




Safety of administration of BNT162b2 mRNA (Pfizer-BioNTech) COVID-19 vaccine in youths and young adults with a history of acute lymphoblastic leukemia and allergy to PEG-asparaginase

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Abstract

Vaccination is a critical tool in the prevention of COVID-19 infection for individuals and for communities. The mRNA vaccines contain polyethylene glycol (PEG) as a stabilizer. Currently, in North America, only the BNT162b2 (Pfizer-BioNTech) mRNA vaccine is approved for individuals aged 12–17. Most patients treated with contemporary regimens for acute lymphoblastic leukemia receive PEG-asparaginase (PEG-ASNase) and 10%–30% will develop allergic reactions. Optimizing access and safety for vaccine administration for these patients is critical. This report describes a process developed to support COVID vaccination in a cohort of adolescents and young adults with a history of PEG-ASNase allergy.

KEYWORDS

allergy, COVID, PEG-asparaginase, vaccine

1 | INTRODUCTION

The COVID-19 virus has been responsible for a global health crisis with, to date, over 150 million cases and 3.7 million deaths worldwide.^{1,2} Those with a malignant diagnosis are at risk of poor outcome following COVID-19 infection.^{3–7}

Vaccination is a critical infection prevention tool and several vaccines have been proven to prevent serious infection with COVID-19, including mRNA-based and adenovirus-vector vaccines.^{8–12} For pediatric patients, aged 12–17, only the BNT162b2 mRNA (Pfizer-BioNTech) vaccine is currently approved by Health Canada and

the American Federal Drug Administration under Emergency Use Authorization.^{13,14}

mRNA vaccines contain polyethylene glycol (PEG) as a stabilizing agent for lipid nanoparticles.¹⁵ Anaphylaxis has been reported, at a rate of 4.7 cases/million doses, following BNT162b2 vaccination, and PEG has been identified as a candidate allergen.^{16–19} Prevacination screening questionnaires, if aligned with World Health Organization recommendations, advise enquiring about PEG allergy.^{20,21}

PEG-asparaginase (PEG-ASNase), an important component of modern-day treatment regimens for acute lymphoblastic leukemia (ALL), is associated with a uniphasic hypersensitivity reaction in 10%–30% of exposed pediatric patients with cancer.^{22,23} Investigations to determine if these allergic reactions are due to the PEG-moiety or the asparaginase component are not routine.

Abbreviations: ALL, acute lymphoblastic leukemia; CDC, Center for Disease Control; CTCAE, Common Terminology Criteria for Adverse Events; EMR, electronic medical records; PEG, polyethylene glycol; PEG-ASNase, PEG-asparaginase.

The US Center for Disease Control (CDC) advises "precautions" be taken in individuals with "a history of immediate allergic reaction" to an injectable medication containing components that are also components of the COVID-19 vaccine.²⁰ Both CDC and Health Canada state that mRNA vaccines are contraindicated in patients with known PEG allergy and advise that, if BNT162b2 is considered, patients should be evaluated by an allergist before vaccination.^{24–27}

Given that PEG-ASNase allergy is commonly encountered in patients with ALL and considering the lack of clarity as to the most effective means of evaluating PEG allergy risk, we designed a strategy to provide safe BNT162b2 vaccination to this population.

2 | METHODS

Participants were patients at The Hospital for Sick Children (SickKids), a tertiary pediatric facility in Toronto, Canada. All current patients, with a documented allergy to PEG-ASNase and an age of 12 or older, as of June 1, 2021, were identified from electronic medical records (EMR). A small number of young adult patients were identified from Princess Margaret Cancer Centre, a Toronto-based adult oncology hospital.

Patients received a phone call from a "COVID-19 vaccine program" nurse and a standardized questionnaire was employed. Patients were asked whether they had received the first COVID-19 vaccine dose. Patients who had not yet received the vaccine were asked to confirm previous allergy to PEG-ASNase. They were asked to report if they experienced symptoms of allergy to other PEG-containing products, specifically PEG 3350-based laxatives. Questionnaire responses were reviewed, patients triaged, and assigned to vaccine clinic booking, allergy service referral, or scheduled follow-up with their primary oncology team.

Those with no positive history of allergy to other PEG-containing products, including those for whom no "challenge" by exposure to such products could be identified, were booked for vaccination clinic. Any patient identified as having a suspected allergy to other PEG-containing products was referred to the SickKids allergy service. Those reluctant to proceed with vaccination received a follow-up phone call from their oncology staff to facilitate discussion.

The vaccination clinic was staffed by "COVID-19 vaccine program" nurses and four pediatric oncologists. Psychosocial personnel were in attendance to provide reassurance to hesitant clinic attendees. All patients received BNT162b2 and were observed for 30 min postvaccine.

For those vaccinated at the clinic, chart review was performed to confirm date and severity of PEG-ASNase allergy. Severity was graded as per Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 criteria. In addition, EMR medication review was performed to confirm exposure to PEG-based laxative.

3 | RESULTS

In total, 65 patients were identified as having a PEG-ASNase allergy. Four patients could not be contacted. Of the 61 contacted, 1 patient had severe pancreatitis and not allergic reaction to PEG-ASNase and

15 had already received their first COVID-19 vaccine dose. None of those vaccinated self-reported a subsequent allergic reaction. Though not systematically assessed, to our knowledge, none of these patients received allergy directed premedications prior to vaccination.

Of the remaining 45 patients, 12 declined the invitation for vaccination: 4 based on distance from the vaccine clinic, 1 due to pending allergy appointment, and the other 7 due to concerns regarding vaccine safety/undeclared reasons.

One patient had a history of grade 4 allergic reaction to PEG-ASNase and grade 2 reaction to PEG 3350-based laxative. This patient was referred to the allergy service.

Thirty-two patients attended the vaccination clinic (Table 1). All had a positive history of CTCAE grades 2–4 allergy to PEG-ASNase. No patients were premedicated with antihistamines or otherwise. All received the Pfizer-BioNTech vaccine and were observed for 30 min following vaccination. No patients had signs or symptoms of allergic reaction.

4 | DISCUSSION

Vaccination is a critical tool in protecting individuals and communities from COVID-19 infection. Children and adolescents, with a history of PEG-ASNase allergy, need careful consideration. Proceeding, in a timely fashion, with COVID-19 vaccination offers the benefit of infection prevention and may have ramifications for schooling, employment and travel.

In some settings, consultation with the allergy service to investigate PEG allergy, is a barrier to timely vaccination. The utility of PEG skin testing in pediatric and immunocompromised patient remains unclear.^{18,28,29}

For patients with PEG-ASNase allergy, the risk of anaphylaxis to BNT162b2 may be lower than in other patient groups with suspected/known PEG allergy. This is because some patients labeled as PEG-ASNase allergic are sensitized to the asparaginase component and not the PEG-moiety.^{22,23,29} Additionally, PEG-ASNase and BNT162b2 contain PEG of differing molecular weight; allergenicity correlates with molecular weight.^{24,28–30} To the best of our knowledge, there have been no allergic reactions to BNT162b2 in patients with PEG-ASNase allergy.

Risk-mitigating strategies that we employed included screening for allergy to other PEG-containing products. It is unclear if tolerance to oral PEG is a reasonable screen prior to intramuscular administration of BNT162b2, but this strategy has been suggested for the oncology population.³¹ Additionally, we provided vaccination in a hospital setting with a well-staffed clinic and, as is recommended for high-risk groups, mandated that patients be observed 30 min after vaccination.³²

It is acknowledged that the number of patients enrolled in our clinic was small and that findings may not be reducible across a larger cohort. This is an obvious limitation. However, it is encouraging that no significant allergic events were observed and suggests that, with an appropriate triage process, patients with PEG-ASNase allergy can avoid formal allergy consultation and safely receive BNT162b2.

TABLE 1 Patients with PEG-ASNase allergy who received the Pfizer-BioNTech vaccine in clinic

Patient demographics	
Age in years (mean, range)	16 (12–29)
Interval from PEG-asparaginase allergy in years (mean, range)	7 (0.5–14) ^a
Grade of PEG-asparaginase reaction (n, %)	
2	2 (6%)
3	19 (59%)
4	11 (34%)
Tolerance of PEG containing oral agent (n, %)	
Evidence of exposure	22 (69%) ^b
No evidence of exposure	10 (31%)

^aUnknown date for two patients.

^bAll patients with documentation of exposure in medical record; in addition, 15 of 22 had parent or patient recall of receipt of PEG containing oral agent.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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