

Thank you for the opportunity to comment on the draft scoping document. Our general comment is concerning how missing data from emerging evidence will be addressed in the assessment (e.g. use of an abstract versus a full publication).

Please find below our comments in each section as recommended by ICER

**Population:**

- For the scope of the evaluation, ICER should also define the type of prior treatment and quality of response to prior therapies.
- For patient selection, it is important to consider disease and patient characteristics relevant to treatment choice.

**Interventions:**

- Since olaparib and rucaprib are FDA approved for treatment, we would like the scope to define the comparator/s for the analysis.
- As watchful waiting is one of the options being considered for maintenance, the scope should define “watchful waiting”.
- The standard of care is changing in ovarian cancer. The evaluation may be more informative if the focus of the evaluation is among PARP inhibitors.

**Comparators:**

- The scope should be clear about inclusion of data sources, level of evidence and limitations associated with them.
- It should be clear from the scope, how breadth of clinical usage of PARP inhibitor’s is reflected in the model. Due to the emerging science and evolving treatment patterns of PARP inhibitor use is important.
- The assumption is that a comprehensive network will be developed to include all possible comparators, which will include single arm trials as well. Is this correct?

**Outcomes:**

- For both treatment and maintenance trials, the scope should clarify how overall survival and its estimates. will be handled. Further, how cross-overs occur in trials, which may impact overall survival estimate is handled.
- Since QoL assessment is within scope, more detail should be given on how to handle limited information available around health utilities.
- In situations where you have not received the full manuscripts but you have abstracts, how will missing data be addressed?

Yours Sincerely,

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March 27, 2017

Steven D. Pearson, MD, MSc, FRCP  
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RE: Institute for Clinical and Economic Review: Background and Scope Document on Poly ADP-ribose polymerase (PARP) Inhibitors for Ovarian Cancer: Effectiveness, Value, and Value-Based Price Benchmarks

Dear Dr. Pearson,

On behalf of the Cancer Support Community (CSC), an international nonprofit organization that provides support, education, and hope to cancer patients, survivors, and their loved ones, we appreciate the opportunity to respond to the request for comments regarding the Institute for Clinical and Economic Review's Background and Scope Document on Poly ADP-ribose polymerase (PARP) Inhibitors for Ovarian Cancer: Effectiveness, Value, and Value-Based Price Benchmarks. CSC is pleased to offer the following comments on this background and scope document:

### ***Unrealistic Timeframe to Respond***

The timeframe to read, consider, and respond to ICER documents continues to pose a challenge to many organizations and individuals who wish to respond. Starting with the open input period and timeframe to comment on background and scope documents, three weeks is simply not sufficient to devote the appropriate amount of time and resources to review a background and scope document. Further, ICER is currently calling for comments on the 2017-2018 Value Framework, Patient Engagement Guide, and Manufacturer Engagement Guide. As we draft comments in response to several of those documents, the timeframe to comment on this background and scope document becomes even more onerous. CSC recommends the following:

1. Provide ample time (at minimum 60 days) to respond.
2. Documents available for comment should not overlap. However, if this is unavoidable an additional time should be allowed for comments.
3. Allow stakeholders to submit comments in PDF form.
4. Post all comments to all documents on ICER's website in perpetuity.

### ***Process for Patient Representation***

A transparent process must be in place to involve patients in every step of the value assessment process. CSC recommends the following:

1. Include a sufficient number of diverse patient representatives (throughout the entire value assessment process) who have experience and knowledge of that specific disease state.

For example, patients who have had ovarian cancer should be commenting on ovarian cancer treatments specifically.

2. Provide patient representatives with information in a transparent, timely, and understandable manner. CSC would be pleased to work with ICER to pilot such information.
3. Obtain patient feedback PRIOR to the release of the scoping document.

### ***Concept of Value***

In this background and scope document, ICER identifies both cost-effectiveness as well as the “potential budgetary impact of each regimen over a 5-year time horizon...” It is critical to clearly delineate the differences between the concept of “value” as it pertains to medical treatments and devices, and assessment based primarily on the financial implications of those treatments and devices. Although cost-effectiveness is a reasonable endpoint in the value discussion, the use of budget impact is inappropriate. Further, meaningful patient and stakeholder representation is vital to all institutions determining value, including ICER. CSC recommends the following:

1. Limit inclusion of budget impact in the final value assessment, but rather report it as one endpoint.
2. Recognize value beyond 5-year timeline including late and long-term benefits and effects.
3. Include and apply weights to user preferences. Ensure that user preferences are appropriately reflected in final assessment.
4. Value endpoints that are important to patients.

### ***Population Perspective***

Although the intent of ICER is to take a “population” level perspective as opposed to trying to create shared decision making tools to be used by individuals and their clinicians, this intention belies the real-world implications of ICER determinations. Our concern is that ICER assessments will be used at all levels within the care system from the micro/individual to the macro/policy and payer levels. CSC recommends the following:

1. Recognize the potential and applied use of ICER value assessments by a variety of stakeholders, regardless of intended use and audience.
2. Define patient perspective as opposed to societal perspective.
3. Outline when and how ICER will incorporate the relative impact of different care options on work productivity as a scenario analysis.

### ***Evidence and Outcomes***

Patient-definitions of value must be included in any assessment. This information should come from real-world settings and be reported by patients directly. Outcomes should be important to patients and capture their experiences. We applaud ICER’s statement that “recognition that what matters to patients is not limited to measured “clinical” outcomes. Patient registries and survey databases could provide opportunities to better understand patient experiences from a wide-range of individuals. While we appreciate ICER’s use of health-related quality of life, we ask that additional patient-defined outcomes be included in the assessment. These should be aligned with the list of “other benefits and disadvantages” and “other contextual considerations” that were included in the 2017-2018 ICER Value Framework update. CSC will be submitting comments on



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the value framework update which includes suggestions to this particularly component but of note for this background and scope document. CSC recommends the following:

1. Ensure transparency at each point of the methodological process including not only the specifics of the method but also the rationale behind the choice and literature to support those decisions.
2. Include a balance of data derived from controlled clinical trials (including observational trials) and real world evidence including data and information from patient and patient advocacy groups.
3. Create principles to ensure that the use of data meets a high level of scientific credibility.
4. Provide a transparent a priori statement of key assumptions.
5. Include weights to accommodate varying user preferences.
6. Incorporate a timeframe that is sufficient to reflect the full range of immediate and late- and long-term treatment benefits and effects.
7. Ensure that outcomes reflect patient experiences and preferences.
8. Utilize existing patient registries and survey databases to explore and incorporate patient experience data.
9. Incorporate review and approval from multidisciplinary, disease-specific experts.
10. In addition to the ICER-defined “other benefits and disadvantages” and “other contextual considerations” the concepts of “financial toxicity” and “costs associated with late and long-term side effects” should be included in outcomes.

### ***Conclusion***

We appreciate the opportunity to provide feedback on ICER’s Background and Scope Document on Poly ADP-ribose polymerase (PARP) Inhibitors for Ovarian Cancer: Effectiveness, Value, and Value-Based Price Benchmarks. As always, we encourage ICER to provide meaningful opportunities to engage patients in each step of the value assessment process. CSC would be pleased to work with ICER to identify and encourage patient participation. Please feel free to contact me at 202.650.5382 or [linda@cancersupportcommunity.org](mailto:linda@cancersupportcommunity.org) if you have questions or if we can serve as a resource to your work.

Sincerely,

Linda House, MSM, BSN, RN  
President  
Cancer Support Community Global Headquarters

## References

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Clovis Oncology, Inc.  
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USA

28 March 2017

Dear Madam or Sir:

Clovis Oncology respectfully submits the following comments on the draft scoping document for the planned report on “Poly ADP-ribose polymerase (PARP) inhibitors for ovarian cancer: effectiveness, value, and value-based price benchmarks.”

- Page 1: “Only 40% of women are cured.”: Unfortunately, there is no ‘cure’ for ovarian cancer; approximately 80% of all ovarian cancer patients relapse following first-line platinum therapy (see, for example: Wiedemeyer WR, Beach JA, Karlan BY. Reversing Platinum Resistance in High-Grade Serous Ovarian Carcinoma: Targeting BRCA and the Homologous Recombination System. *Front. Oncol.* 2014;4:34.)
- Page 1: “...agents known as Poly ADP-ribose polymerase...”: “poly” does not need to be capitalized.
- Page 2: “...and the subset of non-*gBRCA* patients who were positive for homologous recombination DNA repair deficiency (HRD).”: Two additional PARP inhibitors are undergoing clinical trials in ovarian cancer, veliparib and talazoparib. will these two PARP inhibitors be included in ICER's research as well?
- Page 2: “This report will evaluate the health outcomes and economic effects of the PARP inhibitors olaparib, rucaparib, and niraparib in the treatment of ovarian cancer patients with and without germline BRCA mutations.”: What is the source of the data that will be used for analysis of the sub-populations with and without germline *BRCA* for each of the PARP inhibitors?
- Figure 1: “Population” box: Suggest considering analysis of platinum-resistant sub-populations.
- Figure 1: “Key Measures of Clinical Benefit” box: When no HRQOL data are available for an intervention, how will these data be extrapolated?

- Page 3: “For example, rucaparib is approved for use in patients with two or more prior lines of chemotherapy, so we will access appropriate fourth-line subgroup data for between-agent comparisons.”: From where will these data be obtained if ICER does not have access to the source data of the various clinical trials?
- Page 3: “P1) Olaparib, rucaparib, or niraparib as fourth line or later treatment”: See above comment. What is the rationale for evaluating the PARP inhibitors in fourth-line treatment (rather than third-line treatment) and from where will those data be obtained for rucaparib?
- Page 3: “P2) Olaparib, rucaparib, or niraparib as maintenance therapy”: Clovis Oncology will be submitting data from the ARIEL3 clinical trial for FDA approval in the maintenance setting. Data from the ARIEL3 trial be not be publicly available before the 2017 ESMO Annual Meeting on Sept. 8-12, 2017.
- Page 4: “P1) Other fourth line therapies (e.g., docetaxel, paclitaxel, gemcitabine)”: Suggest adding bevacizumab (Avastin) as comparator.
- Page 4: “...in addition, response measures are likely to be less sensitive in populations that have shown response to their most recent treatment.”: Suggest revising this statement. Patients who are platinum-sensitive respond well to PARP inhibitor treatment (see, for example: 2017 SGO Annual Meeting presentation by Konecny *et al.* "Rucaparib in patients with relapsed, primary platinum-sensitive high-grade ovarian carcinoma with germline or somatic *BRCA* mutations: integrated summary of efficacy and safety from the Phase 2 study ARIEL2."
- Page 4: “Health-related quality of life (e.g., EQ-5D-5L)”: If PRO data are not available, what assumptions will be taken into account instead?
- Page 4: “Costs and cost-effectiveness”: What data will be utilized for calculation of QALY and from where will it be obtained?
- Page 5: “Effectiveness will be estimated based on the clinical review of progression-free and/or overall survival.”: What methodology will be used to project OS based on PFS?
- Page 5: “P1: Recurrent disease, 3+ prior lines of chemotherapy”: Please see comment above regarding 2+ versus 3+ lines of chemotherapy in rucaparib’s indication statement.
- No comments on page 6
- Page 7: “2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA: a cancer journal for clinicians*. 2016;66(1):7-30.”: The 2017 Siegel *et al.* publication is now available.





Many thanks for taking Clovis Oncology's feedback on the scoping document into consideration, despite the late submission of our comments. We look forward to working closely with the ICER team on this interesting and exciting project.

With best regards,

Liisa Eisenlohr, Sr. Director, Global Medical Information

On behalf of Jeff Ladwig, VP, Market Access



**Pfizer Inc**  
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March 27, 2017

Steven D. Pearson, MD, MSc  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
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*Submitted via email: [publiccomments@icer-review.org](mailto:publiccomments@icer-review.org)*

RE: Draft scoping document for ovarian cancer review

Dear Dr. Pearson,

On behalf of Pfizer Inc, I am pleased to submit comments in response to the Institute for Clinical and Economic Review's (ICER) draft scoping document<sup>1</sup> for the planned review of poly ADP-ribose polymerase (PARP) inhibitors for the treatment of ovarian cancer (OC).

We appreciate ICER's efforts to seek input from a broad range of stakeholders. Life sciences companies like Pfizer devote significant resources to research, and our scientists have developed deep expertise in understanding the clinical, economic, and quality of life impacts of cancer.

Our experts in health outcomes and economics research have carefully reviewed the draft scoping document, and would like to offer the following recommendations for ICER's consideration, as it continues to shape its review.

**Recommendation:**

**ICER should clarify its process for how patient input was/is gathered and considered as part of the review.**

In recent months, ICER has stated its intent to increase its level of patient engagement as part of its reviews. In the draft scoping document's opening paragraphs, ICER notes that the scope "was developed with important input from ovarian cancer patients and patient organizations".<sup>1</sup>

We commend ICER for seeking to engage patients and their representatives. However, as have noted in prior communications, we urge ICER to increase transparency around its process for how inputs on patient perspectives were gathered, and how inputs from patients will be used specifically in the review. This transparency is needed to help resolve a number of questions that we (and likely other stakeholders) have, including:

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<sup>1</sup> Institute for Clinical and Economic Research. Poly ADP-ribose polymerase (PARP) Inhibitors for Ovarian Cancer: Effectiveness, Value, and Value-Based Price Benchmarks. Background and Scope. Available at: [https://icer-review.org/wp-content/uploads/2017/02/MWCEPAC\\_OVARIAN\\_Draft\\_Scoping\\_Document\\_030617.pdf](https://icer-review.org/wp-content/uploads/2017/02/MWCEPAC_OVARIAN_Draft_Scoping_Document_030617.pdf). Accessed March 20, 2017.

- How many and which specific organization(s) did ICER engage? Is ICER confident that it has the full perspective sufficiently reflecting the entire OC patient community, which spans many different types of patient stakeholder subgroups (e.g., based on age, disease severity, expected outcomes of treatment, caregivers etc)?
- Did ICER speak to OC patients in addition to advocates (who, while knowledgeable, may not be OC patients themselves, and therefore may have a different set of perspectives)?
- How knowledgeable are these organization(s) with respect to the intent and processes of value assessment? Do they understand what the objectives of the review are, and do they understand the underlying methodologies to be implemented? What are their expectations for how their inputs will be utilized?
- What kinds of questions were posed by ICER to the patient advocacy groups? How were the questions chosen/ derived? Did ICER send surveys? Did ICER engage in open-ended dialogue?
- How, specifically, will ICER “engage with patient groups and clinical experts to ascertain which outcomes are of greatest importance to patients”<sup>1</sup>? Similarly, will ICER ask patients what outcomes matter less to them?
- How, specifically, will ICER prioritize and select patient feedback for incorporation as part of the review? Will ICER also re-engage patients and their advocates to discuss what elements of the feedback provided were and were not incorporated into the analysis, and why?

We believe that these types of questions are critically important to answer, as they will allow ICER and its stakeholders to have an informed discussion in full context about how patient engagement is currently being incorporated into ICERs value assessment analyses, and how that process could be improved – in particular, with respect to input that is not utilized.

#### **Recommendation:**

**ICER should specify which quality of life measures will be included in its review, and should consider additional outcomes in its review.**

With respect to outcomes of interest, the draft scoping documents indicates that ICER will include health-related quality of life (HRQoL) measures “e.g., EQ-5D-5L”.<sup>1</sup> We ask that ICER be more specific about which measures will be included, and would suggest that ICER add disease specific HRQoL tools such as EORTC QLQ-C30 or FACT-G (where available) in addition to EQ-5D-5L, which is a generic measure of health status that may not reflect the same sensitivity as a disease-specific measure.

Further, we recommend that in addition to the list of outcomes of interest offered in the draft scoping document, ICER specifically consider adding two additional measures to the review: (1) patient preferences (as elicited from patient preference analyses methods) and (2) cost minimization (as elicited from cost minimization analyses).

#### **Recommendation:**

**ICER should share its planned methodology for extrapolating / forecasting PARP inhibitor uptake.**

The draft scoping document notes ICER’s intent to develop budget impact models for the PARP inhibitor regimens of interest. A critical underlying assumption for the budget impact models relates to the uptake rate for these treatments. However, the draft scoping document offers no

detail on what assumptions ICER will make with respect to this uptake. We strongly recommend that ICER update the scoping document with specific details on its assumptions surrounding uptake for PARP inhibitor treatments of interest to allow for a public discussion around these variables.

**Recommendation:**

**ICER should share its assumptions around PARP inhibitor pricing/discounting.**

ICER notes that that as part of its budget impact analyses it “will calculate the percentage of patients that could be treated at selected prices without crossing a budget impact threshold over the 5-year period”. We recommend that ICER offer more clarity and information about this process, specifically as it relates to assumptions around product discounting during the period of interest. In prior communications we have raised significant concerns regarding ICER’s assumptions for net pricing used in its cost-effectiveness and budget impact models; we ask that ICER engage in an open and transparent discussion around the PARP inhibitor discount rates to avoid additional confusion or lack of consensus.

**Concluding remarks**

We hope that these comments have been thought-provoking and useful to ICER as the organization continues to shape its review of PARP inhibitor treatments for OC. My colleagues and I would welcome an opportunity to discuss the scope and methodology of the planned review with you in more detail.

Kind regards,

A handwritten signature in black ink, appearing to read 'PS', with a stylized flourish at the end.

**Prasun Subedi, PhD**  
Senior Director  
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Pfizer Inc.

## GENERAL COMMENTS

My main concern is the assumption that PARP inhibitors be used as fourth line or later, for treatment. Rucaparib is approved for patients with germline or somatic who have had two prior chemotherapy drugs. In theory, it could be used after Taxol & Carboplatin although we don't know how insurance companies will respond to this request yet. Because PARP resistance is associated with platinum resistance, incorporating these drugs earlier into the treatment course makes sense. So comparing other 4th line therapies may not be the best comparison. Consider other regimens for platinum sensitive disease--Carboplatin/Gemcitabine +/- Bevacizumab, Taxol/Carboplatin +/- Bevacizumab.

Watchful waiting isn't really the best term to consider for this patient population either. Perhaps best supportive care? Use of PARP inhibitors also assumes genetic testing, either germline, somatic, or both to optimize targeted therapy. The cost of this testing should also be included in the model as some health care systems limit somatic testing.

## SPECIFIC REPORT COMMENTS

Ovarian cancer is the most common cause of gynecologic cancer death and fifth leading cause of cancer death in women.<sup>1</sup> There are nearly 200,000 women currently living with ovarian cancer; each year over 22,000 new cases are diagnosed and there are approximately 14,000 deaths attributable to the disease.<sup>1</sup> The median age at diagnosis is 63 years.<sup>2</sup> Due to the lack of early symptoms and absence of an accurate screening strategy, nearly 75% of women with ovarian cancer are diagnosed with advanced disease at presentation (Stage IIIC or IV).<sup>3</sup> Only 40% of women are cured.<sup>2</sup> For patients who present with Stage III cancer, the median overall survival is less than two years.<sup>4</sup> Of these women, those who continue through three or more lines of therapy have a median survival without evidence of disease progression ("progression-free survival") of less than six months.<sup>5</sup>

COMMENT: This is a dated reference, and the median survival for stage III ovarian cancer is greater than 2 years at this time with optimal treatment strategies.

Those who experience remission for greater than six months are considered to be "platinum sensitive." Several therapies may be considered for patients when they experience recurrence, including a newer class of biologic agents known as Poly ADP-ribose polymerase (PARP) inhibitors. Patients with mutations to BRCA are at increased risk for ovarian cancer and have a worse prognosis. PARP inhibitors interfere with a pathway of DNA repair. As such, PARP inhibitors were initially evaluated for patients with germline mutations that affect DNA repair, such as mutations to BRCA1 or BRCA2. Patients with BRCA mutations who have recurrent platinum-sensitive ovarian cancer appear to respond to PARP inhibitors. Two of these PARP inhibitors (rucaparib [Rubraca™; Clovis Oncology] and olaparib [Lynparza™; AstraZeneca]) have been most widely tested in this group of patients.

Comment: BRCA mutated patients likely have a short term survival benefit and no difference compared to long term survival in sporadic cancers (McLaughlin, et al. **J Natl Cancer Inst.** 2013;105(2):141-148)

March 27, 2017

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Re: Draft Scoping Document for “Poly ADP-ribose polymerase (PARP) Inhibitors for Ovarian Cancer: Effectiveness, Value, and Value-Based Price Benchmarks”

We at TESARO appreciate the opportunity to submit comments on the draft scoping document. TESARO is a biopharmaceutical company devoted to providing transformative therapies to people bravely facing cancer. We are committed to ensuring access for our therapies to patients who could benefit from them, and we offer the comments below in that spirit:

1. We believe the group listed as “Population P1” needs to be defined more precisely and consistently for the purposes of the review

There is a discrepancy in how P1 is described in two different sections of the draft scoping document. On page 3, P1 is described as: “Adults with platinum-sensitive, recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer of high-grade serous or endometrioid histology who have a germline *BRCA* mutation and who have relapsed after cytoreductive surgery and three or more prior lines of chemotherapy”. On page 5, P1 is described as either “adult women with platinum-sensitive recurrent ovarian cancer who have previously been treated with at least three lines of platinum-based therapy”, or as “Recurrent disease, 3+ prior lines of chemotherapy.” We recommend that the description of P1 on page 5 be updated to be consistent with that on page 3.

Additionally, we recommend that the population P1 be expanded to include the following two subgroups, just as with population P2, to include all potential ovarian cancer patients who could be eligible for niraparib:

- Patients with *gBRCA* mutation (originally proposed P1): as proposed in the draft scoping document, the relevant interventions for this population would be olaparib, rucaparib, or niraparib
- Patients without *gBRCA* mutation: these patients are included in the niraparib QUADRA trial.<sup>1</sup> These patients are not included in the indication for olaparib or rucaparib. Hence, the only relevant intervention for this population would be niraparib. The relevant comparators will be single-agent chemotherapies used in this setting

2. We believe that the Population P2 HRD positive subset should be removed from consideration for niraparib

In the ENGOT OV-16/NOVA trial a hierarchical-testing procedure was predefined for the non-gBRCAmut cohort in which statistical analysis was first performed in patients with HRD-positive tumors, and if the results were significant, a test of the overall non-gBRCAmut cohort was performed.<sup>2</sup> The hazard ratio (HR) for Progression Free Survival (PFS) was statistically significant indicating a treatment benefit with niraparib in the HRD-positive subgroup, as well as in the overall non-gBRCAmut cohort. The HRD-positive patients comprised only about 46% (162/350) of the non-gBRCA cohort. The HR (95% Confidence Interval) in the HRD-positive subgroup was 0.38 (0.243,0.586), while the corresponding HR in the overall non-gBRCAmut cohort was 0.45 (0.338, 0.607). Given the consistency of these estimates there is no reason to consider HRD positive patients as a subgroup different from the overall non-gBRCAmut cohort regarding treatment effects. Hence, we recommend that the HRD positive subgroup be removed from the P2 population for niraparib.

In addition, as a point of clarification, the tests used to identify the HRD positive population were different in the niraparib ENGOT OV-16/NOVA trial<sup>2</sup> and the rucaparib ARIEL3 trials<sup>3</sup>. Hence, the HRD positive populations from the two trials may not be comparable.

### 3. Indirect comparisons across therapies should be limited to endpoints assessed in a similar fashion

Page 4 of the scope states that “to the extent feasible, techniques of network meta-analysis will be used to generate indirect comparisons across therapies”. We recommend that indirect comparisons be conducted only in cases where endpoints were assessed in a similar fashion. As an example, in the niraparib ENGOT OV-16/NOVA trial, imaging was done to assess progression every 8 weeks through cycle 14, and then every 12 weeks until treatment discontinuation. Imaging assessments were conducted much less frequently in the olaparib SOLO-2 trial<sup>4</sup> (every 12 weeks through week 72, and every 24 weeks thereafter). Hence, it would not be appropriate to compare PFS in the niraparib ENGOT OV-16/NOVA trial to that in the olaparib SOLO-2 trial.

### 4. We recommend using only data from peer-reviewed studies for the assessment

The evidence to support the assessment of PARP inhibitors in ovarian cancer is still emerging, as noted on page 3 of the scope: “data to support use of the PARP inhibitors in these populations is currently emerging. For example, an ongoing study of niraparib in fourth-line or later use is expected in the second half of 2017. In addition, trials of olaparib and rucaparib for maintenance treatment have recently been completed or are nearing completion.” Full information regarding the study design is often not available in conference abstracts. As the details of the study design will be critical to ensure appropriate assessment (please refer to comments on point 3 above), we recommend that studies be published in peer reviewed journals before they are included in the assessment.

### 5. We suggest including bevacizumab as an intervention or comparator

Bevacizumab is approved in the U.S. for recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer that is platinum-sensitive in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by bevacizumab as a single agent. Thus, the

indication of bevacizumab overlaps with the population P2 in the scope. Hence, we recommend that bevacizumab be included in the set of interventions or comparators for population P2.

6. We suggest presenting results for a range of extrapolation approaches

The economic evaluation will require extrapolation of PFS and overall survival (OS) data beyond what was observed in the clinical trials. It is very likely that the results of the cost-effectiveness model will be sensitive to the methodology used for extrapolation. Given the uncertainty, rather than focusing on a single estimate, we recommend presenting the range of QALY gain and cost-effectiveness estimates assuming different parametric survival functions used for extrapolating PFS and OS.

We appreciate the opportunity to provide feedback on the draft scoping document, and we hope that you will reflect our recommendations in the final scope.

Sincerely,

Martin Huber, M.D.  
Senior Vice President, Chief Medical Officer  
TESARO, Inc.

## References

1. TESARO. A Study of Niraparib in Patients With Ovarian Cancer Who Have Received Three or Four Previous Chemotherapy Regimens (QUADRA). *ClinicalTrials.gov [Internet]*. Bethesda (MD): National Library of Medicine (US); 2017.
2. Mirza MR, Monk BJ, Herrstedt J, et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. *N Engl J Med*. 2016.
3. Clovis. A Study of Rucaparib as Switch Maintenance Following Platinum-Based Chemotherapy in Patients With Platinum-Sensitive, High-Grade Serous or Endometrioid Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancer (ARIEL3). *ClinicalTrials.gov [Internet]*. Bethesda (MD): National Library of Medicine (US); 2017.
4. AstraZeneca. Olaparib Treatment in BRCA Mutated Ovarian Cancer Patients After Complete or Partial Response to Platinum Chemotherapy. *ClinicalTrials.gov [Internet]*. Bethesda (MD): National Library of Medicine (US); 2017.



