

FIXED VS WEIGHT-BASED DOSING OF PEMBROLIZUMAB FOR PATIENTS UNDER 80 KG, BASED ON OBSERVED ADRS IN ONE CANCER SETTING

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Background

Monoclonal antibodies are usually dosed by the kilogram of the patient's weight, due to perceived contribution of body size in pharmacokinetic variability. Lately, especially during the COVID pandemic, a lot of monoclonal antibodies, including pembrolizumab, were switched to fixed dosing. Pembrolizumab was initially dosed at 2 mg/kg, fixed dosing includes 200 mg every three weeks or 400 mg every six weeks (Freshwater, 2017). The fixed dosing is more convenient, eliminates the waste, might improve patient's compliance and reduces dosing errors. However, for the patients that weigh less than 80 kg, fixed dose is associated with almost maximum exposure, which is also associated with greater occurrence of toxicity (CADTH, 2020).

Purpose

The aim of this retrospective study was to determine whether it is better to use fixed or weight-based dosing of pembrolizumab for patients under 80 kg in order to avoid serious ADRs.

Materials and methods

We observed ADRs that occurred with 391 patients receiving pembrolizumab in 2021, regardless the diagnosis. We collected the data by reviewing patients' documentation. The patients were distributed across oncology indications, including NSCLC, melanoma, breast cancer, urothelial carcinoma, cervical cancer, Hodgkin lymphoma, head and neck squamous cell carcinoma, oesophageal cancer and renal cell carcinoma.

Results

The patients were split into two subgroups, under and over 80 kg in weight (group 1 and 2). For 29 patients, data about weight was not available. 198 patients were in group 1, whereas in group 2 there were 164 patients. The ADRs occurred in 69 patients (34,8 %) from group 1 and 46 patients from group 2 (28,0 %). The most common ADRs occurred were skin toxicities, hypothyreosis, muscle and joint pain, diarrhea and fatigue. There were no significant differences in the occurred ADRs between group 1 and 2.

Number of patients

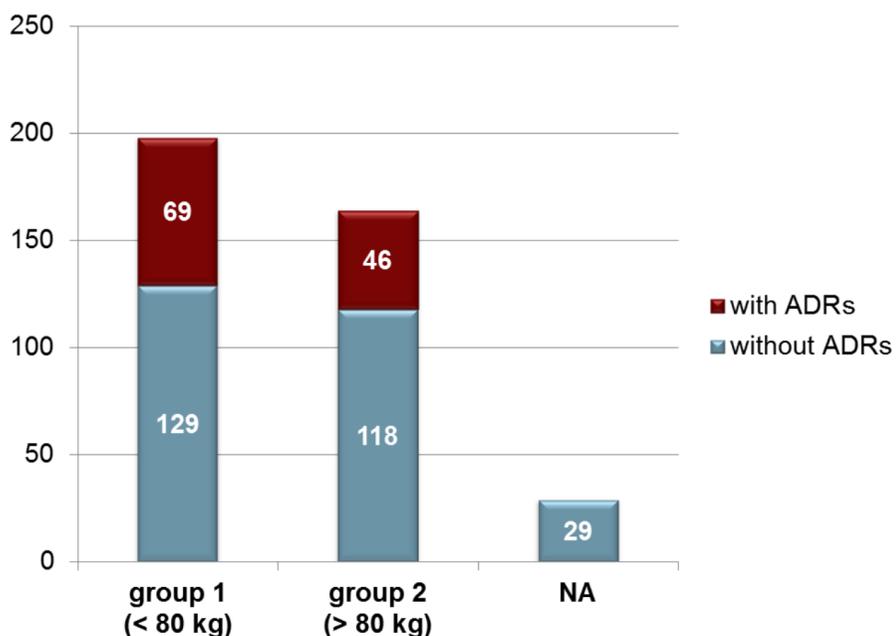


Figure 1. Number of patients with / without ADRs in two subgroups.

Common ADRs in group 1 (< 80 kg)

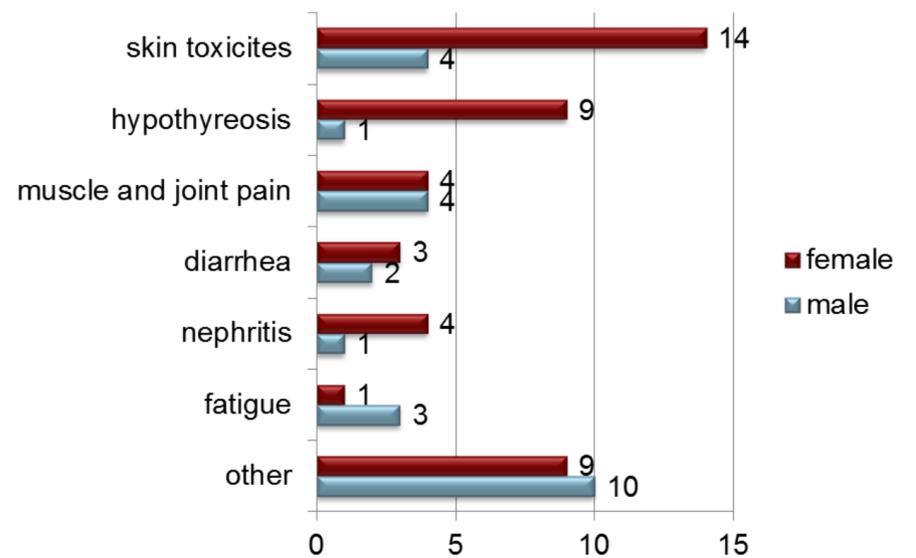


Figure 2. Common ADRs in group 1 (patients under 80 kg).

Common ADRs in group 2 (> 80 kg)

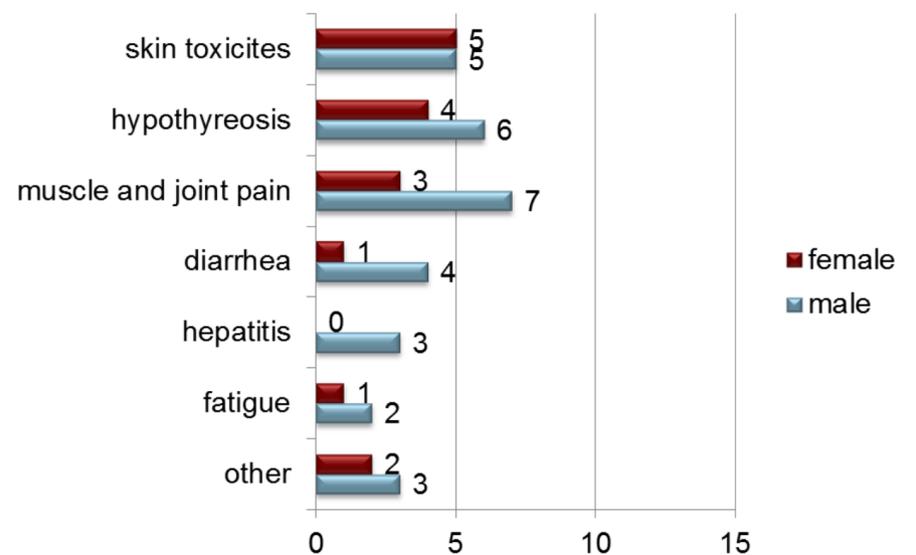


Figure 3. Common ADRs in group 2 (patients over 80 kg).

Conclusion

The results indicated that for patients under 80 kg, weight-based dose would not only be better in terms of less toxicity, but it would also be more cost effective. The adaptation of fixed dosing regimens would lead to the estimated 26 % of additional cost (e.g. 50 kg patient would receive 100 mg dose, which means half price of the fixed dose) (Monirul et al, 2020).

References

- https://www.cadth.ca/sites/default/files/pdf/dosing_and_timing_of_immuno-oncology_drugs_in_brief.pdf
- Freshwater, T. et al. (2017). 'Evaluation of dosing strategy for pembrolizumab for oncology indications', Journal for ImmunoTherapy of Cancer, 5:43, pp.1-9.
- Monirul, S. et al. (2020). 'Budget Impact Analysis of Fixed Dose Versus Weight-Based Dosing Regimen of Nivolumab and Pembrolizumab in the Treatment of Non-Small Cell Lung Cancer', Vaccines (Basel), 3;8(4):730.