Newly FDA Approved Docetaxel + Albumin Formulation for Breast Cancer Treatment

Hirak Biswas, Ph.D *,^; Dhaval Desai, PharmD*; Qun Sun, MD, Ph.D#

*Zydus Pharmaceuticals, Pennington, NJ, USA ^Syneos Health, Morrisville, NC,USA #Zhuhai Beihai Biotech Co., Ltd, Zhuhai, China

Introduction

- Breast cancer remains the most diagnosed malignancy among women and a leading cause of cancer-related death, despite substantial advances in detection and therapy.[1]
- Among systemic therapies, Docetaxel, (marketed as Taxotere®) has become a cornerstone for both early-stage and metastatic disease, consistently improving disease-free and overall survival in randomized trials.
- Conventional formulation of docetaxel relies on the surfactant polysorbate 80 for solubilization, which is linked to hypersensitivity reactions, fluid retention, and other formulation-related toxicities such as peripheral neuropathy.[2,3]
- Novel albumin-based formulations have been developed that eliminate the use of Polysorbate 80, utilizing the natural transport properties and biocompatibility of human serum albumin to increase solubility and reduce hypersensitivity risk[4]. Albumin is a proven excipient for drug delivery multiple formulations and nab-paclitaxel (Abraxane® for injectable suspension) is an example of this novel formulation.
- This advancement in docetaxel formulation has led to the FDA approval of BH009 (albumin-solubilized docetaxel injection) under the 505(b)(2) regulatory pathway, which allowed manufacturers to partly leverage prior findings of safety and efficacy for docetaxel while demonstrating bioequivalence and relatively lower severe AEs for BH009.[5]

Materials and Methods

In-Vivo

- RBC Hemolysis study: The study compared BH009, Taxotere®, saline, and water on 2% rabbit RBCs.
- *Procedure*: Incubated tubes at 37°C, monitored hemolysis for 3 hours, then centrifuged and measured absorbance on the spectrophotometer at 545 nm-OD values of each tube were read, with pure water used as the blank.
- *Assessment*: Classified hemolysis/aggregation visually and calculated hemolysis rate, with >5% indicating hemolysis.

In-Vivo

- The N-87 gastric adenocarcinoma model used 10-week-old female nude mice implanted with tumors averaging ~400 mm^3 at dosing
- A 6.4 mg/kg IV bolus via tail vein was administered, chosen based on formulation and volume limits, with 3 mice studied at each timepoint
- Plasma and tumor concentrations of the drug were determined using validated LC-MS/MS methods at 0, 1, 4-, 12-, 24-, and 48-hour timepoints

Bioequivalence Trial Design[6]

Study Design

- Open label, randomized two-period crossover in solid tumor patients
- Inclusion criteria:
  - 18 years of age
  - Histologically or cytologically confirmed advanced solid tumors who are scheduled to receive treatment with single-agent docetaxel
  - ECOG performance status 0 or 1 and life expectancy ≥ 3months
  - Adequate hematopoietic, renal and liver function
  - Prior chemotherapy completed 30 days prior to randomization
- *Comparators:* BH009 (Test product or T) vs. Taxotere ® (Winthrop injection-Reference product or R)
- *Randomization:* Balanced T-R & R-T sequences
- BH009 or Taxotere® Dose: 75mg/m^2
- Patients in each cohort received the crossover drug at the second assessment
- *PK assessment:*
  - Blood samples collected pre- and post-infusion on Day 1 and Day 22
  - Plasma levels of Free & Total Docetaxel analyzed using validated LC-MS/MS
  - Statistical analysis performed in SAS® 9.4 to confirm bioequivalence

Endpoints assessed

Primary Outcomes (assessed on Day 1 and 24):

- C_{max} of docetaxel injection- Peak Plasma Concentration
- AUC of docetaxel injection- Area under the plasma concentration versus time curve

Secondary Outcomes:

- Safety and tolerability of BH009-
  AE assessments included lab test values, patient reports, and investigator observations

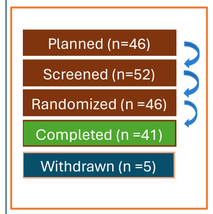


Figure 1. Patient Flow

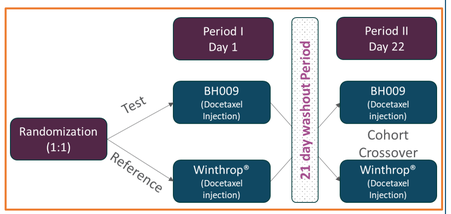


Figure 2. Study Schematic

Preclinical and Bioequivalence Results

In-Vitro

- BH009 Injection (0.25 mg/mL) did not cause hemolysis and aggregation of rabbit RBCs in vitro
- The result of Taxotere® (0.3mg/mL) was weakly positive likely due to PS-80

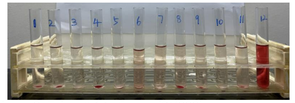


Figure 3. Tubes # 1 to 5 were(BH009); Tubes # 6 to 10 were control (Taxotere®); tubes # 11 and #12 are negative & positive control respectively.

In-vivo

- The intratumoral elimination half-life ($t_{1/2}$) of BH009 was approximately 90 hours
- The $AUC_{0\text{-}48h}$ and $AUC_{0\text{-}\infty}$ ratio of BH009 in tumor and plasma was approximately 12:1 and 36:1, respectively

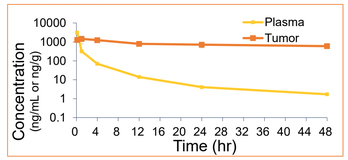


Figure 4. Mean plasma and tumor concentration-time data of single dose BH009 in N87 tumor mouse model

Bioequivalence Study

- Of the 41 patients completing both periods of the study, pharmacokinetic assessments were performed for 41 patients and statistical analyses were performed for 40 patients
- The 90% confidence intervals for the geometric least square mean ratios were within the FDA-defined bioequivalence range of 80.00%- 125.00%, confirming bioequivalence between BH009 and Taxotere®

PK Parameters (Units)	Geometric least square means ratio (T/R)%	90% Confidence Interval
Total Docetaxel		
C_{max} *(ng/ml)*	99.78	92.18% - 108.00%
$AUC_{0\text{-}t}$ *(hr*ng/ml)*	99.24	91.89% - 107.18%
$AUC_{0\text{-}\infty}$ *(hr*ng/ml)*	98.29	91.10% - 106.04%
Free Docetaxel		
C_{max} *(ng/ml)*	93.10	85.22% - 101.70%
$AUC_{0\text{-}t}$ *(hr*ng/ml)*	96.34	89.98% - 103.15%
$AUC_{0\text{-}\infty}$ *(hr*ng/ml)*	96.29	90.24% - 102.75%

Table 1. Statistical results for PK parameters to demonstrate bioequivalence

Safety Results

- The test and reference product were well tolerated by the patients, and the safety profile of the test product complies with the known safety profile of the reference product.
- A total of 198 treatment-emergent adverse events (TEAEs) were reported of which 94 were reported for BH009 and 104 for Taxotere®. There were no serious AEs or deaths
- Grade 3/4 toxicities were limited to hematologic events, which occurred significantly less often with BH009 than with Taxotere® (2.3% vs 15.9%)
- Only one BH009-treated patient experienced grade 3 anemia, whereas the Taxotere® group showed higher rates of grade 3/4 leukopenia (6.8%), neutropenia (4.6%), and lymphopenia (2.3%)

	BH009 (n=43), No.(%)		*Taxotere® (n=44), No.(%)*	
	Any Grade	*Grade3/4*	*Any Grade*	*Grade3/4*
Anemia	3 (7.0)	1 (2.3)	2 (4.6)	1 (2.3)
Leukopenia	5 (11.7)	0 (0)	6 (13.6)	3 (6.8)
Neutropenia	4 (9.3)	0 (0)	8 (18.2)	2 (4.6)
Lymphopenia	0 (0)	0 (0)	1 (2.3)	1 (2.3)

Table 2. Rate of Hematological Toxicity

Conclusion and Discussion

- In the in-vitro study, BH009 demonstrated excellent blood compatibility, whereas Taxotere® showed weakly positive hemolysis, likely related to PS-80.
- In the in-vivo study, BH009 demonstrated a prolonged presence and substantially higher exposure in tumor tissue compared to plasma, supporting sustained intratumoral retention.
- The bioequivalence study demonstrated high completion rates, while PK analyses confirmed that BH009 is bioequivalent to Taxotere®, with key parameters falling within the FDA's accepted range.
- The safety profile of BH009 was also favorable with no serious events or deaths reported. Notably, higher grade hematologic toxicities were infrequent overall and occurred less often with BH009. Taxotere® showed higher rates of serious leukopenia, neutropenia, and lymphopenia.
- The combined evidence demonstrates that BH009 is well-tolerated by blood components, shows prolonged intratumoral exposure, and achieves clinical bioequivalence with superior hematological toxicity profile, all supporting its FDA approval and clinical relevance.
- Using albumin in the formulation, BH009 (BEIZRAY™) will avoid PS-80 related toxicities in patients and theoretically can reduce or eliminate the use of corticosteroid premedication in the treatment regimen. This is being evaluated in a real-world evidence (RWE) study.

Contact

Hirak Biswas Ph.D.
Zydus Pharmaceuticals (USA) Inc
Email: hbiswas@zydususa.com
Website: www.zydususa.com
Phone: +1 410-807-6636

Abbreviations

AE: Adverse event; AUC: Area under curve; FDA: Food and drug administration; LC-MS: Liquid chromatography-mass spectrometry; OD: Optical density; PK: Pharmacokinetic; PS: Polysorbate; R: Reference product; RBC: Red blood cells; T: Test product

This presentation is the intellectual property of the author/presenter. Contact them at hbiswas@zydususa.com for permission to reprint and/or distribute.

References

1. Caswell-Jin et al. *JAMA*. 2024;331(3):233–241
2. Schwartzberg et al. *Advances in Therapy*. 2018; 35(6): 754–767
3. Crown et al. *Oncologist*. 2004; 9 (S2):24-32
4. Tang et al. *Drug Delivery. 2015.* 23(8), 2686–2696
5. BEIZRAY FDA Label. Available online at www.accessdata.fda.gov. Accessed: 11/12/2025
6. Clinicaltrials.gov ID: NCT04889599

Beizray™ is a trademark of Zhuhai Beihai Biotech Co., Ltd. Non-Zydus USA brands are trademarks or registered trademarks of their respective owners.

© 2025 Zydus Pharmaceuticals (USA) Inc.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com