NON-INTERVENTIONAL (NI) STUDY PROTOCOL

Study information

Title	Real-World Patient Characteristics, Treatment Patterns, and Clinical Outcomes Among Talazoparib-Treated Patients with HER2-Negative, Locally Advanced or Metastatic Breast Cancer and Germline BRCA1/2 Mutations: US Chart Review
Protocol number	C3441053
Protocol version identifier	1.0
Date	22 June 2021
Active substance	Talazoparib
Medicinal product	TALZENNA®
Research question and objectives	**Primary objectives**: The following primary objectives will be assessed among adult patients with human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer (ABC) with germline breast cancer susceptibility gene 1 or 2 (gBRCA1/2) mutations treated with talazoparib in the real-world (RW) practice setting in the United States (US): 1. Describe demographic and clinical characteristics. 2. Describe patterns of treatment with talazoparib monotherapy CCI [redacted] 3. Describe RW clinical outcomes of talazoparib monotherapy-treated patients, including: a. Time to treatment failure (TTF) for talazoparib

	b. RW progression-free survival (rwPFS) CCI d. RW overall response rate (rwORR) CCI f. Time to chemotherapy administered following talazoparib CCI
Authors	PPD **MA** PPD PPD Pfizer, Inc PPD PPD **PhD** PPD PPD **MPH** PPD

	PPD [redacted]

1. TABLE OF CONTENTS

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ABC	Advanced breast cancer
AE	Adverse event
AEM	Adverse event monitoring
BC	Breast cancer
BRCA1	Breast cancer susceptibility gene 1
BRCA2	Breast cancer susceptibility gene 2
CDK	Cyclin-dependent kinase
CHSS	Cardinal Health Specialty Solutions
CI	Confidence interval
CNS	Central nervous system
CR	Complete response
CRF	Case report form
CSA	Clinical study agreement
ECOG-PS	Eastern Cooperative Oncology Group performance status
eCRF	Electronic case report form
EHR	Electronic health record
ER	Estrogen receptor
ESR1	Estrogen receptor 1
FDA	Food and Drug Administration
FISH	Fluorescent in situ hybridization
gBRCA1/2	Germline BRCA1 or 2

Abbreviation	Definition
GPO	Group purchasing organization
GPP	Good Pharmacoepidemiology Practices
HCP	Healthcare professional
HER2	Human epidermal growth factor receptor 2
HIPAA	Health Insurance Portability and Accountability Act
HR	Hormone receptor
IEC	Independent ethics committee
IHC	Immunohistochemistry
IQR	Interquartile range
IRB	Institutional review board
ISPE	International Society for Pharmacoepidemiology
KM	Kaplan-Meier
KPS	Karnofsky performance status
LOT	Line of therapy
NIS	Non-interventional study
OPEN	Oncology Provider Extended Network
OR	Odds ratio
ORR	Objective response rate
CCI	[redacted]
PARP	Poly(adenosine diphosphate–ribose) polymerase
PD	Progressive disease
PD-1	Programmed cell death protein 1

Abbreviation	Definition
PD-L1	Programmed death ligand 1
PFS	Progression-free survival
PgR	Progesterone receptor
PH	Proportional hazards
PHI	Protected health information
PIK3CA	Phosphoinositide 3-kinase
PR	Partial response
PV	Pharmacovigilance
QA	Quality assurance
QC	Quality control
RW	Real-world
CCI	[redacted]
rwORR	Real-world overall response rate
rwPFS	Real-world progression-free survival
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Stable disease
STD	Standard deviation
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TNBC	Triple-negative breast cancer
TTF	Time to treatment failure

Abbreviation	Definition
UAT	User acceptance testing
US	United States
YRR	Your Reporting Responsibilities (Pfizer AE training)

3. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

Name, degree(s)	Job Title	Affiliation	Address
PPD MA	PPD	Pfizer, Inc.	235 East 42nd Street New York, NY 10017
PPD PharmD, RPh, MPH,	PPD	Pfizer, Inc.	235 East 42nd Street New York, NY 10017
PPD PhD, RN	PPD	Pfizer, Inc.	235 East 42nd Street New York, NY 10017
PPD PhD	Senior Scientist, PPD	PPD	PPD
PPD MPH	Scientist, PPD	PPD	PPD

4. ABSTRACT

Real-World Patient Characteristics, Treatment Patterns, and Clinical Outcomes Among Talazoparib-Treated Patients with HER2-Negative, Locally Advanced or Metastatic Breast Cancer and Germline BRCA1/2 Mutations: US Chart Review

Version 1, 22 June 2021

PPD

Rationale and background

Talazoparib (TALZENNA®) is an orally available poly (adenosine diphosphate–ribose) polymerase (PARP) inhibitor indicated for treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer (ABC, including locally advanced or metastatic breast cancer) and germline breast cancer susceptibility gene 1 or 2 (gBRCA1/2) mutations. To date, there is no published information about the characteristics, treatment patterns, and clinical outcomes of talazoparib-treated patients in the real-world (RW) United States (US) setting. The RW assessment of ABC patients with gBRCA1/2 mutations treated with talazoparib since its approval in 2018 will provide information about the patient characteristics, treatment patterns, and clinical outcomes of talazoparib-treated patients in the US.

Research question and objectives

Primary objectives:

The following primary objectives will be assessed among adult patients with HER2-negative ABC with gBRCA1/2 mutations treated with talazoparib in the RW practice setting in the US.

1. Describe demographic and clinical characteristics.
2. Describe patterns of treatment with talazoparib monotherapy CCI [redacted]
3. Describe RW clinical outcomes of talazoparib monotherapy-treated patients, including:
    a. Time to treatment failure (TTF) for talazoparib
    b. RW progression-free survival (rwPFS)
    CCI [redacted]
    d. RW overall response rate (rwORR)

CCI [redacted]

f. Time to chemotherapy administered following talazoparib

CCI [redacted]

Study design

This study consists of a retrospective, multi-site, patient-level medical chart review of US adult ABC patients who initiated talazoparib on or after October 16, 2018 and were managed by participating providers from Cardinal Health's Oncology Provider Extended Network (OPEN). A minimum of 6 months follow-up is required unless the patient died within this follow-up period.

Population

Data from primary CCI [redacted] populations will be analyzed CCI [redacted]

Primary population:

1. HER2-negative ABC patients with gBRCA1/2 mutations treated with talazoparib monotherapy initiated on or after October 16, 2018 and ≥18 years of age at initiation of talazoparib.

All patients in the primary population will have had a minimum of 6 months follow-up time after initiation of talazoparib unless the patient died within this follow-up period. No patients will have participated in any breast cancer (BC) clinical trial after initiation of talazoparib, been treated with a PARP inhibitor as neoadjuvant/adjuvant therapy, have unknown gBRCA1/2 status, or have been diagnosed with any other malignancy within the 5 years prior to data collection.

CCI [redacted]

CCI

CCI

Variables

Patient demographics, clinical characteristics, patterns of treatment with talazoparib and therapy administered prior to and following talazoparib, and clinical outcomes will be collected and analyzed CCI for primary and CCI cohort.

Data sources

The patient's treating physician will abstract data from the patient's electronic health record (EHR) into the data capture forms. All study data are secondary. Providers will be trained on data collection to ensure accuracy and reliability. No protected health information (PHI), except for dates of diagnosis, treatment, and outcomes, will be collected. The patient's EHR data will not be shared directly with Cardinal Health Specialty Solutions (CHSS) or Pfizer.

Study size

The total targeted sample sizes for the CCI primary and CCI population are as follows:

Primary population:

1. Approximately 110 HER2-negative ABC patients with gBRCA1/2 mutations treated with talazoparib.

CCI

CCI

An estimated data exclusion rate of 3% following quality control (QC) processes is expected.

Data analysis

Primary CCI cohorts will be delineated and analyzed CCI Descriptive analyses will be conducted on patient demographics, clinical characteristics, treatment patterns and history, biomarker status (e.g., mutation of BRCA1 or BRCA2), and clinical outcomes. For CCI rwPFS, and all other time-to-event endpoint analyses, the Kaplan-Meier (KM) method will be used, accounting for right-censoring. To assess differences in the odds of disease response, logistic regression may be used to calculate the odds ratio (OR) and associated P-values CCI Cox proportional hazards (PH) regression will be applied for time-to-event data analysis. If post-hoc analyses are performed, the log-rank test may be used to assess a difference in median time-to-event data among subgroups for the primary analysis cohort. CCI The comparison of means (medians where appropriate) and proportions across cohorts will be performed using t-tests (Wilcoxon where appropriate) and chi-square tests (Fisher exact where cell size is fewer than 5 patients). The numbers of missing and unknown observations will be described for both categorical and continuous variables. No data imputation will be conducted. Patients with missing/unknown data will be reported as such.

If sample size allows, clinical outcomes will also be reported for analytic subgroups of interest

CCI for the primary population CCI Subgroups may include the following, to be determined once data collection is complete: hormone receptor (HR)-positive/HER2-negative patients and patients with triple-negative BC (TNBC), CCI

Milestones

Start of data collection: Q3 2021

End of data collection: Q3 2021

Final study report: Q4 2021

5. AMENDMENTS AND UPDATES

None.

6. MILESTONES

Milestone	Planned date
Completion of feasibility assessment	01 March 2021
Project kickoff	10 March 2021
Study protocol	26 March 2021
Study protocol finalization/approval	Q2 2021
Case report form (CRF)	Q2 2021
CRF finalization/approval	Q2 2021
Institutional review board (IRB) preparation/submission/approval	Q3 2021
Electronic CRF (eCRF) programming & testing completion	Q3 2021
eCRF pre-test completion/eCRF finalized	Q3 2021
Statistical Analysis Plan (SAP) & table shells	Q3 2021
SAP & table shells finalization/approval	Q3 2021
Start of data collection	Q3 2021
End of data collection	Q3 2021
Analytic/Clinical data quality review completion	Q4 2021
Data analysis completion	Q4 2021
Summary report	Q4 2021
Final study report	Q4 2021

7. RATIONALE AND BACKGROUND

Breast cancer (BC) represents a major public health problem, with 284,200 new cases and 44,130 deaths estimated in the United States (US) during 2021.[1] Prognosis with metastatic BC is poor, with an estimated 5-year survival rate of approximately 28.1%.[2] Although the advent of novel therapeutic interventions such as immunotherapy and targeted agents have brought major strides in the treatment of advanced breast cancer (ABC, including locally advanced or metastatic breast cancer), patients may continue to experience minimal or short-lived responses to these agents.[2] As such, the development and characterization of effective interventions are greatly needed in order to ensure patient-specific, appropriate, and tolerable treatment that achieves meaningful improvement in survival and quality of life. By increasing understanding of the true efficacy, safety, effectiveness, and treatment patterns of ABC-focused regimens in a broad, real-world (RW) patient population, RW studies can add tremendous value to this process.[3]

BC is classified into 4 main disease subtypes based on hormone receptor (HR) status (i.e., estrogen receptor [ER] and progesterone receptor [PgR]) and human epidermal growth factor receptor 2 (HER2) expression, including HR-positive/HER2-negative (luminal A), HR-negative/HER2-negative (triple-negative breast cancer [TNBC]), HR-positive/HER2-positive (luminal B), and HR-negative/HER2-positive (HER2-enriched).[4] Each subtype is associated with distinct disease features as well as treatment recommendations.[4,5] Treatment strategy may also be driven by mutation status of certain genes, including the BC susceptibility gene 1 or 2 (BRCA1 or BRCA2), in which mutations may render cells deficient in the repair of DNA double-strand breaks, thereby increasing reliance on poly(adenosine diphosphate–ribose) polymerase (PARP)-dependent, single-strand break repair mechanisms.[5-8] Germline BRCA1 or BRCA2 (gBRCA1/2) mutations account for approximately 5% of all BC cases, with prevalence of these mutations higher among those with HER2-negative disease.[9-11]

Talazoparib (TALZENNA®), which was approved by the US Food and Drug Administration (FDA) on October 16, 2018, is an orally available PARP inhibitor indicated for treatment of adult patients with HER2-negative ABC having gBRCA1/2 mutations.[12] This approval was based on the Phase 3 EMBRACA trial (NCT01945775), which demonstrated that, in comparison to single-agent chemotherapy of the physician's choice (capecitabine, eribulin, gemcitabine, or vinorelbine), talazoparib improved median progression-free survival (PFS) by approximately 3 months in adult patients diagnosed with HER2-negative ABC with gBRCA1/2 mutations (8.6 months vs 5.6 months [hazard ratio for disease progression or death, 0.54]; 95% confidence interval [CI], 0.41 to 0.71; P<0.001).[13,14] Additionally, the objective response rate (ORR) was 62.6% in the talazoparib arm versus 27.2% in the chemotherapy arm (odds ratio [OR], 5.0; 95% CI, 2.9 to 8.8; P<0.001).[13,14] Grade 3-4 hematologic adverse events (AEs) occurred in 55% of talazoparib-treated patients (primarily anemia) versus in 38% of chemotherapy-treated patients, whereas nonhematologic Grade 3 adverse events (AEs) occurred in 32% and 38% of patients, respectively.[13]

To date, there is no published information related to the characteristics, treatment patterns, and clinical outcomes of talazoparib-treated patients in the RW US setting. CCI

CCI

CCI

CCI

8. RESEARCH QUESTION AND OBJECTIVES

Among patients managed by oncologists in the Cardinal Health OPEN, this study aims to achieve the following research objectives. CCI

8.1. Primary population objectives:

The following primary objectives will be assessed among adult patients with HER2-negative ABC with gBRCA1/2 mutations treated with talazoparib monotherapy in the RW US practice setting:

1. Describe demographic and clinical characteristics.
2. Describe patterns of treatment with talazoparib monotherapy [redacted]
3. Describe RW clinical outcomes of talazoparib monotherapy-treated patients, including:
    a. Time to treatment failure (TTF) for talazoparib
    b. RW progression-free survival (rwPFS)
    [redacted]
    d. RW overall response rate (rwORR)
    [redacted]
    f. Time to chemotherapy administered following talazoparib

[redacted]

9. RESEARCH METHODS

9.1. Study design

To achieve the research objectives described above, retrospective, multi-site, medical chart review will be conducted of study-eligible, talazoparib-treated ABC patients at community oncology clinics in the US. Providers in the OPEN who have previously indicated treating patients meeting the study selection criteria will be recruited and invited to participate (see Section 8.2. for further details) in the patient identification and data abstraction. Additional providers in OPEN may be recruited to aid in patient recruitment. All study data are secondary and will have been collected retrospectively from existing clinical data originally collected as part of routine care.

Patient eligibility will be confirmed by the treating physician. Providers will abstract de-identified patient-level data necessary to achieve the research objectives into an eCRF. No protected health information (PHI), except for dates of diagnosis, treatment, and outcomes,

will be collected. The patient's electronic health record (EHR) data will not be shared directly with Cardinal Health or Pfizer.

Data related to RW patient characteristics, treatment patterns, and clinical outcomes among talazoparib-treated patients will be captured and reported separately for the following 3 distinct cohorts of patients (cohorts will never be combined during analysis):

<u>One primary population</u>:

- HER2-negative ABC patients with gBRCA1/2 mutations treated with talazoparib monotherapy initiated on or after October 16, 2018 and ≥18 years of age at initiation of talazoparib.

CCI [redacted]

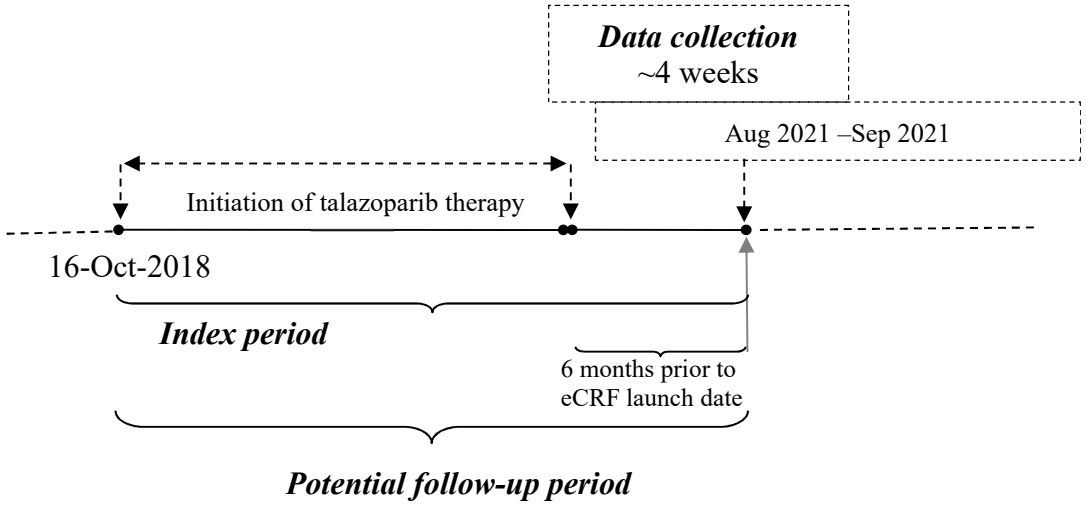
- [redacted]
- [redacted]

If sample size allows, clinical outcomes will also be reported for post-hoc analytic subgroups of interest CCI for the primary population CCI [redacted] Subgroups may include the following, to be determined once data collection is complete: patients with HR-positive/HER2-negative BC and patients with TNBC, CCI [redacted]

For all study-eligible patients, talazoparib treatment for ABC will have been initiated on or after October 16, 2018 and a minimum of 6 months follow-up is required unless the patient died within this follow-up period. Data collection is scheduled to begin in August 2021 and end in September 2021. The pre-index period will be variable and will encompass events and data occurring prior to the initiation of talazoparib treatment (e.g., initial breast cancer diagnosis, initial diagnosis of ABC, neoadjuvant/adjuvant therapy). Index date is defined as the date of initiation of talazoparib. The index period is defined as the period of time spanning the initiation of talazoparib on or after October 16, 2018 and the date of last follow-up. A minimum of 6 months follow-up after initiation of talazoparib is required for all patients, with the exception of patients who died within the follow-up period. The exact length of follow-up will be variable between patients (Figure 1).

F1

Figure 1. Study period



9.1.1. Other Aspects of Study Design

Although data on AEs will not be collected in the CRF, all clinicians who participate in this research will be required to complete Pfizer training related to the identification and reporting of AEs/serious adverse events (SAEs). AE/SAE training materials will be provided to the participating clinicians prior to any data collection. Providers will complete the AE/SAE training and electronically sign the certificate.

9.2. Setting

Providers who participated in the prior related feasibility surveys and short chart review study and who reported having treated potentially eligible patients will be invited to participate in this study. These providers volunteered to participate in the feasibility surveys and/or short chart review after receiving invitations to participate that were sent out to a subset (approximately 800) of CHSS' OPEN providers. Additional physicians from the OPEN may also be recruited to achieve the targeted patient numbers. Recruited providers who volunteer to participate in this study will identify patients meeting the study selection criteria through a series of screener questions. Additionally, these physicians will provide an estimate of their total eligible patient population.

As of 2020, the OPEN community comprised more than 7,000 unique providers in oncology, hematology, and urology across the US who had participated in Cardinal Health internal market research, educational summits, industry-sponsored research, or whose practices had

used the Cardinal Health proprietary point-of-care claims remittance software over the past 7 years. Of the providers, approximately 800 composed the RW research community, and 300 unique investigators have contributed patient-level data to retrospective chart abstraction research since 2016. OPEN is group purchasing organization (GPO)- and EHR- software agnostic. Providers are predominantly in community practices (>75%), ranging in size from solo practitioners to hospital systems, and participate in centralized institutional board review (IRB) approval. Because OPEN is a provider-level (as opposed to site-based) community, CHSS can obtain large, representative samples of patients and collect detailed clinical data from their treating providers. Due to the purposive sampling that selects physicians and patients based on pre-specified selection criteria, however, this study may not be representative of all ABC patients treated with talazoparib or of all providers treating these types of patients.

To be eligible for participation in this research study, a board-certified hematologist/oncologist must have treated or be treating at least 1 ABC patient meeting the eligibility criteria for the study, agree to participate in a study sponsored by Pfizer, and agree to complete and adhere to the Pfizer AE/SAE reporting protocols. Providers must also be able to participate in research monitored by a central IRB. No site-specific IRB approval will be sought, and providers requiring this approval will not be eligible.

After IRB approval of the research protocol, the eCRF will be pre-tested with 2 providers. Data collected as part of the pre-test will not be used in the final analytic dataset. After testing and revisions (if necessary), providers from OPEN will be contacted and asked to participate in the research. Data collection will be conducted over the course of 4 weeks**.** Providers will submit a maximum of 10 eCRFs each (the maximum number of eCRFs per provider may be increased, if necessary, to achieve target patient numbers following pre-approval from Pfizer). Physicians will be asked to identify all eligible patients, report the total number of eligible patients, and chronologically select consecutive eligible patients, starting with the earliest eligible.

9.2.1. Inclusion criteria

Patients must meet all of the following inclusion criteria to be eligible for inclusion in the study:

- ≥18 years of age at initiation of talazoparib
- A minimum of 6 months follow-up time after initiation of talazoparib unless the patient died within this follow-up period

For HER2-**negative** patients with gBRCA1/2 mutations (population for primary analysis, approximately 110 patients):

- Diagnosed with HER2-negative ABC
- gBRCA1/2 mutation(s)
- Treatment with talazoparib monotherapy initiated on or after October 16, 2018

CCI [redacted]

- [redacted]
- [redacted]
- [redacted]

CCI [redacted]

- [redacted]
- [redacted]
- [redacted]

9.2.2. Exclusion criteria

Patients meeting any of the following criteria will not be included in the study:

- Participation in any BC clinical trial after initiation of talazoparib
- Treatment with a PARP inhibitor as neoadjuvant/adjuvant therapy
- gBRCA1/2 or HER2 status unknown
- Diagnosis of any other malignancy, except carcinoma in situ or nonmelanoma skin cancer, within the 5 years prior to data collection

9.3. Variables

The following subsections summarize the key variables to be collected from patient medical records via the eCRF by their treating providers. Detailed definitions will be included in the statistical analysis plan (SAP) and case report form (CRF) documents, which may include variables not listed below.

9.3.1. Provider/Practice Characteristics

- Primary practice setting (e.g., small private practice)
- Whether physician is practicing in a BC-only clinical practice
- US region
- Years in practice
- Specialty
- Total number of talazoparib-treated patients who meet study eligibility requirements
- Estimated ABC patient volumes in study period:

- overall
- talazoparib-treated
- HER2-negative
  - with gBRCA1/2 mutation(s)

CCI

CCI

9.3.2. Patient Demographic & Clinical Characteristics

- Sex at birth, year of birth, payer, state of residence, race/ethnicity
- Family history of BRCA-related cancers, if known (e.g., breast, ovarian, fallopian tube, peritoneal, prostate, pancreatic, gastric, colon)
- Biomarker testing (findings, type, lab, test dates), which may include immunohistochemistry (IHC) score, test type (e.g., IHC/fluorescent in situ hybridization [FISH]), name of lab performing tests, sample used for BRCA1/2 testing (e.g., blood, saliva, tumor tissue), somatic or germline test for BRCA1/2, and dates of tests for the following:
  - BRCA1/2 mutation analysis
  - ER expression analysis
  - PgR expression analysis
  - Estrogen receptor 1 (ESR1) expression analysis
  - HER2 expression analysis
  - PD-L1 expression analysis
  - Phosphoinositide 3-kinase (PIK3CA) mutation analysis
- Stage/date at initial diagnosis of BC
- Date of ABC diagnosis
- Sites of metastasis at initiation of therapy
- Comorbidities (included in the Charlson Comorbidity Index)
- Eastern Cooperative Oncology Group performance status (ECOG-PS)
- Karnofsky performance status (KPS)

9.3.3. Talazoparib Treatment Patterns

- Start/stop dates of therapy

9.3.4. Treatment Patterns Prior to/Following Talazoparib

- Total lines of therapy (LOT) in the ABC setting:
    - For the purposes of this study, one LOT ends when the patient discontinued treatment with a regimen; if a drug was added to the ongoing treatment, this should be considered a new LOT. If a drug within a combination is held or discontinued, this should not be considered a new LOT.
- Prior platinum- or non-platinum-based chemotherapy, hormone therapy, HER2-directed therapy, or immunotherapy in the neoadjuvant/adjuvant setting:
- Pre- and post-talazoparib systemic therapies in the ABC setting:
    - Start/stop dates

9.3.5. Clinical Outcomes of Talazoparib Therapy

Collected data elements:

- Provider-reported/charted best response to therapy (i.e., complete response [CR], partial response [PR], stable disease [SD], progressive disease [PD], not evaluable, too early to tell, or unable to substantiate) during talazoparib therapy
- Date of initial response during talazoparib therapy
- Date of disease progression/recurrence during talazoparib therapy
- Date of last follow-up
- Date of death, if applicable

Clinical outcomes that will be assessed based on the collected data elements:

- TTF – time from initiation of talazoparib to discontinuation for any reason, including disease progression, treatment toxicity, and death

- rwPFS – time from initiation of talazoparib to charted disease progression based on radiographic imaging or death from any cause, whichever occurs first

[redacted]

- rwORR – sum of complete and partial responses divided by all patients with reported disease response assessment

[redacted]

- Time to chemotherapy – time from initiation of talazoparib to initiation of subsequent chemotherapy

9.4. Data sources

Data will be abstracted and entered into the eCRFs by patients' treating physicians within the OPEN. The source documents are the patient chart/medical record data housed within the EHRs and accessed by the participating providers. Data abstracted into the eCRFs must match those charts. To adhere to Pfizer's requirements for non-interventional studies (NIS) collecting data for patients treated with a Pfizer product, all providers who wish to participate will complete the required Pfizer pharmacovigilance (PV) training for reporting of AEs.

Through the chart review approach, data elements contained in unstructured fields of the EHR (e.g., clinical progress notes, radiographic scans/reports, pathology reports) or those elements requiring a provider's interpretation (e.g., date of progression) can be collected. The eCRF is a custom data abstraction tool allowing the provider chart abstractor to input de-identified data directly from the patient EHR into a secure, web-based platform. The data elements that can be collected are limited by the length of time required for the participating provider to conduct the data abstraction, which may vary depending upon the complexity of data elements required and the patient's health record. Based on the study objectives, a preliminary outline of key variables and datapoints to be abstracted into the eCRF by participating physicians is included in Section 9.3 above.

No source document verification can be conducted by CHSS; however, data quality control (QC), quality assurance (QA), and validation processes will be performed as described. These processes and systems are vetted during field testing with volunteer physicians, as described in Section 9.8.

9.5. Study size

As there are no a priori hypotheses specified, sample size calculations are not applicable, and power calculations were not performed. To estimate the numbers of potentially available eCRFs, an initial feasibility survey and subsequent, in-depth feasibility/short CRF study were conducted that identified the numbers of HER2-negative or HER2-positive ABC patients with gBRCA1/2 mutations treated with talazoparib since 2018 by providers in the Cardinal Health OPEN. In the short CRF study, providers were required to confirm whether germline mutations were detected in BRCA1, BRCA2, or both, as well as the sample type used to detect gBRCA mutation(s). Participating physicians were also required to provide other basic demographic, clinical, and treatment descriptors of patients.

CCI [redacted] For the main analysis aimed to address the primary objectives of this study, sample size will be approximately 110 patients. CCI [redacted]

9.6. Data management

Patient-level data are entered by the treating provider into the eCRF, a custom data abstraction tool for capturing deidentified patient-level data directly into a secure, web-based survey platform (Qualtrics). The eCRF structure and format are designed to allow providers to efficiently move through the EHR while documenting the patient journey throughout the course of disease. The eCRF conforms to the rules and regulations of the Health Insurance Portability and Accountability Act (HIPAA) of 1996 governing the abstraction and storage of PHI. Limited and necessary to achieve study objectives PHI (e.g., start and end of treatment dates, date of death) will be collected in the course of the chart review or stored in the eCRF. The CHSS research team is responsible for the programming, testing, and hosting of data from submitted eCRFs, and all data are stored on encrypted, password-protected, and HIPAA-compliant servers housed within the Cardinal Health electronic data storage infrastructure.

Participating physicians will be asked to complete the chart review individually, meaning that site research staff or support staff will not complete any data abstraction. Physicians are instructed to consult all available sources and indicate whether data points have been substantiated by source materials in the EHR. The study variables that can be collected are limited to those that can be captured within the allotted 45 to 60 minutes.

Following protocol finalization, a text version of the CRF will be created, and once finalized, an eCRF will be programmed in Qualtrics. Variables are captured in numeric and text format, as appropriate, and grouped according to the study objectives as described in the protocol. The Qualtrics interface used for data entry and management provides screens for data entry and includes study-specific programming checks to help control for data quality, consistency, and validity. No source document verification can be conducted by Cardinal Health; however, data QC, QA, and validation processes will be performed as described. The raw data entered into Qualtrics will be vetted through QA, QC, and validation procedures as described in Section 9.8, and a CHSS analyst will export them into SAS v9.4 for data transformation and analysis, which will be used for all manipulations of data. Pfizer will not have access to the individual data collected.

9.6.1. Case report forms (CRFs) /Electronic data record

As used in this protocol, the term CRF should be understood to refer to either a paper form or an electronic data record both, depending on the data collection method used in this study.

A CRF is required and should be completed for each included patient. The completed original CRFs are the sole property of Pfizer and should not be made available in any form to third parties, except for authorized representatives of Pfizer or appropriate regulatory authorities, without written permission from Pfizer. The investigator shall ensure that the CRFs are securely stored at the study site in encrypted electronic form and will be password-protected to prevent access by unauthorized third parties.

The investigator has ultimate responsibility for the collection and reporting of all clinical, safety, and laboratory data entered on the CRFs and any other data collection forms (source

documents) and ensuring that they are accurate, authentic/original, attributable, complete, consistent, legible, timely (contemporaneous), enduring, and available when required. The CRFs must be signed by the investigator or by an authorized staff member to attest that the data contained on the CRFs are true. Any corrections to entries made in the CRFs or source documents must be dated, initialed, and explained (if necessary) and should not obscure the original entry.

The source documents are the hospital or the physician's chart. In these cases, data collected on the CRFs must match those charts.

9.6.2. Record retention

To enable evaluations and/or inspections/audits from regulatory authorities or Pfizer, the investigator agrees to keep records, including the identity of all participating patients (sufficient information to link records, e.g., CRFs and hospital records), all original signed informed consent documents, copies of all CRFs, safety reporting forms, source documents, detailed records of treatment disposition, and adequate documentation of relevant correspondence (e.g., letters, meeting minutes, and telephone call reports). The records should be retained by the investigator according to local regulations or as specified in the clinical study agreement (CSA), whichever is longer. The investigator must ensure that the records continue to be stored securely for so long as they are retained.

If the investigator becomes unable for any reason to continue to retain study records for the required period, (e.g., retirement, relocation), Pfizer should be prospectively notified. The study records must be transferred to a designee acceptable to Pfizer, such as another investigator, another institution, or to an independent third party arranged by Pfizer.

Study records must be kept for a minimum of 15 years after completion or discontinuation of the study unless CHSS and Pfizer have expressly agreed to a different period of retention via a separate written agreement. Record must be retained for longer than 15 years or as required by applicable local regulations.

The investigator must obtain Pfizer's written permission before disposing of any records, even if retention requirements have been met.

9.7. Data analysis

9.7.1. Analysis overview

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in the SAP, which will be dated, filed, and maintained by the sponsor. Due to the descriptive nature of this retrospective, observational study, no hypotheses have been specified a priori and no formal hypothesis testing will be performed.

Descriptive analyses will be conducted on variables related to provider characteristics, patient demographics, clinical characteristics, treatment patterns and history, biomarker status, and clinical outcomes. For CCI rwPFS, and all other time-to-event endpoint analyses, the Kaplan-

Meier (KM) method will be used, accounting for right-censoring. To assess differences in the odds of disease response, logistic regression may be used to calculate the OR and associated P-values CCI [redacted] If post-hoc analyses are performed, the log-rank test may be used to assess a difference in median time-to-event data among subgroups for the primary analysis cohort. CCI [redacted] The comparison of means (medians where appropriate) and proportions across cohorts will be performed using t-tests (Wilcoxon where appropriate) and chi-square tests (Fisher exact where cell size is fewer than 5 patients). The numbers of missing and unknown observations will be described for both categorical and continuous variables. No data imputation will be conducted. Patients with missing/unknown data will be reported as such. Primary CCI [redacted] cohorts will be delineated and analyzed CCI [redacted] as follows CCI [redacted] The primary analysis cohort will consist of adult HER2-negative ABC patients with gBRCA1/2 mutations treated with talazoparib monotherapy in a RW practice setting in the US. CCI [redacted]

If sample size allows, clinical outcomes will also be reported for post-hoc analytic subgroups of interest only for the primary population CCI [redacted] Subgroups may include the following and will be determined once data collection is complete: patients with HR-positive/HER2-negative BC and patients with TNBC, CCI [redacted]

Post-hoc statistical comparisons between subgroups of interest in the primary analysis cohort may be performed if sample size allows, using chi-square tests and t-tests or their non-parametric equivalents.

Statistical analyses will be performed using SAS v9.4. All tests will be 2-tailed, and the level of significance will be set at α=0.05. Statistical tests will only be conducted if the sample size is adequate for comparisons.

9.7.2. Analysis of baseline characteristics in the primary analysis population

Baseline characteristics of adult HER2-negative ABC patients with gBRCA1/2 mutations treated with talazoparib monotherapy in a RW practice setting in the US will be assessed in the primary analysis. Patient demographics and clinical characteristics will be summarized

using descriptive statistics: mean, standard deviation (STD), median, interquartile range (IQR), and minimum/maximum values will be calculated for continuous variables and for categorical data, counts and proportions will be calculated.

9.7.3. Analysis of clinical outcomes in the primary analysis population

All categorical and continuous non–time-to-event variables collected for the primary analysis population of adult HER2-negative ABC patients with gBRCA1/2 mutations treated with talazoparib monotherapy in a RW practice setting in the US will be analyzed using descriptive statistical techniques. For continuous/numeric variables, the mean, STD, median, interquartile range (IQR), and minimum/maximum values will be calculated. For categorical variables, frequencies and percentages will be provided.

All time-to-event endpoints will be estimated using univariate analysis and KM methods, as appropriate. KM survival curves, KM survival proportions at specified intervals, the number of events, and the number of patients censored will be provided. KM-estimated median values, first and third quartiles, and 95% CIs around each point estimate will be reported when estimable.

If post-hoc analyses are performed, the log-rank test may be used to assess a difference in median time-to-event data among subgroups for the primary analysis cohort. To assess whether differences exist in the odds of disease response to treatment, the OR and associated P-values may be calculated, CCI [redacted]

Analytic study endpoints for the primary analysis population will include (but are not limited to) the following:

- TTF – time from initiation of talazoparib to discontinuation for any reason, including disease progression, treatment toxicity, and death
    - Patients still on therapy at last encounter will be censored at last encounter date
- rwPFS – time from initiation of talazoparib to disease progression based on radiographic imaging or death from any cause, whichever occurs first
    - Patients who discontinued talazoparib for a reason other than progression or death will be censored at talazoparib discontinuation date. Patients still receiving talazoparib at last encounter will be censored on date of last encounter.

[redacted]

- Patients who are known to be alive or lost to follow-up will be censored on the date of last encounter

- rwORR – sum of patients with reported complete and partial responses to talazoparib divided by all patients assessed for disease response

- Time to chemotherapy – time from initiation of talazoparib to initiation of subsequent chemotherapy

9.7.4. Subgroup analyses for the primary analysis population

All or a selected set of variables may also be reported for subgroups of patient cohorts of the primary analysis population of adult HER2-negative ABC patients with gBRCA1/2 mutations treated with talazoparib monotherapy in a RW practice setting in the US. If sample size allows, clinical outcomes will also be reported for post-hoc analytic subgroups of interest only for the primary population CCI

Subgroups may include the following, to be determined once data collection is complete:

- HR-positive/HER2-negative BC
- TNBC

CCI

CCI

[redacted]

[redacted]

9.8. Quality control

CHSS will be responsible for the programming, testing, and hosting of data from submitted CRFs. Testing includes ensuring functionality across web-based user environments, looping logic to ensure proper alignment of data-related fields (required responses to certain fields prior to entering data into subsequent field), and other programmatic checks to reduce input of erroneous data (such as specifying maximums for year of birth or initiation of index treatment within the dates of the enrollment period).

In addition, the eCRF will be field-tested with 2 providers to ensure its functionality, the correct interpretation of the questions in relation to the data points of interest, and the proper length of time for completion of data abstraction on a single patient. The pre-test results will be reviewed by CHSS with Pfizer. No data from the pre-testing phase will be used in the current study. Additionally, prior to data collection (during the field test and actual study launch), CHSS will complete the previously described user acceptance testing (UAT), inputting various clinical scenarios and identifying function edit checks and checks that are required to be made manually post-data collection. Results of the UAT will be included in the data QC log. Any changes made to the CRF document as a result of the pre-test will require the resubmission of the CRF and study protocol to the IRB.

Participating providers are informed in their contractual agreement that follow-up with CHSS may be required and are contacted for query resolution and/or data validation as needed. For medical queries and random data validation, providers will be asked to create a 4-digit unique identifier for each patient, which will be transmitted to Cardinal Health and used for identifying the patient record for data validation. Data will be reviewed by a licensed healthcare professional (HCP) employee of Cardinal Health to identify medical queries. Data will be further reviewed by an analyst and scientist to check for face validity of aggregate results (e.g., statistical outliers; eCRF completion in an unexpectedly short time; treatment regimens unknown to be used for the disease under study; individual provider responses compared with aggregate responses; laboratory, pathology, and radiology results inconsistent with known clinical parameters; other clinical data inconsistent with known standards and outcomes; and distribution and content of key variables needed for analysis). Issues flagged for potential data validation will be resolved with the providers directly on a case-by-case basis. Any eCRF

flagged during QC will be reviewed by the team to determine the level of follow-up needed. Individual eCRFs that cannot be validated will be removed from the dataset, and the respective provider will not be compensated for the eCRF that is removed.

Random data validation occurs by selecting a random eCRF from each provider submitting a patient. Providers subjected to random validation are asked to complete a 3 data point-validation exercise for the patient, whereby the provider is given the unique patient identifier but no other information. The provider is then asked to re-enter the data elements. The 3 data points may include: month/year of treatment initiation, stage at diagnosis, and date of treatment discontinuation (or date of last treatment/prescription if patient is still on therapy). Providers who had been previously verified by CHSS will not be subject to random validation. A verified provider is any physician abstractor who has completed at least 2 of the following: (1) completed and acknowledged CHSS web-based chart data abstraction training in the past 2 years, (2) participated in a chart review pre-test with screen sharing, (3) participated in two previous chart review studies in the past 2 years and accurately validated data, and (4) completed a phone interview with the CHSS team for data validation. Despite a provider having been verified, however, he or she will still be required to answer questions regarding patients with data flagged by the research operations or research analytics teams. A provider who fails to validate all data points for a selected patient will be required to submit to further clinical data review. No resampling to replace any excluded eCRF will be conducted.

After completion of QC/QA reviews and for all completed eCRFs, the study database will be locked, and all data will be downloaded and stored on a secured server housed within the Cardinal Health Information Technology infrastructure. Analyses for all research objectives will be performed at that time.

9.9. Strengths and limitations of the research methods

9.9.1. Strengths

The extensive CHSS network of oncologists/hematologists is geographically diverse, EHR/GPO-agnostic, and inclusive of multiple settings of community oncology care, thus making the survey results representative of the US oncology provider pool and patient population. Retrospective medical chart review provides in-depth knowledge of biomarker testing, diagnostic testing, treatment patterns, clinical outcomes, and rationale for treatment decisions using an efficient, reliable, and verifiable method. Chart review studies are therefore well suited for oncology as these clinical parameters are important to assess the patient journey, especially with the current focus on targeted, precision, and personalized medicine. Further, data are abstracted by providers for patients under their care, ensuring high data quality as the abstractor does not have to make assumptions about data elements. The majority of physicians invited to participate in this study have undergone various training sessions with CHSS staff related to abstraction of data from patients' medical charts and completion of eCRFs and are well versed with the chart abstraction process. Finally, many of the data elements of interest, including biomarker results, are often not available in structured or unstructured EHR fields, and physician-abstracted chart review allows for collection of these difficult-to-retrieve patient-level data elements.

9.9.2. Limitations

As is a limitation of any observational research study, not all patient characteristics will be included in the data collection (e.g., income and other variables that may influence physician prescribing behavior or treatment decisions), thereby allowing for potential unmeasured and residual confounding that cannot be accounted for in descriptive, univariate, multivariate, or subgroup analyses.

CHSS does not, and cannot, conduct source document verification. CHSS requires that all physicians submit to at least 1 random data validation check during the study whereby they are asked to re-enter 3 data points regarding a patient. Physicians failing to correctly re-enter data are subject to further review, and at the discretion of CHSS, may have all patient records submitted removed from the analytic dataset.

This study employs purposive sampling that selects physicians and patients based on pre-specified selection criteria and hence, this may not be representative of all patients within the cohorts of interest or representative of all physicians treating these patients. Physicians invited to participate in this study will represent a subset of OPEN physicians. Importantly, treatment patterns reflected in the study will represent only the practices of physicians who have volunteered to participate, and may vary from non-responding physicians (i.e., those who refused study participation or who did not respond to the screening invitation). No data will be available to describe non-participating providers or non-selected patients. CHSS cannot verify that all patients who meet the study eligibility criteria are included in the final dataset, and participating providers will initially be limited to submitting a maximum of 10 eCRFs in an aim to minimize provider bias (this maximum number of eCRFs may be increased if necessary, to aid in recruitment following prior approval from Pfizer). However, based on estimates of eligible patients reported by physicians who participated in the short chart review study, we expect the majority of providers to manage 10 or fewer eligible patients. Although bias related to selection of patient subsets within practices may occur, physicians will be instructed to identify all eligible patients and to select patients chronologically starting with eligible patients who initiated talazoparib the earliest within the study index period.

Additionally, this study may be subject to bias due to missing data. Although physicians will be required to record all relevant patient experiences in the medical charts, there may be undercounting of events that are unknown to them due to having occurred outside the office/clinical setting. Further, loss to follow-up may occur if patients transfer care to other providers or clinics. As such, treatments, visits, and outcomes occurring after the date of last visit may be missing. Further, this study involves retrospective extraction of data from medical records. Thus, the accuracy and completeness of the data collected are limited by the quality and nature of data available in the EHR and abstracted into the eCRF. Further, loss to follow-up may occur if patients transfer care to other providers or clinics. As such, treatments, visits, and outcomes occurring after the date of last visit may be missing. Additionally, the follow-up period may not be long enough to observe all disease progression events during therapy. CCI [redacted]

Finally, findings from this study may be impacted by a lack of uniform assessment criteria for certain variables such as disease response.

9.10. Other aspects

Not applicable.

10. PROTECTION OF HUMAN SUBJECTS

At all times, patient PHI is kept confidential in accordance with HIPAA. The eCRF will not capture any data related to the patient's name, full date of birth, social security number, health insurance plan number, medical record number, or other such PHI. However, date of disease diagnosis, date(s) of treatment(s) administered (including dates of dose changes), date of development of health states of interest (e.g., disease progression), and dates of death (if available) will be collected. These items are considered PHI under HIPAA. At no time will Pfizer be provided with PHI in the form of a dataset or otherwise; all study results will be reported in aggregate. Additionally, exact dates (e.g., of dose changes) will not be reported during analysis but will be used to calculate intervals of time between relevant anchor date and end dates of interest.

10.1. Patient information

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of patient personal data. Such measures will include omitting patient names or other directly identifiable data in any reports, publications, or other disclosures, except where required by applicable laws.

The personal data will be stored at the study site in encrypted electronic form and will be password protected to ensure that only authorized study staff have access. The study site will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, the study site shall be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of natural persons with regard to the processing of personal data, when study data are compiled for transfer to Pfizer and other authorized parties, any patient names will be removed and will be replaced by a single, specific, numerical code. All other identifiable data transferred to Pfizer or other authorized parties will be identified by this single, patient-specific code. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of patients' personal data consistent with the vendor contract, research agreement and applicable privacy laws.

10.2. Patient consent

As this study does not involve data subject to privacy laws according to applicable legal requirements, obtaining informed consent from patients by Pfizer is not required.

10.3. Institutional review board (IRB)/Independent ethics committee (IEC)

There must be prospective approval of the study protocol, protocol amendments, and other relevant documents (e.g., informed consent forms if applicable) from the relevant IRBs/IECs. All correspondence with the IRB/IEC must be retained. Copies of IRB/IEC approvals must be forwarded to Pfizer.

10.4. Ethical conduct of the study

The study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and follow generally accepted research practices described in the Guidelines for Good Pharmacoepidemiology Practices (GPP) of the International Society for Pharmacoepidemiology (ISPE 2008), the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, and with the ethical principles laid down in the Declaration of Helsinki.

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This study protocol requires human review of patient-level unstructured data; unstructured data refer to verbatim medical data, including text-based descriptions and visual depictions of medical information, such as medical records, images of physician notes, neurological scans, X-rays, or narrative fields in a database. The reviewer is obligated to report AEs with explicit attribution to any Pfizer drug that appear in the reviewed information (defined per the patient population and study period specified in the protocol). Explicit attribution is not inferred by a temporal relationship between drug administration and an AE but must be based on a definite statement of causality by a healthcare provider linking drug administration to the AE.

The requirements for reporting safety events on the NIS adverse event monitoring (AEM) Report Form to Pfizer Safety are as follows:

- All serious and non-serious AEs with explicit attribution to **any Pfizer drug** that appear in the reviewed information must be recorded on the eCRF and reported, within 24 hours of awareness, to Pfizer Safety using the NIS AEM Report Form.

- Scenarios involving drug exposure, including exposure during pregnancy, exposure during breast feeding, medication error, overdose, misuse, extravasation, lack of efficacy, and occupational exposure associated with the use of a Pfizer product must be reported, within 24 hours of awareness, to Pfizer Safety using the NIS AEM Report Form.

For these AEs with an explicit attribution or scenarios involving exposure to a Pfizer product, the safety information identified in the unstructured data reviewed is captured in the Event Narrative section of the report form, and constitutes all clinical information known regarding these AEs. No follow-up on related AEs will be conducted.

All the demographic fields on the NIS AEM Report Form may not necessarily be completed, as the form designates, since not all elements will be available due to privacy concerns with the use of secondary data sources. While not all demographic fields will be completed, at the very least, at least one patient identifier (e.g., gender, age as captured in the narrative field of the form) will be reported on the NIS AEM Report Form, thus allowing the report to be considered a valid one in accordance with pharmacovigilance legislation. All identifiers will be limited to generalities, such as the statement "A 35-year-old female..." or "An elderly male..." Other identifiers will have been removed.

Additionally, the onset/start dates and stop dates for "Illness", "Study Drug", and "Drug Name" may be documented in month/year (mmm/yyyy) format rather than identifying the actual date of occurrence within the month /year of occurrence in the day/month/year (DD/MMM/YYYY) format.

All research staff members must complete the following Pfizer training requirements:

- "YRR Training for Vendors Working on Pfizer Studies (excluding interventional clinical studies and non-interventional primary data collection studies with sites/investigators)".

These trainings must be completed by research staff members prior to the start of data collection. All trainings include a "Confirmation of Training Certificate" (for signature by the trainee) as a record of completion of the training, which must be kept in a retrievable format. Copies of all signed training certificates must be provided to Pfizer. Re-training must be completed on an annual basis using the most current Your Reporting Responsibilities training materials.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Results from the final analysis may be submitted in the form of peer-reviewed publications and/or presented as an abstract or poster at scientific conferences.

In the event of any prohibition or restriction imposed (e.g., clinical hold) by an applicable competent authority in any area of the world, or if the party responsible for collecting data from the participant is aware of any new information which might influence the evaluation of the benefits and risks of a Pfizer product, Pfizer should be informed immediately.

13. REFERENCES

1. ACS. American Cancer Society Cancer Statistics Center: Breast Cancer. 2021; https://cancerstatisticscenter.cancer.org/?_ga=2.72864211.1312339105.1586458273-885389106.1584627111#!/cancer-site/Breast.
2. Liang Y, Zhang H, Song X, Yang Q. Metastatic heterogeneity of breast cancer: Molecular mechanism and potential therapeutic targets. *Semin Cancer Biol.* 2020;60:14-27.

3. Batra A, Cheung WY. Role of real-world evidence in informing cancer care: lessons from colorectal cancer. *Curr Oncol.* 2019;26(Suppl 1):S53-S56.
4. Masuda H, Brewer TM, Liu DD, et al. Long-term treatment efficacy in primary inflammatory breast cancer by hormonal receptor- and HER2-defined subtypes. *Ann Oncol.* 2014;25(2):384-391.
5. Testa U, Castelli G, Pelosi E. Breast Cancer: A Molecularly Heterogenous Disease Needing Subtype-Specific Treatments. *Medical sciences (Basel, Switzerland).* 2020;8(1).
6. Lee A, Moon BI, Kim TH. BRCA1/BRCA2 Pathogenic Variant Breast Cancer: Treatment and Prevention Strategies. *Annals of laboratory medicine.* 2020;40(2):114-121.
7. Patel M, Nowsheen S, Maraboyina S, Xia F. The role of poly(ADP-ribose) polymerase inhibitors in the treatment of cancer and methods to overcome resistance: a review. *Cell & bioscience.* 2020;10:35.
8. Antolin AA, Ameratunga M, Banerji U, Clarke PA, Workman P, Al-Lazikani B. The kinase polypharmacology landscape of clinical PARP inhibitors. *Scientific reports.* 2020;10(1):2585.
9. Malone KE, Daling JR, Doody DR, et al. Prevalence and predictors of BRCA1 and BRCA2 mutations in a population-based study of breast cancer in white and black American women ages 35 to 64 years. *Cancer Res.* 2006;66(16):8297-8308.
10. Kurian AW, Gong GD, John EM, et al. Performance of prediction models for BRCA mutation carriage in three racial/ethnic groups: findings from the Northern California Breast Cancer Family Registry. *Cancer Epidemiol Biomarkers Prev.* 2009;18(4):1084-1091.
11. De Talhouet S, Peron J, Vuilleumier A, et al. Clinical outcome of breast cancer in carriers of BRCA1 and BRCA2 mutations according to molecular subtypes. *Sci Rep.* 2020;10(1):7073.
12. FDA. US. Food and Drug Administration: FDA approves talazoparib for gBRCAm HER2-negative locally advanced or metastatic breast cancer. 2018; https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-talazoparib-gbrcam-her2-negative-locally-advanced-or-metastatic-breast-cancer.
13. Litton JK, Rugo HS, Ettl J, et al. Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation. *The New England journal of medicine.* 2018;379(8):753-763.
14. Zimmer AS, Gillard M, Lipkowitz S, Lee J-M. Update on PARP Inhibitors in Breast Cancer. *Current Treatment Options in Oncology.* 2018;19(5):21.

14. LIST OF TABLES

None

15. LIST OF FIGURES

ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

None.

ANNEX 2. ENCEPP CHECKLIST FOR STUDY PROTOCOLS

Not applicable.

ANNEX 3. ADDITIONAL INFORMATION

Not applicable.