PRICKLY BUSINESS

Developing Skin Prick Testing for Antineoplastic Therapy

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Background

Cancer may be treated with a variety of medicines, including conventional chemotherapy, immunotherapy such as atezolizumab, and antineoplastic antibodies such as bevacizumab or cetuximab.

Hypersensitivity reactions to antineoplastic therapy may limit treatment options for patients with cancer.

Skin prick testing for cytotoxic or hazardous medicines had not been previously performed at our large tertiary referral hospital.

Case Introduction

Case 1: A 45-year old male with non-small cell lung cancer developed a late-onset rash following cycle 1 of chemo-immunotherapy treatment with bevacizumab, atezolizumab, paclitaxel and carboplatin. During his second cycle, the patient developed a rash during infusion of atezolizumab and bevacizumab, and then anaphylaxis during the paclitaxel infusion. Immunology was consulted and recommended skin prick testing for bevacizumab, atezolizumab and paclitaxel to confirm the cause of hypersensitivity.

Cases 2 and 3: A 64-year old male and 51-year old female with EGFR-positive colorectal cancer experienced anaphylaxis to their first dose of cetuximab. Immunology was consulted and recommended skin prick testing with an alternative anti-epidermal growth factor antibody, panitumumab, to determine safety with using this alternative.

Case Progress

Immunologists requested skin prick tests to be manufactured by the cytotoxic production pharmacy.

For case 1, the immunologist requested the following dilutions for each drug: 1:1 (neat), 1:5, 1:10, 1:50, 1:100, 1:500, 1:1000, 1:5000, 1:10,000, 1:50,000, 1:100,000. For cases 2 and 3, the immunologist requested dilutions of 2, 0.2, 0.02, 0.002 mg/mL.

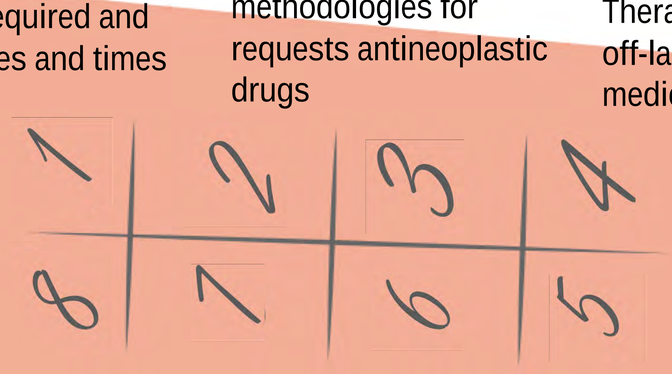
Skin prick tests were manufactured in the aseptic cytotoxic production unit by validated pharmacy technicians. Sodium chloride 0.9% was used as a diluent based on compatibility data. Half or one millilitre of each dilution was provided to the immunologist for skin prick testing. Due to the absence of stability data, the products were manufactured for use on the day of testing.

Pharmacist Interventions

1. Liaise with immunologists regarding dilutions required and testing dates and times

2. Perform literature search for available methodologies for requests antineoplastic drugs

3. Assist with governance approval from Drug and Therapeutics Committee for off-label use of high cost medications



4. Perform calculations for requested dilution (Image 1)

5. Generate clear methodology, worksheets and product labels (Image 2)

6. Seek independent review of calculations and methodology from Senior Production Pharmacist

7. Organise rostering of an extra pharmacy technician dedicated to making the dilutions due to lengthy time of production

8. Educate immunologists about the necessary personal protective equipment to be worn during administration

Atezolizumab					
Strength (mg)	Volume (mL)	C (mg/mL)	Vial details		
1200	20	60			
Dilution (1:*x*)	Volume (mL)	Added to (mL)	Total V (mL)	C (mg/mL)	Dilution check (concentration x dilution factor)
1	1	0	1	60	60
5	1	4	5	12	60
50	1	9	10	1.2	60
500	1	9	10	0.12	60
5,000	1	9	10	0.012	60
50,000	1	9	10	0.0012	60
Dilution (1:*x*)	Volume (mL)	Added to (mL)	Total V (mL)	C (mg/mL)	Dilution check (concentration x dilution factor)
1	1	0	1	60	60
10	1	9	10	6	60
100	1	9	10	0.6	60
1,000	1	9	10	0.06	60
10,000	1	9	10	0.006	60
100,000	1	9	10	0.0006	60

Image 1: Example of serial dilution calculation performed for atezolizumab.

Case Outcomes

Case 1: Skin prick testing demonstrated hypersensitivity to paclitaxel from 1:50,000, atezolizumab from 1:5000 and bevacizumab from 1:1000. Immunology recommended discontinuation of paclitaxel and offered a desensitisation to atezolizumab and bevacizumab. Combination chemo-immunotherapy was ceased and the patient was commenced on chemotherapy with carboplatin and pemetrexed. Due to disease progression, the patient was commenced on immunotherapy with nivolumab monotherapy. Unfortunately, the patient experienced a hypersensitivity reaction to nivolumab. Immunology were consulted again and recommended desensitisation to nivolumab. The patient currently remains on treatment with nivolumab via a desensitisation protocol each cycle.

Cases 2 and 3: Skin prick testing was negative to panitumumab. Both patients were subsequently administered intravenous panitumumab as part of their cancer treatment without hypersensitivity complications.

Conclusion

Skin prick testing for antineoplastic therapy required multidisciplinary consultation, considerable planning and production time.

Skin prick testing confirmed hypersensitivity to all three agents in case 1. Negative results to panitumumab skin prick testing correctly predicted nil hypersensitivity to systemic treatment in Cases 2 and 3.

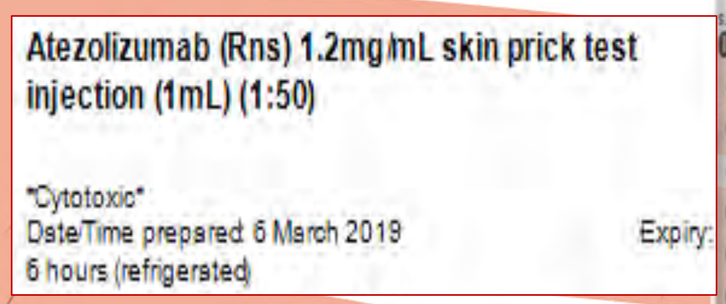


Image 2: Example of label generated for atezolizumab skin prick test

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