Cancer Drugs Fund

Managed Access Agreement

Niraparib for maintenance treatment of platinum-sensitive ovarian cancer after second response to chemotherapy

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Niraparib in Ovarian Cancer ID1041

Company name: Tesaro

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

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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 (to be updated with TA number after final guidance has been published). 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 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the data collection period has ended and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of guidance follows the standard timelines described in the addendum to NICE's methods and processes when appraising cancer technologies.

3 Patient eligibility

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:

- Clinician is aware of the likely toxicities of niraparib, the associated monitoring required and the reasons why 48% of patients in the ENGOT-OV16/NOVA trial had dose interruptions in the 1st cycle and 47% commenced their 2nd cycle at a reduced niraparib dosage
- 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
- Patient has a documented germline BRCA mutation
- Patient has relapsed following 1st line chemotherapy (i.e. the penultimate line of treatment) and had platinum-sensitive disease at

this relapse, platinum sensitivity defined by a complete or partial remission which lasted for more than 6 months following completion of 1st line platinum-based chemotherapy (whether given pre- and/or post-operatively or if the patient did not have surgery)

- Patient is in a complete or partial response following completion of 2nd line platinum-based chemotherapy (i.e. the most recent chemotherapy) and that the serum CA125 is either normal or has demonstrated a >90% decrease from before the initiation of 2nd line chemotherapy and is stable
- It has been less than 12 weeks since the patient completed 2nd line chemotherapy
- Patient has not previously received any PARP inhibitor
- 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:

- Clinician is aware of the likely toxicities of niraparib, the associated monitoring required and the reasons why 48% of patients in the ENGOT-OV16/NOVA trial had dose interruptions in the 1st cycle and 47% commenced their 2nd cycle at a reduced niraparib dosage

- Patient has a confirmed histological diagnosis of predominantly high grade serous epithelial ovarian, fallopian tube or primary peritoneal carcinoma
- Patient does not have a documented germline BRCA mutation.
- Patients must have had a germline BRCA test.
- Patient relapsed following penultimate line of chemotherapy (i.e. the line of treatment preceding the most recent line of chemotherapy) and had platinum-sensitive disease at this relapse, platinum sensitivity defined by a complete or partial remission which lasted for more than 6 months following completion of penultimate line of platinum-based chemotherapy (whether given pre- and/or post-operatively or if the patient did not have surgery)
- Patient is in a complete or partial response following completion of the most recent line platinum-based chemotherapy which must be at least second line treatment and that the serum CA125 is either normal or has demonstrated a >90% decrease from before the initiation of 2nd line chemotherapy and is stable
- It has been less than 12 weeks since the patient completed 2nd line chemotherapy
- Patient has not previously received any PARP inhibitor
- Patient has an ECOG performance status of either 0 or 1. A patient with a performance status of 2or 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.

Table 1 Trial description

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

5.2 NHS England's Blueteq database captures the CDF population. NHS England shares Blueteq data with Public Health England for the CDF evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and Public Health England.

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 Tesaro in advance of the planned review of guidance.

7.4 Completeness of SACT dataset reporting will be shared with NHS England and the Tesaro on a quarterly basis. Public Health England will provide summary results for time on treatment and survival to NHS England and Tesaro 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, TESARO 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. TESARO 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 TESARO 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.

Commercial Access Agreement

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The contents of this document have been redacted as they are confidential

- A glossary of terms relating to managed access agreements in the Cancer Drugs Fund is available here.