Cancer Drugs Fund – Data Collection Arrangement

Niraparib in Ovarian Cancer [TA528]

Company name: GlaxoSmithKline
Primary source of data collection: ENGOT-OV16/NOVA
Secondary source of data collection: Public Health England routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy data set

<table>
<thead>
<tr>
<th>NICE Agreement Manager</th>
<th>Brad Groves</th>
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<tr>
<td>NHS England Agreement Manager</td>
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<td>Public Health England Agreement Manager</td>
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<td>GlaxoSmithKline Agreement Manager</td>
<td>Toni Maslen</td>
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1 Purpose of data collection arrangement

1.1 The purpose of the agreement is to describe the arrangements and responsibilities for further data collection for niraparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer [TA528]. An invitation to submit a proposal within the context of a managed access agreement has been decided by the appraisal committee.

2 Commencement and period of agreement

2.1 This data collection arrangement shall take effect on publication of the managed access agreement. The data collection period is anticipated to conclude in June 2020, when it is expected that mature overall survival data will be available from the pivotal ENGOT-OV16/NOVA trial (see section 5.1). The process for exiting the Cancer Drugs Fund will begin at this point and the review of the NICE guidance will start.
2.2 Estimated dates for data collection, reporting and submission for CDF guidance review are:

<table>
<thead>
<tr>
<th>End of data collection (primary source)</th>
<th>June 2020</th>
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<tr>
<td>Data available for development of company submission</td>
<td>June 2020</td>
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<tr>
<td>Anticipated company submission to NICE for Cancer Drugs Fund review</td>
<td>August 2020</td>
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2.3 GlaxoSmithKline anticipate the results from the additional data collected during the Cancer Drugs Fund period will be incorporated into an evidence submission and the updated economic model by end of August 2020.

2.4 GlaxoSmithKline acknowledge their responsibility to adhere as closely as possible to the timelines presented in the document.

2.5 NICE will, as far as is practicable, schedule a Cancer Drugs Fund review into the technology appraisal work programme to align with the estimated dates for the end of data collection. The review will use the process and methods in place at the time the invitation to participate in the guidance review is issued, which will be no earlier than 4 weeks prior to the anticipated company submission date. For further details of the expected timelines for the Cancer Drugs Fund guidance review see 6.27 of the technology appraisal process guide.

2.6 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the end of data collection and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of guidance follows the Cancer Drugs Fund guidance review timelines described in NICE’s guide to the processes of technology appraisal.
2.7 The company is responsible for paying all associated charges for a Cancer Drugs Fund review. Further information is available on the NICE website.

2.8 The company must inform NICE and NHS England of any anticipated changes to the estimated dates for data collection at the earliest opportunity.

2.9 Any changes to the terms or duration of any part of the data collection arrangement must be approved by NICE and NHS England.

2.10 If data collection is anticipated to conclude earlier than the estimated dates for data collection, for example due to earlier than anticipated reporting of an ongoing clinical trial, the company should note:

- Where capacity allows, NICE will explore options to reschedule the Cancer Drugs Fund guidance review date to align with the earlier reporting timelines.
- It may be necessary to amend the content of the final SACT or real-world data report (for example if planned outputs will no longer provide meaningful data).

2.11 If data collection is anticipated to conclude later than the estimated dates for data collection, the company should note:

- The company must submit a written request to NICE and NHS England, with details of the extension requested, including an explanation of the factors contributing to the request.
- It may be necessary for the company to mitigate any risks.
- In the event of an extension, it may not be possible to amend the date of the final SACT or real-world data report, although NICE will explore options with Public Health England to provide data over the extended period.

2.12 If a primary source of data is delayed or no longer reports outcome data that could resolve the uncertainties identified by the technology appraisal committee, NICE and NHSE may consider the data collection agreement no longer valid, and withdraw the technology from the Cancer Drugs Fund.
3 Patient eligibility

The patient eligibility for this Data Collection Arrangement has been updated in November 2019. Rucaparib (TA611) has subsequently been made available as a treatment option for those who have received 2 or more courses of platinum-based chemotherapy. Patient eligibility has been modified to align the eligibility criteria between these treatment options. Where any alignment occurred, the most permissive criterion was used.

People who started treatment under the previous patient eligibility criteria may continue without change to the funding arrangements in place for them.

3.1 Niraparib has been recommended for use in the Cancer Drugs Fund (CDF) as an option for maintenance treatment of platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer that has responded to the most recent course of platinum-based chemotherapy:

- in adults with a germline BRCA mutation who have received 2 courses of platinum-based chemotherapy and
- in adults without a germline BRCA mutation who have received 2 or more courses of platinum-based chemotherapy

3.2 Key patient eligibility criteria for the use of niraparib in the Cancer Drugs Fund in adults with a germline BRCA mutation who have received 2 courses of platinum based chemotherapy include:

- Patient has a confirmed histological diagnosis of predominantly high grade serous epithelial ovarian, fallopian tube or primary peritoneal carcinoma
- Patient has had a germline BRCA test and/or somatic (tumour) BRCA testing
- Patient has a documented deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour or in both
- Patient responded to initial (1st line) platinum-based chemotherapy ie the recent 1st relapse has occurred after a previous response to initial (first line) platinum-based treatment
• Patient has recently completed a second platinum-based chemotherapy and has received a minimum of 4 cycles of platinum-based treatment
• Patient has responded to the recently completed 2nd line platinum-based chemotherapy and has achieved a partial or complete response to treatment and there is no evidence of progressive disease on the post-treatment scan or a rising CA125 level
• It has been less than 8 weeks from the date of the last infusion of the last cycle of the 2nd platinum-based chemotherapy
• Patient has not previously received any PARP inhibitor unless olaparib or rucaparib via the CDF has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression
• Patient has an ECOG performance status of either 0 or 1. A patient with a performance status of 2 or more is not eligible for niraparib
• Niraparib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment
• A formal medical review as to whether maintenance treatment with niraparib should continue or not and at what dose will be scheduled to occur at least by the start of the second cycle of treatment
• Niraparib will be used as monotherapy
• No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve)
• Niraparib is to be otherwise used as set out in its Summary of Product Characteristics

3.3 Key patient eligibility criteria for the use of niraparib in the Cancer Drugs Fund in adults without a germline BRCA mutation who have received 2 or more courses of platinum-based chemotherapy include:

• Patient has a confirmed histological diagnosis of predominantly high grade serous epithelial ovarian, fallopian tube or primary peritoneal carcinoma
• Patient has had germline and/or somatic (tumour) BRCA testing
• Patient does not have a documented deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour
• Patient had disease which was sensitive to the penultimate line of platinum-based chemotherapy (ie the disease responded to the line of platinum-based chemotherapy preceding the most recent line of platinum-based chemotherapy)
• Patient has recently completed a further line of platinum-based chemotherapy and has received a minimum of 4 cycles of platinum-based treatment
• Patient has responded to the recently completed 2nd or subsequent line of platinum-based chemotherapy and has achieved a partial or complete response to treatment and there is no evidence of progressive disease on the post-treatment scan or a rising CA125 level
• It has been less than 8 weeks from the date of the last infusion of the last cycle of the recent 2nd or subsequent line platinum-based chemotherapy
• Patient has not previously received any PARP unless rucaparib via the CDF has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression
• Patient has an ECOG performance status of either 0 or 1. A patient with a performance status of 2 or more is not eligible for niraparib
• Niraparib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment
• A formal medical review as to whether maintenance treatment with niraparib should continue or not and at what dose will be scheduled to occur at least by the start of the second cycle of treatment
• Niraparib will be used as monotherapy
• No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve)
Niraparib is to be otherwise used as set out in its Summary of Product Characteristics

3.4 There are no additional patients that would form part of the data collection for the CDF, other than those initiated following the initiation of this agreement.

3.5 It is estimated that there will be 688 new patients per year for the non-germline breast cancer susceptibility gene mutation second line plus (non-gBRCA 2l+) cohort and 158 new patients per year for the germline breast cancer susceptibility gene mutation second line therapy (gBRCA 2l) cohort.

3.6 The mean time to treatment discontinuation from the ENGOT-OVA16/NOVA is estimated to be 1.32 years for patients in the non-gBRCA 2l+ cohort and 2.76 years for the gBRCA 2l cohort.

4 Area(s) of clinical uncertainty

4.1 The main clinical uncertainty is the immaturity of the overall survival data. Evidence from NOVA suggests that niraparib improves progression-free survival and extends the chemotherapy-free interval compared with placebo. Although niraparib has shown promising clinical benefits compared with placebo, it is unclear whether, and by how much, it will extend overall survival. However, the NICE appraisal committee concluded that there is no reason to suppose that the overall survival benefit will be less than the progression-free survival benefit.

5 Source(s) of data collection

Clinical trial

5.1 Data collection from the ongoing clinical trial (ENGOT-OV16/NOVA) will be the primary source of data collection. Mature overall survival data from this trial is expected in June 2020. The timeframe for overall survival is driven by the need to observe approximately 250 events. Table 1 provides a brief description of the trial.
ENGOT-OV16/NOVA: Randomized, Phase III Trial of Niraparib Maintenance Therapy in Patients with Recurrent Ovarian Cancer

| Population | Adults with platinum-sensitive recurrent, high-grade serous ovarian, fallopian tube or primary peritoneal cancer  
|            | Previously received ≥2 platinum-based regimens  
|            | Responsive (partial or complete) to last platinum regimen  

| Cohorts | With (n=203)/without (n=350) hereditary germline BRCA mutation  

| Primary endpoint | Progression-free survival (RECIST v 1.1 blinded central review)  

| Key secondary endpoints | Time to first and time to second subsequent therapy  
|                        | Chemotherapy free interval  
|                        | Progression-free survival 2 (i.e. PFS on next line of therapy)  
|                        | Overall survival  
|                        | Quality of life (EQ-5D-5L)  

**Other data**

5.3 Public Health England identifies, collects, collates, quality-assures and analyses large population-level datasets for specific diseases and conditions, including cancer. These datasets include the Systemic Anti-cancer Therapy (SACT) dataset, which is a mandated dataset as part of the Health and Social Care Information Standards. Public Health England will use the routinely-captured data collected during the period of the data collection arrangement to provide analyses as defined in sections 6.2 and 7.3.

5.4 Public Health England will collect data, including via the SACT dataset, alongside the primary source of data collection.

6 Outcome data

Clinical trial

6.1 The most pertinent outcome to be measured is long-term overall survival. At the end of the data collection, mature overall survival data will be available from the ongoing ENGOT-OV16/NOVA trial. This will be provided to NICE when the guidance is reviewed and will be supplemented by the data collected in SACT.

Other data, including SACT

6.2 Data will be collected via Public Health England’s routine population-wide datasets, including the SACT dataset. This collection will support data collected in the ongoing clinical trial. During the managed access agreement period, Public Health England will collect data to provide information on overall survival, duration of therapy and time to first subsequent treatment (if available).

7 Data analysis plan

Clinical trials

7.1 The number of overall survival events will drive the minimum time frame for data collection.

7.2 No interim analysis are planned for overall survival data.
Other data

7.3 At the end of the data collection period Public Health England will provide a final report for NHS England based on routinely collected population-wide data, including that collected via SACT. The report will present depersonalised summary data, including the total number of patients starting treatment, overall survival and treatment duration, and time to first subsequent treatment (if available). The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with GlaxoSmithKline in advance of the planned review of guidance.

7.4 Completeness of SACT dataset reporting will be shared with NHS England and the GlaxoSmithKline on a quarterly basis. Public Health England will provide summary results for time on treatment and survival to NHS England and GlaxoSmithKline on an annual basis, to check the continuing validity of the period of the data collection arrangement.

8 Ownership of the data

8.1 For all clinical trial data listed above from the ENGOT-OV16/NOVA study, GlaxoSmithKline will be the owner

8.2 No additional governance arrangements are required as data will be collected through on-going clinical trials and routine PHE data collection.

8.3 The data analysed by Public Health England is derived from patient-level information collected by the NHS, as part of the care and support of cancer patients. The data is collated, maintained, quality-assured and analysed by the National Cancer Registration and Analysis Service, which is part of Public Health England. Access to the data was facilitated by the Public Health England Office for Data Release. GlaxoSmithKline will not have access to the Public Health England patient data, but will receive de-personalised summary data, with appropriate controls in place to cover this. Public Health England will provide a report to NHS England and GlaxoSmithKline at the end of the managed access period.
8.4 The SACT dataset is a mandated dataset as part of the Health and Social Care Information Standards. All necessary governance arrangements through SACT, and other datasets brought together by Public Health England, have been established with NHS Trusts and NHS England.

8.5 Blueteq’s CDF system data is owned by NHS England. NHS England is responsible for implementing Blueteq data collection and generally for analysis of these data. NHS England, however, shares Blueteq data with Public Health England for CDF evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and Public Health England.

9 Publication

9.1 The details/authorship of any proposed publications arising from these studies will be planned with the publication of the final study results.

9.2 Publication of the analysis results of data collected by Public Health England, including through SACT and the data from Blueteq’s CDF system, will be planned and implemented by Public Health England.