TALZENNA

Table of Content

Please click on either of the following links to access the required information:

TALZENNA
(talazoparib)

1. NAME OF THE MEDICINAL PRODUCT

TALZENNA 0.1 mg hard capsules
TALZENNA 0.25 mg hard capsules
TALZENNA 0.35 mg hard capsules
TALZENNA 0.5 mg hard capsules
TALZENNA 1 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TALZENNA 0.1 mg hard capsules
Each capsule contains 0.145 mg talazoparib tosylate equivalent to 0.1 mg talazoparib free base.

TALZENNA 0.25 mg hard capsules
Each capsule contains 0.363 mg talazoparib tosylate equivalent to 0.25 mg talazoparib free base.

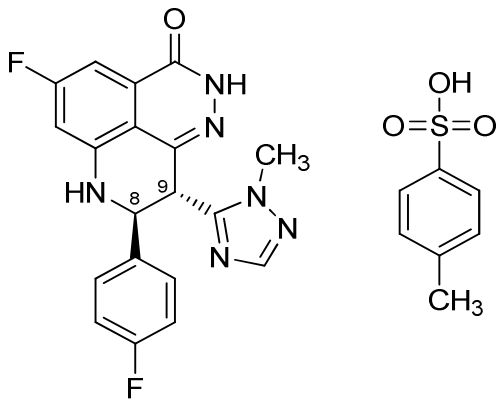
TALZENNA 0.35 mg hard capsules
Each capsule contains 0.509 mg talazoparib tosylate equivalent to 0.35 mg talazoparib free base.

TALZENNA 0.5 mg hard capsules
Each capsule contains 0.727 mg talazoparib tosylate equivalent to 0.5 mg talazoparib free base.

TALZENNA 1 mg hard capsules
Each capsule contains 1.453 mg talazoparib tosylate equivalent to 1 mg talazoparib free base.

For the full list of excipients, see Section 6.1.

Structure:



3. PHARMACEUTICAL FORM

Hard capsule.

TALZENNA 0.1 mg hard capsules
Opaque, size #4 hard hypromellose (HPMC) capsule with a white cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.1” in black).

TALZENNA 0.25 mg hard capsules
Opaque, size #4 hard hypromellose (HPMC) capsule with an ivory cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.25” in black).

TALZENNA 0.35 mg hard capsules
Opaque, size #4 hard hypromellose (HPMC) capsule with an ivory cap (printed with “Pfizer” in black) and an ivory body (printed with “TLZ 0.35” in black).

TALZENNA 0.5 mg hard capsules
Opaque, size #4 hard hypromellose (HPMC) capsule with a light pink cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.5” in black).

TALZENNA 1 mg hard capsules
Opaque, size #4 hard hypromellose (HPMC) capsule with a light red cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 1” in black).

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Breast cancer

TALZENNA is indicated for the treatment of adult patients with germline breast cancer susceptibility gene (BRCA)-mutated (gBRCAm) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer who have previously been treated with chemotherapy. These patients could have received chemotherapy in the neoadjuvant, adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments.

Prostate cancer

TALZENNA is indicated in combination with enzalutamide for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated.

4.2. Posology and method of administration

Treatment with TALZENNA should be initiated and supervised by a physician experienced in the use of anticancer medicinal products.

Treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer

Detection of mutations in hereditary breast cancer-related BRCA1 and BRCA2 genes should be determined by an experienced laboratory using a validated test method (see Section 5.1).

Recommended dosing for gBRCAm HER2-negative locally advanced or metastatic breast cancer
The recommended dose of TALZENNA is 1 mg capsule taken orally once daily. Patients should be treated until disease progression or unacceptable toxicity occurs.

Treatment of mCRPC

Recommended dosing for mCRPC
The recommended dose of TALZENNA is 0.5 mg administered orally once daily in combination with enzalutamide 160 mg orally once daily. Patients should be treated until disease progression or unacceptable toxicity occurs.

Patients receiving TALZENNA and enzalutamide should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

The 0.35 mg, 0.25 mg and 0.1 mg capsules are available for dose reduction.

Missing dose
TALZENNA may be taken with or without food. If the patient vomits or misses a dose, an additional dose should not be taken. The next prescribed dose should be taken at the usual time.

Dose modifications and reductions
To manage adverse reactions, consider interruption of treatment or dose reduction based on severity and clinical presentation. Recommended dose reductions are indicated in Tables 2 and 3.

Complete blood count should be obtained prior to starting TALZENNA therapy and monitored monthly and as clinically indicated (see Table 1 and Section 4.4).

Table 1. Dose adjustments for adverse reactions

	Withhold TALZENNA until levels resolve to	**Resume TALZENNA**
Hemoglobin <8 g/dL	≥9 g/dL	Resume TALZENNA at a reduced dose
Platelet count <50,000/μL	≥75,000/μL	
Neutrophil count <1,000/μL	≥1,500/μL	
Non-hematologic adverse reaction Grade 3 or Grade 4	≤Grade 1	Consider resuming TALZENNA at a reduced dose or discontinue

gBRCAm HER2-negative locally advanced or metastatic breast cancer
Table 2. Dose reduction levels for talazoparib monotherapy (breast cancer)

	Talazoparib dose level (breast cancer)
Recommended starting dose	1 mg once daily

First dose reduction	0.75 mg once daily
Second dose reduction	0.5 mg once daily
Third dose reduction	0.25 mg once daily

mCRPC

Table 3. Dose reduction levels for talazoparib when used in combination with enzalutamide (prostate cancer)

	Talazoparib dose level (prostate cancer)
Recommended starting dose	0.5 mg once daily
First dose reduction	0.35 mg once daily
Second dose reduction	0.25 mg once daily
Third dose reduction	0.1 mg once daily

Please refer to the enzalutamide prescribing information for dose modifications for adverse reactions associated with enzalutamide.

Concomitant treatment with inhibitors of P-glycoprotein (P-gp)

gBRCAm HER2-negative locally advanced or metastatic breast cancer
Strong inhibitors of P-gp may lead to increased talazoparib exposure. Concomitant use of strong P-gp inhibitors during treatment with talazoparib should be avoided. Coadministration should only be considered after careful evaluation of the potential benefits and risks. If coadministration with a strong P-gp inhibitor is unavoidable, the TALZENNA dose should be reduced to the next lower dose. When the strong P-gp inhibitor is discontinued, the TALZENNA dose should be increased (after 3 to 5 half-lives of the P-gp inhibitor) to the dose used prior to the initiation of the strong P-gp inhibitor (see Section 4.5).

mCRPC
The effect of coadministration of P-gp inhibitors on talazoparib exposure when talazoparib is given in combination with enzalutamide has not been studied. Therefore, concomitant use of P-gp inhibitors during treatment with talazoparib should be avoided (see Section 4.5).

Concomitant treatment with inhibitors of Breast Cancer Resistance Protein (BCRP)
The effect of coadministration of BCRP inhibitors with TALZENNA has not been studied. Therefore, concomitant use of strong BCRP inhibitors during treatment with talazoparib should be avoided (see Section 4.5).

Special populations

Hepatic impairment
No dose adjustment is required for patients with mild hepatic impairment (total bilirubin ≤1 × upper limit of normal [ULN] and aspartate aminotransferase (AST) >ULN, or total bilirubin >1.0 to 1.5 × ULN and any AST), moderate hepatic impairment (total bilirubin >1.5 to 3.0 × ULN and any AST), or severe hepatic impairment (total bilirubin >3.0 × ULN and any AST) (see Section 5.2). TALZENNA in combination with enzalutamide is not recommended for use in patients with severe hepatic impairment (Child-Pugh classification C), as pharmacokinetics and safety have not been established in these patients (see Section 5.2).

Renal impairment

gBRCAm HER2-negative locally advanced or metastatic breast cancer
No dose adjustment is required for patients with mild renal impairment (60 mL/min ≤ creatinine clearance [CrCL] < 90 mL/min). For patients with moderate renal impairment (30 mL/min ≤ CrCL < 60 mL/min), the recommended dose of TALZENNA is 0.75 mg once daily. For patients with severe renal impairment (15 mL/min ≤ CrCL < 30 mL/min), the recommended dose of TALZENNA is 0.5 mg once daily. TALZENNA has not been studied in patients requiring hemodialysis (see Section 5.2).

mCRPC
No dose adjustment is necessary for patients with mild renal impairment (60 mL/min ≤ creatinine clearance [CrCL] <90 mL/min). For patients with moderate renal impairment (30 mL/min ≤ CrCL <60 mL/min), the recommended dose of TALZENNA is 0.35 mg once daily in combination with enzalutamide orally once daily. For patients with severe renal impairment (15 mL/min ≤ CrCL <30 mL/min), the recommended dose of TALZENNA is 0.25 mg once daily in combination with enzalutamide once daily. TALZENNA has not been studied in patients with CrCL <15 mL/min or patients requiring hemodialysis (see Section 5.2).

Elderly population
No dose adjustment is necessary in elderly (≥65 years of age) patients (see Section 5.2).

Pediatric population
The safety and efficacy of TALZENNA in children and adolescents <18 years of age have not been established.

4.3. Contraindications

None.

4.4. Special warnings and precautions for use

Myelosuppression
Myelosuppression consisting of anemia, leukopenia/neutropenia, and/or thrombocytopenia, have been reported in patients treated with talazoparib (see Section 4.8). Do not start talazoparib until patients have recovered from hematological toxicity caused by previous therapy (≤Grade 1).

Precautions should be taken to routinely monitor hematology parameters and signs and symptoms associated with anemia, leukopenia/neutropenia, and/or thrombocytopenia in patients receiving talazoparib. If such events occur, dose modifications (reduction or interruption) are recommended (see Section 4.2). Supportive care with or without blood and/or platelet transfusions and/or administration of colony stimulating factors may be used as appropriate.

Myelodysplastic syndrome/Acute Myeloid Leukemia
Myelodysplastic syndrome/Acute Myeloid Leukemia (MDS/AML) have been reported in patients who received poly (adenosine diphosphate [ADP] ribose) polymerase (PARP) inhibitors. Overall, MDS/AML has been reported in <1% of solid tumor patients treated with

talazoparib in clinical studies. Potential contributing factors for the development of MDS/AML include previous platinum-containing chemotherapy, other DNA damaging agents or radiotherapy. Complete blood counts should be obtained at baseline and monitored monthly for signs of hematologic toxicity during treatment. If MDS/AML is confirmed, talazoparib should be discontinued.

Venous thromboembolic events
In patients with mCRPC a higher incidence of venous thromboembolic events was observed with TALZENNA in combination with enzalutamide compared with enzalutamide alone. Patients should be monitored for clinical signs and symptoms of deep venous thrombosis and pulmonary embolism and treated as medically appropriate (see Section 4.8).

Embryo-fetal toxicity
Studies in animals have shown embryo-fetal toxicity and talazoparib was clastogenic in *in vitro* and in *in vivo* assays (see Section 5.3). Talazoparib should not be given to pregnant patients or those who plan to become pregnant during treatment. Women of childbearing potential should be advised to avoid becoming pregnant while receiving TALZENNA. TALZENNA may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus (see Section 4.6).

A highly effective method of contraception is required for female patients during treatment with TALZENNA, and for at least 7 months after completing therapy. Since the use of hormonal contraception is not recommended in patients with breast cancer, two non-hormonal and complementary contraception methods should be used. Advise male patients with female partners of reproductive potential and pregnant partners to use effective contraception (even after vasectomy), during treatment with TALZENNA and for at least 4 months after the final dose.

4.5. Interaction with other medicinal products and other forms of interaction

Talazoparib is a substrate for drug transporters P-gp and BCRP and mainly eliminated by renal clearance as unchanged compound.

Agents that may affect talazoparib plasma concentrations

Effect of enzalutamide
Coadministration with enzalutamide increases talazoparib exposure approximately 2-fold. Administration of talazoparib 0.5 mg daily in combination with enzalutamide achieves approximately the same steady-state trough (C_{trough}) concentration reported for talazoparib 1 mg daily (see Section 5.2). When TALZENNA is coadministered with enzalutamide, the TALZENNA starting dose is 0.5 mg (see Section 4.2). The interaction effect of doses other than 160 mg enzalutamide on talazoparib has not been quantified.

Effect of P-gp inhibitors
Data from a drug-drug interaction study in patients with advanced solid tumors indicated that coadministration of multiple daily doses of a P-gp inhibitor, itraconazole 100 mg twice daily with a single 0.5 mg talazoparib dose increased talazoparib total exposure (AUC_{inf}) and peak concentration (C_{max}) by approximately 56% and 40%, respectively, relative to a single 0.5 mg talazoparib dose administered alone. Population pharmacokinetic (PK) analysis has shown that concomitant use of strong P-gp inhibitors with TALZENNA increased talazoparib

exposure by 44.7%, relative to TALZENNA given alone. If patients must be coadministered a strong P-gp inhibitor, those that result in ≥2-fold increase in the exposure of an *in vivo* probe P-gp substrate, (including but not limited to amiodarone, carvedilol, clarithromycin, cobicistat, darunavir, dronedarone, erythromycin, indinavir, itraconazole, ketoconazole, lapatinib, lopinavir, propafenone, quinidine, ranolazine, ritonavir, saquinavir, telaprevir, tipranavir, valspodar, and verapamil), the TALZENNA dose should be reduced to the next lower dose (see Section 4.2).

Population PK analysis has shown that coadministration with relatively weak P-gp inhibitors (including azithromycin, atorvastatin, diltiazem, felodipine, fluvoxamine, and quercetin) in clinical studies had no significant effect on talazoparib exposure.

The effect of coadministration of P-gp inhibitors on talazoparib exposure when talazoparib is given in combination with enzalutamide has not been studied. If coadministration of P-gp inhibitors cannot be avoided, when TALZENNA is given with enzalutamide, the patient should be monitored for potential increased adverse reactions.

Effect of P-gp inducers
Data from a drug-drug interaction study in patients with advanced solid tumors indicated that coadministration of a P-gp inducer (rifampin 600 mg once daily) with a single 1 mg talazoparib dose increased talazoparib C_{max} by 37% with no effect on talazoparib exposure. This is probably the net effect of both P-gp induction and inhibition by rifampin under the tested conditions in the drug-drug interaction study. No talazoparib dose adjustments are required when coadministered with rifampin. However, the effect of other P-gp inducers on talazoparib exposure has not been studied. Other P-gp inducers (including but not limited to carbamazepine, phenytoin, and St. John's wort) may decrease talazoparib exposure.

Effect of BCRP inhibitors
The effect of BCRP inhibitors on PK of talazoparib has not been studied. Concomitant use of strong BCRP inhibitors (including but not limited to curcumin, cyclosporine, and elacridar [GF120918]) should be avoided (see Section 4.2).

Effect of acid-reducing agents
Population PK analysis indicates that coadministration of acid-reducing agents including proton pump inhibitors (PPI), histamine receptor 2 antagonists (H_2RA), or other acid-reducing agents had no significant impact on the absorption of talazoparib.

4.6. Fertility, pregnancy and lactation

Women of childbearing potential/contraception in males and females
Women of childbearing potential should not become pregnant while receiving TALZENNA and should not be pregnant at the beginning of treatment. A pregnancy test should be performed on all women of childbearing potential prior to treatment (see Section 4.4).

A highly effective method of contraception is required for female patients during treatment with TALZENNA, and for at least 7 months after completing therapy. Since the use of hormonal contraception is not recommended in patients with breast cancer, two non-hormonal and complementary contraception methods should be used. Advise male patients with female partners of reproductive potential and pregnant partners to use effective

contraception (even after vasectomy) during treatment with TALZENNA and for at least 4 months after the final dose (see Section 4.4).

Pregnancy
There are no data from the use of TALZENNA in pregnant women. Studies in animals have shown embryo-fetal toxicity (see Section 5.3). TALZENNA may cause fetal harm when administered to a pregnant woman. TALZENNA is not recommended during pregnancy or for women of childbearing potential not using contraception (see Section 4.4).

Breastfeeding
It is unknown whether TALZENNA is excreted in human breast milk. A risk to newborns/infants cannot be excluded and therefore breastfeeding is not recommended during treatment with TALZENNA and for at least 1 month after the final dose.

Fertility
There is no information on fertility in patients. Based on non-clinical findings in testes and ovary, male and female fertility may be compromised by treatment with TALZENNA (see Section 5.3).

4.7. Effects on ability to drive and use machines

No studies have been conducted on the effects of talazoparib on the ability to drive or operate machinery. However, patients experiencing fatigue/asthenia or dizziness while taking talazoparib should exercise caution when driving or operating machinery.

4.8. Undesirable effects

The overall safety profile of TALZENNA is based on pooled data from 1,088 patients, including 690 patients who received talazoparib monotherapy at 1 mg daily in clinical studies for solid tumors and 398 patients with mCRPC who received talazoparib 0.5 mg in combination with enzalutamide 160 mg in the TALAPRO-2 study.

The most common (≥20%) adverse reactions in patients receiving talazoparib in these clinical studies were anemia (55.6%), fatigue (52.5%), nausea (35.8%), neutropenia (30.3%), thrombocytopenia (25.2%), and decreased appetite (21.1%). The most common (≥10%) Grade ≥3 adverse reactions of talazoparib were anemia (39.2%), neutropenia (16.5%), and thrombocytopenia (11.1%).

Dose modifications (dose reductions or dose interruptions) due to any adverse reaction occurred in 58.7% of patients receiving TALZENNA 1 mg monotherapy. The most common adverse reactions leading to dose modifications were anemia (33.5%), neutropenia (11.7%), and thrombocytopenia (9.9%).

Permanent discontinuation due to an adverse reaction occurred in 2.9% of patients receiving TALZENNA; the most common was anemia (0.6%). The median duration of exposure was 5.6 months (range 0.00 to 70.2).

Dosing interruptions due to adverse reactions occurred in 62.1% of patients with mCRPC receiving TALZENNA in combination with enzalutamide; the most common was anemia (44%). Dose reductions due to adverse reactions occurred in 52.8% of patients

receiving TALZENNA; the most common was anemia (43.2%). Permanent discontinuation of TALZENNA due to adverse reactions occurred in 18.8% of patients; the most common was anemia (8.3%). The median duration of talazoparib exposure was 86 weeks (range 0.29 to 186.14).

Table 4 summarizes adverse reactions based on pooled dataset listed by system organ class, and frequency category. Frequency categories defined as: very common (≥1/10), common (≥1/100 to <1/10), and uncommon (≥1/1,000 to <1/100). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 4. Adverse reactions based on pooled dataset from 8 studies (N=1,088)

System organ class **Frequency** **Preferred term**	**All grades*** **N (%)**	**Grade 3 N (%)**	**Grade 4 N (%)**
Neoplasms benign, malignant, and unspecified (including cysts and polyps)			
Uncommon			
Myelodysplastic syndrome/Acute myeloid leukemia	2 (0.2)	1 (<0.1)	1 (<0.1)
Blood and lymphatic system disorders			
Very common			
Thrombocytopenia[a]	274 (25.2)	88 (8.1)	33 (3.0)
Anemia[b]	605 (55.6)	411 (37.8)	16 (1.5)
Neutropenia[c]	330 (30.3)	163 (15.0)	17 (1.6)
Leukopenia[d]	195 (17.9)	52 (4.8)	2 (0.2)
Common			
Lymphopenia[e]	88 (8.1)	37 (3.4)	4 (0.4)
Metabolism and nutrition disorders			
Very common			
Decreased appetite	230 (21.1)	11 (1.0)	0 (0.0)
Nervous system disorders			
Very common			
Dizziness	157 (14.4)	4 (0.4)	1 (<0.1)
Headache	207 (19.0)	8 (0.7)	N/A
Common			
Dysgeusia	68 (6.3)	0 (0.0)	0 (0.0)
Vascular disorders			
Common			
Venous thromboembolism[f]	36 (3.3%)	23 (2.1%)	2 (0.2%)
Gastrointestinal disorders			
Very common			
Vomiting	167 (15.3)	9 (0.8)	0 (0.0)
Diarrhea	205 (18.8)	4 (0.4)	0 (0.0)
Nausea	389 (35.8)	10 (0.9)	N/A
Abdominal pain[g]	162 (14.9)	12 (1.1)	N/A
Common			
Stomatitis	54 (5.0)	0 (0.0)	0 (0.0)
Dyspepsia	69 (6.3)	0 (0.0)	N/A
Skin and subcutaneous tissue disorders			
Very common			

System organ class Frequency Preferred term	All grades* N (%)	Grade 3 N (%)	Grade 4 N (%)
Alopecia	189 (17.4)	N/A	N/A
General disorders and administration site conditions *Very common*			
Fatigue[h]	571 (52.5)	58 (5.3)	N/A

Abbreviations: N=number of patients; N/A=not applicable.

* There were no Grade 5 adverse drug reactions.

a. Includes preferred terms of thrombocytopenia and platelet count decreased.

b. Includes preferred terms of anemia, hematocrit decreased, hemoglobin decreased, and red blood cell count decreased.

c. Includes preferred terms of neutropenia and neutrophil count decreased.

d. Includes preferred terms of leukopenia and white blood cell count decreased.

e. Includes preferred terms of lymphocyte count decreased and lymphopenia.

f. Includes preferred terms of pulmonary embolism, deep vein thrombosis, embolism venous and venous thrombosis.

g. Includes preferred terms of abdominal pain, abdominal pain upper, abdominal discomfort and abdominal pain lower.

h. Includes preferred terms of fatigue and asthenia.

Description of selected adverse reactions

Myelosuppression

Myelosuppression-related adverse reactions of anemia, neutropenia, and thrombocytopenia were very commonly reported in patients treated with talazoparib. Grade 3 and Grade 4 myelosuppression-related events were reported for anemia in 37.8% and 1.5% of patients, neutropenia in 15.0% and 1.6%, and thrombocytopenia in 8.1% and 3.0%. No deaths were reported due to myelosuppression-related adverse reactions.

In monotherapy studies (1 mg/day population), the most frequent myelosuppression-related adverse events associated with dose modifications were anemia (33.5%), neutropenia (11.7%) and thrombocytopenia (9.9%) reported for up to approximately 30% of patients in the talazoparib 1 mg/day population and the one associated with permanent study drug discontinuation was anemia reported in 0.6% of patients.

In patients with mCRPC treated with talazoparib in combination with enzalutamide, anemia led to talazoparib dose interruption in 44.0% of patients, decreased neutrophil count in 13.6%, and decreased platelet count in 7.8%. Overall, 42.5% of patients required blood transfusions. The most common blood transfusion was of packed red blood cells 39.2%. Discontinuation due to anemia, neutropenia and thrombocytopenia occurred, respectively, in 8.3%, 3.3% and 0.5% of patients.

4.9. Overdose

There is no specific treatment in the event of talazoparib overdose, and symptoms of overdose are not established. In the event of overdose, treatment with talazoparib should be stopped, and physicians should consider gastric decontamination, follow general supportive measures and treat symptomatically.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: antineoplastic agents, other antineoplastic agents, ATC code: L01XK04.

Mechanism of action and pharmacodynamics effects
TALZENNA is a potent inhibitor of PARP enzymes, PARP1 (IC_{50}=0.7 nM), and PARP2 (IC_{50}=0.3 nM). PARP enzymes are involved in cellular DNA damage response signaling pathways such as DNA repair, gene transcription, cell cycle regulation, and cell death. PARP inhibitors (PARPi) exert cytotoxic effects on cancer cells by 2 mechanisms, inhibition of PARP catalytic activity and by PARP trapping, whereby PARP protein bound to a PARPi does not readily dissociate from a DNA lesion, thus preventing DNA repair, replication, and transcription and ultimately leading to apoptosis and/or cell death. Treatment of cancer cell lines that are harboring defects in DNA repair genes with talazoparib single agent leads to increased γH2AX, which is a marker of double stranded DNA breaks, resulting in decreased cell proliferation and increased apoptosis. The potent cytotoxicity observed with talazoparib against multiple tumor cell lines harboring mutations in the DNA damage response (DDR) pathways, can be attributed to its inhibition of PARP catalytic activity and robust PARP trapping. Talazoparib anti-tumor activity was also observed in a patient-derived xenograft (PDX) BRCA-mutant breast cancer model that was previously treated with a platinum-based regimen, as well as in an androgen receptor (AR) positive prostate cancer xenograft model. In these PDX models, talazoparib decreased tumor growth and increased γH2AX level and apoptosis in the tumors.

The anti-tumor effects of combined inhibition of PARP and AR activity is based on the following mechanisms: AR signaling inhibition suppresses the expression of homologous recombination repair (HRR) genes including BRCA1, resulting in sensitivity to PARP inhibition. PARP1 activity has been shown to be required for maximal AR function and thus inhibiting PARP may reduce AR signaling and increase sensitivity to AR signaling inhibitors. Clinical resistance to AR blockade is sometimes associated with co-deletion of RB1 and BRCA2, which is in turn associated with sensitivity to PARP inhibition.

Detection of BRCA mutation in breast cancer
Patients are eligible for TALZENNA treatment if they have a confirmed deleterious or suspected deleterious germline BRCA mutation (i.e., a mutation that disrupts normal gene function; detected using an appropriately validated test).

Clinical efficacy and safety

Treatment of gBRCAm HER2-negative locally advanced or metastatic breast cancer

Randomized phase 3 study EMBRACA
EMBRACA was an open-label, randomized, parallel, 2-arm multicenter study of TALZENNA versus chemotherapy (capecitabine, eribulin, gemcitabine, vinorelbine) in patients with germline BRCA-mutated HER2-negative locally advanced or metastatic breast cancer who received no more than 3 prior cytotoxic chemotherapy regimens for their metastatic or locally advanced disease. Patients were required to have received treatment with an anthracycline and/or a taxane (unless contraindicated) in the neoadjuvant, adjuvant and/or

metastatic setting. Patients with prior platinum therapy for advanced disease were required to have no evidence of disease progression during platinum therapy. No prior treatment with a PARPi was permitted.

A total of 431 patients were randomized 2:1 to receive TALZENNA 1 mg capsules once daily or chemotherapy at standard doses until progression or unacceptable toxicity. Of the 431 patients randomized onto EMBRACA, 287 were randomized to the TALZENNA arm and 144 to the chemotherapy arm. Randomization was stratified by prior use of chemotherapy for metastatic disease (0 versus 1, 2, or 3), by triple-negative disease status (triple-negative breast cancer [TNBC] versus non-TNBC), and history of central nervous system metastasis (yes versus no). The majority of patients 408/431 (95%) were selected using the BRAC Analysis test and BRCA mutation status (breast cancer susceptibility gene 1 [BRCA1] positive or breast cancer susceptibility gene 2 [BRCA2] positive) was similar across both treatment arms.

Patient demographic and baseline characteristics were generally similar between the study treatment arms. The median age of patients treated with TALZENNA was 45 years (range 27 to 84) and 50 years (range 24 to 88) among patients treated with chemotherapy. Of note, 63% versus 47% of patients were <50 years of age in the talazoparib and chemotherapy arms, respectively, 27% versus 47% were 50 to <65 years of age, and 9% versus 7% were ≥65 years of age. Among all randomized patients, 1% versus 2% were males, 66.9% versus 75.0% were White; 10.8% versus 11.1% were Asian, and 4.2% versus 0.7% were Black or African American in the talazoparib and chemotherapy arms, respectively. Almost all patients (97.7%) in both arms had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Approximately 55.9% of patients had hormone receptor-positive (either estrogen receptor [ER]-positive or progesterone receptor [PR]-positive) disease; 44.1% of patients had triple-negative disease and the proportions were balanced across treatment arms. The median time from initial diagnosis of breast cancer to diagnosis of advanced breast cancer was 1.9 years (range 0 to 22) on the talazoparib arm and 2.7 years (range 0 to 24) on the chemotherapy arm. The reported disease-free interval (DFI) was <12 months in 37.6% of patients on the talazoparib arm and in 29.2% of patients on the chemotherapy arms. Among all patients enrolled, the median number of prior cytotoxic regimens for advanced breast cancer was 1 where 38.3% of patients received no prior regimens for advanced or metastatic disease, 37.4% received 1, 19.7% received 2, and 4.6% received ≥3 prior regimens, respectively. Sixteen percent of patients in the talazoparib arm and 20.8% of patients in the chemotherapy arm had received prior platinum treatment. 54.7% of patients had hormone receptor-positive disease in the talazoparib arm, of which 90.4% took a prior hormonal therapy, while 9.6% did not take any prior endocrine therapy. In the chemotherapy arm, 58.3% of patients had hormone receptor-positive disease, of which 83.3% took a prior hormonal therapy, while 16.7% did not take any prior endocrine therapy.

The primary efficacy endpoint was progression-free survival (PFS) evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, as assessed by blinded independent central review (BICR). The secondary objectives were objective response rate (ORR), overall survival (OS), safety, and PK. Exploratory objectives included duration of response (DOR), Clinical Benefit Rate at 24 weeks (CBR24), quality of life (QoL) assessed using the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire – Core 30 (QLQ-C30)/EORTC Quality of Life Questionnaire – Breast Cancer Module (QLQ-BR23) and biomarker research.

The study met its primary objective of demonstrating a statistically significant improvement in PFS for TALZENNA compared with chemotherapy (hazard ratio [HR] 0.54; 95% confidence interval [CI]: 0.41, 0.71; p-value <0.0001). A sensitivity analysis of investigator-assessed PFS was consistent with the BICR-assessed PFS results. Efficacy data for EMBRACA are summarized in Table 5 and the Kaplan-Meier curves for PFS and OS are shown in Figures 1 and 3. Consistent results were observed across pre-specified patient subgroups (Figure 2).

Table 5. Summary of efficacy results – EMBRACA study*

	Talazoparib	**Chemotherapy**
PFS by BICR	N=287	N=144
Events, number (%)	186 (65%)	83 (58%)
Median (95% CI), months	8.6 (7.2, 9.3)	5.6 (4.2, 6.7)
Hazard ratio (95% CI)	0.54 (0.41, 0.71)	
2-sided p-value[a]	p<0.0001	
OS (final analysis)[b]	N=287	N=144
Events, number (%)	216 (75.3%)	108 (75.0%)
Median (95% CI), months	19.3 (16.6, 22.5)	19.5 (17.4, 22.4)
Hazard ratio** (95% CI)	0.85 (0.67, 1.07)[b]	
2-sided p-value[a]	p=0.1693	
24-Month Survival Probability, % (95% CI)	42 (36, 47)	38 (30, 47)
36-Month Survival Probability, % (95% CI)	27 (22, 33)	21 (14, 29)
Objective Response by Investigator[c,d]	N=219	N=114
ORR, % (95% CI)	62.6 (55.8, 69.0)	27.2 (19.3, 36.3)
Odds ratio (95% CI)	4.99 (2.9, 8.8)	
2-sided p-value[e]	p<0.0001	
Duration of Response by Investigator[c]	N=137	N=31
Median (IQR), months	5.4 (2.8, 11.2)	3.1 (2.4, 6.7)

Abbreviations: BICR=blinded independent central review; CI=confidence interval; CMH=Cochran-Mantel-Haenszel; CR=complete response; IQR=interquartile range; ITT=intent-to-treat; ORR=objective response rate; OS=overall survival; PARP=poly (adenosine diphosphate [ADP] ribose) polymerase; PFS=progression-free survival; PR=partial response; RECIST 1.1=Response Evaluation Criteria in Solid Tumors version 1.1.

* PFS, ORR, and Duration of Response are based on the data cutoff date of 15 September 2017. OS is based on the data cutoff date 30 September 2019, and is based on a median follow up of 44.9 months (95% CI: 37.9, 47.0) in the talazoparib arm and 36.8 months (95% CI: 34.3, 43.0) in the chemotherapy arm.

** Hazard ratio was based on stratified Cox regression model with treatment as the only covariate (stratification factors: number of prior cytotoxic chemotherapy regimens, triple-negative status, history of central nervous system metastasis) and was relative to overall chemotherapy with <1 favoring talazoparib.

a. Stratified Log-rank test.

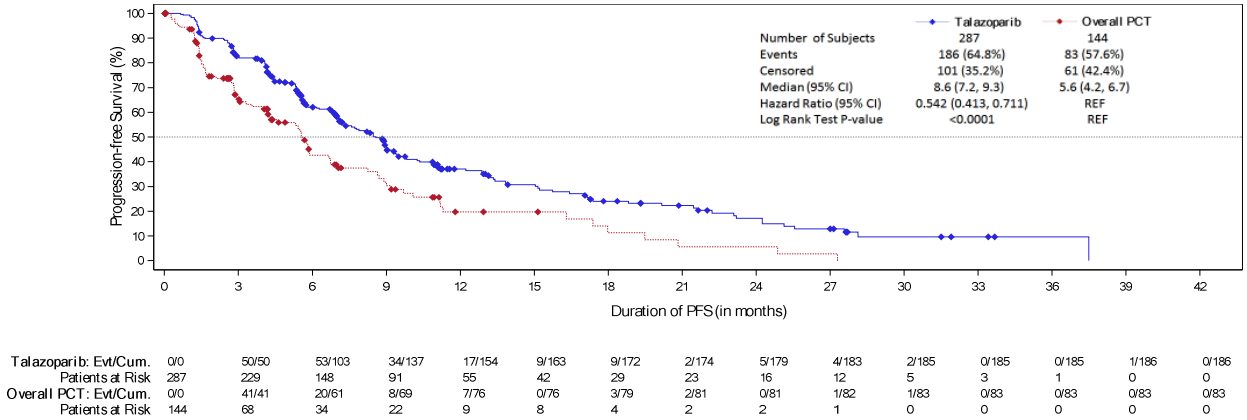
b. At the time of the final OS analysis, 46.3% versus 41.7% of patients randomized in the talazoparib and chemotherapy arms, respectively, received subsequently a platinum therapy, and 4.5% versus 32.6% received subsequently a PARP inhibitor treatment.

c. Conducted in ITT with measurable disease population who had an objective response. The complete response rate was 5.5% for talazoparib compared to 0% for the chemotherapy arm.

d. Per RECIST 1.1, confirmation of CR/PR was not required.

e. Stratified CMH test.

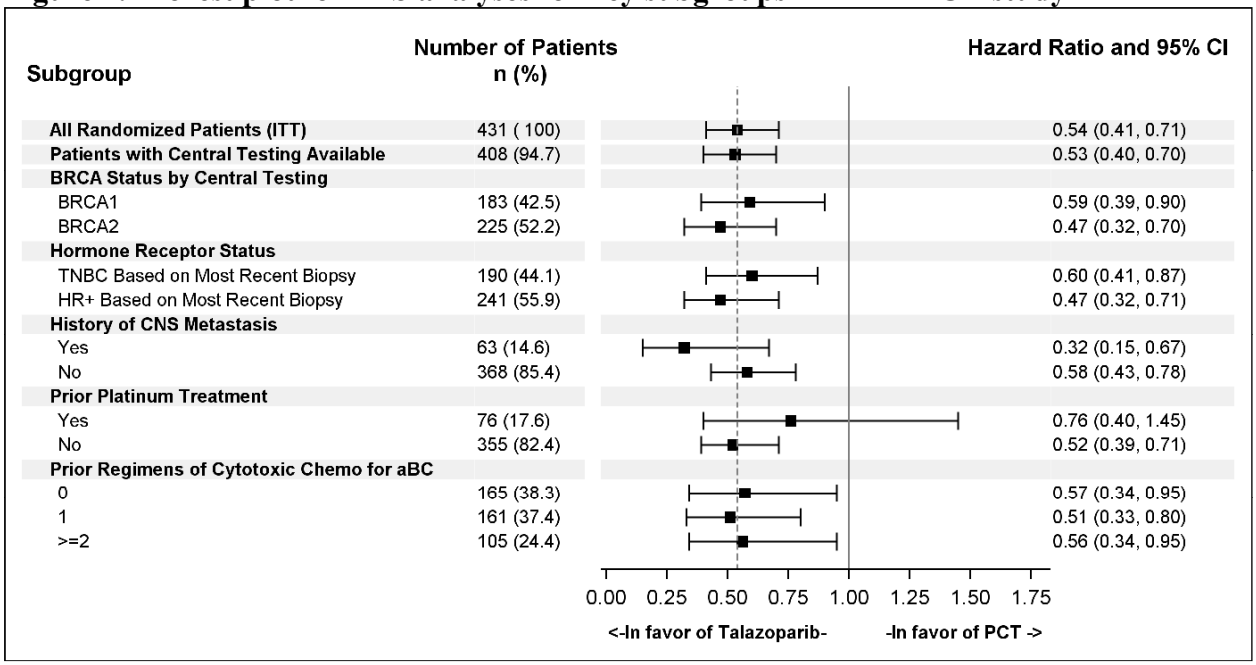
Figure 1. Kaplan-Meier curves of PFS – EMBRACA study



Talazoparib: Evt/Cum.	0/0	50/50	53/103	34/137	17/154	9/163	9/172	2/174	5/179	4/183	2/185	0/185	0/185	1/186	0/186
Patients at Risk	287	229	148	91	55	42	29	23	16	12	5	3	1	0	0
Overall PCT: Evt/Cum.	0/0	41/41	20/61	8/69	7/76	0/76	3/79	2/81	0/81	1/82	1/83	0/83	0/83	0/83	0/83
Patients at Risk	144	68	34	22	9	8	4	2	2	1	0	0	0	0	0

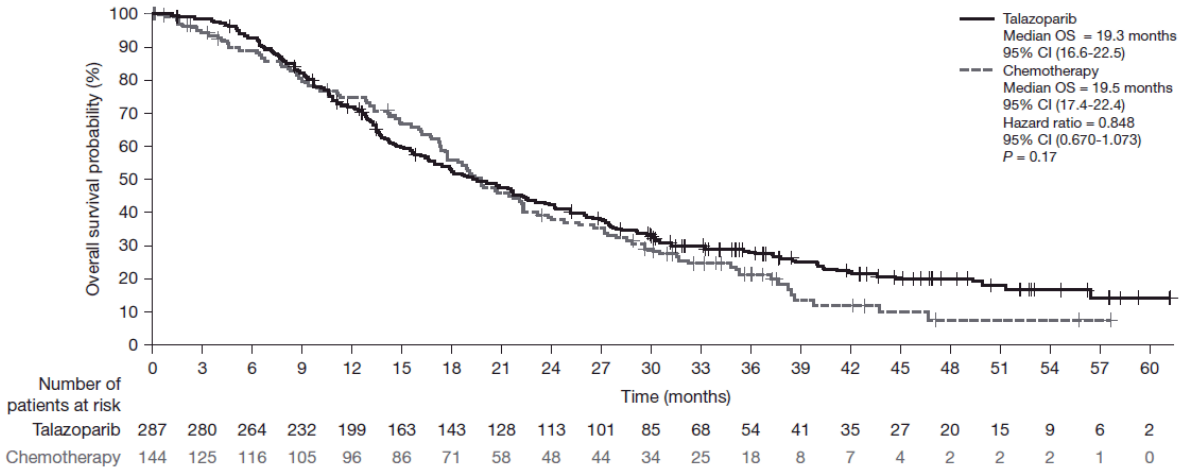
Abbreviations: CI=confidence interval; Cum=cumulative; Evt=event; PFS=progression-free survival; PCT=physician's choice treatment (chemotherapy); REF=reference treatment group.
Primary analysis p-value was based on a stratified log-rank test.

Figure 2. Forest plot for PFS analyses for key subgroups – EMBRACA study



Abbreviations: aBC=advanced breast cancer; BRCA=breast cancer susceptibility gene; CI=confidence interval; CNS=central nervous system; HR+=hormone receptor-positive; ITT=intent-to-treat; PCT=physician's choice treatment (chemotherapy); PFS=progression-free survival; TLZ=talazoparib; TNBC=triple-negative breast cancer.

Figure 3. Kaplan-Meier curves of OS – EMBRACA study



Abbreviations: CI=confidence interval; PCT=physician's choice treatment (chemotherapy); OS=overall survival.
Primary analysis' p-value was based on a stratified log-rank test.

Patient-reported symptoms were assessed using the EORTC QLQ-C30 and its EORTC QLQ-BR23. A total of 262 patients in the talazoparib arm and 114 patients in the chemotherapy arm completed the questionnaire at baseline and at least 1 postbaseline visit.

A significantly greater overall improvement from baseline in global health status (GHS)/QoL was observed in the talazoparib arm (3.0 [95% CI: 1.2, 4.8]) compared to the chemotherapy arm (-5.4 [95% CI: -8.8, -2.0]) (p<0.0001). A significantly greater delay in time to clinically meaningful (≥10 point decrease from baseline) definitive deterioration in GHS/QoL was observed in the talazoparib arm compared with chemotherapy [(HR: 0.38 [95% CI: 0.26, 0.55]; p<0.0001), median 24.3 months versus 6.3 months].

A significantly greater overall improvement from baseline in breast symptoms was observed in the talazoparib arm (-5.1 [95% CI: -6.7, -3.5]) compared to the chemotherapy arm (-0.1 [95% CI: -2.9, 2.6]) (p=0.002). A significantly greater delay in time to clinically meaningful (≥10 point increase from baseline) definitive deterioration in breast symptoms was observed in the talazoparib arm compared with chemotherapy (HR of 0.39 [95% CI: 0.20, 0.78]; p=0.005, median times not reached [NR]).

A significantly greater overall improvement from baseline was observed in the talazoparib arm compared to the chemotherapy arm in role functioning [12.4, 95% CI: (7.1, 17.7) (p<0.0001)] and the following symptoms: fatigue [-12.3, 95% CI: (-17.2, -7.5) (p<0.0001)], pain [-13.3, 95% CI: (-18.5, -8.1) (p<0.0001)] and appetite loss [-11.7, 95% CI: (-17.6, -5.7) (p=0.0001)].

A significantly greater delay in time to clinically meaningful deterioration in the following symptoms was observed in the talazoparib arm compared to the chemotherapy arm for fatigue, [(HR: 0.40 [95% CI: 0.28, 0.56]; p<0.0001), median 17.1 months versus 7.1 months], pain, [(HR: 0.34 [95% CI: 0.23, 0.50]; p<0.0001), median 22.7 months versus 7.5 months], appetite loss, [(HR: 0.32 [95% CI: 0.21, 0.49]; p<0.0001), median NR versus 9.0 months], systemic therapy side effects, [(HR: 0.33 [95% CI: 0.22, 0.51]; p<0.0001), median 24.6 months versus 7.9 months], arm symptoms, [(HR: 0.46 [95% CI: 0.29, 0.73]; p=0.0008), median NR versus 13.2 months]. A significantly greater delay in time to clinically

meaningful deterioration was observed in the talazoparib arm compared to the chemotherapy arm for role functioning, [(HR: 0.36 [95% CI: 0.25, 0.52]; p<0.0001), median 20.5 months versus 5.6 months].

mCRPC

TALAPRO-2 study
TALAPRO-2 was a randomized, double-blind, placebo-controlled study in which patients (N=805) with mCRPC were randomized 1:1 to receive TALZENNA 0.5 mg once daily in combination with enzalutamide 160 mg once daily, versus a comparator arm of placebo in combination with enzalutamide 160 mg once daily. All patients received a GnRH analog or had prior bilateral orchiectomy and needed to have progressed on prior androgen deprivation therapy. Prior treatment with abiraterone or taxane-based chemotherapy for metastatic castration-sensitive prostate cancer (mCSPC) was permitted.

Randomization was stratified by: previous treatment with abiraterone or taxane-based chemotherapy versus no such prior treatment; and by tumor HRR gene mutation status which was prospectively tested by next generation sequencing of tumor tissue using FoundationOne® CDx or circulating tumor DNA (ctDNA) using FoundationOne Liquid® CDx; patients with tumor HRR gene mutations (ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, or RAD51C) versus patients with tumors without HRR gene mutations or with unknown status.

The median age was 71 years (range 36 to 91) in both arms; 62% were White, 31% were Asian, and 2% were Black. Most participants (66%) in both arms had an ECOG performance status of 0. In patients treated with TALZENNA, the proportion of patients with RECIST 1.1 measurable disease at baseline per BICR was 30%. Twenty-eight percent (28%) of patients had received prior abiraterone or taxane-based chemotherapy. Twenty percent (20%) had tumors that had HRR gene mutations and 80% had tumors that did not have HRR gene mutations or had an unknown status.

The major efficacy outcome was radiographic progression-free survival (rPFS) evaluated according to RECIST version 1.1 and Prostate Cancer Clinical Trials Working Group Criteria 3 (PCWG3) (bone) criteria, as assessed by BICR. Key efficacy outcomes included OS and ORR assessed by BICR. Additional secondary efficacy endpoints included prostate-specific antigen (PSA) response (proportion of patients with PSA response ≥50%), time to PSA progression, time to initiation of cytotoxic chemotherapy, time to initiation of antineoplastic therapy, and PFS2 (time from randomization to disease progression on the first subsequent antineoplastic therapy for prostate cancer, or death).

A statistically significant improvement in BICR-assessed rPFS and OS was demonstrated for TALZENNA in combination with enzalutamide compared to placebo in combination with enzalutamide. A sensitivity analysis of investigator-assessed rPFS was consistent with the BICR-assessed rPFS results. Consistent rPFS results were observed across patient subgroups defined by study stratification factors (patients who received or did not receive prior abiraterone or prior taxane-based chemotherapy; and patients with tumors with HRR gene mutations or without HRR gene mutations or unknown status).

Efficacy results of TALAPRO-2 are provided in Tables 6 and 7, and Figures 4, 5, 6, and 7.

Table 6. Summary of efficacy results – TALAPRO-2 (mCRPC)*

	Talazoparib + enzalutamide N=402	Placebo + enzalutamide N=403
rPFS by BICR		
Events, number (%)	151 (37.6)	191 (47.4)
Median months (95% CI)	NR (27.5, NR)	21.9 (16.6, 25.1)
Hazard ratio (95% CI)[a] p-value[b]	0.627 (0.506, 0.777) p<0.0001	
Objective response (OR) by BICR[c]		
Patients with measurable disease N (%)	120 (29.8)	132 (32.7)
ORR, % (95% CI)[d]	61.7 (52.4, 70.4)	43.9 (35.3, 52.8)
CR, %	45 (37.5)	24 (18.2)
Duration of response (DOR)		
Patients with confirmed CR or PR, N	74	58
Median[e] DOR months (95% CI)	20.4 (16.1, NR)	19.8 (12.9, NR)
OS		
Events, number (%)	211 (52.5)	243 (60.3)
Median months (95% CI)	45.8 (39.4, 50.8)	37 (34.1, 40.4)
Hazard ratio (95% CI)[a] p-value[b]	0.796 (0.661, 0.958) p=0.0155	

Abbreviations: BICR=blinded independent central review; CI=confidence interval; CR=complete response; mCRPC=metastatic castration-resistant prostate cancer; CSPC=castration-sensitive prostate cancer; DOR=duration of response; HRR=homologous recombination repair; ITT=intent-to-treat; N=number of patients; NHT=novel hormone therapy; NR=not reached; OR=objective response; ORR=objective response rate; OS=overall survival; PR=partial response; rPFS=radiographic progression-free survival.

* rPFS, OR and DOR are based on the data cutoff date of 16 August 2022 and a median follow-up for rPFS of 24.9 months (95% CI: 24.7, 25.3) in the talazoparib plus enzalutamide arm and 24.6 months (95% CI: 22.1, 24.9) in the placebo plus enzalutamide arm. OS is based on the data cutoff date of 3 September 2024 and a median follow-up for OS of 52.5 months (95% CI: 49.9, 53.4) in the talazoparib plus enzalutamide arm and 53.0 months (95% CI: 50.6, 54.0) in the placebo plus enzalutamide arm.

a. Hazard ratio based on Cox proportional hazards model stratified by previous treatment with NHT (abiraterone) or taxane-based chemotherapy for CSPC (yes vs. no), and by HRR mutational status (deficient vs. non-deficient/unknown), with <1 favoring talazoparib.

b. P-values (2-sided) from the log-rank test stratified by previous treatment with NHT (abiraterone) or taxane-based chemotherapy for CSPC and by HRR mutational status.

c. Conducted in ITT population with measurable disease at baseline.

d. Response rate based on confirmed responses.

e. Median estimated from Kaplan-Meier probabilities.

At the time of the final OS analysis, median rPFS was 33.1 months (95% CI: 27.4, 39.0) for patients who received TALZENNA in combination with enzalutamide and 19.5 months (95% CI: 16.6, 24.7) for patients who received placebo in combination with enzalutamide (hazard ratio=0.667, 95% CI: 0.551, 0.807).

Table 7. Summary of efficacy results for subgroup analysis – TALAPRO-2 (mCRPC)*

	Talazoparib + enzalutamide	Placebo + enzalutamide
HRRm Subgroup Analyses[a]		
HRRm	**N=85**	**N=82**
rPFS by BICR		
Events, number (%)	37 (43.5)	49 (59.7)
Median months (95% CI)	27.9 (16.8, NR)	13.8 (10.9, 19.5)
Hazard ratio (95% CI)[b]	0.424 (0.275, 0.653)	
OS		
Events, number (%)	41 (48.2)	55 (67.1)
Median months (95% CI)	45.8 (36.4, NR)	30.1 (25.6, 38.2)
Hazard ratio (95% CI)[b]	0.524 (0.348, 0.787)	
Non-HRRm	**N=207**	**N=219**
rPFS by BICR		
Events, number (%)	73 (35.3)	95 (43.4)
Median months (95% CI)	NR (25.8, NR)	22.4 (16.6, NR)
Hazard ratio (95% CI)[b]	0.695 (0.511, 0.944)	
OS		
Events, number (%)	112 (54.1)	133 (60.7)
Median months (95% CI)	45 (34.7, 53.3)	37.4 (31.8, 41.4)
Hazard ratio (95% CI)[b]	0.817 (0.635, 1.053)	
BRCAm Subgroup Analyses[a]		
BRCAm	**N=27**	**N=32**
rPFS by BICR		
Events, number (%)	8 (29.6)	22 (68.7)
Median months (95% CI)	NR (16.8, NR)	11 (7.4, 24.6)
Hazard ratio (95% CI)[b]	0.232 (0.101, 0.529)	
OS		
Events, number (%)	14 (51.9)	23 (71.9)
Median months (95% CI)	36.9 (24.9, NR)	26.1 (15.2, 35.4)
Hazard ratio (95% CI)[b]	0.556 (0.285, 1.085)	

Abbreviations: BICR=blinded independent central review; BRCAm=breast cancer gene mutated; CI=confidence interval; CSPC=castration-sensitive prostate cancer; ctDNA=circulating tumor DNA; HRRm=homologous recombination repair gene mutated; mCRPC=metastatic castration-resistant prostate cancer; N=number of patients; NHT=novel hormone therapy; NR=not reached; OS=overall survival; rPFS=radiographic progression-free survival.

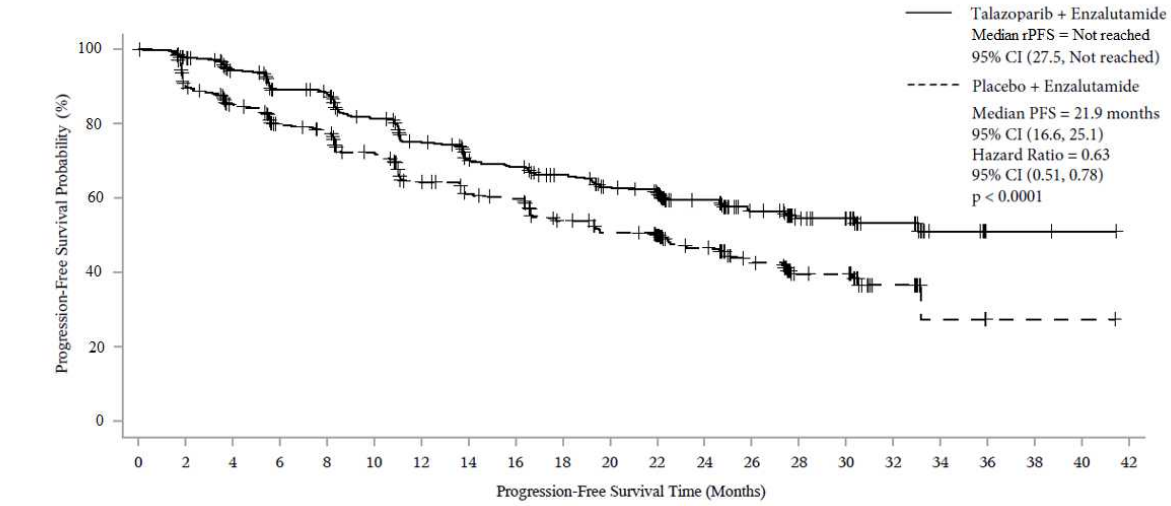
* Based on the data cutoff date of 16 August 2022 and a median follow-up for rPFS of 24.9 months (95% CI: 24.7, 25.3) in the talazoparib plus enzalutamide arm, and 24.6 months (95% CI: 22.1, 24.9) in the placebo plus enzalutamide arm. OS is based on the data cutoff date of 3 September 2024 and a median follow-up for OS of 52.5 months (95% CI: 49.9, 53.4) in the talazoparib plus enzalutamide arm and 53.0 months (95% CI: 50.6, 54.0) in the placebo plus enzalutamide arm.

a. Derived based on prospective tumor tissue-based results (results known prior to randomization) and prospective blood-based ctDNA results (results known prior to randomisation).

b Hazard ratio based on Cox proportional hazard model stratified by previous treatment with NHT (abiraterone) or taxane-based chemotherapy for CSPC (yes versus no) with < 1 favoring talazoparib.

At the time of the final OS analysis, in the HRRm subgroup median rPFS was 27.7 months (95% CI: 19.3, 38.4) for patients who received Talzenna in combination with enzalutamide and 13.8 months (95% CI: 10.8, 19.3) for patients who received placebo in combination with enzalutamide (hazard ratio=0.454, 95% CI: 0.305, 0.674); in the non-HRRm subgroup median rPFS was 33.2 months (95% CI: 25.9, 44.2) for patients who received Talzenna in combination with enzalutamide and 22.1 months (95% CI: 16.6, 30.4) for patients who received placebo in combination with enzalutamide (hazard ratio=0.740, 95% CI: 0.565, 0.969); in the BRCAm subgroup median rPFS was not reached (95% CI: 16.8, Not Reached) for patients who received Talzenna in combination with enzalutamide and 11 months (95% CI: 5.9, 13.8) for patients who received placebo in combination with enzalutamide (hazard ratio=0.259, 95% CI: 0.120, 0.558).

Figure 4. Kaplan-Meier curves of rPFS by BICR – TALAPRO-2 (mCRPC)



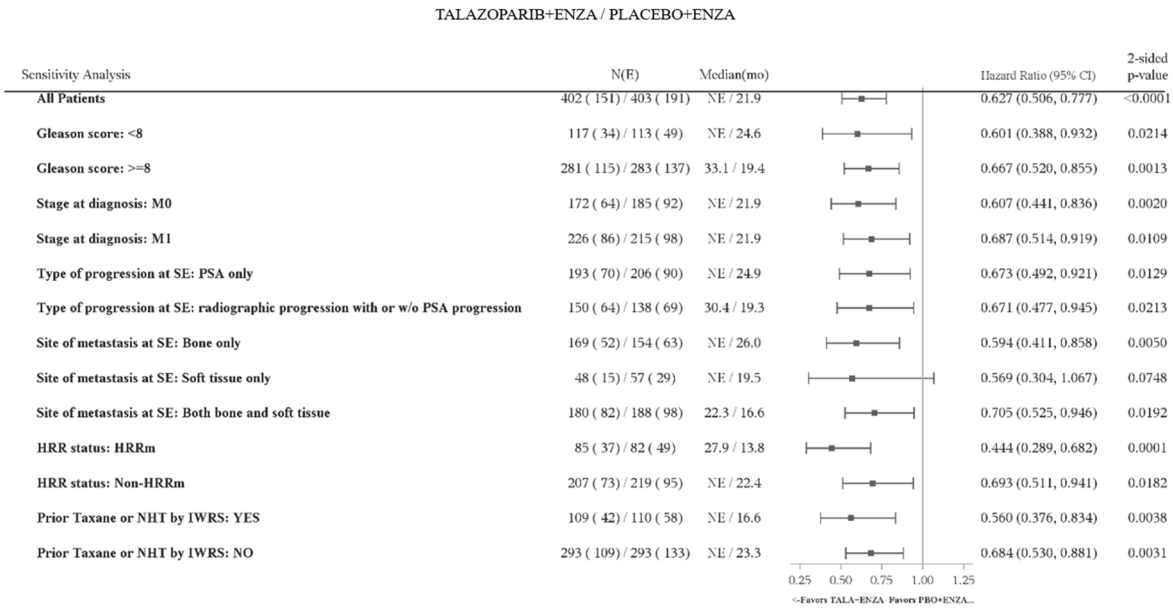
Number of patients at risk

Talazoparib + Enzalutamide	402	379	353	326	318	285	256	234	226	209	193	175	136	97	67	61	29	13	2	2	1	0
Placebo + Enzalutamide	403	346	311	279	272	237	200	185	179	154	140	124	96	68	43	42	14	3	1	1	1	0

Abbreviations: BICR=blinded independent central review; CI=confidence interval; mCRPC=metastatic castration-resistant prostate cancer; PFS=progression-free survival; rPFS=radiographic progression-free survival.

Prespecified subgroup rPFS analyses were performed based on prognostic factors and baseline characteristics to evaluate the internal consistency of the treatment effect. Consistent with the overall results, a reduction in the risk of disease progression or death in favor of talazoparib in combination with enzalutamide was observed in patient subgroups shown in Figure 5.

Figure 5. Forest plot of rPFS analyses for key subgroups – TALAPRO-2 (mCRPC)

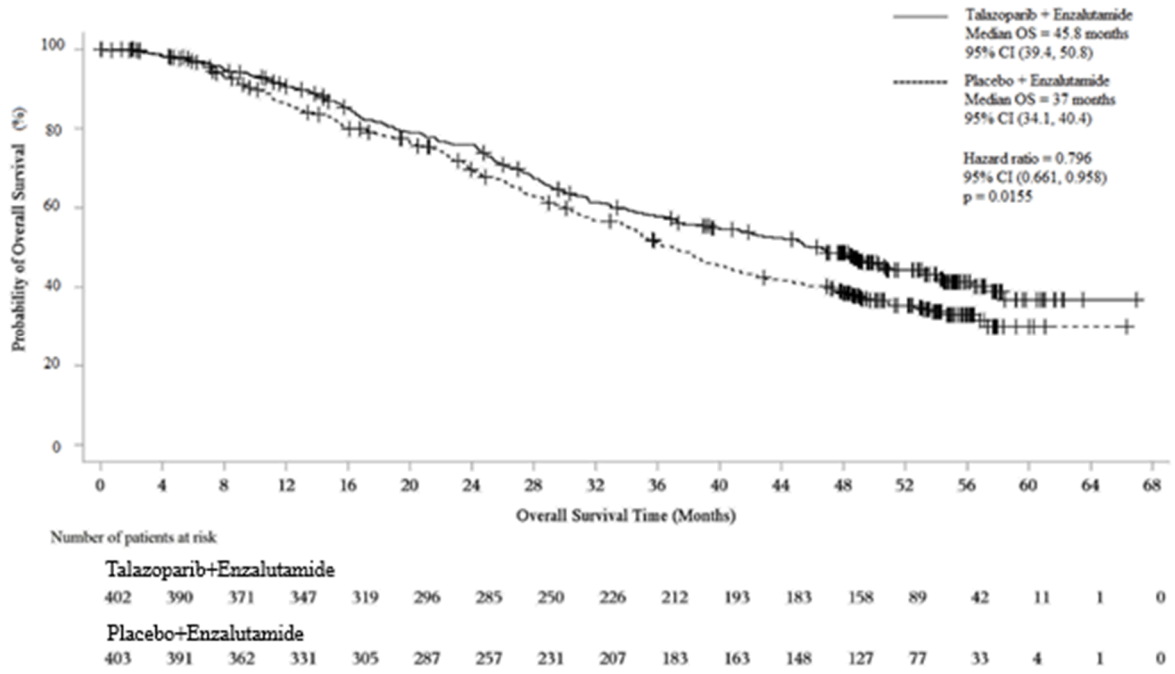


Abbreviations: CI=confidence interval; ctDNA=circulating tumor DNA; E=number of events; ENZA=enzalutamide; HRR=homologous recombination repair; HRRm=homologous recombination repair gene mutated; IWRS=Interactive Web Response System; mCRPC=metastatic castration-resistant prostate cancer; N=number of patients; NE=not evaluable/not reached; NHT=novel hormone therapy; PBO=placebo; PSA=prostate-specific antigen; rPFS=radiographic progression-free survival; SE=study entry; TALA=talazoparib; w/o=without.

Hazard ratio for all patients was based on a Cox model stratified by the randomization stratification factors. For all subgroups, hazard ratio was based on an unstratified Cox model with treatment as the only covariate. A hazard ratio < 1 favors talazoparib.

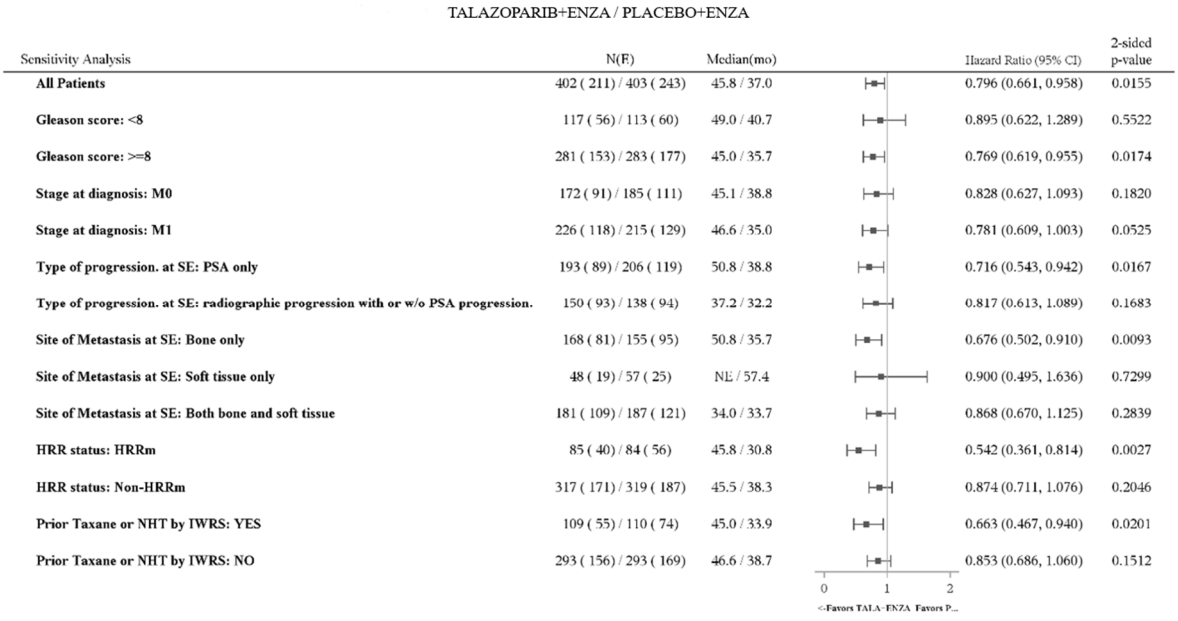
HRR status is derived based on prospective tumor tissue-based results and prospective blood-based ctDNA results.

Figure 6. Kaplan-Meier curves of OS – TALAPRO-2 (mCRPC)



Abbreviations: CI=confidence interval; mCRPC=metastatic castration-resistant prostate cancer; OS=overall survival.

Figure 7. Forest plot of OS analyses for key subgroups – TALAPRO-2 (mCRPC)



Abbreviations: CI=confidence interval; E=number of events; ENZA=enzalutamide; HRR=homologous recombination repair; HRRm=homologous recombination repair gene mutated; IWRS=Interactive Web Response System; mCRPC=metastatic castration-resistant prostate cancer; N=number of patients; NHT=novel hormone therapy; OS=overall survival; PSA=prostate-specific antigen; SE=study entry; TALA=talazoparib; w/o=without.
Hazard ratio for all patients was based on a Cox model stratified by the randomization stratification factors. For all subgroups, hazard ratio was based on an unstratified Cox model with treatment as the only covariate.
Percentages calculated based on N, the number of patients in the full analysis set in each treatment group.

5.2. Pharmacokinetic properties

Talazoparib exposure generally increased proportionally with dose across the range of 0.025 mg to 2 mg after daily administration of multiple doses. Following repeated daily dosing of 1 mg talazoparib monotherapy to breast cancer patients, the geometric mean (% coefficient of variation [CV%]) area under the plasma concentration-time curve (AUC) and maximum observed plasma concentration (C_{max}) of talazoparib at steady-state was in the range of 126 (107) ng•hr/mL to 208 (37) ng•hr/mL and 11 (90) ng/mL to 19 (27) ng/mL, respectively.

After oral administration of 0.5 mg talazoparib once daily in combination with enzalutamide in mCRPC patients, the geometric mean (CV%) steady-state C_{trough} across visits ranged from 3.29 to 3.68 ng/mL (45 to 48%), which is similar to the observed values of 3.53 (61%) ng/mL when talazoparib monotherapy was administered at 1 mg once daily in breast cancer patients.

Following repeated daily dosing, talazoparib plasma concentrations reached steady-state within 2 to 3 weeks when administered alone, and within 9 weeks when coadministered with enzalutamide. The median accumulation ratio of talazoparib following repeated oral administration of 1 mg monotherapy once daily was in the range of 2.3 to 5.2. Talazoparib is a substrate of P-gp and BCRP transporters.

Absorption

Following oral administration of talazoparib, the median time to C_{max} (T_{max}) was generally between 1 to 2 hours after dosing. The absolute bioavailability study has not been conducted in humans. However, based on urinary excretion data the absolute bioavailability is at least 54.6% with fraction absorbed of at least 68.7% (see Elimination).

The effect of food

Food intake decreased the rate but not the extent of talazoparib absorption. Following a single oral dose of talazoparib with high-fat, high-calorie food (approximately 827 calories, 57% fat), the mean C_{max} of talazoparib was decreased by approximately 46%, the median T_{max} was delayed from 1 to 4 hours, while the AUC_{inf} was not affected. Based on these results, TALZENNA can be administered with or without food.

Distribution

The population mean apparent volume of distribution (V_{ss}/F) of talazoparib was 420 L. *In vitro*, talazoparib is approximately 74% bound to plasma proteins with no concentration dependence over the concentration range of 0.01 µM to 1 µM. Renal or hepatic impairment does not appear to impact talazoparib protein binding as there was no obvious trend in the mean talazoparib fraction of unbound drug (f_u) in human plasma *in vivo* with worsening renal or hepatic function.

Metabolism

Talazoparib undergoes minimal hepatic metabolism in humans. Following oral administration of a single 1 mg dose of [^{14}C]talazoparib to humans, no major circulating metabolites were identified in plasma, and talazoparib was the only circulating drug-derived entity identified. No metabolites that individually represented more than 10% of the administered dose were recovered in the urine or feces. The identified metabolic pathways of talazoparib in humans

include: 1) mono-oxidation; 2) dehydrogenation; 3) cysteine conjugation of mono-desfluoro-talazoparib; and 4) glucuronide conjugation.

In vitro, talazoparib was not an inhibitor of cytochrome (CYP)1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4/5 or inducer of CYP1A2, CYP2B6, or CYP3A4 at clinically relevant concentrations.

In vitro, talazoparib did not inhibit any of the major intestinal, hepatic or renal membrane transporters (P-gp, BCRP, organic anion transporting polypeptide [OATP]1B1, OATP1B3, organic cationic transporter [OCT]1 OCT2, organic anion transporter [OAT]1, OAT3, bile salt export pump [BSEP], multidrug and toxin extrusion [MATE]1 and MATE2-K) at clinically relevant concentrations.

In vitro, talazoparib did not inhibit any of the major uridine-diphosphate glucuronosyltransferase (UGT) isoforms (1A1, 1A4, 1A6, 1A9, 2B7, and 2B15) at clinically relevant concentrations.

Elimination

The mean terminal plasma half-life of talazoparib was 89.8 hours and the population mean apparent oral clearance (CL/F) was 6.45 L/h in cancer patients. In 6 female patients with advanced solid tumors given a single oral dose of [^{14}C]talazoparib, a mean of 68.7% and 19.7% of the total administered radioactive dose was recovered in urine and feces, respectively. Excretion of unchanged talazoparib in urine was the major route of elimination accounting for 54.6% of the administered dose, while unchanged talazoparib recovered in the feces accounted for 13.6%.

Special populations

Age, sex, race, and body weight

A population PK analysis was conducted using data from 490 patients with cancer who received talazoparib 1 mg daily as monotherapy to evaluate the impact of age (ranging from 18 to 88 years), sex (53 males and 437 females), race (361 White, 41 Asian, 16 Black, 9 Others, and 63 Not reported), and body weight (ranging from 35.7 kg to 162 kg) on the PK of talazoparib. The results have shown that age, sex, race, and body weight had no clinically relevant effect on the PK of talazoparib.

Pediatric population

Pharmacokinetics of talazoparib have not been evaluated in patients <18 years of age.

Elderly population

Of the 494 patients who received TALZENNA, 85 patients were ≥65 years of age. No overall differences in safety or effectiveness of TALZENNA were observed between these patients and younger patients but greater sensitivity of some older individuals cannot be ruled out.

Renal impairment

Talazoparib monotherapy

Data from a PK trial in advanced cancer patients with varying degrees of renal impairment indicate that talazoparib total exposure (AUC_{0-24}) after multiple talazoparib once-daily doses increased by 12%, 43%, and 163% in patients with mild (eGFR 60 – 89 mL/min/1.73 m^2),

moderate (eGFR 30 – 59 mL/min/1.73 m^2), and severe (eGFR 15 – 29 mL/min/1.73 m^2) renal impairment, respectively, relative to patients with normal renal function (eGFR ≥90mL/min/1.73 m^2). Talazoparib C_{max} increased by 11%, 32%, and 89% in patients with mild, moderate, and severe renal impairment, respectively, relative to patients with normal renal function. Consistent with these findings, a population PK analysis that included 490 patients, where 132 patients had mild renal impairment (60 mL/min ≤ CrCL <90 mL/min), 33 patients had moderate renal impairment (30 mL/min ≤ CrCL <60 mL/min), and 1 patient had severe renal impairment (CrCL <30 mL/min), showed that talazoparib CL/F was decreased by 14.4% and 37.1% in patients with mild and moderate renal impairment, corresponding to 17% and 59% increase in AUC, respectively, when compared to patients with normal renal function (CrCL ≥90 mL/min). The PK of talazoparib has not been studied in patients requiring hemodialysis.

Talazoparib coadministered with enzalutamide
Based on a population PK analysis that included 412 mCRPC patients who received talazoparib coadministered with enzalutamide, where 152 patients had mild renal impairment (60 mL/min ≤ CrCL <90 mL/min), 72 patients had moderate renal impairment (30 mL/min ≤ CrCL <60 mL/min), and 2 patients had severe renal impairment (CrCL <30 mL/min). Predicted talazoparib CL/F was decreased by 8.0%, 27.1%, and 46.7% in patients with mild, moderate, and severe renal impairment, corresponding to increases of 9%, 37%, and 88% in AUC, respectively, compared to patients with normal renal function. The PK of talazoparib has not been studied in patients requiring hemodialysis (see Section 4.2).

Hepatic impairment

Talazoparib monotherapy
Based on a population PK analysis that included 490 patients who received talazoparib 1 mg daily as monotherapy, where 118 patients had mild hepatic impairment (total bilirubin ≤1.0 × ULN and AST >ULN, or total bilirubin >1.0 to 1.5 × ULN and any AST), mild hepatic impairment had no effect on the PK of talazoparib. The PK of talazoparib in patients with normal hepatic function, mild hepatic impairment, moderate hepatic impairment (total bilirubin >1.5 to 3.0 × ULN and any AST), or severe hepatic impairment (total bilirubin >3.0 × ULN and any AST) was studied in a PK trial. Population PK analysis using data from this PK trial indicated that mild, moderate, or severe hepatic impairment had no significant impact on the PK of talazoparib.

Talazoparib coadministered with enzalutamide
The PK of talazoparib in combination with enzalutamide has not been studied in patients with hepatic impairment (see Section 4.2).

Cardiac electrophysiology
The effect of talazoparib on cardiac repolarization was evaluated using time-matched electrocardiograms (ECGs) in assessing the relationship between the change of the QT interval corrected for heart rate (QTc) from baseline and the corresponding plasma talazoparib concentrations in 37 patients with advanced solid tumors. Talazoparib did not have a clinically relevant effect on QTc prolongation at the maximum clinically recommended dose of 1 mg once daily.

5.3. Preclinical safety data

Carcinogenicity
Carcinogenicity studies have not been conducted with talazoparib.

Genotoxicity
Talazoparib was not mutagenic in a bacterial reverse mutation (Ames) test. Talazoparib was clastogenic in an *in vitro* chromosomal aberration assay in human peripheral blood lymphocytes and in an *in vivo* micronucleus assay in rats at exposures similar to clinically relevant doses. This clastogenicity is consistent with genomic instability resulting from the primary pharmacology of talazoparib, indicating the potential for genotoxicity in humans.

Repeat-dose toxicity
In repeat-dose toxicity studies of up to 13-week duration, talazoparib was clinically tolerated in rats at 0.04 mg/kg/day and in dogs at 0.01 mg/kg/day and the AUC_{24} exposure margins at the no adverse effect level are 0.2-fold the relevant human exposure. The main findings at subtherapeutic exposures included bone marrow hypocellularity with dose-dependent decrease in hematopoietic cells, depletion of lymphoid tissue in multiple organs and atrophy and/or degenerative changes in testes, epididymis, and seminiferous tubules. Additional findings at higher exposures included dose-dependent increase in apoptosis/necrosis in the gastrointestinal (GI) tract, liver, and ovary. Most of the histopathologic findings were generally reversible while the testes findings were partially reversible after 4 weeks of dosing cessation. These toxicity findings are consistent with the pharmacology of talazoparib and its tissue distribution pattern.

Reproductive toxicology
In an embryo-fetal development study in rats, talazoparib resulted in embryo-fetal death, fetal malformation (depressed eye bulge, small eye, split sternebra, fused cervical vertebral arch) and structural variations in bones at a maternal systemic AUC_{24} exposure approximately 0.09-fold the relevant human exposure at the recommended dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Talazoparib capsules content
Silicified microcrystalline cellulose (sMCC)

Capsule shell

White body shell or white cap
Hypromellose (HPMC)
Titanium dioxide (E171)

Ivory body shell or ivory cap
Hypromellose (HPMC)
Yellow iron oxide (E172)
Titanium dioxide (E171)

Light pink cap
Hypromellose (HPMC)
Red iron oxide (E172)
Titanium dioxide (E171)

Light red cap
Hypromellose (HPMC)
Red iron oxide (E172)
Yellow iron oxide (E172)
Titanium dioxide (E171)

Printing ink
Shellac
Propylene glycol
Ammonium hydroxide
Black iron oxide
Potassium hydroxide

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

Refer to outer carton for expiration date.

6.4. Special precautions for storage

Store at or below 30°C.
Store in original container, in order to protect capsules from light.

6.5. Nature and contents of container

TALZENNA 0.1 mg hard capsules
High-density polyethylene (HDPE) bottle and polypropylene (PP) closure with heat induction seal (HIS) liner, containing 30 hard capsules.

TALZENNA 0.25 mg hard capsules
High-density polyethylene (HDPE) bottle and polypropylene (PP) closure with heat induction seal (HIS) liner, containing 30 or 60 or 90 hard capsules.

Polyvinyl chloride/polyvinylidene chloride (PVC/PVdC) blister with an aluminum peel off foil lidding in cartons of 30 × 1, or 60 × 1, or 90 × 1 hard capsules.

TALZENNA 0.35 mg hard capsules
High-density polyethylene (HDPE) bottle and polypropylene (PP) closure with heat induction seal (HIS) liner, containing 30 hard capsules.

TALZENNA 0.5 mg hard capsules
High-density polyethylene (HDPE) bottle and polypropylene (PP) closure with heat induction seal (HIS) liner, containing 30 hard capsules.

TALZENNA 1 mg hard capsules
High-density polyethylene (HDPE) bottle and polypropylene (PP) closure with heat induction seal (HIS) liner, containing 30 hard capsules.

Polyvinyl chloride/polyvinylidene chloride (PVC/PVdC) blister with an aluminum foil lidding in cartons of 30 × 1 hard capsules.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. NAME AND ADDRESS OF PRODUCT OWNER

Pfizer Inc
New York,
United States

TAL-SIN-0525/0
Date of last revision: May 2025

Package leaflet: Information for the patient

TALZENNA 0.1 mg hard capsules
TALZENNA 0.25 mg hard capsules
TALZENNA 0.35 mg hard capsules
TALZENNA 0.5 mg hard capsules
TALZENNA 1 mg hard capsules
talazoparib

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What TALZENNA is and what it is used for

What TALZENNA is and how it works
TALZENNA contains the active substance talazoparib. It is a type of anticancer medicine known as a 'PARP (poly-ADP ribose polymerase) inhibitor'.

TALZENNA works by blocking PARP, which is an enzyme that repairs damaged DNA in certain cancer cells. As a result, the cancer cells can no longer repair themselves and they die.

What TALZENNA is used for
TALZENNA is used to treat adults with breast cancer (BC) of a type known as HER2-negative breast cancer who have an abnormal inherited BRCA gene. Your healthcare provider will perform a test to make sure that TALZENNA is right for you.

TALZENNA is used in combination with a medicine called enzalutamide, to treat adults with prostate cancer who no longer respond to a hormone therapy or surgical treatment to lower testosterone.

TALZENNA is used when the cancer has spread beyond the original tumor or to other parts of the body.

If you have any questions about how TALZENNA works or why this medicine has been prescribed for you, ask your doctor.

2. What you need to know before you take TALZENNA

Do not take TALZENNA
- If you are allergic to talazoparib or any of the other ingredients of this medicine (listed in section 6).
- If you are breast-feeding.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking TALZENNA and during your treatment if you experience signs or symptoms described in this section.

Low blood cell counts
TALZENNA lowers your blood cell counts, such as your red blood cell count (anemia), white blood cell count (neutropenia), or blood platelet count (thrombocytopenia). Signs and symptoms you need to look out for include:
- **Anemia:** Being short of breath, feeling very tired, pale skin, or fast heartbeat – these may be signs of a low red blood cell count
- **Neutropenia:** Infection, developing chills or shivering, or fever – these may be signs of a low white blood cell count
- **Thrombocytopenia:** Bruising or bleeding for longer than usual if you hurt yourself – these may be signs of a low blood platelet count

You will have regular blood tests during treatment with TALZENNA to check your blood cells (white blood cells, red blood cells, and platelets).

Serious problems with the bone marrow
Rarely, low blood cell counts may be a sign of more serious problems with the bone marrow such as myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). Your doctor may want to test your bone marrow to check for these problems.

Blood clots
TALZENNA may cause blood clots in the veins. Tell your doctor, pharmacist or nurse if you experience signs or symptoms of blood clots in the veins such as pain or stiffness, swelling and redness in the affected leg (or arm), chest pain, shortness of breath or light-headedness.

Male and female contraception
Women who can become pregnant and men with partners who are or can become pregnant should use effective contraception.

Please see section “Male and female contraception” below.

Children and adolescents
TALZENNA is not to be used in children or adolescents (under 18 years of age).

Other medicines and TALZENNA
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines. This is because TALZENNA can affect the way some other medicines work. Also some medicines can affect the way TALZENNA works.

In particular, the following may increase the risk of side effects with TALZENNA:
- Amiodarone, carvedilol, dronedarone, propafenone, quinidine, ranolazine and verapamil – generally used to treat heart problems.
- Clarithromycin and erythromycin antibiotics – used to treat bacterial infections.
- Itraconazole and ketoconazole – used to treat fungal infections.
- Cobicistat, darunavir, indinavir, lopinavir, ritonavir, saquinavir, telaprevir and tipranavir – used to treat HIV infections/AIDS.
- Cyclosporin – used in organ transplantation to prevent rejection.
- Lapatinib – used to treat patients with certain types of breast cancer.
- Curcumin (e.g., found in turmeric root) in some medicines (see also section TALZENNA with food and drink below).
- Other products such as valspodar.

The following medicines may reduce the effect of TALZENNA:
- Carbamazepine and phenytoin – anti-epileptics used to treat seizures or fits.
- St. John's wort (*Hypericum perforatum*) – a herbal remedy used to treat mild depression and anxiety.

TALZENNA with food and drink
Do not use curcumin in food supplements while you are taking TALZENNA as it may increase TALZENNA's side effects. Curcumin is found in turmeric root and you should not use large amounts of turmeric root, but using spices in food is not likely to cause a problem.

Pregnancy
TALZENNA may harm an unborn baby. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Your doctor will perform a pregnancy test prior to starting TALZENNA. TALZENNA is not recommended during pregnancy or for women of childbearing potential not using contraception.

- You should not use TALZENNA if you are pregnant.
- You should not become pregnant while taking TALZENNA.
- Discuss contraception with your doctor if there is any possibility that you or your partner may become pregnant.

Male and female contraception
Women who are able to become pregnant should use effective birth control (contraception) during treatment with TALZENNA and for at least 7 months after the last dose of TALZENNA. Since the use of hormonal contraception is not recommended if you have breast cancer, you should use two non-hormonal contraception methods.

Talk to your healthcare provider about birth control methods that may be right for you.

Men with female partners who are pregnant or able to become pregnant should use effective birth control (contraception), even after a vasectomy, during treatment with TALZENNA and for at least 4 months after the last dose.

Breast-feeding
You should not breast-feed while taking TALZENNA and for at least 1 month after the last dose. It is not known if TALZENNA passes into breast milk.

Fertility
Male and female fertility may be compromised by treatment with TALZENNA.

Driving and using machines
TALZENNA may have a minor influence on the ability to drive and use machines. If you feel dizzy, weak, or tired (these are very common side effects of TALZENNA), you should not drive or use machines.

3. How to take TALZENNA

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take
TALZENNA is taken by mouth once daily. The recommended dose is:
- For breast cancer: one 1 mg capsule.
- For prostate cancer: TALZENNA is taken with a medicine called enzalutamide. The usual dose of TALZENNA is 0.5 mg.

If you get certain side effects while you are taking TALZENNA alone or in combination with enzalutamide (see section 4), your doctor may lower your dose or stop treatment, either temporarily or permanently. Take TALZENNA and enzalutamide exactly as your doctor has told you.

Swallow the capsule whole with a glass of water. Do not chew or crush the capsules. You can take TALZENNA with food or between meals. Do not open the capsules. Contact with the capsule content should be avoided.

If you take more TALZENNA than you should
If you have taken more TALZENNA than your normal dose, contact your doctor or nearest hospital right away. Urgent treatment may be necessary.

Take the carton and this leaflet so that the doctor knows what you have been taking.

If you forget to take TALZENNA
If you miss a dose or vomit, take your next dose as scheduled. Do not take a double dose to make up for the forgotten or vomited capsules.

If you stop taking TALZENNA
Do not stop taking TALZENNA unless your doctor tells you to.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor straight away if you notice any of the following symptoms which could be a sign of serious blood disorder:

Very common (may affect more than 1 in 10 people)
- Being short of breath, feeling very tired, having pale skin, or fast heartbeat – these may be signs of a low red blood cell count (anemia).
- Infection, developing chills or shivering, or fever or feeling hot – these may be signs of a low white blood cell count (neutropenia, leukopenia).
- Bruising or bleeding for longer than usual if you hurt yourself – these may be signs of a low blood platelet count (thrombocytopenia).

Talk to your doctor if you get any other side effects. These can include:

Very common (may affect more than 1 in 10 people)
- Low counts of white blood cells, red blood cells, and blood platelets
- Decreased appetite
- Feeling dizzy
- Headache
- Feeling sick (nausea)
- Being sick (vomiting)
- Diarrhea
- Pain in the abdomen
- Hair loss (alopecia)
- Tiredness

Common (may affect up to 1 in 10 people)
- Low levels of lymphocytes
- Alteration in taste (dysgeusia)
- Painful swollen leg, chest pain, shortness of breath, rapid breathing or rapid heart rate as these can be signs of blood clots in the vein
- Indigestion
- Mouth inflammation

Uncommon (may affect up to 1 in 100 people)
- Abnormal blood cell counts due to serious problems with bone marrow (myelodysplastic syndrome or acute myeloid leukaemia). See Warnings and precautions in Section 2.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store TALZENNA

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the bottle or blister after EXP. The expiry date refers to the last day of that month.

Store at or below 30°C. Store in original container, in order to protect capsules from light.

Do not use this medicine if the pack is damaged or shows signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What TALZENNA contains

- The active substance is talazoparib. TALZENNA hard capsules come in different strengths.
- TALZENNA 0.1 mg hard capsules: each capsule contains talazoparib tosylate equivalent to 0.1 mg talazoparib.
- TALZENNA 0.25 mg hard capsules: each capsule contains talazoparib tosylate equivalent to 0.25 mg talazoparib.
- TALZENNA 0.35 mg hard capsules: each capsule contains talazoparib tosylate equivalent to 0.35 mg talazoparib.
- TALZENNA 0.5 mg hard capsules: each capsule contains talazoparib tosylate equivalent to 0.5 mg talazoparib.
- TALZENNA 1 mg hard capsules: each capsule contains talazoparib tosylate equivalent to 1 mg talazoparib.

The other ingredients are:

- Capsule content: silicified microcrystalline cellulose (sMCC) (microcrystalline cellulose and silicone dioxide).
- 0.1 mg capsule shell: hypromellose (HPMC), and titanium dioxide (E171).
- 0.25 mg capsule shell: hypromellose (HPMC), yellow iron oxide (E172), and titanium dioxide (E171).
- 0.35 mg capsule shell: hypromellose (HPMC), yellow iron oxide (E172), and titanium dioxide (E171).
- 0.5 mg capsule shell: hypromellose (HPMC), red iron oxide (E172), and titanium dioxide (E171).
- 1 mg capsule shell: hypromellose (HPMC), yellow iron oxide (E172), titanium dioxide (E171), and red iron oxide (E172).

Printing ink: shellac, propylene glycol, ammonium hydroxide, black iron oxide, and potassium hydroxide.

What TALZENNA looks like and contents of the pack
TALZENNA 0.1 mg is supplied as opaque, approximately 14.30 mm x 5.32 mm hard capsule with a white cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.1” in black).

TALZENNA 0.25 mg is supplied as opaque, approximately 14.30 mm x 5.32 mm hard capsule with an ivory cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.25” in black).

TALZENNA 0.35 mg is supplied as opaque, approximately 14.30 mm x 5.32 mm hard capsule with an ivory cap (printed with “Pfizer” in black) and an ivory body (printed with “TLZ 0.35” in black).

TALZENNA 0.5 mg is supplied as opaque, approximately 14.30 mm x 5.32 mm hard capsule with a light pink cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 0.5” in black).

TALZENNA 1 mg is supplied as opaque, approximately 14.30 mm x 5.32 mm hard capsule with a light red cap (printed with “Pfizer” in black) and a white body (printed with “TLZ 1” in black).

TALZENNA 0.1 mg is available in plastic bottles of 30 hard capsules.

TALZENNA 0.25 mg is available in blister packs of 30 x 1, or 60 x 1, or 90 x 1 hard capsules and in plastic bottles of 30 or 60 or 90 hard capsules.

TALZENNA 0.35 mg is available in plastic bottles of 30 hard capsules.

TALZENNA 0.5 mg is available in plastic bottles of 30 hard capsules.

TALZENNA 1 mg is available in blister pack of 30 x 1 hard capsule and in plastic bottles of 30 hard capsules.

Not all pack sizes may be marketed.

TAL-SIN-0525/PIL/0
Date of last revision: May 2025