INDICATION

TALZENNA® (talazoparib) 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.[1]

The only once-daily oral PARP inhibitor for the treatment of g*BRCA*-mutated hormone receptor-positive (HR+)/HER2- or triple-negative locally advanced or metastatic breast cancer (LABC or MBC).[1,2]

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

EMBRACA is the largest Phase 3, open-label, 2:1 randomized study of a PARP inhibitor in patients with g*BRCA*-mutated HER2- LABC or MBC (N=431). TALZENNA significantly outperformed chemotherapy in progression-free survival (PFS): median of 8.6 months (95% CI: 7.2-9.3) vs 5.6 months (95% CI: 4.2-6.7) (HR=0.54 [95% CI: 0.41-0.71]; *P*<0.0001).[1-3]

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 <1% (3 out of 787, 0.4%) of solid tumor patients treated with TALZENNA in clinical studies. The duration of TALZENNA treatment in these three patients prior to developing MDS/AML was 4 months, 24 months, and 60 months respectively. These patients had received previous chemotherapy with platinum agents and/or other DNA damaging agents including radiotherapy.

*Capecitabine, eribulin, gemcitabine, or vinorelbine.

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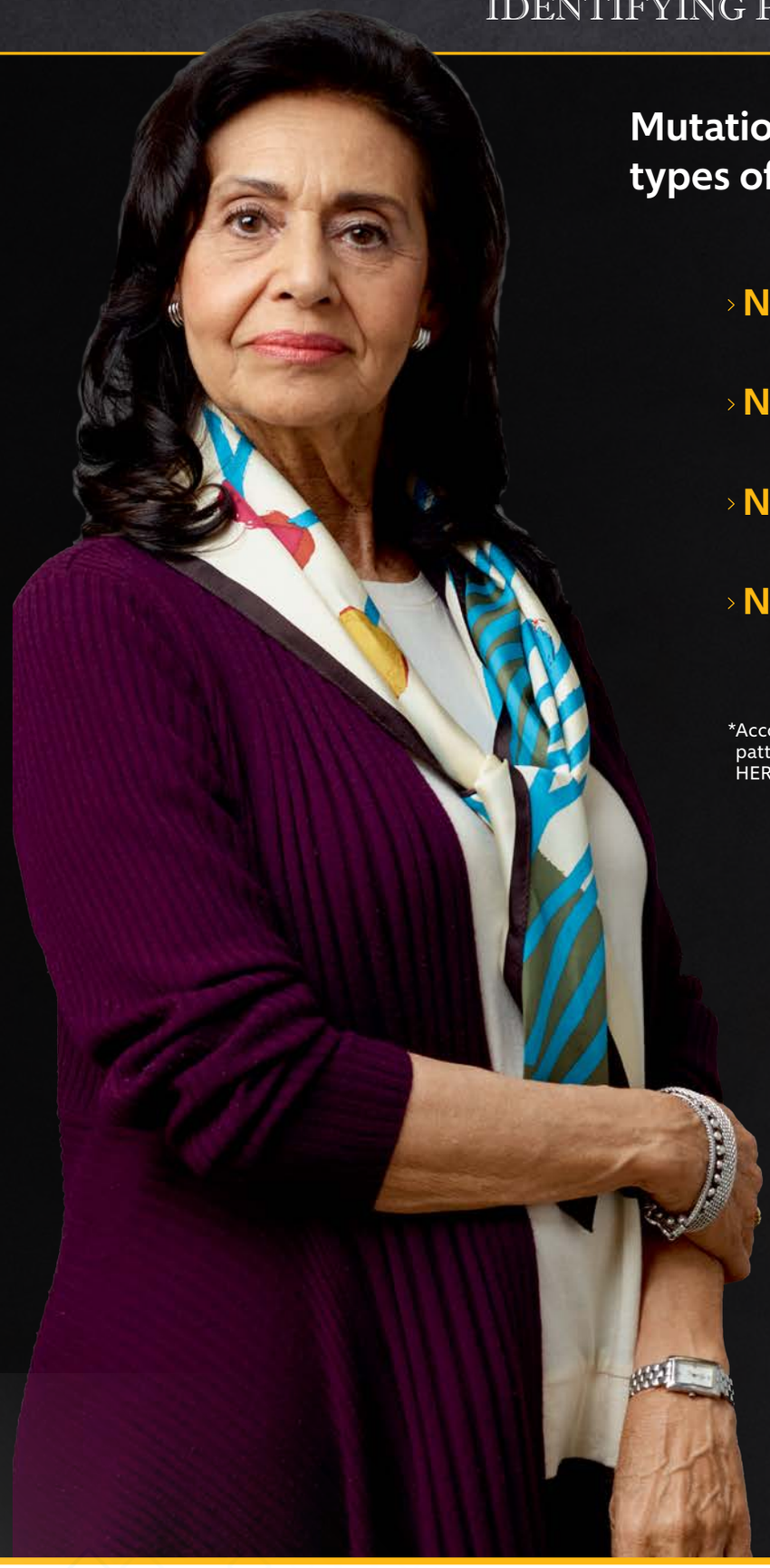

Mutations in g*BRCA* may be present in many types of patients with MBC[4*]

- Not all have triple-negative disease
- Not all are young
- Not all are white
- Not all are women

*According to a retrospective real-world analysis of clinical outcomes, treatment patterns, and health resource utilization among 229 patients diagnosed with HER2- g*BRCA*1/2-mutated MBC, between January 2011 and February 2018.[4]

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IMPORTANT SAFETY INFORMATION (continued)

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.

Test patients with recurrent or metastatic breast cancer for g*BRCA*1/2 mutations to inform treatment planning[5]

Assess for g*BRCA* Mutations to Inform Treatment Planning[5]

- All patients with recurrent or metastatic breast cancer should be assessed for g*BRCA*1/2 mutations to identify candidates for PARP inhibitor therapy.[5]

Talazoparib (TALZENNA®) received a Category 1 recommendation from the National Comprehensive Cancer Network® (NCCN®)[5]

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.

IMPORTANT SAFETY INFORMATION (continued)

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.

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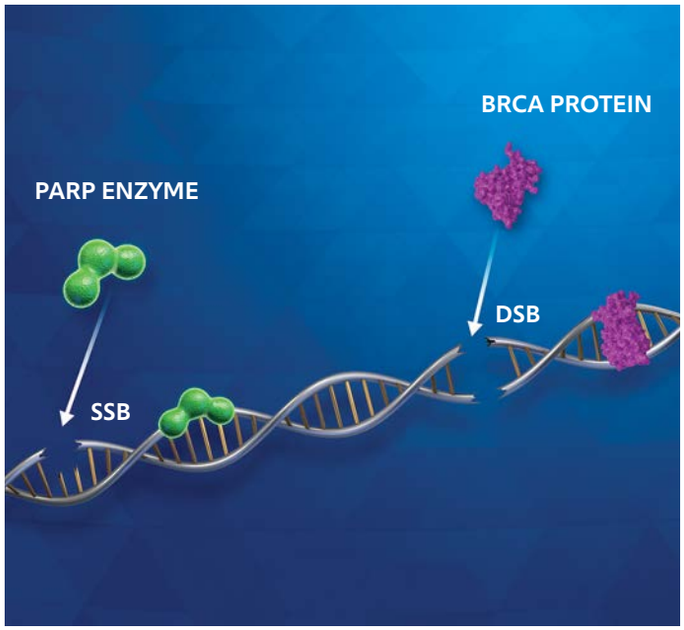
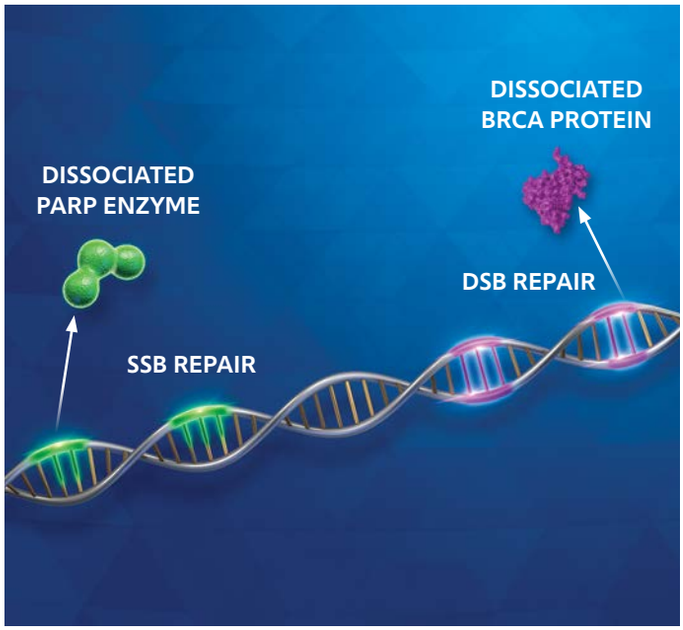
PARP enzymes and BRCA1/2 proteins both function in DNA repair[6,7]

NORMAL CELLS





In normal cells

- The role of PARP enzymes is to repair single-strand breaks (SSBs) in DNA generated during DNA replication or by DNA damage[6]
- The role of BRCA1/2 proteins is to repair double-strand breaks (DSBs) in DNA via a repair mechanism called homologous recombination (HR)[7]

IMPORTANT SAFETY INFORMATION (continued)

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.

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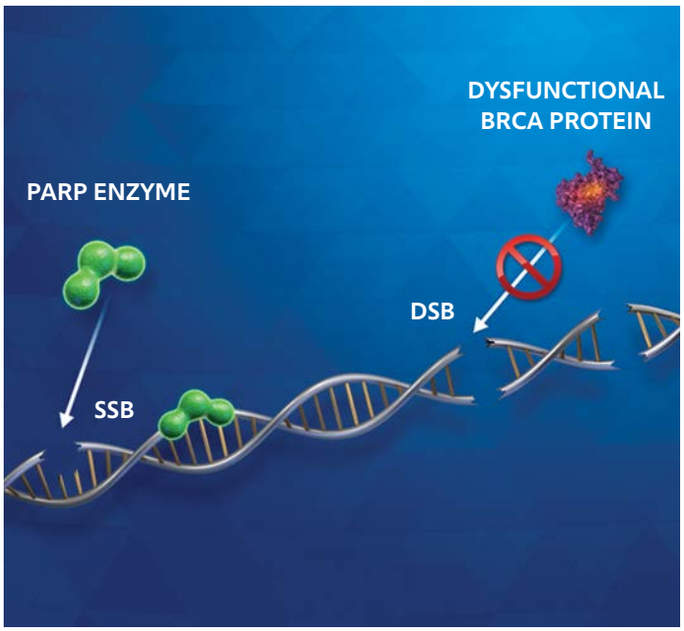
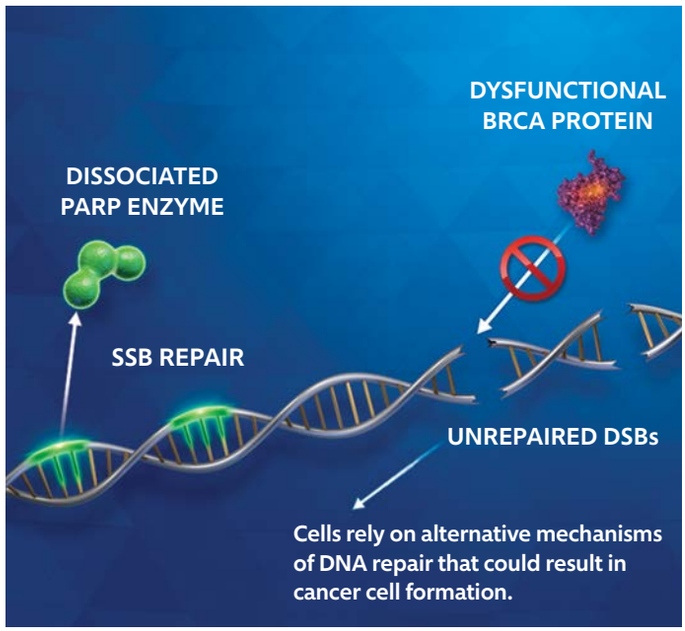
CANCER CELLS





In cancer cells

- In g*BRCA*-mutated cells, HR, the mechanism that repairs harmful DSBs in DNA, is defective[7,8]
- These cells become reliant on PARP enzymes, in addition to other, less accurate repair mechanisms, to maintain DNA repair and cell proliferation[7,8]
- Cancer cell overreliance on these alternative repair mechanisms can lead to the accumulation of genetic mutations, promoting the formation and survival of tumor cells[8]

IMPORTANT SAFETY INFORMATION (continued)

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%).

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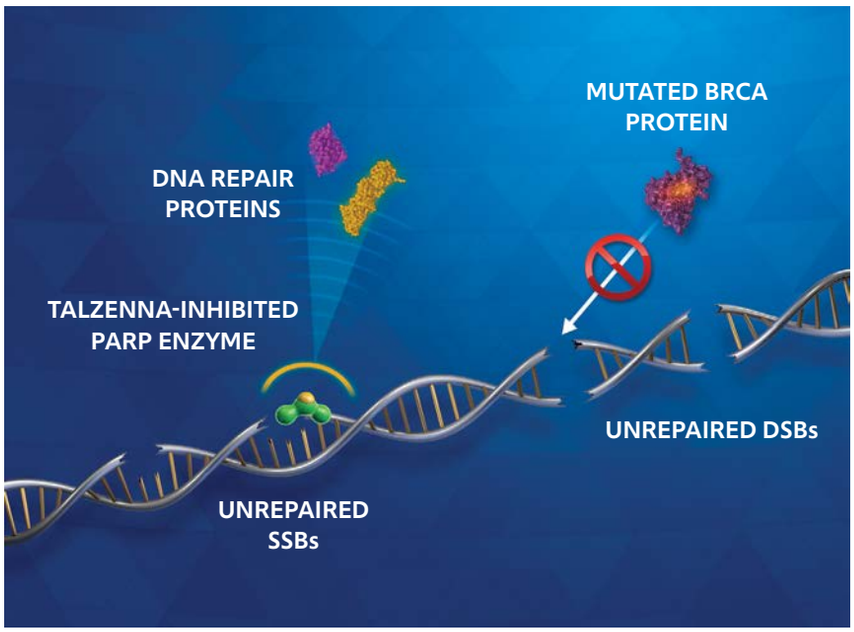
TALZENNA is a targeted treatment that induces cancer cell death via 2 complementary mechanisms[1]*

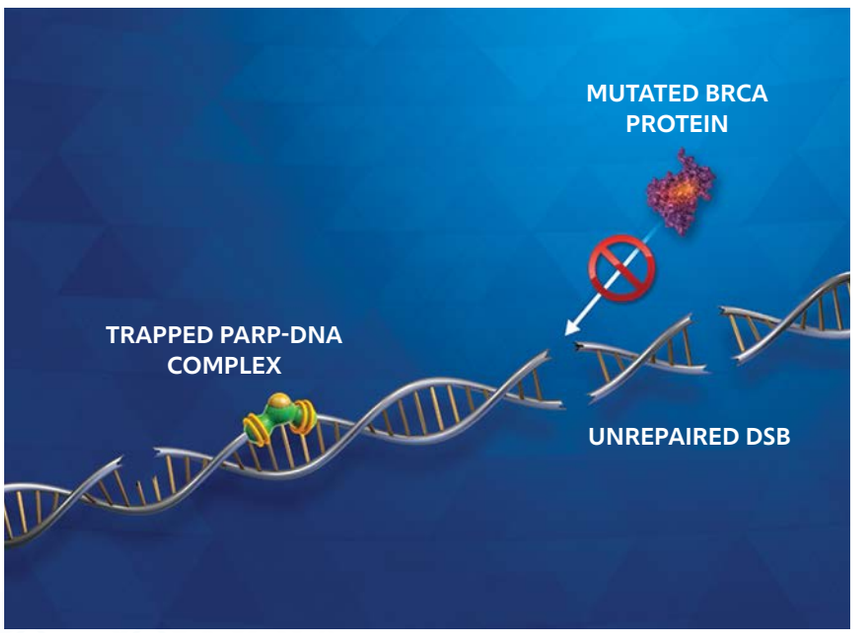
PARP ENZYME INHIBITION



- PARP enzymatic inhibition disrupts the subsequent recruitment of DNA repair proteins to the site of SSBs. This results in the accumulation of SSBs, which eventually leads to DSBs during DNA replication[9,10]
- In vitro studies demonstrated that *BRCA*1/2-mutated, HR-deficient cells are highly sensitive to cell death induced by TALZENNA[10,11]

*TALZENNA can also affect healthy cells.

HIGHLY POTENT PARP TRAPPING



- Preclinical studies have shown that TALZENNA has the capacity to trap PARP enzymes to DNA, forming PARP-DNA complexes[10,11]
- In preclinical studies, TALZENNA demonstrated highly potent PARP trapping, which may be correlated with tumor cell death[10,11]

IMPORTANT SAFETY INFORMATION (continued)

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%).

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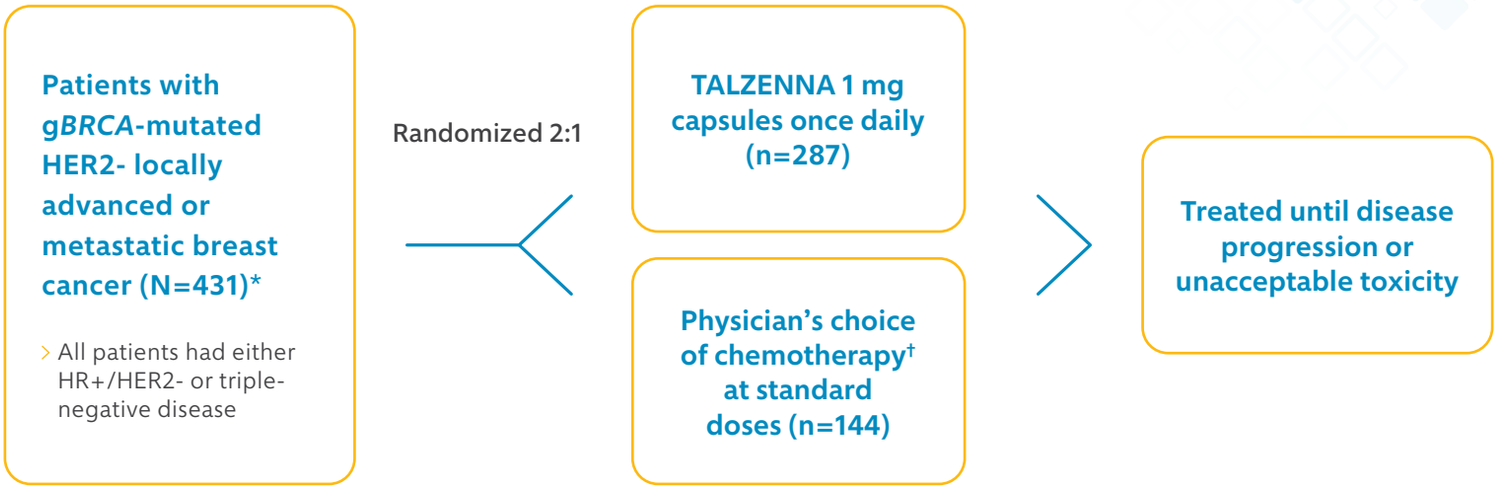
EMBRACA: the largest Phase 3, open-label study of a PARP inhibitor monotherapy in g*BRCA*-mutated HER2- locally advanced or metastatic breast cancer[1-3]



› **Additional inclusion criteria:**

- Patients received 0, 1, 2, or 3 prior cytotoxic chemotherapy regimens for locally advanced or metastatic 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 treated with prior platinum therapy for advanced disease were required to have no evidence of disease progression during platinum therapy
- No prior treatment with a PARP inhibitor was permitted

› **Randomization stratified by:**

- Prior lines of chemotherapy for locally advanced or metastatic disease (0 vs 1, 2, or 3)
- Hormone receptor status (HR+/HER2- vs TNBC)
- History of CNS metastases (yes vs no)

Primary endpoint[12]	Secondary endpoints included[12]	Exploratory endpoints included[12]
› PFS per RECIST v1.1, as assessed by BICR	› Objective response rate (ORR) › Overall survival (OS) › Safety	› Duration of response (DoR) for objective responders

BICR=blinded independent central review; CNS=central nervous system; RECIST=Response Evaluation Criteria in Solid Tumors; TNBC=triple-negative breast cancer.
*Patients had a deleterious or suspected deleterious g*BRCA* mutation detected using a clinical trial assay.
†Capecitabine, eribulin, gemcitabine, or vinorelbine.

IMPORTANT SAFETY INFORMATION (continued)

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%).

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TALZENNA was evaluated in a broad range of patients[3]

Baseline characteristics (ITT population)

	TALZENNA (n=287)	Chemotherapy (n=144)
Demographics		
Age, median (range), y[1]	46 (28.0-84.0)	51 (24.0-89.0)
<50 y, No. (%)	182 (63.4)	67 (46.5)
Female, (%)	98.6	97.9
Clinical status		
Stage of breast cancer (BC)		
Locally advanced, No. (%)	15 (5.2)	9 (6.2)
Metastatic, No. (%)	271 (94.4)	135 (93.8)
ECOG PS 0/1/2, (%)	53.3/44.3/2.1	58.3/39.6/1.4
Measurable disease by investigator, No. (%)	219 (76.3)	114 (79.2)
History of CNS metastases, No. (%)	43 (15.0)	20 (13.9)
Visceral disease, No. (%)	200 (69.7)	103 (71.5)
Disease-free interval (initial diagnosis to ABC) <12 months, No. (%)	108 (37.6)	42 (29.2)
Hormone receptor status, No. (%)		
TNBC	130 (45.3)	60 (41.7)
HR+	157 (54.7)	84 (58.3)
BRCA* status, No. (%)		
*BRCA*1+	133 (46.3)	63 (43.8)
*BRCA*2+	154 (53.7)	81 (56.2)
Prior treatment		
Prior adjuvant/neoadjuvant therapy, No. (%)	238 (82.9)	121 (84.0)
No. of previous hormone-therapy–based regimens for HR+ BC in the TALZENNA group (n=157) and the standard-therapy group (n=84), Median (range)	2.0 (0-6)	2.0 (0-6)
Prior platinum therapy, No. (%)	46 (16.0)	30 (20.8)
Prior cytotoxic regimens for ABC, No. (%)		
0	111 (38.7)	54 (37.5)
1	107 (37.3)	54 (37.5)
2	57 (19.9)	28 (19.4)
3	12 (4.2)	8 (5.6)

The majority of patients (76%) had received 0 or 1 chemotherapy regimens for locally advanced or metastatic breast cancer prior to receiving TALZENNA (38.7% received 0 prior regimens and 37.3% received 1 prior regimen)[3]

ABC=advanced breast cancer; ECOG PS=Eastern Cooperative Oncology Group performance status; ITT=intent-to-treat.
*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.

IMPORTANT SAFETY INFORMATION (continued)

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.

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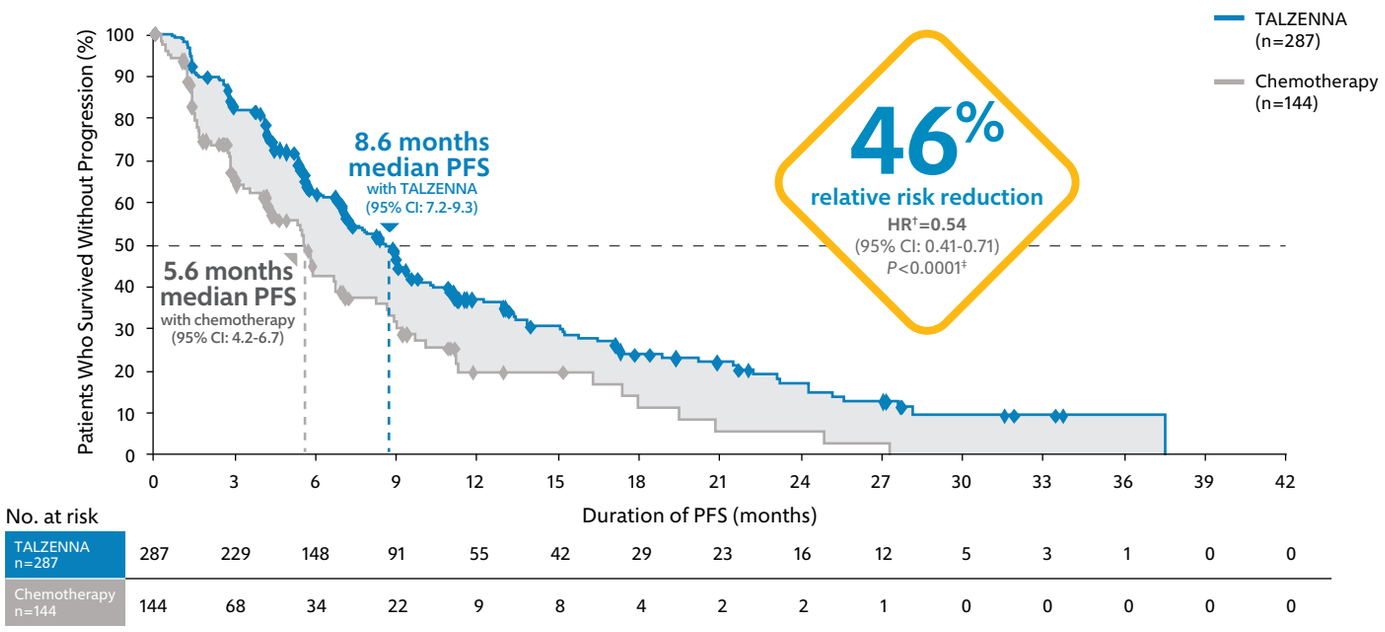
TALZENNA was superior to chemotherapy* in delaying disease progression[1]

Kaplan-Meier Curves of PFS



No. at risk

TALZENNA n=287	287	229	148	91	55	42	29	23	16	12	5	3	1	0	0
Chemotherapy n=144	144	68	34	22	9	8	4	2	2	1	0	0	0	0	0

*Capecitabine, eribulin, gemcitabine, vinorelbine.
†Hazard ratio is estimated from a Cox proportional hazards model stratified by prior use of chemotherapy for metastatic disease (0 vs 1, 2, or 3), by TNBC status (TNBC vs non-TNBC), and by history of CNS metastasis (yes vs no).
‡*P* values from stratified log-rank test (2-sided).

› **Nearly twice as many patients remained on TALZENNA without disease progression or death at 1 year vs chemotherapy (37% vs 20%)[3]**

IMPORTANT SAFETY INFORMATION (continued)

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.

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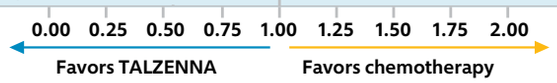
Consistent PFS results were observed across patient subgroups defined by number of prior cytotoxic regimens, hormone receptor status (HR+ or TNBC), and history of CNS metastases[1]

PFS according to prespecified subgroups[3]

› The below table depicts subgroup analyses from the overall EMBRACA study population. Small patient numbers can be a limitation of subgroup analyses. These analyses are not intended to demonstrate efficacy in particular subgroups

SUBGROUP	PATIENT, n (%)	HAZARD RATIO (95% CI)
All patients	431 (100.0)	0.54 (0.41-0.71)
***BRCA* mutation type, according to central testing**		
*BRCA*1	183 (42.5)	0.59 (0.39-0.90)
*BRCA*2	225 (52.2)	0.47 (0.32-0.70)
Hormone receptor status according to most recent biopsy		
TNBC	190 (44.1)	0.60 (0.41-0.87)
HR+	241 (55.9)	0.47 (0.32-0.71)
History of CNS metastasis		
Yes	63 (14.6)	0.32 (0.15-0.68)
No	368 (85.4)	0.58 (0.43-0.78)
Visceral disease assessed by investigator		
Yes	303 (70.3)	0.51 (0.37-0.70)
No	128 (29.7)	0.59 (0.34-1.02)
Previous platinum treatment		
Yes	76 (17.6)	0.76 (0.40-1.45)
No	355 (82.4)	0.52 (0.39-0.71)
Previous regimens of cytotoxic chemo for ABC		
0	165 (38.3)	0.57 (0.34-0.95)
1	161 (37.4)	0.51 (0.33-0.80)
≥2	105 (24.4)	0.56 (0.34-0.95)



SELECTED SAFETY INFORMATION

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) have been reported in patients who received TALZENNA. Overall, MDS/AML has been reported in <1% (3 out of 787, 0.4%) of solid tumor patients treated with TALZENNA in clinical studies. The duration of TALZENNA treatment in these three patients prior to developing MDS/AML was 4 months, 24 months, and 60 months respectively. These patients had received previous chemotherapy with platinum agents and/or other DNA damaging agents including radiotherapy.

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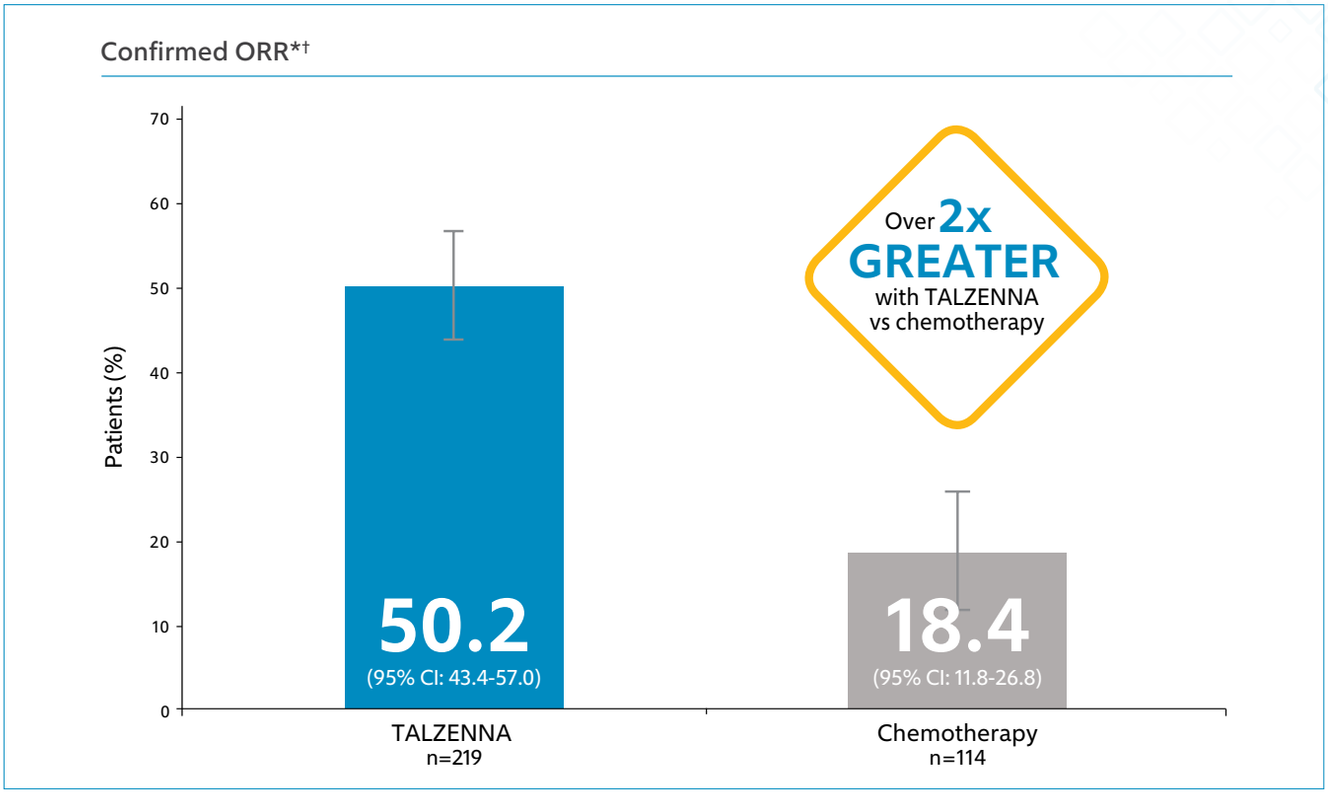
TALZENNA more than doubled ORR vs chemotherapy[1]



› **Unconfirmed ORR†‡**—Unconfirmed ORR was 62.6% (95% CI: 55.8-69.0) for patients treated with TALZENNA vs 27.2% (95% CI: 19.3-36.3) for patients treated with chemotherapy[1,3,13]

- **Complete response†‡**—5.5% achieved a complete response with TALZENNA vs 0% with chemotherapy[1,13]
- **Partial response†‡**—57.1% achieved a partial response with TALZENNA vs 27.2% with chemotherapy[1,13]

› **Time to response‡§**—Patients in both groups experienced a response at either the first or second imaging time point[3,12,13]

- At the first imaging time point (6 weeks ± 7 days), an objective response was observed in 44.5% and 45.2% of patients who experienced a response in the TALZENNA and chemotherapy arms, respectively
- At the second imaging time point (12 weeks ± 7 days), an objective response was observed in 35.0% and 35.5% of patients who experienced a response in the TALZENNA and chemotherapy arms, respectively
- The median time to response was 2.6 months for the TALZENNA group and 1.7 months for the chemotherapy group[3]

› **Final OS analysis did not reach statistical significance[14]**

- **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)

*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 ITT population with measurable disease at baseline.
‡Includes patients with confirmed and unconfirmed responses.
§Analyzed in the ITT patients who experienced an objective response as assessed by the investigator.

SELECTED SAFETY INFORMATION

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.

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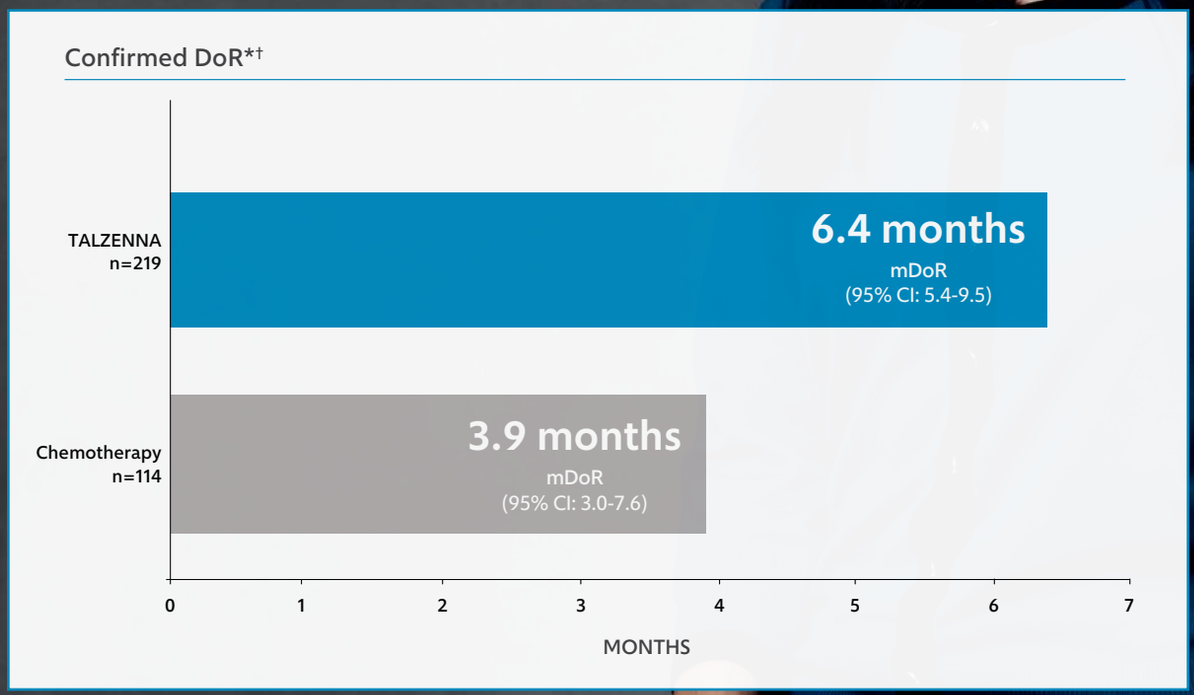
Median DoR (mDoR) was longer with TALZENNA vs chemotherapy[1*†]



*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.
†Analyzed in the ITT patients who experienced an objective response as assessed by the investigator.

SELECTED SAFETY INFORMATION

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.

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TALZENNA offers proven safety and tolerability

Adverse Reactions* (in ≥20% of Patients Receiving TALZENNA) in EMBRACA[1]

Adverse Reactions	TALZENNA n=286 (%)			Chemotherapy n=126 (%)		
	Grades 1-4	Grade 3	Grade 4	Grades 1-4	Grade 3	Grade 4
Blood and lymphatic system disorders						
Anemia†	53	38	1	18	4	1
Neutropenia‡	35	18	3	43	20	16
Thrombocytopenia§	27	11	4	7	2	0
Metabolism and nutrition disorders						
Decreased appetite	21	<1	0	22	1	0
Nervous system disorders						
Headache	33	2	0	22	1	0
Gastrointestinal disorders						
Nausea	49	<1	0	47	2	0
Vomiting	25	2	0	23	2	0
Diarrhea	22	1	0	26	6	0
Skin and subcutaneous tissue disorders						
Alopecia	25	0	0	28	0	0
General disorders and administration site conditions						
Fatigue‖	62	3	0	50	5	0

› 25.2% of patients who received TALZENNA experienced alopecia, of which 22.7% was Grade 1¶ (hair loss of <50%) and 2.4% was Grade 2# (hair loss of ≥50%), vs 27.8% of patients who received chemotherapy (19.8% Grade 1; 7.9% Grade 2)[1,12,15]

CTCAE=Common Terminology Criteria for Adverse Events; NCI=National Cancer Institute.
*Graded according to NCI CTCAE 4.03.
†Includes anemia, hematocrit decreased, hemoglobin decreased, and red blood cell count decreased.
‡Includes febrile neutropenia, neutropenia, and neutrophil count decreased.
§Includes thrombocytopenia and platelet count decreased.
‖Includes fatigue and asthenia.
¶Grade 1 defined as hair loss of <50% of normal for that individual that is not obvious from a distance but only on close inspection. A different hairstyle may be required to cover the hair loss, but it does not require a wig or hairpiece to camouflage.[15]
#Grade 2 defined as hair loss of ≥50% of normal for that individual that is readily apparent to others. A wig or hairpiece is necessary if the patient desires to completely camouflage the hair loss.[15]

SELECTED SAFETY INFORMATION

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.

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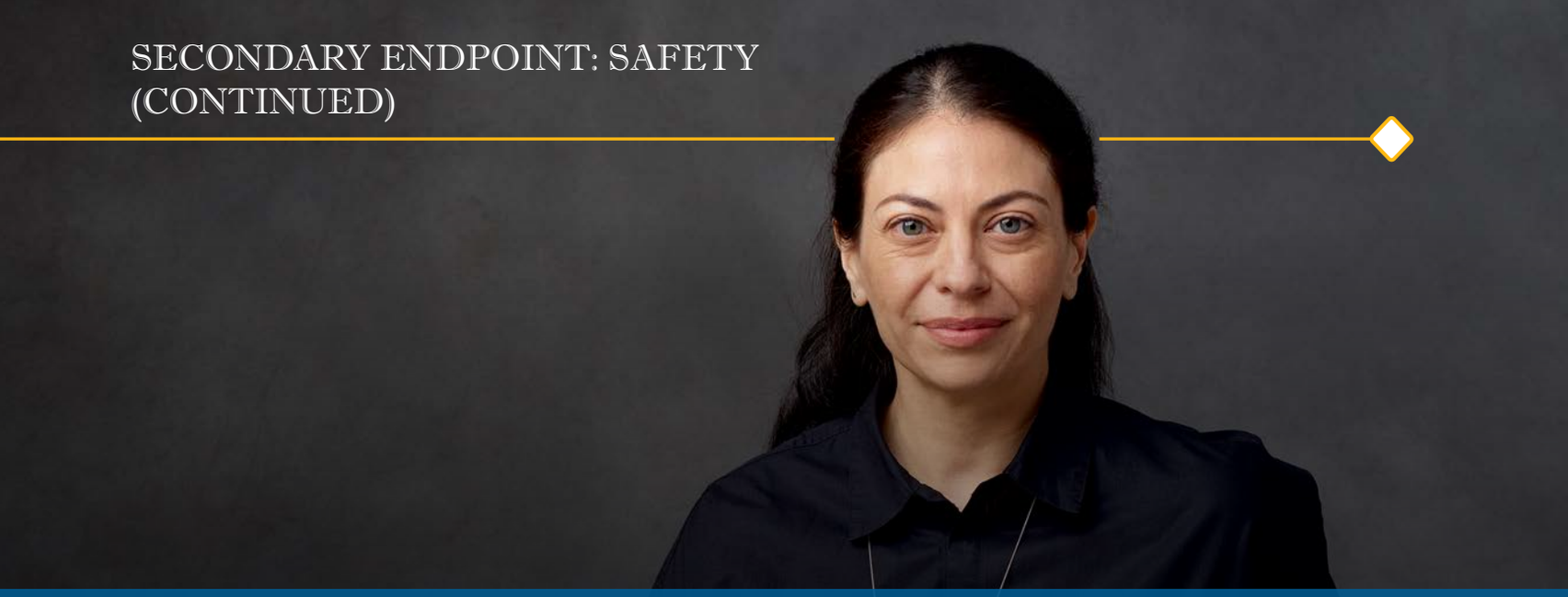
SECONDARY ENDPOINT: SAFETY (CONTINUED)



The most common **hematologic adverse reactions** to TALZENNA were **transient**[16]

With appropriate management, the median duration of Grade 3-4 anemia, neutropenia, and thrombocytopenia was **≤8 days vs ≤18 days** with chemotherapy[16]*

The majority of **nonhematologic** adverse reactions in the TALZENNA group were **Grade 1 in severity**[3]

95% of patients did not discontinue TALZENNA due to an adverse reaction[1]

- **Permanent discontinuation due to an adverse reaction** occurred in 5% of patients receiving TALZENNA vs 6% of patients on chemotherapy[1]
- Most adverse reactions were managed with dose interruption/reduction or standard supportive medical therapy[13,16]
- **The median time to first dose reduction due to an adverse reaction** was 19.3 weeks for TALZENNA vs 9.3 weeks with oral chemotherapy (capecitabine)[13,16]*
  - Dose interruptions due to an adverse reaction of any grade occurred in 65% of patients receiving TALZENNA and 50% of those receiving chemotherapy[1]
  - Dose reductions due to any cause occurred in 53% of TALZENNA patients and 40% of chemotherapy patients[1]

*Post hoc exploratory analysis included median time to first episode, duration, and time to recovery in EMBRACA. Post hoc exploratory analyses were conducted in the safety population with a data cutoff date of September 15, 2017.[16]

SELECTED SAFETY INFORMATION

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%).

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Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) have been reported in patients who received TALZENNA. Overall, MDS/AML has been reported in <1% (3 out of 787, 0.4%) of solid tumor patients treated with TALZENNA in clinical studies. The duration of TALZENNA treatment in these three patients prior to developing MDS/AML was 4 months, 24 months, and 60 months respectively. These 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.[1]

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.[1]

Embryo-fetal toxicity

Based on its mechanism of action and findings from animal data, TALZENNA can cause **fetal harm** when administered to a pregnant woman.[1]

- Apprise pregnant women and females of reproductive potential of the potential risk to a fetus[1]
- Advise females of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose of TALZENNA[1]
- Based on findings from genetic toxicity and animal reproduction studies, advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for at least 4 months following the last dose of TALZENNA[1]

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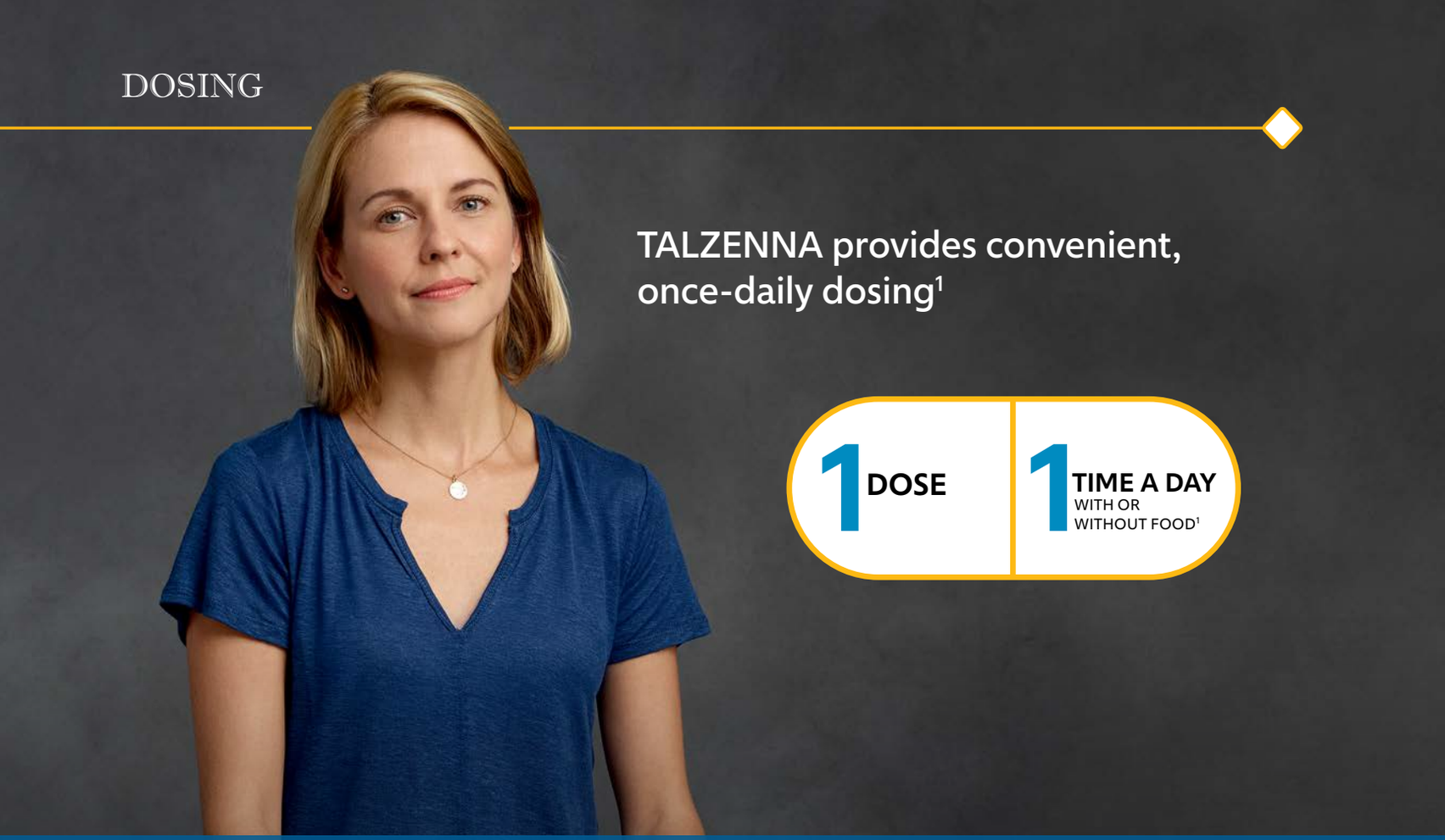
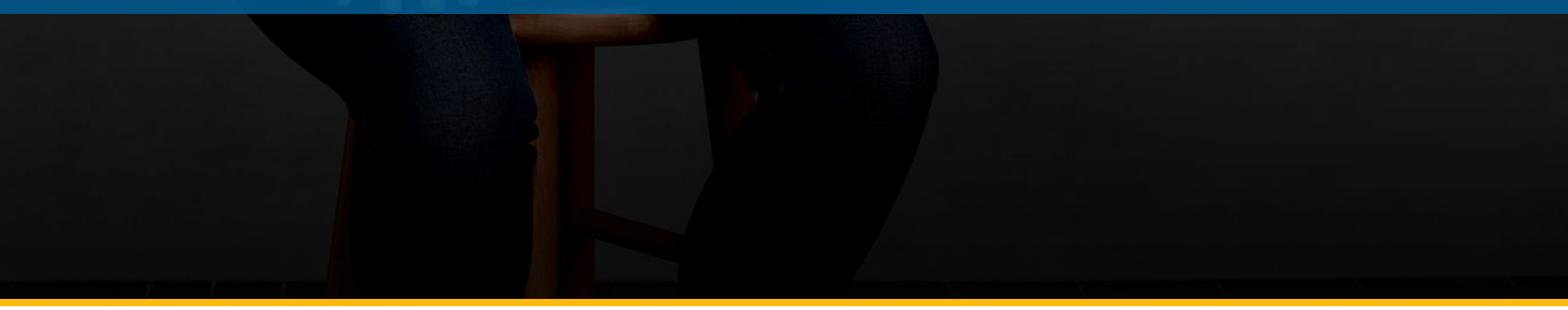


TALZENNA provides convenient, once-daily dosing[1]

1 DOSE

1 TIME A DAY WITH OR WITHOUT FOOD[1]

- The recommended starting dose of TALZENNA is 1 mg taken orally once daily, with or without food
- The 0.25 mg, 0.5 mg, and 0.75 mg capsules are available for dose reduction
- Patients should be treated until disease progression or unacceptable toxicity occurs
- The capsules should be swallowed whole and must not be opened or dissolved
- 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



SELECTED SAFETY INFORMATION

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%).

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TALZENNA® talazoparib 1 mg capsules

Dose modification for adverse reactions[1]

Monitor complete blood counts monthly and as clinically indicated.

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 Grade 3 or Grade 4	≤ Grade 1	Consider resuming TALZENNA at a reduced dose or discontinue

Dose modifications for patients with renal impairment[1]

- For patients with moderate renal impairment (CLcr 30-59 mL/min), the recommended dose of TALZENNA is 0.75 mg once daily
- For patients with severe renal impairment (CLcr 15-29 mL/min), the recommended dose of TALZENNA is 0.5 mg once daily

Dose modifications for use with P-glycoprotein (P-gp) inhibitors[1]

- Reduce the TALZENNA dose to 0.75 mg once daily when coadministered with certain P-gp inhibitors*
- 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

*In the clinical studies, coadministration with P-gp inhibitors including amiodarone, carvedilol, clarithromycin, itraconazole, and verapamil resulted in an approximate 45% increase in TALZENNA exposure and an increase in the rate of TALZENNA dose reduction.

SELECTED SAFETY INFORMATION

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%).

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TALZENNA® talazoparib 1 mg capsules

For patients who require dose modification, TALZENNA offers flexible dosing options[1]

Available in 4 capsule strengths:

1 mg capsule

0.25 mg, 0.5 mg, and 0.75 mg capsules

Capsules not actual size.

› To manage adverse reactions, consider interruption of treatment or dose reduction based on severity and clinical presentation

Once-daily dosing

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**

Treatment with TALZENNA should be discontinued if more than 3 dose reductions are required.

Broad access for patients

TALZENNA is covered for[13]:

96% of the commercially insured population*

100% of the Medicare Part D-insured population*

*TALZENNA is included on formulary/plan policies. Additional requirements may apply. Formulary data are current as of 11/2021.

SELECTED SAFETY INFORMATION

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.

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TALZENNA® talazoparib 1 mg capsules

Pfizer Oncology together™

Making your patients' support needs a priority. Together.

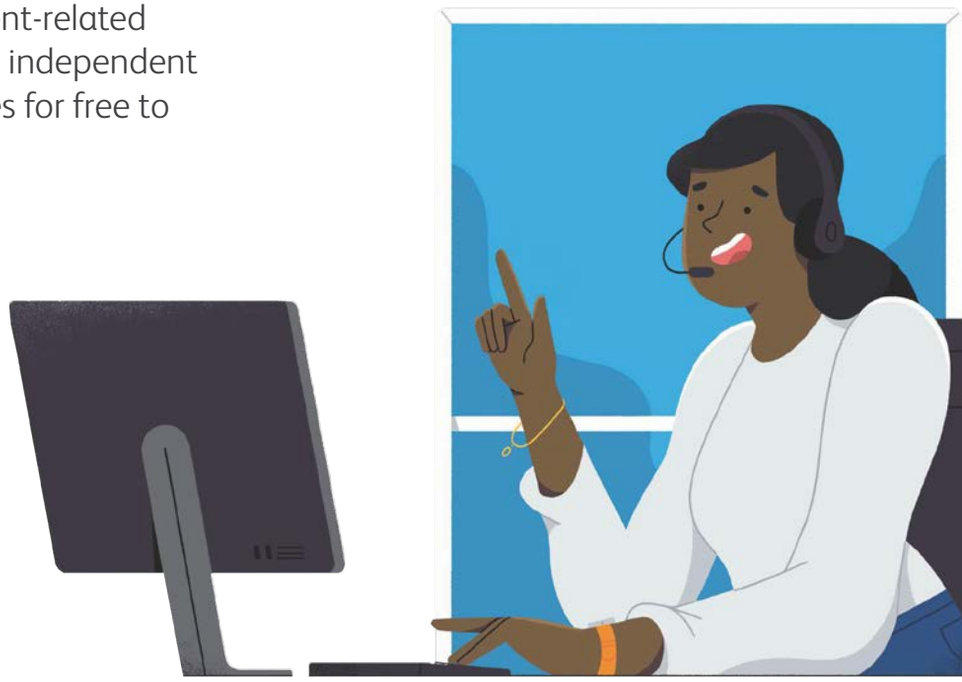
At Pfizer Oncology Together™, patient support is at the core of everything we do. We've gathered resources and developed tools to help patients and their loved ones throughout TALZENNA treatment.

PERSONALIZED PATIENT SUPPORT

When your patients need support for their day-to-day challenges, we want to be a place they can turn to for help. At Pfizer Oncology Together, our Care Champions, who have social work experience, can connect patients prescribed TALZENNA to resources that may help with some of their daily needs.*

- **Emotional Support** We can connect patients to diagnosis-specific support groups, an independent organization that offers short-term counseling, and a free app, developed by Pfizer Oncology, to help patients connect with loved ones and ask for the support they need
- **Educational Support** To help support patients' overall health and well-being, we've created resources about physical and mental health, as well as nutritional tips and healthy recipes developed in partnership with dietitians who specialize in oncology nutrition. We can also provide patients with information to help them understand their prescribed TALZENNA
- **Practical Support** If patients need assistance with transportation or lodging for treatment-related appointments, we'll connect them to independent organizations that offer these services for free to qualifying patients

  And if your patients are leaving work for a period of time during treatment, or preparing to return to work, we can send them information to help make the transition easier



FOR LIVE, PERSONALIZED SUPPORT
Call **1-877-744-5675** (Monday–Friday 8 AM–8 PM ET)

VISIT
PfizerOncologyTogether.com

*Some services are provided through third-party organizations that operate independently and are not controlled by Pfizer. Availability of services and eligibility requirements are determined solely by these organizations.

Finding financial support options. Together.

COMMERCIALLY INSURED

- Co-pay assistance: Eligible, commercially insured patients may pay as little as $0 per month for TALZENNA. Limits, terms, and conditions apply*

*Patients are not eligible to use this card if they are enrolled in a state or federally funded insurance program, including but not limited to Medicare, Medicaid, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico. Patients may receive up to $25,000 per product in savings annually. **The offer will be accepted only at participating pharmacies. This offer is not health insurance.** No membership fees apply. Pfizer reserves the right to rescind, revoke, or amend this offer without notice. For full Terms and Conditions, please see PfizerOncologyTogether.com/terms. For any questions, please call 1-877-744-5675, visit PfizerOncologyTogether.com/terms or write: Pfizer Oncology Together Co-Pay Savings Program, 2250 Perimeter Park Drive, Suite 300, Morrisville, NC 27560.

MEDICARE/GOVERNMENT INSURED

- Assistance for patients with searching for financial support that may be available from independent charitable foundations. These foundations exist independently of Pfizer and have their own eligibility criteria and application processes. Availability of support from the foundations is determined solely by the foundations
- Financial assistance through Extra Help, a Medicare Part D Low-Income Subsidy (LIS) program
- Free medication†

UNINSURED

- Help finding coverage
- Free medication for eligible patients through the Pfizer Patient Assistance Program

†If support from independent charitable foundations or Medicare Extra Help is not available, Pfizer Oncology Together will provide eligible patients with medication for free through the Pfizer Patient Assistance Program. The Pfizer Patient Assistance Program is a joint program of Pfizer Inc. and the Pfizer Patient Assistance Foundation™. The Pfizer Patient Assistance Foundation is a separate legal entity from Pfizer Inc. with distinct legal restrictions.

Navigating access and reimbursement. Together.

If patients need access or reimbursement support, Pfizer Oncology Together is here to help.

BENEFITS VERIFICATION

We can help determine a patient's coverage and out-of-pocket costs.

PRIOR AUTHORIZATIONS (PA)

We can coordinate with a patient's insurer to determine the PA requirements. After your office submits a PA request, we'll follow up with the payer until a final outcome is determined.

APPEALS ASSISTANCE

We can help you and your office staff understand the payer requirements as you prepare an appeal submission. After your office submits an appeal, we'll follow up with the payer to track its progress until a final outcome is determined.

SPECIALTY PHARMACY COORDINATION

To help your patients access the medication you've prescribed, we can identify specialty pharmacy options. If you prefer, you and your staff can also continue to work directly with specialty pharmacies.

INDICATION

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.

GIVE THEM A BIOMARKER-DRIVEN TREATMENT THAT'S

Just for them

TALZENNA was proven superior to chemotherapy* for patients with a g*BRCA* mutation and HR+/HER2- or triple-negative locally advanced or metastatic breast cancer[1,3]

- TALZENNA demonstrated both **PARP enzyme inhibition** and **highly potent PARP trapping** in preclinical studies[1,11]
- **TALZENNA significantly outperformed chemotherapy in PFS**: median of 8.6 months (95% CI: 7.2-9.3) vs 5.6 months (95% CI: 4.2-6.7) (HR=0.54 [95% CI: 0.41-0.71]; *P*<0.0001)[1]
- **Confirmed ORR†‡ more than doubled** with TALZENNA compared with chemotherapy: 50.2% (95% CI: 43.4-57.0) vs 18.4% (95% CI: 11.8-26.8)[1,3,13]
- **Final OS analysis did not reach statistical significance**[14]
  - **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)
- **Median DoR†§ was longer with TALZENNA vs chemotherapy**: 6.4 months (95% CI: 5.4-9.5) vs 3.9 months (95% CI: 3.0-7.6)[1,3]
- **WARNINGS AND PRECAUTIONS:** TALZENNA is associated with serious, potentially fatal risks, including MDS/AML, myelosuppression, and embryo-fetal toxicity.[1] Please see Warnings and Precautions on page 15
- 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%)[1]

1 DAILY DOSE with or without food[1]

*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 as assessed by the investigator.

References: 1. TALZENNA [prescribing information]. New York, NY: Pfizer Inc.; 2021. **2.** Lynparza [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2019. **3.** 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. **4.** Quek RGW, Mardekian J. Clinical outcomes, treatment patterns, and health resource utilization among metastatic breast cancer patients with germline *BRCA1/2* mutation: a real-world retrospective study. *Adv Ther*. 2019;36(3):708-720. **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.8.2021. © 2021 National Comprehensive Cancer Network, Inc. All rights reserved. Accessed October 7, 2021. 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 their content, use or application and disclaims any responsibility for their application or use in any way. **6.** Sonnenblick A, de Azambuja E, Azim HA Jr, Piccart M. An update on PARP inhibitors—moving to the adjuvant setting. *Nat Rev Clin Oncol*. 2015;12(1):27-41. **7.** Lee J-m, Ledermann JA, Kohn EC. PARP inhibitors for BRCA1/2 mutation-associated and BRCA-like malignancies. *Ann Oncol*. 2014;25(1):32-40. **8.** Lupo B, Trusolino L. Inhibition of poly(ADP-ribosyl)ation in cancer: old and new paradigms revisited. *Biochim Biophys Acta*. 2014;1846(1):201-215. **9.** Livraghi L, Garber JE. PARP inhibitors in the management of breast cancer: current data and future prospects. *BMC Med*. 2015;13:188. doi:10.1186/s12916-015-0425-1. **10.** Gavande NS, VanderVere-Carozza PS, Hinshaw HD, et al. DNA repair targeted therapy: the past or future of cancer treatment? *Pharmacol Ther*. 2016;160:65-83. **11.** Murai J, Huang SY, Renaud A, et al. Stereospecific PARP trapping by BMN 673 and comparison with olaparib and rucaparib. *Mol Cancer Ther*. 2014;13(2):433-443. **12.** 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. **13.** Data on file. Pfizer Inc., New York, NY. **14.** 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 Aug 20. doi:org/10.1016/j.annonc.2020;31(11):1526-1535. **15.** National Institutes of Health, US Department of Health and Human Services. *Common Terminology Criteria for Adverse Events (CTCAE)*. Bethesda, MD: National Institutes of Health. Version 5.0. Published November 2017. **16.** Hurvitz SA, Gonçalves A, Rugo HS, et al. Talazoparib in Patients with a Germline *BRCA*-Mutated Advanced Breast Cancer: Detailed Safety Analyses from the Phase III EMBRACA Trial. *Oncologist*. 2020;25(3):e439-e450.

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