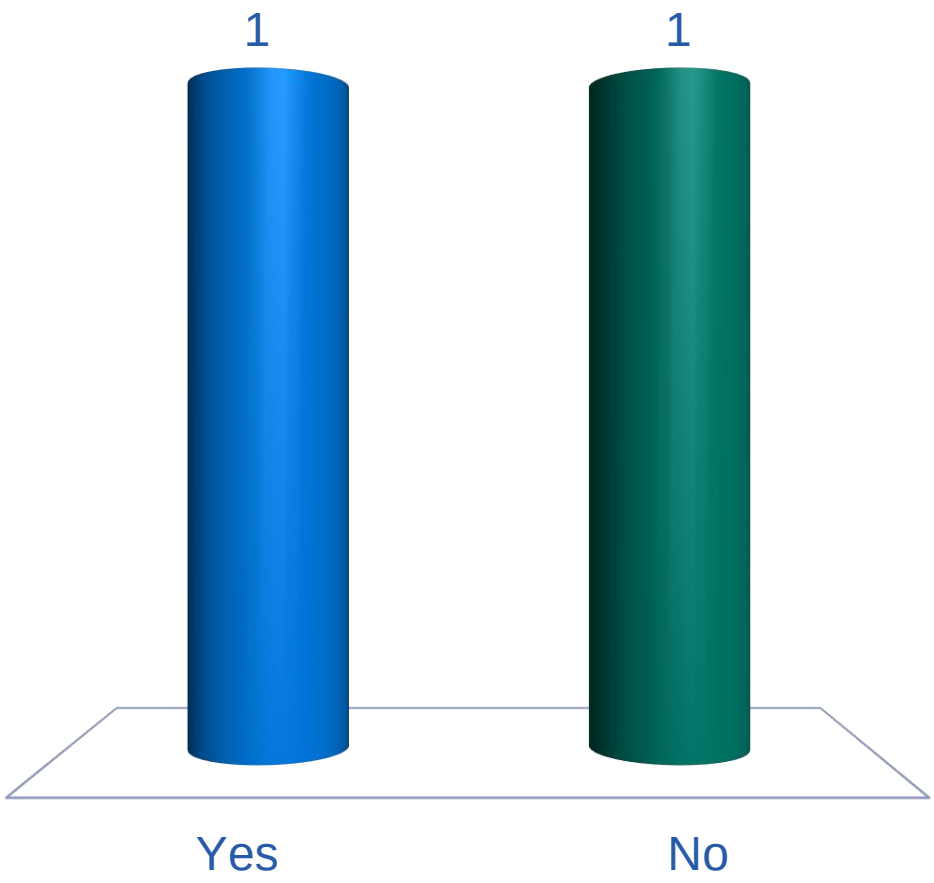
Meeting will resume at 1:00 pm

Voting Questions

1. In patients with recurrent BRCA-mutated disease, is the evidence adequate to demonstrate that the net health benefit of treatment with olaparib is greater than that of treatment with standard chemotherapy?

A. Yes

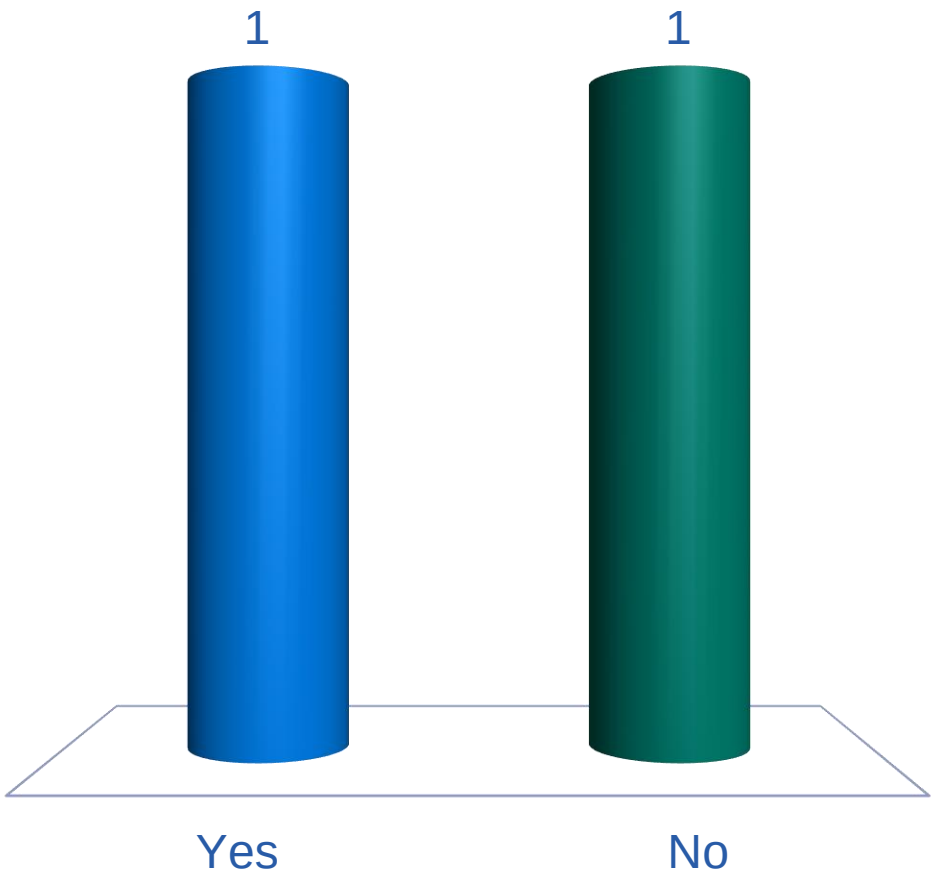
B. No



2. In patients with platinum-sensitive disease who are eligible for maintenance therapy, is the evidence adequate to demonstrate that the net health benefit of treatment with olaparib is greater than that of surveillance alone?

A. Yes

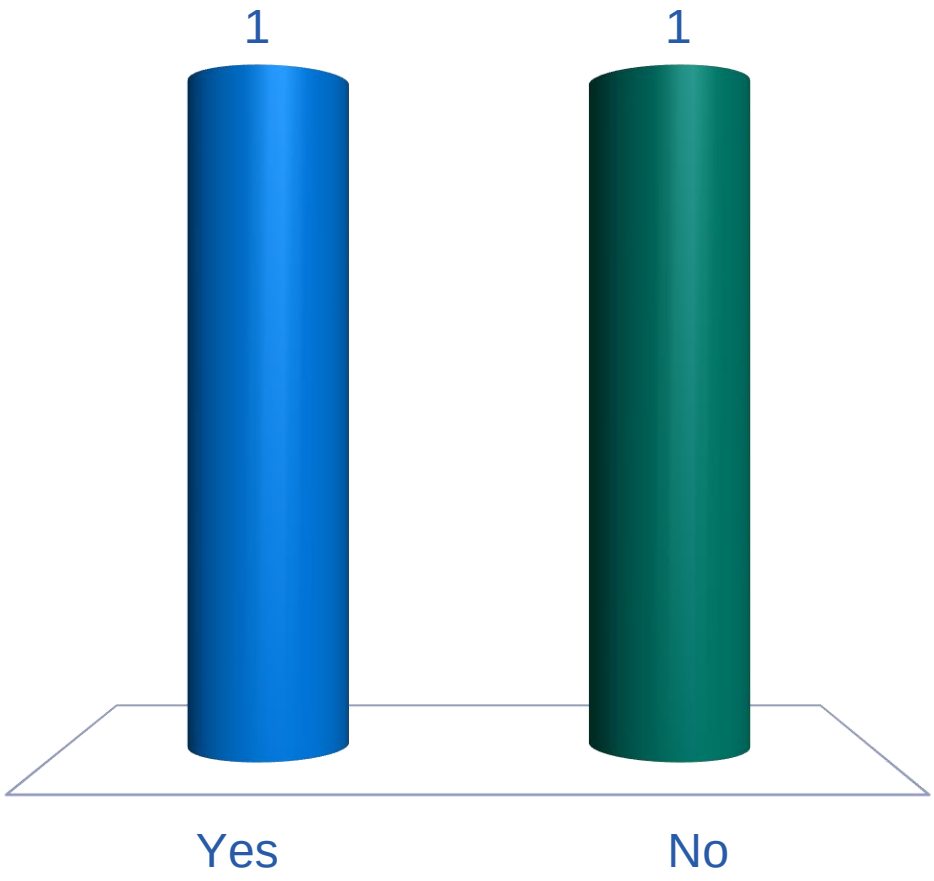
B. No



3. In patients with recurrent platinum-sensitive, germline BRCA-mutated disease who are eligible for maintenance therapy, is the evidence adequate to demonstrate that the net health benefit of treatment with niraparib is greater than that of surveillance alone?

A. Yes

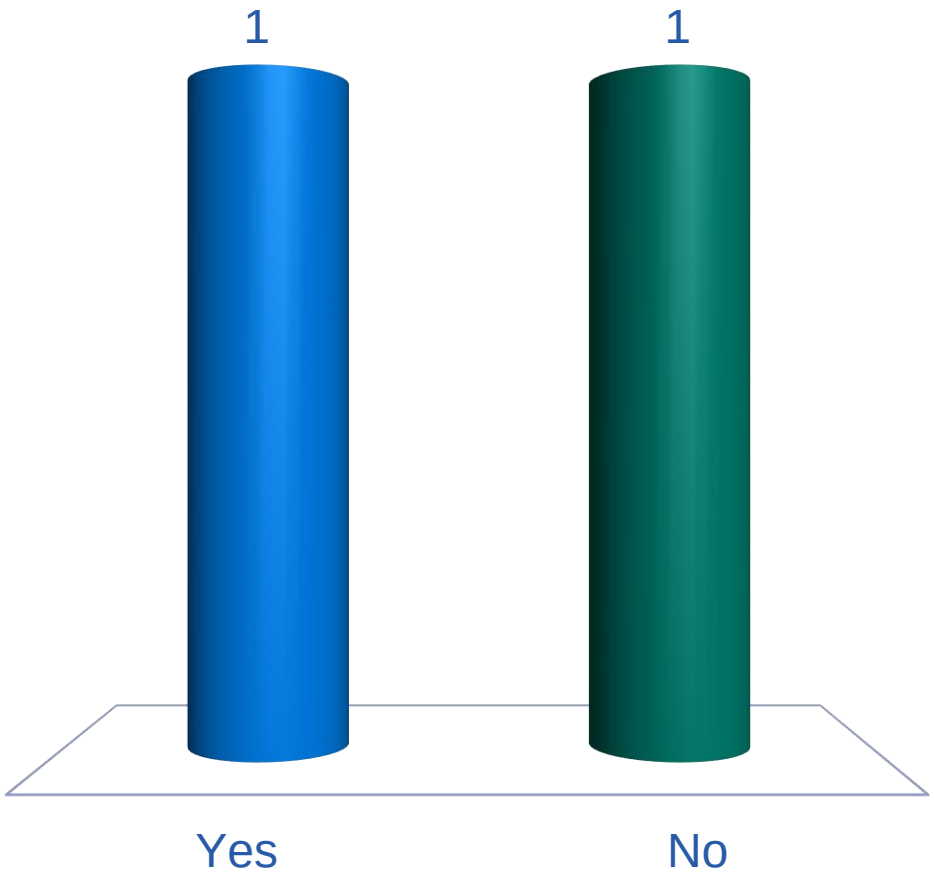
B. No



4. In patients with recurrent platinum-sensitive disease who are eligible for maintenance therapy and do not have germline BRCA mutations, is the evidence adequate to demonstrate that the net health benefit of treatment with niraparib is greater than that of surveillance alone?

A. Yes

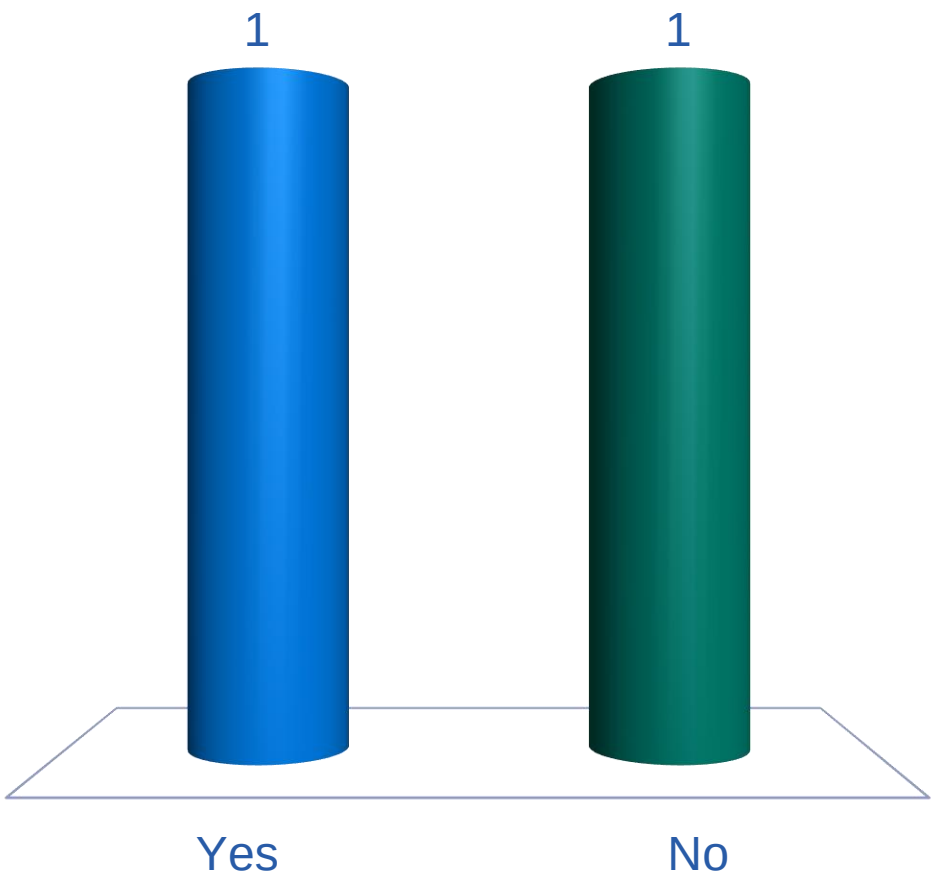
B. No



5. In patients with recurrent BRCA-mutated disease, is the evidence adequate to demonstrate that the net health benefit of treatment with rucaparib is greater than that of treatment with standard chemotherapy?

A. Yes

B. No



6. When compared to the pegylated liposomal doxorubicin and carboplatin does olaparib, for recurrent BRCA-mutated disease offer any of the following “other benefits”? Please select all that apply.

A. Significant direct patient health benefits not adequately captured by the QALY

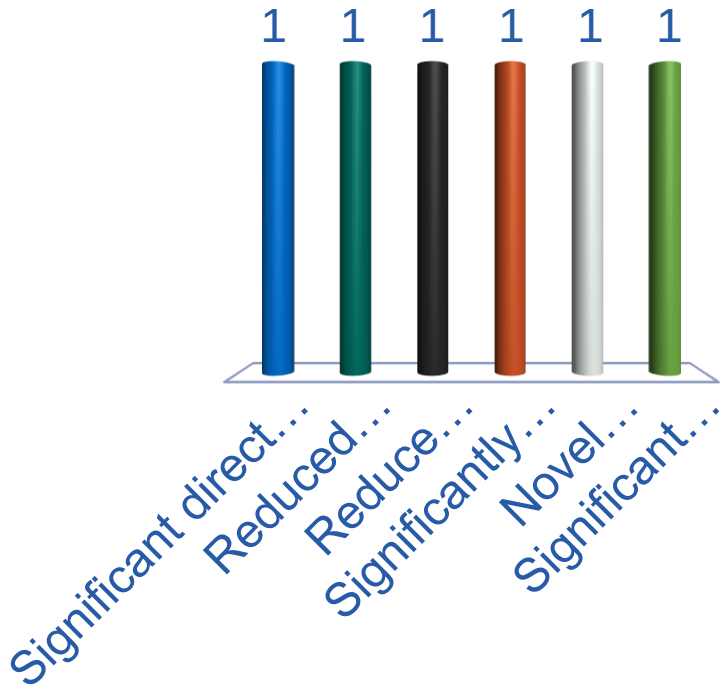
B. Reduced complexity that will significantly improve outcomes

C. Reduce important health disparities

D. Significantly reduce caregiver/family burden

E. Novel mechanism of action or approach….

F. Significant impact on improving return to work/overall productivity



7. Are any of the following contextual considerations important in assessing olaparib's long-term value for money in patients with recurrent BRCA-mutated disease? Please select all that apply.

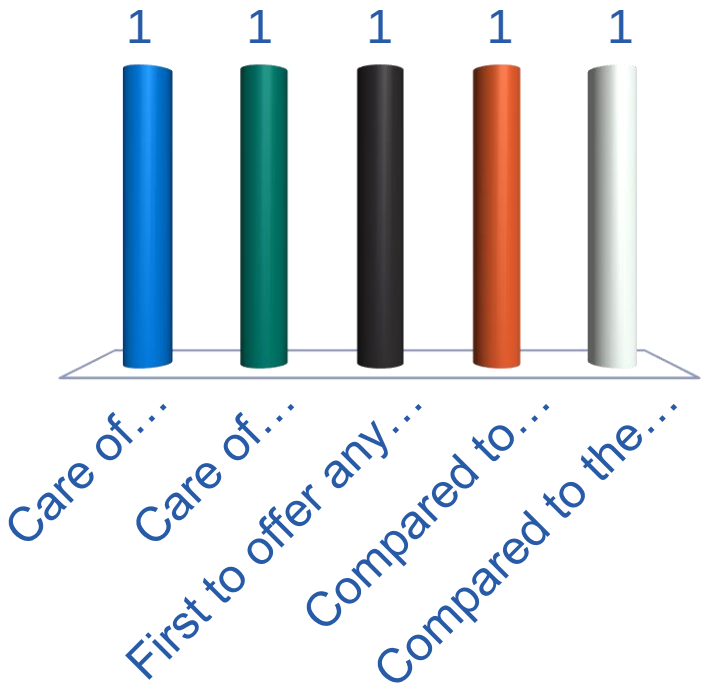
A. Care of individuals with condition of high severity

B. Care of individuals with condition with high lifetime burden of illness

C. First to offer any improvement

D. Compared to comparator, there is significant uncertainty about long-term risk of serious side effects

E. Compared to the comparator, significant uncertainty about magnitude or durability of the long term benefits of this intervention

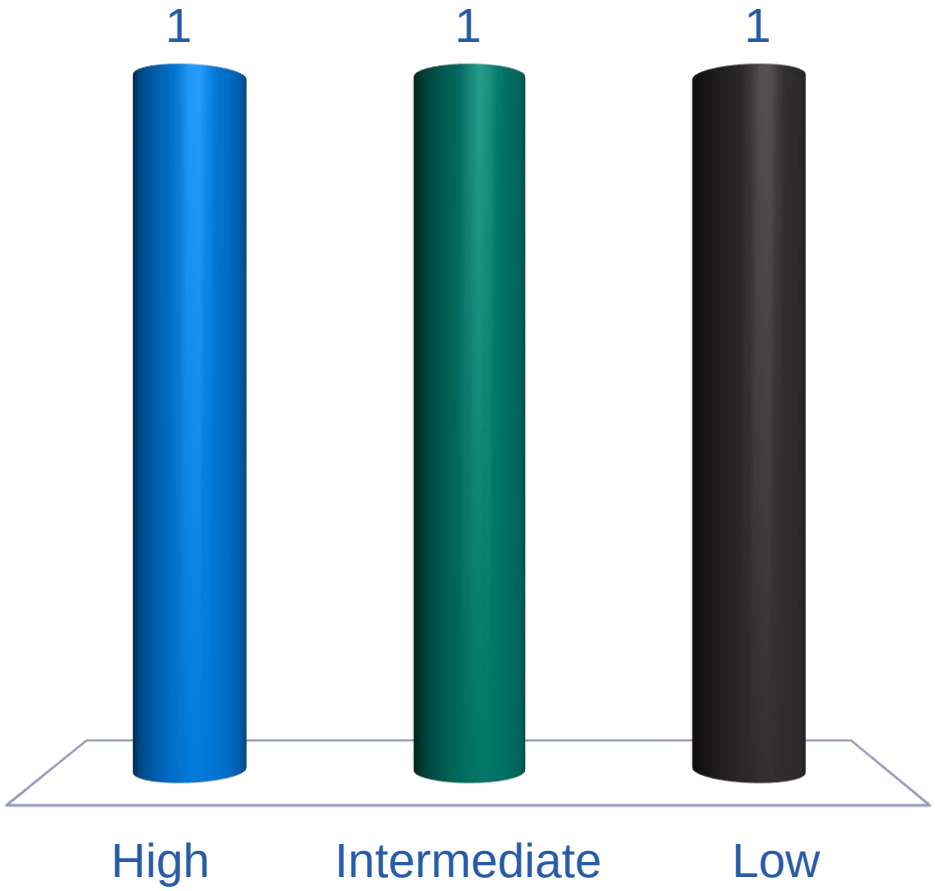


8. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, in patients with recurrent BRCA-mutated disease, what is the long-term value for money of olaparib compared with PLD+C?

A. High

B. Intermediate

C. Low



Policy Roundtable

Policy Roundtable Participants

Policy Roundtable	
Harold Carter Express Scripts	**Matthew Powell, MD** Washington University at St. Louis
Susan Leighton Patient	**Andrea Wahner Hendrickson, MD** Mayo Clinic
Betsy Neisner Patient	

Midwest CEPAC Panel Reflections

Next Steps

- Final Report and accompanying materials expected on or before September 28, 2017

- Meeting materials and outputs: https://icer-review.org/meeting/ovarian-cancer/

For more information please visit:

https://icer-review.org/programs/midwest-cepac/

Adjourn