

# Immune checkpoint inhibitors (immunostimulants) and vaccination

**Influenza.**  
Don't get it.  
Don't give it.

April 2018

## What are immune checkpoint inhibitors?

Immune checkpoint inhibitor treatments are relatively new and evolving forms of immunotherapy that enhance (or augment) the anti-tumour immune system response so it is more effective at eliminating tumour cells. The four immune checkpoint inhibitor treatments currently used in New Zealand are atezolizumab (Tecentriq®), ipilimumab (Yervoy®), nivolumab (Opdivo®) and pembrolizumab (Keytruda®).

## How do they work?

Checkpoint proteins on the outside of our own healthy immune cells help the immune system regulate the immune response by distinguishing 'self' from 'foreign' or in the case of a tumour, 'altered self'. The presence of these proteins stop the immune system from attacking 'self' and causing autoimmune disease, but these proteins also help the tumour cells evade the immune response.

Immune checkpoint inhibitors stimulate the actions of the immune system. For many years it has been noted that the immune system can develop a weak response to some tumour cells. Recently it has been shown that dysregulating the immune system's control mechanism and inhibiting checkpoint proteins greatly increases the natural anti-tumour immune response. The tumour cells can be seen as 'altered self' by the immune system and attacked. However, the immune system may also stop seeing healthy cells as 'self' and attack them too, causing autoimmune disease.

## What are their side effects?

Not every person receiving immune checkpoint inhibitor treatments experiences serious side effects. However, serious immune-mediated side effects have been documented in some people receiving these treatments, including fatal myositis, myocarditis, rhabdomyolysis and other autoimmune conditions.

What makes one person more susceptible to serious immune-mediated side effects compared with a person who isn't is not known. Theoretically, any event that causes the immune system to increase its activity could trigger the immune system to target healthy cells.

## Why is vaccination a precaution for people receiving these treatments?

In a few people receiving a combination of ipilimumab and nivolumab, the onset of fatal myositis, myocarditis and rhabdomyolysis was observed sometime after receipt of an influenza vaccination. It was not possible to identify if the onset of these treatment-related autoimmune side effects was directly related to receipt of the influenza vaccination. However, the theoretical risk that any event that stimulates the immune system could trigger the onset of autoimmune drug side effects means a possible role of influenza vaccination cannot be discounted.

It is for this reason that a new influenza vaccination precaution has been made for people receiving immune checkpoint inhibitor treatments in New Zealand. Other countries, such as Australia and Canada have issued similar precautionary advice, but as this is a rapidly evolving therapy area there are currently no international consensus statements on the use of vaccines in people receiving immune checkpoint inhibitor treatments.

## What do we do before vaccinating a person receiving these treatments?

In New Zealand, specialist advice must be sought before administering any vaccine, including influenza vaccine, to person who has received atezolizumab (Tecentriq®), ipilimumab (Yervoy®), nivolumab (Opdivo®) or pembrolizumab (Keytruda®) within the preceding 6 months.

If you are unable to contact a person's specialist, phone 0800 IMMUNE (0800 466 863) for advice before vaccinating.

## References

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