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CASE REPORT OPEN ACCESS

# Allergy to cabazitaxel: Cross-reactivity between taxanes

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**Abstract**
A 46-year-old man, with HIV infection A2 stage and chronic C hepatitis was diagnosed with stage 4 prostate cancer with bone metastases in September 2019. His treatment was started with docetaxel, receiving five cycles with good tolerance, after which he received hormonal treatment. Currently, he presents progression of the disease and docetaxel is reintroduced. After infusing the first 5 mL, he showed respiratory distress with thoracic pain and low oxygen saturation (88%) together with lumbar pain. Both tryptase and interleukin 6 (IL-6) levels in blood were measured at the time of the reaction, and were elevated. The case was discussed in an oncology clinical round, and it was decided a change to cabazitaxel. Allergy tests were performed, including skin prick and intradermal tests, with docetaxel and cabazitaxel. A positive result to intradermal test with docetaxel, 10 mg/mL, was obtained 24 h later. Then 48 h later, another positive intradermal test reaction with 1-mg/mL docetaxel as skin ulceration was reported. However, skin prick and intradermal tests with cabazitaxel were negative.
Drug provocation test with cabazitaxel was subsequently performed. After the infusion of 11 mL, the patient presented pharyngeal obstruction with dyspnoea, facial erythema, genital pruritus, and cervical pain that required treatment with intramuscular epinephrine. The results of the allergy study were not concordant with clinical presentation and confirmed the poor predictive value of taxane skin tests.


## Introduction

Drug hypersensitivity reactions (DHSRs) to chemotherapeutic drugs are classified as immediate drug hypersensitivity reaction (IDHSRs) or non-immediate drug hypersensitivity reaction (NIDHSRs) depending on the appearance of clinical manifestations.[1]

Phenotypes are defined by clinical presentation, and endotypes refer to the cellular and molecular mechanisms of DHSRs. The phenotypes described in IDHSRs to

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chemotherapeutic drugs include type I reactions, cytokine release reactions, mixed reactions, and indeterminate reactions.[1]

The estimated incidence of taxanes IDHSR is 10% for paclitaxel, around 5% for docetaxel and cabazitaxel, and less than 4% for nab-paclitaxel. Symptoms occur mainly during the first cycle, within minutes of starting the infusion. It is not clear whether taxanes themselves or the vehicles in which they are dissolved are responsible for most reactions. Cross-reactivity between paclitaxel and docetaxel has been reported to reach 50%.[1]

Docetaxel is an antineoplastic agent belonging to the family of taxanes and has a unique mechanism of action as an inhibitor of cellular mitosis. Currently, docetaxel plays a central role in the therapy of many solid tumors, including prostate, breast, and lung cancer.

Cabazitaxel is also an antineoplasic agent that is currently used in the therapy of adults with castration-resistant metastatic prostate cancer refractory to docetaxel. To the best of our knowledge, no DHSRs have been described with cabazitaxel and by cross-reactivity with other taxanes such as docetaxel. Here, we report a case of hypersensitivity to docetaxel and cabazitaxel.

## Case Report

A 46-year-old man, with HIV infection A2 stage and chronic C hepatitis was diagnosed with STAGE 4 prostate cancer with bone metastases in September 2019. His treatment was started with docetaxel, receiving five cycles with good tolerance, after which he received hormonal treatment. Currently, he presents progression of disease, and docetaxel is reintroduced.

After infusing the first 5 mL, he showed respiratory distress with thoracic pain and low oxygen saturation (88%) together with lumbar pain. Tryptase and interleukin 6 (IL-6) levels in blood were measured at the time of reaction; both were elevated, with tryptase level being 24.60 ug/L (normal range: 0–11.40 ug/L) and IL-6 level reported as 8 pg/mL (normal range: 0–7 pg/mL). The case was discussed in an oncology clinical round, and it was decided a change to cabazitaxel.

Allergy tests were performed, including skin prick and intradermal tests, with docetaxel (10 mg/mL and 1 mg/mL, respectively)[1] and cabazitaxel (10 mg/mL and 1 mg/mL, respectively). A positive result to intradermal test with docetaxel 10 mg/mL was obtained 24 h later; and 48 h later, reaction with skin ulceration was reported with 1-mg/mL docetaxel. However, both skin prick and intradermal tests with cabazitaxel were negative.

Drug provocation test (without desensitization) with cabazitaxel was performed subsequently. After the infusion of 11 mL, the patient presented pharyngeal obstruction with dyspnea, facial erythema, genital pruritus, and cervical pain. He was administered 0.5-mg intramuscular epinephrine, corticosteroids, antihistamines, montelukast, and acetaminophen with clinical improvement until he was asymptomatic. Tryptase and IL-6 levels at the time of reaction were both positive: IL 6: 9.4 pg/mL (normal range: 0–7 pg/mL); and tryptase: 30.60 ug/L (normal range 0–11.40 ug/L). Basal tryptase levels at 24 h were 26 ug/L.

## Discussion

Most of chemotherapy agents induce hypersensitivity reactions that associate with higher frequency to certain groups, such as platinums or taxanes.[1,2]

The incidence of DHSRs with either paclitaxel or docetaxel is about 30%, but when administered after corticosteroids and antihistamines, the proportion lowers to 2–4%.

Paclitaxel and docetaxel are the main taxanes used. Docetaxel has a mechanism of action and a safety profile similar to that of paclitaxel and is widely used in the treatment of various cancer types, such as breast, lung, prostate, stomach, and head and neck carcinomas. Paclitaxel is used in the treatment of ovarian, breast and lung cancers.[3,4]

After failure of docetaxel, cabazitaxel is currently used in the therapy of adults with castration-resistant metastatic prostate cancer.

Adverse reactions vary among different taxanes, but common reactions include myelosuppression, neuropathy, and DHSRs.

Paclitaxel and docetaxel cause high proportions of IDHSRs in about 30% of patients, usually during first or second exposure to the drug. Premedication with antihistamines and corticosteroids for paclitaxel and with corticosteroids alone for docetaxel successfully reduces the risk of IDHSRs to less than 10%. However, severe IDHSRs still occur in around 1% of patients.[2,5,6]

Direct mast cell degranulation, complement activation, and, in some cases, specific immunoglobulin E (IgE)-type reaction are involved in adverse events to taxanes. Although an immunological mechanism is not demonstrated, the term IDHSR is used to designate adverse reactions with features suggestive of mast cell–basophil degranulation that occurs during taxane infusions.[5,7]

Taxanes are poorly soluble molecules. DHSRs to taxanes are generally attributed to the surfactants used in their formulation (cremophor EL for paclitaxel, and polysorbate 80 for docetaxel and cabazitaxel). These molecules can cause complement activation, resulting in anaphylatoxin release. Nanoparticle albumin-bound paclitaxel (nab-paclitaxel; Abraxane© [Celgene Corp., Summit, NJ, USA]) is a newer paclitaxel formulation that does not contain cremophor EL.[2,6,8]

The present patient had suffered a hypersensitivity reaction with docetaxel, suggesting IgE-mediated mechanism and cytokine release. In addition, drug provocation test with cabazitaxel was performed, also suggestive of a mixed mechanism.

The patient had high basal tryptase levels; however, the study of a possible mast cell activation syndrome was discarded due to the palliative clinical situation of the patient.

Docetaxel skin tests had delayed positive reactions, while those for cabazitaxel were negative both for immediate and delayed reactions.

The results were not concordant with the clinical presentation of the patient and this confirmed the poor predictive value of taxane skin tests.

The negative results of polysorbate skin tests suggest that hypersensitivity reactions with both taxanes were not due to the excipient but because of active drug.

Therefore, we present a case report of hypersensitivity reactions with docetaxel and cabazitaxel with inconclusive drug allergy study.

After a careful literature search, we could not find any report of DHRSs caused directly by cabazitaxel alone. This could be due to the lower rate of use, as cabazitaxel is not considered a first line of treatment and its use is only indicated if docetaxel fails.

## Mandatory Disclosure on Use of Artificial Intelligence

The authors declare that no AI-assisted tools were used in the preparation of this manuscript. All references have been manually verified for accuracy and relevance.

## Author Contributions

Paola C Fernández -Paredes, Mariola Navarro and Elisa Peñalver were directly responsible for the clinical course of the patient's adverse reactions. Paola C Fernández-Paredes wrote the report and Mariola Navarro, Elisa Peñalver and J D López collaborated to achieve the final version of the manuscript.

## Conflicts of Interests

The authors had no relevant financial interests to disclose.

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