Department:	Pharmacy Management	**Original Approval:**	12/24/2015
Policy #:	PM110	**Last Approval:**	03/14/2019
Title:	Nanoparticle albumin bound paclitaxel (Abraxane®)		
Approved By:	UM Committee		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for Nanoparticle albumin bound paclitaxel (Abraxane): History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis - Medication list (current and past) to include start and end dates of previous trials for all chemotherapy regimens -Prescribed by or in consultation with an oncologist -Labs/diagnostics -Height -Weight -Dosing and duration requested.

BACKGROUND

Abraxane is indicated for the following uses:[1]

1. 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 contraindicated); AND
2. Non-small cell lung cancer (NSCLC) in combination with carboplatin injection for the first-line treatment of locally advanced or metastatic disease in patients who are not candidates for curative surgery or radiation therapy; AND
3. Adenocarcinoma of the pancreas in combination with gemcitabine injection for the first-line treatment of patients with metastatic disease.

Premedication to prevent hypersensitivity reactions is generally not needed before giving Abraxane.

Abraxane, a microtubule inhibitor, is an albumin-bound form of paclitaxel.[1] This formulation of paclitaxel uses nanotechnology to combine human albumin with paclitaxel allowing for the delivery of insoluble paclitaxel in the form of nanoparticles.

Abraxane is available as a lyophilized powder in single-use vials containing 100 mg of paclitaxel bound to approximately 900 mg of human albumin.[1] Abraxane must be reconstituted with 20 mL of 0.9% sodium chloride injection before use. The final solution will contain 5 mg of paclitaxel per mL. The appropriate amount of reconstituted Abraxane is injected into an empty, sterile intravenous bag and administered as a 30-minute intravenous infusion.

DEFINITIONS

None.

INDICATIONS/CRITERIA

Medicaid Members	***Continue to criteria for approval below.***
Medicare Members	***Step-utilization of Part D drugs not required.***

Coverage of Abraxane is recommended in those who meet one of the following criteria:

Food and Drug Administration (FDA)-Approved Indications

Breast Cancer.

1. Criteria. Approve for 1 year if the patient must meet the following criteria (A AND B):

A) Abraxane is prescribed by or in consultation with an oncologist; AND
The patient meets ONE of the following criteria (i or ii):

- **i.** The patient has recurrent or metastatic breast cancer and ONE of the following applies (a or b);[2]
  - **a)** The patient has human epidermal growth factor receptor 2 (HER2)-negative disease AND Abraxane will be used as a single agent; OR
  - **b)** The patient has human epidermal growth factor receptor 2 (HER2)-positive disease and meets the following criteria (1 and 2):
    - **(1)** The patient has previously received Herceptin® (trastuzumab intravenous infusion); AND
    - **(2)** Abraxane will be used in combination with Herceptin (trastuzumab intravenous infusion);

  OR
- **ii.** Abraxane is being used for preoperative or adjuvant therapy and the following criteria apply (a and b);[2]
  - **a)** The patient has had a hypersensitivity reaction to paclitaxel or docetaxel; AND
  - **b)** Abraxane will be used as part of a regimen for human epidermal growth factor receptor 2 (HER2)-negative disease OR as part of a regimen for HER2-positive disease that includes Herceptin (trastuzumab intravenous infusion).

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines on breast cancer (version 3.2018) recommend Abraxane as a single agent for recurrent or metastatic HER2-negative disease in patients with symptomatic visceral disease or visceral crisis or that is either hormone receptor negative or hormone receptor positive and endocrine therapy refractory (category 2A).[2-3] Abraxane is not in the list of "preferred single agents". Abraxane is also recommended in combination with Herceptin for HER2-positive recurrent or metastatic Herceptin-exposed disease with symptomatic visceral disease or visceral crisis or that is hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory (category 2A). For Herceptin-exposed HER2-positive disease, Herceptin can be combined with non-anthracycline agents listed as preferred or other singles agents. This would include paclitaxel, docetaxel, and Abraxane. Abraxane may be substituted for paclitaxel or docetaxel in patients with a

hypersensitivity reaction. Paclitaxel or docetaxel are recommended in many preoperative/adjuvant therapy regimens for HER2-negative or -positive disease and in chemotherapy regimens for recurrent or metastatic breast cancer. If substituted for weekly paclitaxel or docetaxel, the weekly dose of Abraxane should not be greater than 125 mg/m^2. Abraxane is not included in preoperative/adjuvant regimens for HER2-positive or HER2-negative disease. However, in patients with a hypersensitivity reaction to paclitaxel or docetaxel, Abraxane could be used.

A summary of the clinical trials comparing Abraxane with paclitaxel in metastatic breast cancer is included in Appendix A.

Dosing in Recurrent or Metastatic Breast Cancer in Adults. *Dosing must meet ONE of the following (A OR B)*:

- **A)** 260 mg per m^2 given as an intravenous infusion every 3 weeks.[1-2,4]
- **B)** 100 mg per m^2, 125 mg per m^2, or 150 mg per m2 given as an intravenous infusion on Days 1, 8 and 15, cycled every 28 days.[5-6, 17]

Note: Dose modifications are recommended for the management of toxicities and are determined by the prescribing physician. Dosing modifications are recommended in the prescribing information and are dependent on diagnosis, baseline hepatic function, concomitant therapy, patient variability, and toxicity.[1] Alternate dosing will be assessed individually on a case-by-case basis.

Duration of Therapy in Recurrent or Metastatic Breast Cancer. . Extended approvals are allowed if the patient continues to meet the conditions for coverage and dosing for breast cancer.

2. Non-Small Cell Lung Cancer (NSCLC). Approve for 1 year if the patient meets the following criteria (A, B, AND C):[1,7]

- **A)** Abraxane is prescribed by or in consultation with an oncologist; AND
- **B)** The patient has recurrent or metastatic non-small cell lung cancer (NSCLC); AND
- **C)** The patient has one of the following histologic subtypes of NSCLC (i or ii):
  - **i.** Non-squamous cell carcinoma (that is, adenocarcinoma, large cell, or NSCLC not otherwise specified) AND the following conditions are met (a, b, or c):
    - **a)** If the NSCLC tumor is positive for any of the targetable mutations (e.g., epidermal growth factor receptor [*EGFR*] mutation, anaplastic lymphoma kinase [*ALK*] fusions, ROS proto-oncogene 1 [*ROS1*]), at least one of the specific targeted therapy options have been tried and Abraxane is used as subsequent therapy; OR
    - **b)** If the NSCLC tumor is *BRAF V600E* mutation-positive, Abraxane is used as either first-line or subsequent therapy; OR
    - **c)** The NSCLC tumor is negative or unknown for targetable mutations (e.g., *EGFR*, *ALK*, *ROS1*, *BRAF*) and Abraxane is used as initial therapy either as a single agent or in combination with platinum chemotherapy (cisplatin or carboplatin) with or without an immune checkpoint inhibitor (e.g., Keytruda [pembrolizumab intravenous injection], Tecentriq [atezolizumab intravenous injection]); OR
  - **ii.** Squamous cell carcinoma and Abraxane is used as a single agent or in combination with platinum chemotherapy (cisplatin or carboplatin) with or without an immune checkpoint

inhibitor (e.g., Keytruda [pembrolizumab intravenous injection], Tecentriq [atezolizumab intravenous injection]).

The NCCN clinical practice guidelines on NSCLC (version 1.2019) recommend Abraxane for treatment of recurrence or metastasis of adenocarcinoma (with mixed subtypes), squamous cell carcinoma, or large cell carcinoma as a single-agent in patients with performance status (PS) 2 or in combination with carboplatin for patients with PS 0 to 2 for the following uses:[3,7]

- first-line therapy for *EGFR*, *ALK*, *ROS1*, and PD-L1 negative or unknown;
- first-line or subsequent therapy for *BRAF V600E*-mutation positive tumors;
- subsequent therapy for sensitizing *EGFR* mutation-positive tumors after targeted therapy;
- subsequent therapy for *ROS1* rearrangement-positive tumors and prior Xalkori therapy;
- subsequent therapy for PD-L1 expression-positive (≥ 50%) and *EGFR, ALK*, *ROS1* and *BRAF* negative or unknown and prior Keytruda therapy.

Abraxane plus carboplatin for patients with PS 0 to 1 is a category 1 recommendation and for patients with PS 2 is category 2A. Single agent therapy has a category 2A recommendation. These guidelines also state that Abraxane may be substituted for either paclitaxel or docetaxel in patients who have hypersensitivity reactions after receiving paclitaxel or docetaxel despite premedication, or if patients have contraindications to standard hypersensitivity pre-medications (category 2A). Abraxane is not included in NCCN chemotherapy regimens for neoadjuvant and adjuvant therapy or as a chemotherapy regimen that is used with radiation therapy in NSCLC.[7] However, paclitaxel and docetaxel are taxanes that may be used for neoadjuvant/adjuvant therapy and paclitaxel may be used sequentially or concurrently with radiation therapy. The NCCN guidelines also do not include Abraxane in the recommendations for continuation maintenance (i.e., continuing at least one of the agents given first line beyond 4 to 6 cycles, in the absence of disease progression). A summary of the clinical trial comparing Abraxane to paclitaxel in patients with unresectable Stage IIIb or IV NSCLC is included in Appendix A.

A summary of the clinical trial comparing Abraxane to paclitaxel in patients with unresectable Stage IIIb or IV NSCLC is included in Appendix A.

Dosing in NSCLC in Adults. *Dosing must meet the following:* 100 mg per m^2 as an intravenous infusion on Days 1, 8, and 15 of each 21-day cycle.[1,8] Abraxane is usually administered for 4 to 6 cycles.[7]

Note: Dose modifications are recommended for the management of toxicities and are determined by the prescribing physician. Dosing modifications are recommended in the prescribing information and are dependent on diagnosis, baseline hepatic function, concomitant therapy, patient variability, and toxicity.[1] Alternate dosing will be assessed individually on a case-by-case basis.

Duration of Therapy in NSCLC. Duration of treatment is usually 4 to 6 cycles.[7] Extended approvals are allowed if the patient continues to meet the conditions for coverage and dosing for NSCLC.

3. Pancreatic Adenocarcinoma.

Approve for 1 year if the patient t meets the following criteria (A, B, AND C):[3,9]

A) Abraxane is prescribed by or in consultation with an oncologist; AND
B) The patient has locally advanced unresectable or metastatic disease OR Abraxane is being used for neoadjuvant therapy; AND
C) Abraxane will be used in combination with gemcitabine.

The NCCN clinical practice guidelines on pancreatic adenocarcinoma (version 2.2018) recommend therapy with Abraxane for the following uses:[9]

- Neoadjuvant therapy in combination with gemcitabine with or without subsequent chemoradiation [category 2A];
- In combination with gemcitabine as first-line chemotherapy, or as induction therapy followed by chemoradiation in selected patients without systemic metastases, for patients with locally advanced unresectable disease and good performance status (category 2A);
- Preferred first-line therapy for metastatic disease in patients with good performance status (Karnofsky Performance Scale [KPS] ≥ 70) in combination with gemcitabine (category 1);
- Second-line therapy in combination with gemcitabine for locally advanced unresectable or metastatic disease as gemcitabine-based therapy (category 2A);
- Second-line therapy for recurrence after resection in combination with gemcitabine for local recurrence in the pancreatic bed OR for metastatic disease with or without local recurrence (category 2A).

Dosing in Pancreatic Adenocarcinoma in Adults. *Dosing must meet the following*: 125 mg per m^2 as an intravenous infusion on Days 1, 8, and 15 of each 28-day cycle for 4 cycles.[10]

Duration of Therapy in Pancreatic Adenocarcinoma.
Extended approvals are allowed if the patient continues to meet the conditions for coverage and dosing for pancreatic adenocarcinoma.

Other Uses with Supportive Evidence
4. Melanoma.

Melanoma. Approve for 1 year if the patient meets the following criteria (A, B, AND C):
A) Abraxane is prescribed by or in consultation with an oncologist; AND
B) The patient has unresectable, advanced or metastatic melanoma; AND
C) At least one other systemic therapy for melanoma has been tried (e.g., Keytruda [pembrolizumab for intravenous use], Opdivo® [nivolumab injection for intravenous use], Yervoy® [ipilimumab intravenous injection], high dose Proleukin® [aldesleukin for intravenous infusion]; cytotoxic agents [e.g., dacarbazine, temozolomide, paclitaxel, carboplatin]; Gleevec® [imatinib tablets]; Zelboraf® [vemurafenib tablets]; Tafinlar® [dabrafenib capsules]; Mekinist® [trametinib tablets]).

The NCCN clinical practice guidelines on melanoma (version 3.2018) recommend Abraxane as a single-agent for metastatic or unresectable disease as second-line or subsequent therapy for disease progression or after maximum benefit from *BRAF*-targeted therapy for patients with PS 0 to 2.[11] Other cytotoxic regimens for systemic therapy of metastatic disease include dacarbazine, temozolomide, and paclitaxel with or without carboplatin. In general, options for front-line therapy for metastatic melanoma include immunotherapy (e.g., Keytruda, Opdivo) or targeted therapy.

Dosing in Melanoma in Adults. *Dosing must meet the following:* 100 mg per m^2 or 150 mg per m^2 given as an intravenous infusion on Days 1, 8, and 15, cycled every 28 days.[12-13.22]

Note: Dose modifications are recommended for the management of toxicities and are determined by the prescribing physician.

Duration of Therapy in Melanoma. Extended approvals are allowed if the patient continues to meet the conditions for coverage and dosing for Melanoma.[12,13]

5. Ovarian, Fallopian Tube, or Primary Peritoneal Cancer.

Criteria.
Approve for 1 year if the patient meets the following criteria (A, B, AND C):

- **A)** Abraxane is prescribed by or in consultation with an oncologist; AND
- **B)** The patient has persistent or recurrent disease; AND
- **C)** At least one other systemic chemotherapy regimen has been tried (e.g., docetaxel or paclitaxel plus carboplatin).

The NCCN clinical practice guidelines on ovarian cancer (version 2.2018) recommend Abraxane as therapy for persistent disease or recurrence (including epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer) 1) as preferred therapy, if platinum sensitive, in combination with carboplatin, for patients with confirmed taxane hypersensitivity or 2) as a single agent (category 2A).[17] For platinum-sensitive disease, carboplatin plus Doxil® (doxorubicin liposome injection for intravenous use) and carboplatin plus paclitaxel are preferred agents (category 1 recommendations). The NCCN panel, in general, recommends combination platinum-based regimens for platinum-sensitive recurrent disease, especially in first relapses. Single-agent therapy with Abraxane is included as a potentially active agent.

Dosing in Ovarian, Fallopian Tube, or Primary Peritoneal Cancer in Adults. *Dosing must meet one of the following (A OR B)*:

- **A)** 260 mg per m^2 given as an intravenous infusion every 3 weeks;[18] OR
- **B)** 100 mg/m^2 on Days 1, 8, and 15 of a 28-day cycle.[19]

Note: Dose modifications are recommended for the management of toxicities and are determined by the prescribing physician.

Duration of Therapy in Ovarian, Fallopian Tube, or Primary Peritoneal Cancer. Limited information is available. Therapy may be extended based on the opinion of the prescribing physician and if the patient continues to meet the conditions for coverage and dosing for this condition.

6. Urothelial Carcinoma.

Criteria. Approve for 1 year if the patient meets the following criteria (A, B, AND C):

A) Abraxane is prescribed by or in consultation with an oncologist; AND
B) The patient has recurrent, locally advanced or metastatic urothelial carcinoma; AND
C) Abraxane is used as subsequent therapy after disease progression on at least one prior therapy (e.g., cisplatin- or carboplatin-containing regimen, immunotherapy [Keytruda® {pembrolizumab injection}, Tecentriq® {atezolizumab injection}, Imfinzi™ {durvalumab injection}, Bavencio® {avelumab injection}], gemcitabine plus carboplatin, gemcitabine alone, gemcitabine plus paclitaxel, ifosfamide with doxorubicin plus gemcitabine).

The NCCN clinical practice guidelines on bladder cancer (version 5.2018) recommend Abraxane as a single agent for urothelial carcinoma of the bladder for clinical Stage T4b or T2-T4a, N1-3 disease, or for recurrence post cystectomy or for metastatic disease subsequent systemic therapy as an alternate regimen for select patients.[20] Abraxane is also recommended as a single agent for the following: for recurrent or metastatic disease as subsequent systemic therapy as an alternate regimen for select patients for urothelial carcinoma of the urethra; as subsequent systemic therapy for metastatic upper genitourinary tract tumors as an alternate regimen for select patients; or for subsequent systemic therapy for metastatic urothelial carcinoma of the prostate as an alternate regimen for select patients.

Dosing in Urothelial Carcinoma in Adults. *Dosing must meet the following*: 260 mg per m^2 as an intravenous infusion every 3 weeks.[20]

Note: Dose modifications are recommended for the management of toxicities and are determined by the prescribing physician

Duration of Therapy in Urothelial Carcinoma. Limited information is available. Therapy may be extended based on the opinion of the prescribing physician and if the patient continues to meet the conditions for coverage and dosing for urothelial carcinoma. .

7. Uveal Melanoma. Approve for 1 year if the patient meets the following criteria (A, B, and C):
A) Abraxane is prescribed by or in consultation with an oncologist; AND
B) The patient has metastatic or unresectable disease; AND
C) Abraxane will be used as a single agent.

The NCCN guidelines for uveal melanoma (version 1.2018) recommends Abraxane as a single agent option for metastatic or unresectable disease.[22]

Dosing in Uveal Melanoma in Adults. *Dosing must meet the following*: Although limited dosing is available for this condition, doses between 100 mg/m^2 and 260 mg/m^2 administered every 21 or 28 days are recommended in the product labeling for approved uses.[1]

Duration of Therapy in Uveal Melanoma. Limited information is available. Determined by the prescriber. Patient must meet criteria and dosing above.

NOTE TO NURSE CLINICIAN: Approval duration should align with the criteria and requested dosing up to a maximum 1 year approval per review.

8. **Endometrial Carcinoma.** Approve for 1 year if the patient meets the following criteria (A and B):
   A) Abraxane is prescribed by or in consultation with an oncologist; AND
   B) The patient has metastatic, recurrent, or high-risk disease.

   Dosing in Endometrial Carcinoma in Adults. *Dosing must meet the following*: Although limited dosing is available for this condition, doses between 100 mg/m^2 and 260 mg/m^2 administered every 21 days or 28 days are recommended in the product labeling for approved uses.[1]

   Duration of Therapy in Endometrial Carcinoma. Limited information is available. Determined by the prescriber. Patient must meet criteria and dosing above.

   NOTE TO NURSE CLINICIAN: Approval duration should align with the criteria and requested dosing up to a maximum 1 year approval per review.

Other Cancer Indications. Forward to the Medical Director for review on a case-by-case basis.
An example of another indications supported in the *NCCN Compendium*: AIDS-related Kaposi Sarcoma (category 2A), and cervical cancer (category 2B).[3]

Waste Management for All Indications.
Dosing is based on body surface area (m^2). The dose should be calculated and the number of vials needed assessed.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Abraxane has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

SPECIAL CONSIDERATIONS
None.

LIMITATIONS/EXCLUSIONS
Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

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patients with recurrent ovarian, peritoneal, or fallopian tube cancer. *J Clin Oncol*. 2009;27:1426-1431.
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CFR		
WAC	284-43-2050	
RCW		
Contract Citation	☐ WAH	
	☐ IMC	
	☐ MA	
Other Requirements		
NCQA Elements		

Revision History

Revision Date	Revision Description	Revision Made By
12/02/2015	New	Kelly Force; Yusuf Rashid, RPh
12/24/2015	Approval	MMLT
01/11/2017	No revisions	Fran McGaugh
01/12/2017	Approval	MMLT
06/18/2017	Updated indications and references	Sonya Ou, Pharm.D.
07/24/2017	Formatted to current approved template	Sophia Yun, PharmD
07/25/2017	Approved	MMLT
04/16/2018	Transferred to new template	Cindy Bush
04/23/18	Updated indications and references	Jennifer Farley, PharmD
05/10/2018	Approval	UM Committee
03/08/2019	Updated indications and references	Jennifer Farley, PharmD
03/14/2019	Approval	UM Committee

Appendix A: Metastatic Breast Cancer Clinical Trials

In one Phase III open-label, non-inferiority trial, patients (n = 460) with metastatic breast cancer were randomized to therapy every 3 weeks with Abraxane 260 mg/m^2 as a 30-minute intravenous infusion without corticosteroid or antihistamine premedication (n = 229) or paclitaxel 175 mg/m^2 as a 3-hour intravenous infusion with premedication (n = 225).[1,4] The intent-to-treat population was 454 patients (Abraxane, n = 229; paclitaxel, n = 225).[4] At study entry 64% of patients had impaired PS (ECOG 1 or 2). Fifty-nine percent of patients received the study drug as second or greater than second-line therapy. Seventy-seven percent of patients had previously received an anthracycline. *Results:* ORR based on the investigator reported response rates and on all cycles of therapy for all patients was 33% of patients on Abraxane (95% CI: 27.09, 39.29) vs. 19% of patients on paclitaxel (95% CI: 13.58, 23.76) [P =0.001]. In all of the randomized patients, the Abraxane group had a statistically significantly higher reconciled target lesion response rate (TLRR) of 21.5% (95% CI: 16.2%, 26.7%) vs. 11.1% (95% CI: 6.9%, 15.1%) of patients receiving paclitaxel (P = 0.003).[1] In patients who had failed combination chemotherapy or relapsed within 6 months of adjuvant chemotherapy, the reconciled TLRR (which was based on the first 6 cycles of therapy) was15.5% (n = 20/129) with Abraxane (95% CI: 9.26, 21.75) and 8.4% (n = 12/143) with paclitaxel (95% CI: 3.85, 12.94).[1] Median time to progression (TTP) was 23.0 weeks with Abraxane and 16.9 weeks with paclitaxel (HR: 0.75; P = 0.006).[4] Median survival for Abraxane and paclitaxel was 65.0 weeks and 55.7 weeks, respectively (P = 0.374) for all patients. There was no statistically significant difference in overall survival between the two therapies.[1] There was no difference between the two groups in survival in patients receiving first-line therapy.[4] In patients who received second-line or greater therapy, survival was 56.4 weeks and 46.7 weeks for Abraxane and paclitaxel, respectively (HR: 0.73; P = 0.024). There was no difference in quality of life between the two groups. The incidence of hypersensitivity reactions of any grade was < 1% with Abraxane vs. 2% with paclitaxel. Grade 3 hypersensitivity reactions occurred in five patients receiving paclitaxel. No Grade 3 or 4 hypersensitivity reactions occurred with Abraxane, but premedication was given for emesis, myalgia/arthralgia, or anorexia in 18 patients (8%) in the Abraxane group in 2% of the treatment cycles. Grade 4 neutropenia (< 500 cell/mm^3) was reported in 9% of patients on Abraxane and in 22% of patients on paclitaxel (P < 0.001);[1,4] neutropenia (< 2,000 cells/mm^3) was reported in 80% vs. 82% with Abraxane and paclitaxel, respectively.[1] Grade 3 sensory neuropathy occurred in 10% vs. 2% of patients on Abraxane and paclitaxel, respectively (P < 0.001) and were managed with dose reduction and treatment interruption.[4]

In one Phase III trial, the efficacy of weekly paclitaxel was compare to weekly Abraxane or Ixempra with or without Avastin as *first-line therapy* in patients with chemotherapy naïve locally recurrent or metastatic breast cancer.[5] Patients were randomized to paclitaxel 90 mg/m^2, Ixempra 16 mg/m^2, or Abraxane 150 mg/m^2 given once weekly for 3 weeks with 1 week off. Initially all patients received Avastin but this became optional after the study was started. The primary endpoint was PFS. ***Results:*** In all, 799 patients were enrolled (n = 283, paclitaxel; n = 271 Abraxane; n = 245, Ixempra) and 783 patients received treatment (97% of patients received Avastin). At the first interim analysis (165 events) accrual to Ixempra was closed for futility. At the second interim analysis (236 events) the study was closed for futility. Median PFS was 11 months, 9.3 months, and 7.4 months for paclitaxel, Abraxane, and Ixempra, respectively. Ixempra was inferior to paclitaxel (HR: 1.59; 95% CI: 1.31, 1.93; P < 0.001). Abraxane was not superior to paclitaxel (HR: 1.20; 95% CI: 1.00, 1.45; P = 0.054). Grade ≥ 2 sensory neuropathy occurred in 54% of patients on Abraxane, and 46% of patients on paclitaxel. The percentage of patients with Grade ≥ 3 hematologic toxicity was 55% with Abraxane, 12% for Ixempra, and 22% for paclitaxel. Grade ≥ 3 non-hematologic toxicity was reported in 49% of patients on paclitaxel, 65% of

patients on Abraxane, and 58% of patients on Ixempra. When compared with paclitaxel, Abraxane was reported to have worse hematologic and non-hematologic toxicity (P < 0.001 for both), including peripheral neuropathy, with more frequent and earlier dose reductions with Abraxane than with paclitaxel. In the 783 patients who began treatment, the ORR was 38% for paclitaxel, 34% for Abraxane, and 27% for Ixempra with no difference in response between paclitaxel and Abraxane (odds ratio 0.84; P = 0.33). Time to treatment failure was a median of 5.2 months vs. 6.6 months (P < 0.001) for Abraxane and paclitaxel, respectively. Regarding overall survival, a post hoc test of inferiority did not reach significance for Abraxane compared with paclitaxel (median overall survival was 23.5 months with Abraxane vs. 26.5 months with paclitaxel [HR: 1.17; 95% CI: 0.92, 1.47; P = 0.20]).

Unresectable NSCLC Clinical Trial

In one multicenter Phase III open-label trial, 1052 chemotherapy naïve patients with unresectable Stage IIIb or IV NSCLC were randomized to Abraxane 100 mg/m^2 given over 30 minutes on Days 1, 8, and 15 of each 21-day cycle or to paclitaxel 200 mg/m^2 given over 3 hours every 21 days.[1,8] Patients receiving paclitaxel were premedicated. In both treatment arms carboplatin AUC 6 mg•minute/mL was given on Day 1 of every 21-day cycle after completing the Abraxane or paclitaxel infusion. Patients had an ECOG PS of 0 to 1. Treatment was given until disease progression or unacceptable toxicity. The primary outcome was the ORR as determined by a central independent committee. For all randomized patients the median age was 60 years; 75% of patients were men; 49% of patients had adenocarcinoma and 43% had squamous cell carcinoma. The median number of cycles was six in both study arms. ***Results:*** The ORR in patients receiving Abraxane/carboplatin was 33% (95% CI: 28.6%, 36.7%) vs. 23% of patients receiving paclitaxel/carboplatin (95% CI: 21.2%, 28.5%) [P = 0.005].[8] For Abraxane/carboplatin and paclitaxel/carboplatin, the respective ORRs in patients with squamous cell histology were 41% (95% CI: 34.7%, 47.4%) vs. 24% (95% CI: 18.8%, 30.1%) [P < 0.001]. For patients with non-squamous cell histology, the ORR were 26% vs. 25%, respectively (P = 0.808). There was no statistically significant difference in median overall survival between the two groups (12.1 months with Abraxane vs. 11.2 months with paclitaxel) [HR: 0.922; 95% CI: 0.797, 1.066; P = 0.271]. Median PFS was 6.3 months with Abraxane/carboplatin vs. 5.8 months with paclitaxel/carboplatin (HR: 0.902; 95% CI: 0.767, 1.060; P = 0.214). Median duration of response was 6.9 months (95% CI: 5.6, 8.0) in patients on Abraxane/carboplatin and 6.0 months (95% CI: 5.6, 7.1) in patients on paclitaxel/carboplatin.

Paclitaxel has been given <u>weekly</u> in combination with carboplatin in patients with advanced NSCLC.[14]