TALZENNA® (talazoparib)

Patient Profiles

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TALZENNA® (talazoparib) Indication and Important Safety Information[1]

INDICATION

TALZENNA is indicated for the treatment of adult patients with deleterious or suspected deleterious germline breast cancer susceptibility gene (BRCA)-mutated (*gBRCAm*) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for TALZENNA.

IMPORTANT SAFETY INFORMATION

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) have been reported in patients who received TALZENNA. Overall, MDS/AML has been reported in 2 out of 584 (0.3%) solid tumor patients treated with TALZENNA in clinical studies. The duration of TALZENNA treatment in these two patients prior to developing MDS/AML was 4 months and 24 months, respectively. Both patients had received previous chemotherapy with platinum agents and/or other DNA damaging agents including radiotherapy.

Myelosuppression consisting of anemia, leukopenia/neutropenia, and/or thrombocytopenia have been reported in patients treated with TALZENNA. Grade ≥3 anemia, neutropenia, and thrombocytopenia were reported, respectively, in 39%, 21%, and 15% of patients receiving TALZENNA. Discontinuation due to anemia, neutropenia, and thrombocytopenia occurred, respectively, in 0.7%, 0.3%, and 0.3% of patients.

Monitor complete blood counts for cytopenia at baseline and monthly thereafter. Do not start TALZENNA until patients have adequately recovered from hematological toxicity caused by previous therapy. If hematological toxicity occurs, dose modifications (dosing interruption with or without dose reduction) are recommended. **With respect to MDS/AML**, for prolonged hematological toxicities, interrupt TALZENNA and monitor blood counts weekly until recovery. If the levels have not recovered after 4 weeks, refer the patient to a hematologist for further investigations. If MDS/AML is confirmed, discontinue TALZENNA.

TALZENNA can cause **fetal harm** when administered to pregnant women. Advise women of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose. A pregnancy test is recommended for females of reproductive potential prior to initiating TALZENNA treatment. Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment with TALZENNA and for at least 4 months after receiving the last dose. Based on animal studies, TALZENNA may impair fertility in males of reproductive potential. Advise women not to breastfeed while taking TALZENNA and for at least 1 month after receiving the last dose because of the potential for serious adverse reactions in nursing infants.

The **most common adverse reactions (≥20%)** of any grade for TALZENNA vs chemotherapy were fatigue (62% vs 50%), anemia (53% vs 18%), nausea (49% vs 47%), neutropenia (35% vs 43%), headache (33% vs 22%), thrombocytopenia (27% vs 7%), vomiting (25% vs 23%), alopecia (25% vs 28%), diarrhea (22% vs 26%), and decreased appetite (21% vs 22%).

The **most frequently reported Grade ≥3 adverse reactions (≥10%)** for TALZENNA vs chemotherapy were anemia (39% vs 5%), neutropenia (21% vs 35%), and thrombocytopenia (15% vs 2%).

The **most common lab abnormalities (≥25%)** for TALZENNA vs chemotherapy were decreases in hemoglobin (90% vs 77%), leukocytes (84% vs 73%), lymphocytes (76% vs 53%), neutrophils (68% vs 70%), platelets (55% vs 29%), and calcium (28% vs 16%) and increases in glucose (54% vs 51%), aspartate aminotransferase (37% vs 48%), alkaline phosphatase (36% vs 34%), and alanine aminotransferase (33% vs 37%).

Coadministration with P-gp inhibitors or **BCRP inhibitors** may increase TALZENNA exposure. If coadministering with the P-gp inhibitors amiodarone, carvedilol, clarithromycin, itraconazole, or verapamil is unavoidable, reduce the TALZENNA dose to 0.75 mg once daily. When the P-gp inhibitor is discontinued, increase the TALZENNA dose (after 3–5 half-lives of the P-gp inhibitor) to the dose used prior to the initiation of the P-gp inhibitor. When coadministering TALZENNA with other known P-gp inhibitors or BCRP inhibitors, monitor patients for potential increased adverse reactions.

For patients with moderate **renal impairment**, the recommended dose of TALZENNA is 0.75 mg once daily. For patients with severe renal impairment, the recommended dose of TALZENNA is 0.5 mg once daily. No dose adjustment is required for patients with mild renal impairment. TALZENNA has not been studied in patients requiring hemodialysis.

TALZENNA has not been studied in patients with moderate or severe **hepatic impairment**. No dose adjustment is required for patients with mild hepatic impairment.

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National Comprehensive Cancer Network® (NCCN®)

Assess for g*BRCA* mutations to inform treatment planning.[2,3]

According to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®):

- All patients with recurrent or metastatic breast cancer (mBC) should be assessed for g*BRCA*1/2 mutations to identify candidates for PARP inhibitor therapy[2]
- Testing is clinically indicated for patients with a personal history of certain cancers* to aid in systemic therapy decision-making, such as for HER2- mBC[3]

*May include breast, ovarian, pancreatic, and prostate cancer. Please see detailed criteria for testing for high-penetrance breast and/or ovarian cancer susceptibility genes (such as *BRCA*1/2) in the NCCN Guidelines® for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.

Talazoparib (TALZENNA®) received a Category 1 recommendation from the NCCN.[2]

Category 1 definition: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

NCCN Category 1

Talazoparib (TALZENNA) is a preferred treatment option for recurrent or stage IV breast cancer patients with a germline *BRCA*1/2 mutation.†

†Assess for germline *BRCA*1/2 mutations in all patients with recurrent or metastatic breast cancer to identify candidates for PARP inhibitor therapy.

The NCCN Guidelines above fall outside the talazoparib (TALZENNA) US Prescribing Information

TALZENNA Indication[1]

TALZENNA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with deleterious or suspected deleterious germline breast cancer susceptibility gene (BRCA)-mutated (*gBRCAm*) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for TALZENNA.

The appropriate use of TALZENNA should be based on risk/benefit assessment by the practitioner for an individual patient.

NCCN Category 2A

Capecitabine, gemcitabine, vinorelbine, and eribulin are some of the preferred chemotherapy treatment options for recurrent or stage IV HER2-negative patients.

Category 2A definition: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

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MEET ADELA*

A Patient With Metastatic HR+/HER2- Breast Cancer and a g*BRCA* Mutation[4-8]

- 54-year-old college history professor
- Postmenopausal
- Single, with 2 adult children living out of town
- Father died of prostate cancer

Initial HR+/HER2- diagnosis and treatment

- Age 50 at initial diagnosis
- 2.2-cm nodule in left breast with involvement of 2 axillary lymph nodes (stage IIB)
- Treatment included neoadjuvant taxane-based chemotherapy, surgery, and radiation
- Started on adjuvant anastrozole

2-year disease-free interval†
Recurred while on anastrozole treatment

Recurrence and first-line treatment for mBC

- Imaging revealed solitary lung metastasis
- Was not offered genetic testing in the past
- Started on CDK4/6 inhibitor + fulvestrant
- Comorbidities: self-limiting microscopic colitis

2-year progression-free interval
Progressed while on CDK4/6 inhibitor + fulvestrant treatment

Today: Progression; initiating second-line treatment for g*BRCA*2-mutated mBC

- Started experiencing cough and shortness of breath
- ECOG PS=1
- Imaging revealed 3 lung metastases (up to 2.7 cm) and pleural effusion
- Genetic testing performed, revealed g*BRCA*2 mutation

Adela and her care team are considering second-line treatment options for her g*BRCA*2-positive HR+/HER2- mBC. She has a strong desire to continue working while on treatment. If possible, she wants to avoid time-consuming infusions.

How Does Adela* Compare With Patients in the EMBRACA Trial?

Adela's* Profile		EMBRACA TALZENNA ARM Phase 3, open-label, randomized clinical trial: ITT Population (n=287)[4]	EMBRACA TALZENNA ARM Phase 3, open-label, randomized clinical trial: HR+ Subgroup (n=157)[9-11]
✓	HR+/HER2- disease	55%	100%
✓	g*BRCA*2 mutation–positive	54%	81%
✓	Measurable disease‡	76%	NR
✓	Visceral metastases	70%	NR
✓	ECOG PS=1	44%	45%
✓	Previous adjuvant or neoadjuvant therapy	83%	84.1%

‡Assessed by investigator.
ITT=intent-to-treat; NR=not reported.

Consider TALZENNA® to treat a patient like Adela*

*Hypothetical patient.
†Defined as period of time from post-surgery to diagnosis of advanced breast cancer.
CDK4/6=cyclin-dependent kinase 4 and 6; ECOG PS=Eastern Cooperative Oncology Group performance status; HR=hormone receptor.

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MEET KAYLA*

A Patient With Metastatic Triple-Negative Breast Cancer With a g*BRCA* Mutation[4,7,12-14]

- 43-year-old engineer
- Premenopausal
- Married, with 3 young children at home
- No family history of breast, ovarian, pancreatic, or prostate cancer

Initial TNBC diagnosis and treatment

- Age 40 at initial diagnosis
- 2.9-cm tumor without lymph node involvement in her left breast (stage II TNBC)
- Refused genetic testing due to potential implications for her family
- Treatment included lumpectomy and whole-breast radiation; completed adjuvant anthracycline/taxane chemotherapy

2.5-year disease-free interval†

Today: Recurrence; initiating first-line treatment for metastatic g*BRCA*1-mutated TNBC

- During one of her follow-up appointments, she complained about new-onset headache characterized as severe, with dizziness and nausea, and unintentional weight loss of 15 pounds
- ECOG PS=1; no comorbidities
- Physical exam: numbness in the right arm
- Diagnosis of stage IV disease: Imaging revealed 4 CNS metastases (range: 0.1–1.6 cm) and multiple bone metastases
- CNS metastases were treated with whole-brain radiation, and local control was achieved
- Genetic testing performed after consultation with genetic counselor, revealing a g*BRCA*1 mutation

Kayla and her care team are considering first-line treatment options for her g*BRCA*1-mutated metastatic TNBC. She wants to avoid time-consuming infusions and delay time to chemotherapy as long as possible.

*Hypothetical patient.
†Defined as period of time from post-surgery to diagnosis of advanced breast cancer.
CNS=central nervous system; TNBC=triple-negative breast cancer.

How Does Kayla* Compare With Patients in the EMBRACA Trial?

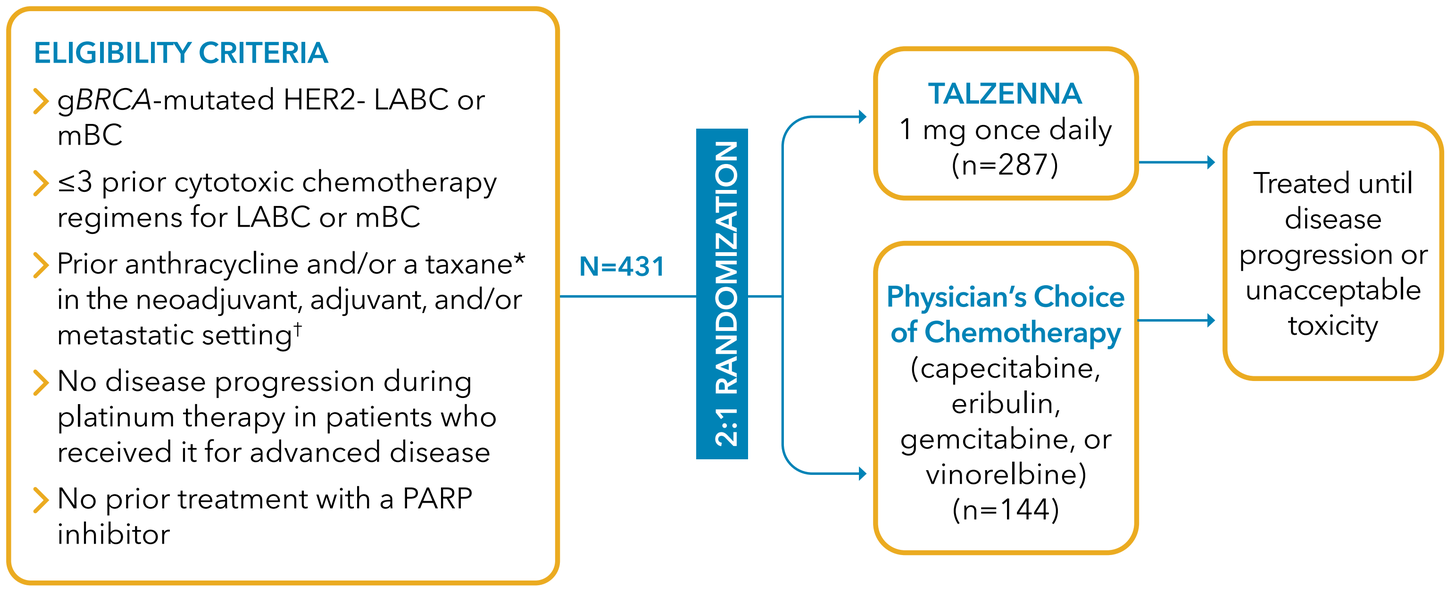
Kayla's* Profile		EMBRACA TALZENNA ARM Phase 3, open-label, randomized clinical trial: ITT Population (n=287)[4,11]	EMBRACA TALZENNA ARM Phase 3, open-label, randomized clinical trial: TNBC Subgroup (n=130)[9,10]
✓	TNBC	45%	100%
✓	g*BRCA*1 mutation–positive	46%	75%
✓	<50 years old	63%	71%
✓	ECOG PS=1	44%	44%
✓	No prior cytotoxic regimens for aBC	39%	40%
✓	≥12-month disease-free interval from initial diagnosis to aBC	62%	NR
✓	History of CNS metastases	15%	NR

aBC=advanced breast cancer.

Consider TALZENNA® to treat a patient like Kayla*

EMBRACA Clinical Trial: Study Design[1,4]

Phase 3, open-label, randomized, multicenter study



Stratification factors

- Prior use of chemotherapy for metastatic disease (0 vs 1, 2, or 3)
- Triple-negative disease status (TNBC vs non-TNBC)
- History of central nervous system metastases (yes vs no)

Primary endpoint

- Progression-free survival (PFS) by RECIST version 1.1 as assessed by BICR

Secondary endpoints

- Overall survival (OS)
- Objective response rate (ORR)
- Safety

Exploratory endpoint

- Duration of response (DoR) for objective responders

*Unless contraindicated.
†First-line treatment for advanced or metastatic disease with no prior adjuvant chemotherapy was allowed if the investigator determined that 1 of the 4 chemotherapy choices in the control arm would be an appropriate treatment option for the patient.
BICR=blinded independent central review; LABC=locally advanced breast cancer; PARP=poly (ADP-ribose) polymerase; RECIST=Response Evaluation Criteria in Solid Tumors.

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EMBRACA Clinical Trial: Patient Baseline Characteristics[4]

EMBRACA Clinical Trial Included HR+/HER2- or TNBC Patients With g*BRCA* Mutations and Various Patient Characteristics

Baseline characteristics (ITT population)

	TALZENNA® (talazoparib) (n=287)	Chemotherapy (n=144)
Demographics		
Age, median (years)	45 (27.0–84.0)	50 (24.0–88.0)
<50 y, %	63.4	46.5
Female, %	98.6	97.9
Clinical status, %		
Breast cancer stage		
Locally advanced	5.2	6.2
Metastatic	94.4	93.8
ECOG PS 0/1/2	53.3/44.3/2.1	58.3/39.6/1.4
Measurable disease by investigator	76.3	79.2
History of CNS metastasis	15.0	13.9
Visceral disease	69.7	71.5
Disease-free interval (initial diagnosis to aBC), <12 months	37.6	29.2
Hormone receptor status, %		
TNBC	45.3	41.7
HR+	54.7	58.3
BRCA* status, %		
*BRCA*1+	46.3	43.8
*BRCA*2+	53.7	56.2
Prior treatment		
Prior adjuvant/neoadjuvant therapy, %	82.9	84.0
No. of **previous hormone therapy–based regimens** for HR+ breast cancer in TALZENNA group (n=157) and chemotherapy group (n=84), **median (range)**	2.0 (0–6)	2.0 (0–6)
Prior platinum therapy, %	16.0	20.8
Prior cytotoxic regimens for patients with aBC, %		
0	38.7	37.5
1	37.3	37.5
2	19.9	19.4
3	4.2	5.6

*Only 10 patients (6 and 4 patients in the TALZENNA and standard-therapy groups, respectively) were identified as having a suspected deleterious mutation. The remainder who underwent central testing with BRACAnalysis CDx® had a known pathogenic variant.

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EMBRACA Clinical Trial: Summary of Efficacy and Safety

TALZENNA® is a proven alternative to chemotherapy* that provides patients with greater efficacy in a convenient, once-daily oral dose[1]

EMBRACA: a Phase 3, open-label, 2:1 randomized study in patients with g*BRCA*-mutated HER2- locally advanced or metastatic breast cancer[1,4]

Primary endpoint: PFS[1]

- **TALZENNA reduced the risk of disease progression by 46%** compared to chemotherapy

8.6 months (95% CI: 7.2-9.3) mPFS with TALZENNA (n=287)

vs **5.6 months (95% CI: 4.2-6.7) mPFS** with chemotherapy (n=144); HR=0.54 (0.41-0.71); *P*<0.0001

Secondary and exploratory endpoints[1]:

- **Confirmed ORR†‡:** 50.2% (95% CI: 43.4-57.0) with TALZENNA vs 18.4% (95% CI: 11.8-26.8) with chemotherapy
- **OS:** Final OS analysis did not reach statistical significance[15]
  - Median OS: 19.3 months (95% CI: 16.6-22.5) with TALZENNA vs 19.5 months (95% CI: 17.4-22.4) with chemotherapy (HR=0.85 [95% CI: 0.67-1.07]; *P*=0.17)
- **mDoR†§:** 6.4 months (95% CI: 5.4–9.5) mDoR with TALZENNA vs 3.9 months (95% CI: 3.0–7.6) mDoR with chemotherapy

Safety[1]:

- **WARNINGS AND PRECAUTIONS:** TALZENNA is associated with serious, potentially fatal risks, including MDS/AML, myelosuppression, and embryo-fetal toxicity. Please see Important Safety Information on page 2
- The **most common adverse reactions (≥20%)** of any grade for TALZENNA vs chemotherapy were fatigue (62% vs 50%), anemia (53% vs 18%), nausea (49% vs 47%), neutropenia (35% vs 43%), headache (33% vs 22%), thrombocytopenia (27% vs 7%), vomiting (25% vs 23%), alopecia (25% vs 28%), diarrhea (22% vs 26%), and decreased appetite (21% vs 22%)

*Capecitabine, eribulin, gemcitabine, vinorelbine.
†Response rate based on confirmed responses. Confirmed response: best overall response of partial response or complete response, confirmed by a subsequent tumor assessment (at least 4 weeks later) by investigator assessment.
‡Conducted in the intent-to-treat (ITT) population with measurable disease at baseline.
§Analyzed in the ITT patients who experienced an objective response assessed by investigator.
CI=confidence interval; DoR=duration of response; HR=hazard ratio; MDS/AML=myelodysplastic syndrome/acute myeloid leukemia; mPFS=median PFS; ORR=objective response rate; OS=overall survival.

References: 1. TALZENNA® U.S. Prescribing Information. New York, NY: Pfizer Inc.; 2020. **2.** Referenced with permission from NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.6.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed September 16, 2020. To view the most recent and complete version of the guideline, go online to www.NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic V.1.2021. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed September 30, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding the content, use or application and disclaims any responsibility for the application or use in any way. **4.** Litton JK, Rugo HS, Ettl J, et al. Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. *N Engl J Med*. 2018;379(8):753-763. **5.** Wang H, Zhang C, Zhang J, Kong L, Zhu H, Yu J. The prognosis analysis of different metastasis pattern in patients with different breast cancer subtypes: a SEER based study. *Oncotarget*. 2017;8(16):26368-26379. **6.** Nombela P, Lozano R, Aytes A, Mateo J, Olmos D, Castro E. BRCA2 and other DDR genes in prostate cancer. *Cancers* (*Basel*). 2019;11(3):e352. **7.** National Cancer Institute. Classic BRCA2 pedigree. https://visualsonline.cancer.gov/details.cfm?imageid=10437. Accessed April 20, 2020. **8.** Saguil A, Wyrick K, Hallgren J. Diagnostic approach to pleural effusion. *Am Fam Physician*. 2014;90(2):99-104. **9.** Eiermann W, Rugo HS, Ettl J, et al. Abstract presented at: Annual Meeting of the American Society of Clinical Oncology; June 1-5, 2018; Chicago, IL. Abstract 1070. **10.** Goncalves A, Eiermann W, Rugo HS, et al. Abstract presented at: European Society of Medical Oncology. October 19-22, 2018. Munich, Germany. Abstract 304P. **11.** Data on file. Pfizer Inc., New York, NY. **12.** Metastatic Breast Cancer Symptoms and Diagnosis. https://www.breastcancer.org/symptoms/types/recur_metast/metastic. Accessed April 20, 2020. **13.** Breast Cancer Care. Secondary breast cancer symptoms. https://www.breastcancercare.org.uk/information-support/secondary-metastatic-breast-cancer/signs-symptoms-secondary-breast-cancer. Accessed April 20, 2020. **14.** Lin NU, Claus E, Sohl J, Razzak AR, Arnaout A, Winer EP. Sites of distant recurrence and clinical outcomes in patients with metastatic triple-negative breast cancer: high incidence of central nervous system metastases. *Cancer*. 2008;113(10):2638-2645. **15.** Litton JK, Hurvitz SA, Mina LA, et al. Talazoparib versus chemotherapy in patients with germline BRCA1/2-mutated HER2-negative advanced breast cancer: final overall survival results from the EMBRACA trial. *Ann Oncol*. 2020. doi:10.1016/j.annonc.2020.08.2098.

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