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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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COVID-19 vaccines tolerated in patients with paclitaxel and docetaxel allergy

To the Editor,

After initial reports of anaphylaxis to the messenger RNA (mRNA) COVID-19 vaccines, the Centers for Disease Control and Prevention (CDC) put forth guidance stating that patients with a history of anaphylaxis to vaccine components like polyethylene glycol (PEG) should not receive the mRNA COVID-19 vaccines.[1] To address this clinical challenge and decrease vaccine hesitancy, we published an approach to guide COVID-19 vaccination in high-risk allergy individuals.[2–4] While the etiology of anaphylaxis to mRNA COVID-19 vaccines remains unclear, PEG continues to be an important focus.[5,6] Paclitaxel contains polyoxyl-35 castor oil—a PEG derivative and structurally similar to the excipient in Pfizer-BioNTech and Moderna COVID-19 vaccines—and docetaxel contains polysorbate 80—the excipient in Janssen COVID-19 vaccine. Given this, we sought to assess the utility of pre-vaccine excipient skin testing (ST), risk stratification, and COVID-19 vaccine tolerability in oncology patients with a history of paclitaxel or docetaxel hypersensitivity reaction (HSR).

We included consecutive paclitaxel or docetaxel HSR patients referred to Mass General Brigham allergy/immunology for evaluation prior to COVID-19 vaccination. Evaluation included clinical risk assessment and excipient ST as previously described.[2,4] Clinical details were obtained by electronic health record (EHR) review. COVID-19 vaccine tolerance was determined by an allergy/immunology physician (AB) using EHR review, phone call, and/or e-mail. This study was approved by the Massachusetts General Brigham Institutional Review Board and deemed minimal risk.

Between December 30, 2020, and April 2, 2021, 21 patients with paclitaxel (n = 17) or docetaxel (n = 4) HSR were referred (Table 1). Most were female (n = 20, 95%) and white (n = 20, 95%). Approximately half of HSRs occurred in the past 4 years (n = 11, 52%), and 14 (67%) HSRs were severe grade 3.[7] Twenty patients (95%) had negative excipient ST. One paclitaxel HSR patient had positive ST (methyl-prednisolone acetate PEG3350, 0.4 mg/ml intradermal) and tolerated the Janssen COVID-19 vaccine (Table 2). All patients completed COVID-19 vaccination with no reaction (n = 19, 90%) or with mild symptoms treated with antihistamines alone (n = 2, 10%). Of 17 patients with history of paclitaxel HSR, 12 (71%) received an mRNA COVID-19 vaccine and none had a reaction.

This case series of 21 patients suggests that patients with paclitaxel (containing the excipient polyoxyl-35 castor oil/PEG derivative) or docetaxel (containing the excipient polysorbate 80) HSRs tolerate COVID-19 vaccination. While 2 patients (10%) developed reactions after COVID-19 vaccination, symptoms resolved with antihistamines alone. The reactions do not appear related to the patient's specific excipient allergy history (e.g., docetaxel HSR patient developed reaction with mRNA vaccine), and in fact, no reactions occurred in paclitaxel HSR patients that received an mRNA COVID-19 vaccine. It remains unclear if the paclitaxel HSR patient with positive intradermal PEG ST would have tolerated mRNA COVID-19 vaccination, but experience to date indicates that positive PEG intradermal ST does not predict reactions to mRNA COVID-19 vaccines.[4]

CDC guidance advises patients with PEG allergy to proceed with Janssen COVID-19 vaccination while patients with polysorbate 80 allergy can proceed with mRNA COVID-19 vaccines.[1] However, if both COVID-19 vaccine platforms are not routinely accessible, allergy/immunology consultation may be useful for allergy risk assessment and vaccine guidance. Furthermore, if mRNA COVID-19 vaccines are proven optimal for oncology patients, allergy assessment and limited excipient ST (e.g., Miralax, PEG-3350)[2,4] can provide reassurance prior to mRNA COVID-19 vaccination in patients with HSR to chemotherapeutics containing PEG. We continue to advise 30-minute monitoring post–COVID-19 vaccination for all patients with any history of anaphylaxis per CDC guidance.[1]

This study was limited by its small sample from a single institution and retrospective study design. Additionally, the study included patients with a history of hypersensitivity to drugs (i.e., paclitaxel) that do not contain the specific form of PEG contained in the vaccines, which is a PEGylated form of PEG forming PEGylated lipids. It has been frequently reported that hypersensitivity to drugs containing PEG (in its native form) or its derivatives (and not containing the

TABLE 1 Characteristics of Patients with a Paclitaxel or Docetaxel Hypersensitivity Reaction Referred for Allergy Evaluation prior to COVID-19 Vaccination.

Characteristics	No. (%)		
	All ($n = 21$)	Paclitaxel allergy ($n = 17$)	Docetaxel allergy ($n = 4$)
Age, mean (SD), year	57 (10.5)	58 (10.7)	52 (8.6)
Female	20 (95)	17 (100)	3 (75)
Race			
White	20 (95)	17 (100)	3 (75)
Asian	1 (5)	0 (0)	1 (25)
History of atopy	14 (67)	12 (71)	2 (50)
Anaphylaxis	12 (57)	11 (65)	1 (25)
Allergic rhinitis	5 (24)	4 (24)	1 (25)
Food allergy	5 (24)	4 (24)	1 (25)
Asthma	4 (19)	3 (18)	1 (25)
Atopic dermatitis	1 (5)	1 (6)	0 (0)
Time since hypersensitivity reaction			
Less than 1 year	8 (38)	6 (35)	2 (50)
1–4 years	3 (14)	3 (18)	0 (0)
5–9 years	3 (14)	2 (12)	1 (25)
10 or more years	6 (29)	6 (35)	0 (0)
Unknown	1 (5)	0 (0)	1 (25)
Hypersensitivity reaction symptoms[a]			
Cutaneous	18 (86)	14 (82)	4 (100)
Respiratory	15 (71)	12 (71)	3 (75)
Gastrointestinal	4 (19)	2 (12)	2 (50)
Cardiovascular	2 (10)	2 (12)	0 (0)
Other	8 (38)	6 (35)	2 (50)
Severity of reaction[b]			
Grade 0	1 (5)	1 (6)	0 (0)
Grade 1	3 (14)	2 (12)	1 (25)
Grade 2	3 (14)	2 (12)	1 (25)
Grade 3	14 (67)	12 (71)	2 (50)
Management of chemotherapy hypersensitivity reaction			
Antihistamines	19 (90)	16 (94)	3 (75)
Corticosteroid	14 (67)	11 (65)	3 (75)
Epinephrine	1 (5)	1 (6)	0 (0)
Other[c]	3 (14)	2 (12)	1 (25)
COVID–19 vaccine(s) received			
mRNA (Pfizer-BioNTech or Moderna)	16 (76)[d]	12 (71)[e]	4 (100)[f]
Janssen	5 (24)	5 (29)	0 (0)

[a]Cutaneous: hives, rash, itching, swelling (not throat), and flushing; respiratory: wheezing, chest tightness, shortness of breath, cough, and sensation of throat closing; gastrointestinal: gastrointestinal upset, abdominal cramping, diarrhea, vomiting, and nausea; cardiovascular: tachycardia and hypotension; other: 7 patients had back pain, 1 patient had lightheadedness, and 1 patient had sinus pressure.

[b]Grading of reaction based on Ring and Messmer criteria.[7]

[c]One patient received acetaminophen and oxycodone, and 2 patients received unknown treatment.

[d]Twelve patients received Pfizer-BioNTech, and 4 patients received Moderna COVID-19 vaccine.

[e]Nine patients received Pfizer-BioNTech, and 3 patients received Moderna COVID-19 vaccine.

[f]Three patients received Pfizer-BioNTech, and 1 patient received Moderna COVID-19 vaccine.

TABLE 2 Patients with a History of Hypersensitivity Reactions to Paclitaxel or Docetaxel with Positive Skin Testing or Reaction to COVID-19 Vaccination

				Reaction to paclitaxel/docetaxel				COVID–19 vaccine		
ID	Age	Sex	Other drug/vaccine allergy history	Drug	Onset	Reaction symptoms	Reaction treatment	Excipient skin testing results[a]	Manufacturer	Outcome
1	53	F	Influenza vaccine (vision changes, wheezing, shortness of breath) Ampicillin (hives)	Paclitaxel	15 mins	Shortness of breath, chest pain, loss of consciousness	Diphenhydramine, unspecified steroid	Positive to PEG[b]	Janssen	Tolerated
2	51	F	Influenza vaccine (facial erythema, dizziness) Pertuzumab and trastuzumab (flushing, swelling, hives) Cefadroxil (itching) Clindamycin (itching, facial swelling, facial erythema, malaise, rhinorrhea, cough)	Docetaxel	5 mins	Flushing, diarrhea	Diphenhydramine, famotidine	Negative to PEG and polysorbate 80	Pfizer-BioNTech	Dose 1: dizziness, lightheadedness, nausea, hives, itching, increase throat secretions, upper lip swelling, rash Treatment: cetirizine and loratadine Dose 2: dizziness, nausea, lip swelling, increased throat secretions, rash Treatment: cetirizine
3	66	F	Tetracycline (shortness of breath) Meperidine (vomiting) Nitrofurantoin (shortness of breath, cough)	Paclitaxel	4–6 h	Flushing, facial edema	Diphenhydramine	Negative to PEG	Janssen	Flushing, facial swelling Treatment: diphenhydramine

Abbreviation: PEG: polyethylene glycol.

[a]Skin testing protocols published previously[2,4]

[b]Positive to methyl-prednisolone acetate intradermal 0.4 mg/ml.

PEGylated form of PEG) is not a contraindication for receiving the COVID-19 mRNA vaccines.[8]

The role of excipient ST prior to COVID-19 vaccination appears limited.[8,9] Patients in our study largely tolerated COVID-19 vaccination despite paclitaxel or docetaxel HSR, and there is no identified role to date for the use of skin testing to PEG/polysorbate 80 prior to COVID-19 vaccination in these patients.[8]

KEYWORDS

COVID, docetaxel, drug allergy, paclitaxel, PEG, SARS-CoV, vaccine allergy

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CONFLICT OF INTEREST

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Mast cells partly contribute to allergic enteritis development: Findings in two different mast cell-deficient mice

To the Editor,

Allergic enteritis (AE) is a gastrointestinal form of food allergy.[1] Compared with other clinical phenotypes of allergy, the pathomechanisms of AE have not been elucidated. In this study, we provide evidence, based on the studies of two mast cell-deficient mouse strains (KIT$^{(W-sh/W-sh)}$ bearing the W-sash (W(sh)) inversion