NON-INTERVENTIONAL (NI) STUDY PROTOCOL

Study information

Title	Treatment Patterns and Clinical Outcomes Among Talazoparib-Treated Adults with HER2-Negative Metastatic Breast Cancer and Germline *BRCA1/2* Mutations: An Observational Study Using Flatiron Electronic Health Record (EHR) Database
Protocol number	C3441055
Protocol version identifier	1.0
Date	16 November 2021
Active substance	Talazoparib
Medicinal product	TALZENNA®
Research question and objectives	**Objectives**: The following objectives will be assessed descriptively among adult patients with human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer (mBC) with germline breast cancer susceptibility gene 1 or 2 (*gBRCA1/2*) mutations treated with talazoparib in first-line or later line of therapy in the real-world (RW) practice setting in the United States (US): *Primary objective* • Describe time to treatment failure (TTF) with talazoparib for talazoparib-treated patients CCI [redacted]

	[redacted]

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1. TABLE OF CONTENTS

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ABC	advanced breast cancer
AE	adverse event
AIDS	acquired immunodeficiency syndrome
ATU	Autorisation Temporaire d'Utilisation (temporary authorization for use)
BC	breast cancer
BRCA1	Breast cancer susceptibility gene 1
BRCA2	Breast cancer susceptibility gene 2
CDK	cyclin-dependent kinase
CI	confidence interval
ECOG	Eastern Cooperative Oncology Group performance status
EHR	Electronic Health Record
ER	estrogen receptor
FDA	Food and Drug Administration
gBRCA1/2	germline BRCA1 or 2
GPP	Good Pharmacoepidemiology Practices
HER2	human epidermal growth factor receptor 2
HIV	human immunodeficiency virus
HR	hormone receptor
IEC	Independent Ethics Committee
IQR	interquartile range
IRB	Institutional Review Board

Abbreviation	Definition
ISPE	International Society for Pharmacoepidemiology
KM	Kaplan-Meier
mBC	metastatic breast cancer
OR	odds ratio
CCI	[redacted]
PARP	Poly(adenosine diphosphate–ribose) polymerase
PDF	portable document format
PD-L1	Programmed death ligand 1
PFS	progression-free survival
PgR	progesterone receptor
PH	proportional hazards
PHI	Protected Health Information
QC	quality control
RW	real-world
CCI	[redacted]
SSDI	Social Security Death Index
STD	standard deviation
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TNBC	triple-negative breast cancer
TTF	time to treatment failure
US	United States

3. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

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4. ABSTRACT

Treatment Patterns, and Clinical Outcomes Among Talazoparib-Treated Adults with HER2-Negative Metastatic Breast and Germline *BRCA1/2* Mutations: An Observational Study Using Flatiron Electronic Health Record (EHR) database

Version 1, 16 November 2021

Main author: PPD PharmD, RPh, MPH
PPD Global Health Economics and Outcomes Research (Oncology)

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, the only information available about the real-world experience with talazoparib, including patient characteristics, treatment patterns, and clinical outcomes comes from compassionate use programs in Turkey, and Russia, and the French temporary authorization for use (ATU) program. Since the approval of talazoparib in the United States (US) in 2018, there is no published data about the real-world (RW) experience of talazoparib-treated patients with HER2-negative ABC with *gBRCA1/2* mutations in the US.

Research question and objectives

The following objectives will be assessed descriptively among adult patients with HER2-negative metastatic breast cancer (mBC) with *gBRCA1/2* mutations treated with talazoparib in first-line or later line of therapy in the RW practice setting in the US.

Primary objective

- Describe time to treatment failure (TTF) with talazoparib for talazoparib-treated patients

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[redacted]

Study design

This is an observational study using de-identified EHR data from Flatiron Health Analytic Database.

Population

The study population includes adult patients with HER2-negative mBC with *gBRCA1/2* mutations who initiated talazoparib in first or later line of therapy identified from the Flatiron Health Analytic Database.

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Data sources

EHR data from Flatiron Health Analytic Database.

Study size

Approximately 40 patients with *gBRCA1/2* mutated HER2- mBC who have received treatment with talazoparib.

Data analysis

CCI

CCI [redacted] For time-to-event analyses endpoints such as TTF, CCI

CCI [redacted] the Kaplan-Meier (KM) method will be used, accounting for right-censoring.

CCI [redacted]

5. AMENDMENTS AND UPDATES

None.

6. MILESTONES

Milestone	Planned date
Tables for Abstract Submission to 2022 Miami Breast, ASCO 2022, ESMO BC	31 December 2021
Start of data collection	22 November 2021
End of data collection	31 December 2021
Final tables	28 February 2022
Final study report	31 March 2022

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 (mBC) 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 (including locally advanced or metastatic breast cancer) and germline breast cancer susceptibility gBRCA1/2 mutations.[12]

To date, the only information available about the real-world experience with talazoparib, including patient characteristics, treatment patterns, and clinical outcomes comes from compassionate use programs in Turkey, and Russia, and the French temporary authorization for use (ATU) program. Since the approval of talazoparib in the United States (US) in 2018, there is no published data about the real-world (RW) experience of talazoparib-treated patients with HER2-negative ABC with *gBRCA1/2* mutations in the US.

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. This study aims to describe patient demographics, clinical characteristics, clinical outcomes, and treatment patterns among patients with *gBRCA1/2* mutated HER2- mBC who have received treatment with talazoparib. The EHR data is collected as part of the routine clinical practice and enables quick access to rich health information in a timely manner.

8. RESEARCH QUESTION AND OBJECTIVES

The following objectives will be assessed among adult patients with HER2-negative mBC with *gBRCA1/2* mutations treated with talazoparib in first-line or later line of therapy in the RW practice setting in the US.

Primary objective

- Describe time to treatment failure (TTF) with talazoparib for talazoparib-treated patients

CCI [redacted]

9. RESEARCH METHODS

9.1. Study design

This is an observational study using de-identified structured EHR data from Flatiron Health Analytic Database. The following table lists 7 key components of the study protocol.

Protocol Component	Description
Eligibility criteria	Talazoparib-treated adult patients with HER2-negative mBC with *gBRCA1/2* mutations identified between 01 January 2011 to 30 September 2020 from Flatiron Health Analytic Database
Study cohorts	Single cohort study of talazoparib-treated patients
Index date	Date of first talazoparib-containing line of therapy between 01 January 2018 to 30 September 2020, as defined by the Flatiron's line of therapy business rules
Baseline period	The baseline period will be variable, and it will encompass events that occur between 01 January 2011 and the index date (e.g., initial breast cancer diagnosis, diagnosis of mBC, neoadjuvant/adjuvant therapy)
Follow-up period	From index date to death or end of study follow-up (earliest of last patient-level structured or abstracted activity (i.e., the

Protocol Component	Description
	last record of patient vitals, medication administrations, or reported laboratory tests/results, or abstracted end date of oral medications) or date of data cut-off (30 September 2020)), whichever occurred first
Primary outcome	TTF for time from talazoparib initiation to discontinuation for any reason, including disease progression, treatment toxicity, and death.
CCI [redacted]	[redacted]

9.2. Setting

The study population includes adult patients with HER2-negative mBC with *gBRCA1/2* mutations who initiated talazoparib treatment in first-line or later identified from Flatiron Health Analytic Database.

9.2.1. Inclusion criteria

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

1. Diagnosed with breast cancer (ICD-9 174.x or 175.x or ICD-10 C50x)
2. At least two visits in the Flatiron database on or after 01 January 2011
3. Pathology consistent with breast cancer
4. Has evidence of stage IV or recurrent metastatic breast cancer with a metastatic diagnosis date on or after 01 January 2011. This includes patients who were diagnosed with stage IV at diagnosis or were diagnosed with earlier stage disease, then developed a distant metastasis later on, or had recurrence of the disease via a distant metastasis
5. Confirmed receipt of talazoparib as treatment for mBC via abstraction initiated on or after 01 January 2018
6. HER2 negative test result on or before the start of patient's first talazoparib-containing line of therapy, as defined by Flatiron's line of therapy rules

7. BRCA1, BRCA2, BRCA1 and BRCA2 germline mutation, or BRCA germline mutation not otherwise specified, identified on or before the start date of patient's first talazoparib-containing line of therapy, as defined by Flatiron's line of therapy business rules

8. Age 18 or older at the time of first talazoparib-containing line of therapy

9.2.2. Exclusion criteria

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

1. Lacking relevant unstructured documents in the Flatiron database for review by the abstraction team

2. Receipt of drug as part of a clinical trial (captured in the database as "clinical study drug" without additional information about active ingredient or whether the patient received placebo), defined as any non-cancelled order, administration, or oral episode for a drug used in a clinical trial, on or prior to start of first talazoparib line of therapy, as defined by Flatiron's line of therapy business rules

9.3. Variables

Key variables include:

Variable	Operational definition
Demographic characteristics	
Age	Age at index date (date of first talazoparib-containing line of therapy in mBC), years
CCI [redacted]	
Gender	Male, female, unknown
CCI [redacted]	
Hispanic/Latino ethnicity	Yes, No/unknown
CCI [redacted]	

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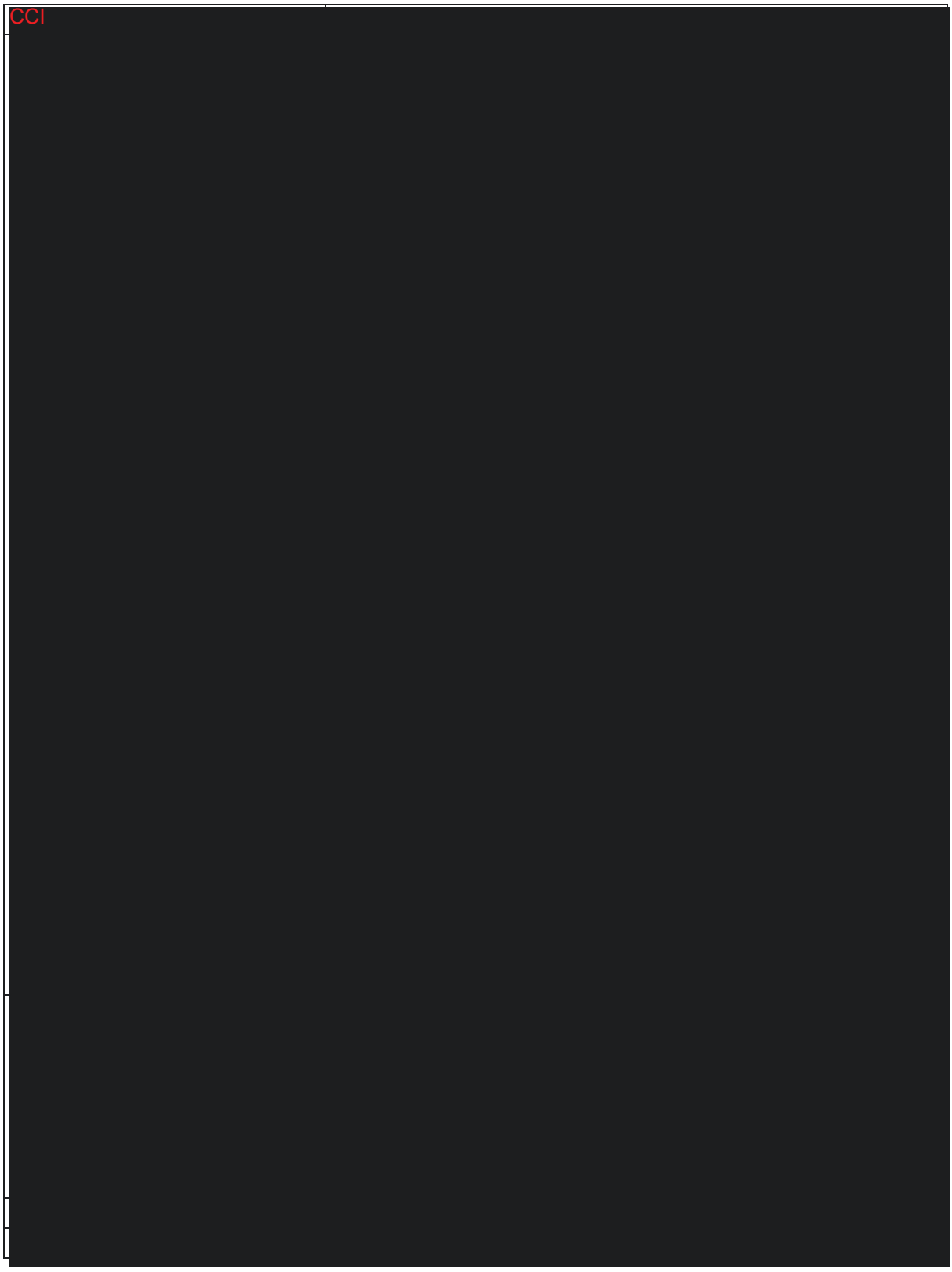

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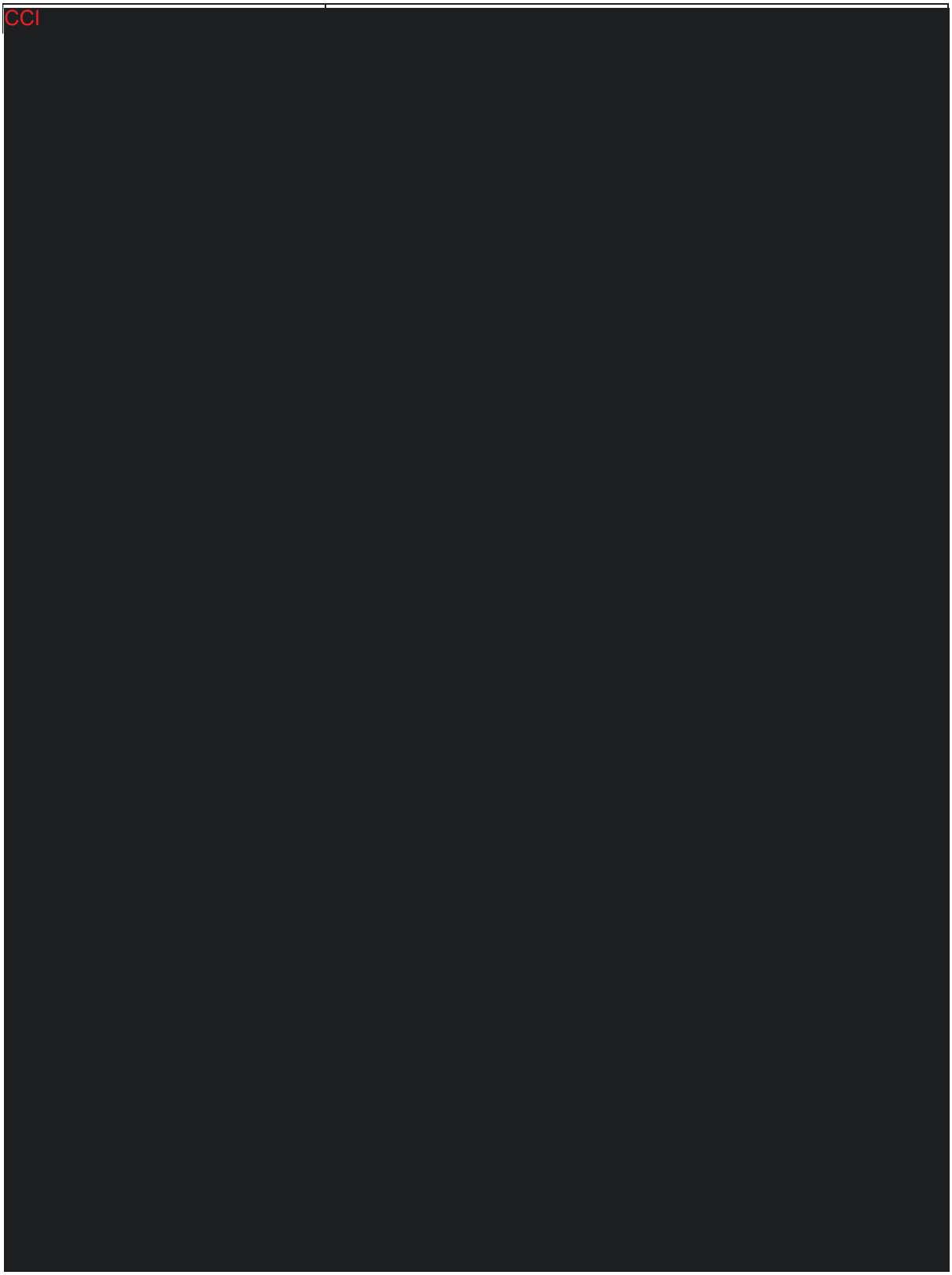

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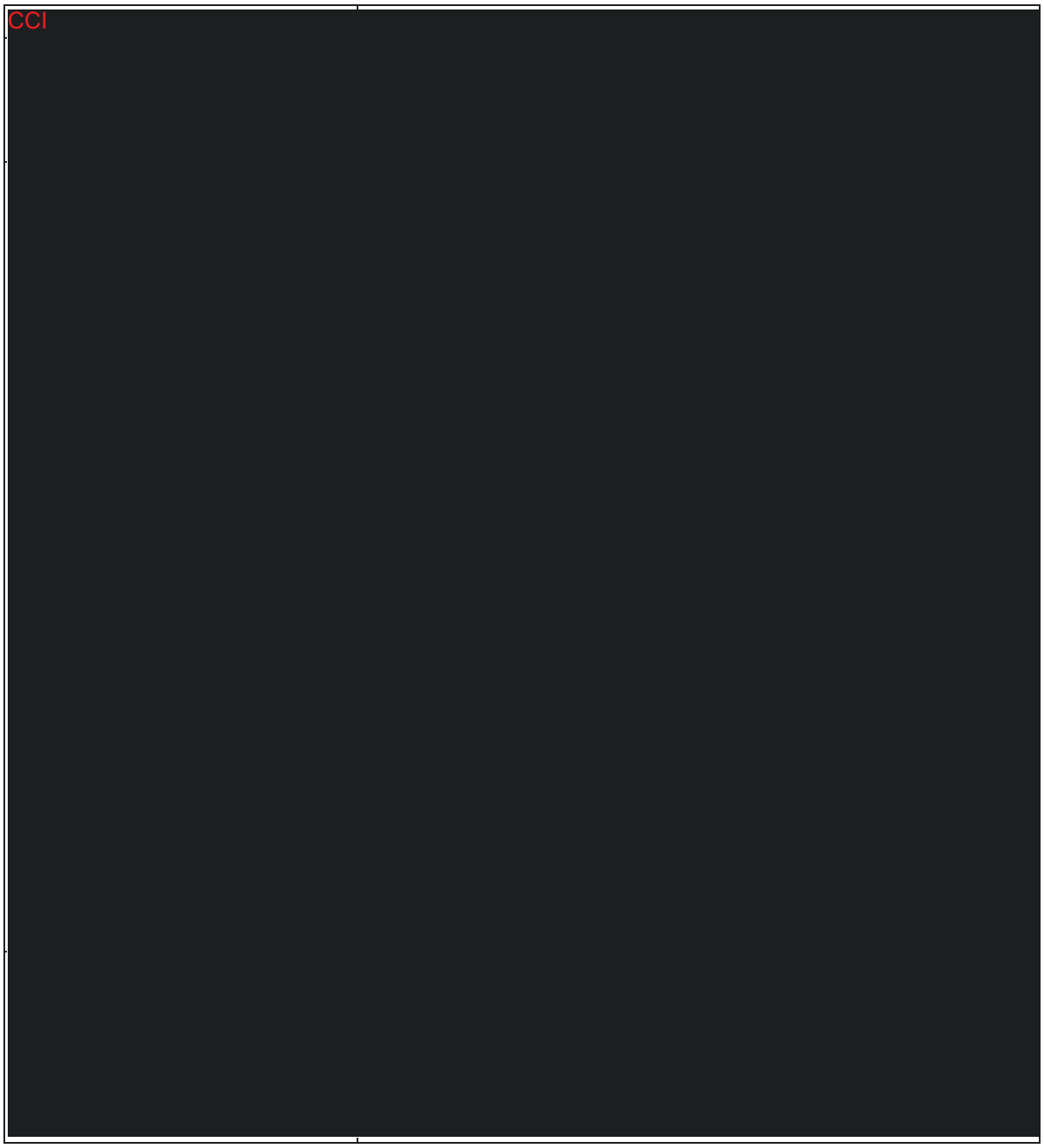
Variable	Operational definition
CCI [redacted]	
Time to treatment failure (TTF)	Months from start of talazoparib to discontinuation for any reason, including disease progression, treatment toxicity, and death. Patients still on therapy at the end of follow-up (earliest of last patient-level structured or abstracted activity (i.e., the last record of patient vitals, medication administrations, or reported laboratory tests/results, or abstracted end date of oral medications) or date of data cut-off (30 September 2020)) will be censored.
CCI [redacted]	[redacted]



9.4. Data sources

This retrospective observational study will utilize Flatiron Health's longitudinal, demographically, and geographically diverse database derived from EHR data from over 265 cancer clinics (~800 sites of care) including more than 2.5 million active US cancer patients available for analysis. The Flatiron EHRs include the entire patient chart of all patients treated in the Flatiron network.

Across the clinics in the Flatiron Health Network, data become available in near real time after each clinical encounter and contribute to Flatiron's continuously aggregating centralized data set. Flatiron accesses both structured data (i.e., data points that are organized in a predefined manner, such as dropdown fields that reside in an EHR to capture a patient's gender or date of birth or laboratory data) as well as unstructured data (i.e., information that is not organized in a preexisting data model, such as free text from a physician note or a portable document format (PDF) laboratory report). The data used in this analysis already exist as structured data in an electronic database.

9.5. Study size

This is a descriptive study and sample size and power calculations are not available. All eligible talazoparib treated patients during the study period will be included in the analysis. This will include approximately 40 patients with *gBRCA1/2* mutated HER2- mBC who have received treatment with talazoparib.

9.6. Data management

De-identified data are prepared by Flatiron and transferred securely to Pfizer in a standard flat file format. Details of de-identification procedure and data management are outlined in the Flatiron's parent database protocol (NEIRB#15-159, "The Flatiron Health Analytic Database"). All data are stored and backed up on Flatiron's servers for at least 7 years.

9.7. Data analysis

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in a statistical analysis plan (SAP), which will be dated, filed and maintained by the sponsor. The SAP may modify the plans outlined in the protocol; any major modifications of primary endpoint definitions or their analyses would be reflected in a protocol amendment.

9.8. Analysis overview

Due to the descriptive exploratory 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 patient demographics, clinical characteristics, treatment patterns and history, and clinical outcomes. For time-to-event endpoint analyses such as TTF, CCI [redacted] CCI [redacted] CCI [redacted] the Kaplan-Meier (KM) method will be used, accounting for right-censoring. Additionally, depending on sample size, Cox proportional hazards (PH) models may be used to assess the impact of specific characteristics on time-to-event outcomes during post-hoc analysis if sample size allows.

If sample size allows, clinical outcomes will also be reported for post-hoc analytic subgroups of interest. Subgroups may include the following and will be determined once data collection is complete: patients with HR-positive/HER2-negative mBC and patients with metastatic TNBC, patients who received prior platinum therapy in mBC and patients who did not,

patients who receive CDK4/6 inhibitors in mBC and those who did not, and subgroups by line of therapy of talazoparib initiation.

Post-hoc statistical comparisons between subgroups of interest may be performed if sample size allows. The comparison of means (medians where appropriate) and proportions across subgroups will be performed using t-tests (Wilcoxon where appropriate) and chi-square tests (Fisher exact where cell size is fewer than 5 patients). If post-hoc analyses of subgroups are performed, the log-rank test may be used to assess a difference in median time-to-event data among subgroups.

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.

9.8.1. Analysis of baseline characteristics

Baseline characteristics of adult patients with HER2-negative mBC and *gBRCA1/2* mutations treated with talazoparib monotherapy in a RW practice setting in the US will be assessed. 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. 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.

9.8.2. Analysis of clinical outcomes

All categorical and continuous non–time-to-event variables 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 subgroup analyses are performed, the log-rank test may be used to assess a difference in median time-to-event data among subgroups. Additionally, depending on sample size Cox PH models may be used to assess the impact of specific characteristics on time-to-event outcomes during post-hoc analysis.

Analytic study endpoints will include (but are not limited to) the following:

- TTF – months from initiation of talazoparib to discontinuation for any reason, including disease progression, treatment toxicity, and death
    - Patients still on therapy at the end of follow-up (earliest of last patient-level structured or abstracted activity (i.e., the last record of patient vitals, medication administrations, or reported laboratory tests/results, or abstracted end date of oral medications) or date of data cut-off (30 September 2020)) will be censored.

[redacted]

9.9. Quality control

Quality control (QC) will follow the Flatiron's standard procedure for quality control and assurance as described in Flatiron Health Analytic Database Parent Protocol. QC for structured and unstructured data is conducted prior to delivery of each dataset. For each data model, Flatiron generates and continually maintains a set of quality standards. These QC standards cover themes such as demographics, biomarkers, treatment, therapy shares, and treatment length/dosage, and include both medical considerations (e.g., what are expected based on the literature and clinical practice) and data considerations (e.g., stability from prior months). Issues identified are methodically logged, prioritized, investigated and resolved. Substantive issues are discussed by the team and a mitigation plan is developed. Any quality concerns and the approaches taken to rectify them will be communicated to the sponsor. All data undergo statistical review prior to locking the data. Statistical review includes: error log search, warning evaluation, logic and critical steps and macro usage. Queries generated are forwarded to the medical lead of the project and resolved prior to the data being locked.

9.10. Limitations of the research methods

One of the main challenges of EHR data is the potential for missing, inaccurate or incomplete data (e.g., EHR contains only that a physician prescribed an oral drug but not whether or not it was filled/refilled). In addition, the quality of information extracted from the EHR depends on the quality of information entered into the EHR by the clinician. Finally, the patient populations in the Flatiron database may not be reflective of the general population nationally. Some skewing in the data is possible if differences exist between patients in this study cohort and general patient population (refer to Flatiron parent protocol). Moreover, the sample size of talazoparib-treated patients in this study is small which could affect the reliability of study findings.

9.11. Other aspects

Not applicable.

10. PROTECTION OF HUMAN SUBJECTS

All parties will ensure protection of patient personal data and will not include patient names on any sponsor forms, reports, publications, or in any other disclosures, except where required by laws. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of patient personal data.

Informed consent is not required for this study as it is the secondary use of the existing health records and the data is de-identified. There will be no direct involvement of patients and patients will receive no direct benefit from participating in the study.

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)

The IRB approval of this observational study with secondary data use from an existing EHR database is covered by IRB approval on Flatiron parent protocol. There are no known risks to the patients beyond the potential of loss of confidentiality; all precautions will be maintained to protect patient confidentiality and protected health information (PHI) as outlined in the parent protocol, NEIRB#15-159.

It is the responsibility of the investigator to have prospective approval of the study protocol, protocol amendments, and informed consent forms, and other relevant documents, (e.g., recruitment advertisements), if applicable, from the IRB/IEC. All correspondence with the IRB/IEC should be retained in the Investigator File. Copies of IRB/IEC approvals should 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 involves a combination of existing structured data and unstructured data, which will be converted to structured form during the implementation of the protocol solely by a computer using automated/algorithmic methods, such as natural language processing.

In these data sources, individual patient data are not retrieved or validated, and it is not possible to link (i.e., identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an adverse event (AE) (i.e., identifiable patient, identifiable reporter, a suspect product, and event) cannot be met.

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.

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14. LIST OF TABLES

Table 1. Tentative List of CDK4/6 Inhibitors, Chemotherapy, and Immunotherapy for the Treatment of HR+/HER2-Negative or TNBC Metastatic Breast Cancer [a]

Drug Name	Brand Name	Type of therapy	Code
Palbociclib	Ibrance	CDK4/6 inhibitor	N/A
Ribociclib	Kisqali	CDK4/6 inhibitor	N/A
Abemaciclib	Verzenio	CDK4/6 inhibitor	N/A
Atezolizumab	Tecentriq	Immunotherapy	J9022
Pembrolizimab	Keytruda	Immunotherapy	J9271
Capecitabine	Xeloda	Chemotherapy	J8520 , J8521
5-fluorouracil	Adrucil	Chemotherapy	• J9190
Cisplatin	Platinol	Chemotherapy; Platinum therapy	• C9418 - Cisplatin (2) *(HCPCS Procedure Drug)* • J9060 - Cisplatin 10 mg injection (2) *(HCPCS Procedure Drug)* • J9062 - Cisplatin 50 mg injection (2) *(HCPCS Procedure Drug)*
Carboplatin	Paraplatin	Chemotherapy; Platinum therapy	○ J9045 - Injection, carboplatin, 50 mg *(HCPCS Procedure Drug)*
Cyclophosphamide	Cytoxan	Chemotherapy	• C9420 - Cyclophosphamide (2) *(HCPCS Procedure Drug)* • C9421 - Cyclophosphamide (2) *(HCPCS Procedure Drug)* • J8530 - Cyclophosphamide oral 25 mg (2) *(HCPCS Procedure Drug)* • J9070 - Cyclophosphamide 100 mg inj (2) *(HCPCS Procedure Drug)*

Table 1. Tentative List of CDK4/6 Inhibitors, Chemotherapy, and Immunotherapy for the Treatment of HR+/HER2-Negative or TNBC Metastatic Breast Cancer [a]

Drug Name	Brand Name	Type of therapy	Code
			• J9080 - Cyclophosphamide 200 mg inj (2) *(HCPCS Procedure Drug)* • J9090 - Cyclophosphamide 500 mg inj (2) *(HCPCS Procedure Drug)* • J9091 - Cyclophosphamide 1.0 grm inj (2) *(HCPCS Procedure Drug)* • J9092 - Cyclophosphamide 2.0 grm inj (2) *(HCPCS Procedure Drug)* • J9093 - Cyclophosphamide lyophilized (2) *(HCPCS Procedure Drug)* • J9094 - Cyclophosphamide lyophilized (2) *(HCPCS Procedure Drug)* • J9095 - Cyclophosphamide lyophilized (2) *(HCPCS Procedure Drug)* • J9096 - Cyclophosphamide lyophilized (2) *(HCPCS Procedure Drug)* • J9097 - Cyclophosphamide lyophilized (2) *(HCPCS Procedure Drug)*

Table 1. Tentative List of CDK4/6 Inhibitors, Chemotherapy, and Immunotherapy for the Treatment of HR+/HER2-Negative or TNBC Metastatic Breast Cancer [a]

Drug Name	Brand Name	Type of therapy	Code
Docetaxel		Chemotherapy	• J9170 - INJECTION, DOCETAXEL, 20 MG *(HCPCS Procedure Drug)* • J9171 - Injection, docetaxel, 1 mg *(HCPCS Procedure Drug)*
Doxorubicin	Taxotere	Chemotherapy	• C9415 - Doxorubicin (2) *(HCPCS Procedure Drug)* • J9000 - Doxorubicin hcl injection (2) *(HCPCS Procedure Drug)* • J9001 - Doxorubicin hcl liposome inj (2) *(HCPCS Procedure Drug)* • Q2050 - Doxorubicin inj 10mg (2) *(HCPCS Procedure Drug)*
Epirubicin	Ellence	Chemotherapy	• J9178
Eribulin	Halaven	Chemotherapy	• C9280 - Injection, eribulin mesylate (2) *(HCPCS Procedure Drug)* • J9179 - Eribulin mesylate injection (2) *(HCPCS Procedure Drug)*
Gemcitabine	Gemzar	Chemotherapy	J9201
Ixabepilone	Ixempra	Chemotherapy	J9207
Methotrexate	NA	Chemotherapy	J8610, J9250, J9260,
Mitomycin	NA	Chemotherapy	J9280
Mitoxantrone	Novantrone	Chemotherapy	J9293
Nab-paclitaxel	Abraxane	Chemotherapy	No code specific to Abraxane

Table 1. Tentative List of CDK4/6 Inhibitors, Chemotherapy, and Immunotherapy for the Treatment of HR+/HER2-Negative or TNBC Metastatic Breast Cancer [a]

Drug Name	Brand Name	Type of therapy	Code
Paclitaxel	Taxol	Chemotherapy	• C9127 - Paclitaxel (2) *(HCPCS Procedure Drug)* • C9431 - Paclitaxel (2) *(HCPCS Procedure Drug)* • I - PACLITAXEL NO STRENGTH *(Uncoded Product Identifier)* • J9264 - Paclitaxel protein bound (2) *(HCPCS Procedure Drug)* • J9265 - Paclitaxel injection (2) *(HCPCS Procedure Drug)* J9267 - Paclitaxel injection (2) *(HCPCS Procedure Drug)*
Vinorelbine	Navelbine	Chemotherapy	• J9390

a The final list of chemotherapies, CDK4/6 inhibitors, and immunotherapies will be determined after evaluating the administered medications and oral therapies among eligible mBC patients.

15. LIST OF FIGURES

Not applicable.

ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

None.

ANNEX 2. ENCEPP CHECKLIST FOR STUDY PROTOCOLS

Not applicable.

ANNEX 3. ADDITIONAL INFORMATION

Not applicable.