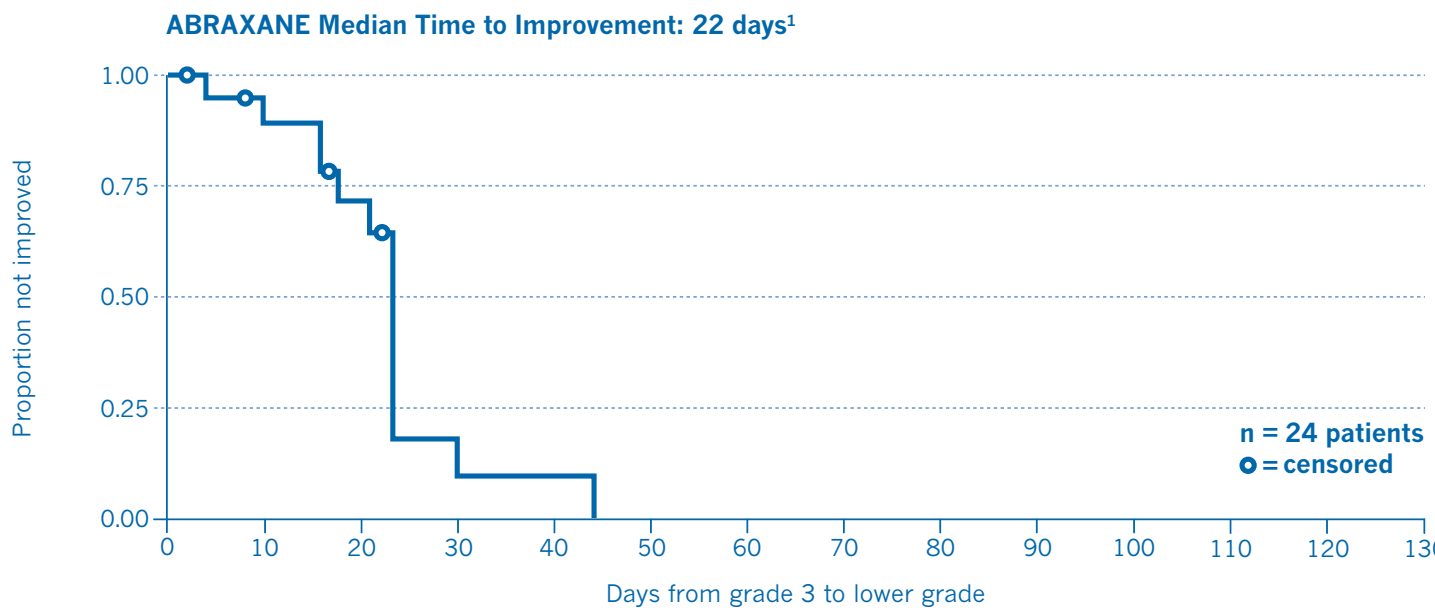
Time to improvement in sensory neuropathy

ABRAXANE® for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.



Improvement in neuropathy score following treatment interruption in 24 ABRAXANE-treated patients who experienced a grade 3 sensory neuropathy adverse event. From an international, randomized, open-label, phase III study comparing treatment with ABRAXANE (260 mg/m² IV over 30 minutes; n=229) vs polyethylated castor oil-based paclitaxel (175 mg/m² IV over 3 hours; n=225) in patients with metastatic breast cancer. Patients were treated every 3 weeks and assessed by imaging at baseline; weeks 5, 9, and 15; and at end of treatment. The primary efficacy measure was overall response rate (ORR).[1]

- **58% (14/24) of ABRAXANE-treated patients who developed grade 3 neuropathy showed documented improvement after a median of 22 days, often allowing a resumption of therapy at a reduced dose[2]**
- **Frequency of severe neuropathy was 10% for ABRAXANE vs 2% for solvent-based paclitaxel[2]**
- **3% (7/229) of patients discontinued ABRAXANE due to sensory neuropathy vs 1% (2/225) for solvent-based paclitaxel[2]**

Deliver a 49% higher dose of paclitaxel than solvent-based paclitaxel without compromising safety[2]

Frequency[a] % of selected treatment-emergent side effects[2]

		ABRAXANE (n=229) 260 mg/m² 30-minute infusion time	**Solvent-based paclitaxel** (n=225) 175 mg/m² 3-hour infusion time[b]
Neutropenia	<2.0 x 10^9/L	80	82
	<0.5 x 10^9/L	9	22
Hypersensitivity reactions[c]*	All	4	12
	Severe[d]	0	2
Sensory neuropathy	Any	71	56
	Severe[d]	10	2
Myalgia/arthralgia	Any	44	49
	Severe[d]	8	4
Gastrointestinal	Nausea - Any	30	22
	- Severe[d]	3	<1
	Vomiting - Any	18	10
	- Severe[d]	4	1
	Diarrhea - Any	27	15
	- Severe[d]	<1	1
Alopecia		90	94

[a]Based on worst grade, [b]paclitaxel injection patients received premedication, [c]includes treatment-related events related to hypersensitivity (eg, flushing, dyspnea, chest pain, hypotension) that began on a day of dosing, [d]severe events are defined as at least grade 3 toxicity.[1]

*>99% of patients treated with solvent-based paclitaxel received premedication vs 8% of patients treated with ABRAXANE.[1]

WARNING: ABRAXANE for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) should be administered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

ABRAXANE therapy should not be administered to patients with metastatic breast cancer who have baseline neutrophil counts of less than 1,500 cells/mm³. In order to monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving ABRAXANE.

Note: An albumin form of paclitaxel may substantially affect a drug's functional properties relative to those of drug in solution. DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS.

IMPORTANT SAFETY INFORMATION

The use of ABRAXANE has not been studied in patients with hepatic or renal dysfunction. In the randomized controlled trial, patients were excluded for baseline serum bilirubin >1.5 mg/dL or baseline serum creatinine >2 mg/dL.

ABRAXANE can cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with ABRAXANE.

Men should be advised to not father a child while receiving treatment with ABRAXANE.

It is recommended that nursing be discontinued when receiving ABRAXANE therapy.

ABRAXANE contains albumin (human), a derivative of human blood.

Caution should be exercised when administering ABRAXANE concomitantly with known substrates or inhibitors of CYP2C8 and CYP3A4.

ABRAXANE therapy should not be administered to patients with metastatic breast cancer who have baseline neutrophil counts of less than 1,500 cells/mm³. It is recommended that frequent peripheral blood cell counts be performed on all patients receiving ABRAXANE. Patients should not be retreated with subsequent cycles of ABRAXANE until neutrophils recover to a level >1,500 cells/mm³ and platelets recover to a level >100,000 cells/mm³.

In the case of severe neutropenia (<500 cells/mm³ for 7 days or more) during a course of ABRAXANE therapy, a dose reduction for subsequent courses is recommended.

Sensory neuropathy occurs frequently with ABRAXANE.

If grade 3 sensory neuropathy develops, treatment should be withheld until resolution to grade 1 or 2 followed by a dose reduction for all subsequent courses of ABRAXANE.

Severe cardiovascular events possibly related to single-agent ABRAXANE occurred in approximately 3% of patients in the randomized trial. These events included chest pain, cardiac arrest, supraventricular tachycardia, edema, thrombosis, pulmonary thromboembolism, pulmonary embolism, and hypertension.

In the randomized metastatic breast cancer study, the most important adverse events included alopecia (90%), neutropenia (all cases 80%; severe 9%), sensory neuropathy (any symptoms 71%; severe 10%), asthenia (any 47%; severe 8%), myalgia/arthralgia (any 44%; severe 8%), anemia (all 33%; severe 1%), infections (24%), nausea (any 30%; severe 3%), vomiting (any 18%; severe 4%), diarrhea (any 27%; severe <1%), and mucositis (any 7%; severe <1%).

Other adverse reactions have included ocular/visual disturbances (any 13%; severe 1%), fluid retention (any 10%; severe 0%), hepatic dysfunction (elevations in bilirubin 7%, alkaline phosphatase 36%, AST [SGOT] 39%), renal dysfunction (any 11%; severe 1%), thrombocytopenia (any 2%; severe <1%), hypersensitivity reactions (any 4%; severe 0%), cardiovascular reactions (severe 3%), and injection site reactions (<1%). During postmarketing surveillance, rare occurrences of severe hypersensitivity reactions have been reported with ABRAXANE.

Please click here for the ABRAXANE full prescribing information.

References: 1. Gradishar WJ, Tjulandin S, Davidson N, et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. *J Clin Oncol.* 2005;23:7794-7803. **2.** ABRAXANE [prescribing information]. Los Angeles, Calif: Abraxis Oncology, a division of Abraxis BioScience, Inc; August 2007.

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Abraxis Oncology

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