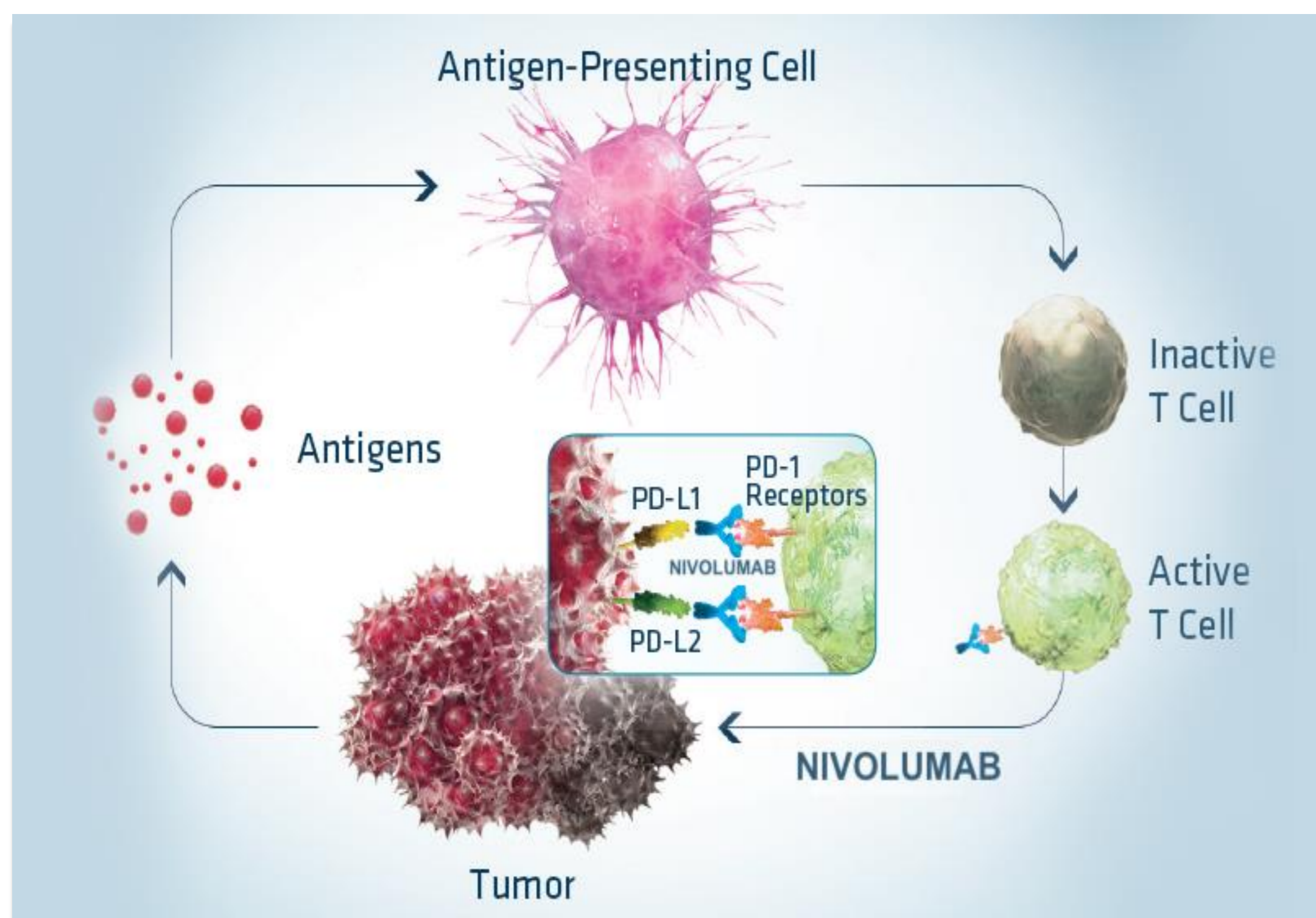


# NIVOLUMAB FLAT DOSE, CLINICAL-ETHICAL AND ECONOMIC IMPLICATIONS

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## Background

In Italy, on 2<sup>nd</sup> of May 2018, was approved the use of **nivolumab** (Opdivo) in monotherapy in the **240 mg** dose every two weeks to replace the weight based dosage (**3 mg/kg**) for all approved indications (melanoma, non-small cell lung cancer -NSCLC-, renal cell carcinoma -RCC-) and a dose of 480 mg every four weeks (melanoma and RCC). The dosage change was based on pharmacokinetic data that showing good safety up to a dose of 10 mg/kg. The previous dosage was defined **OFF-LABEL**.

## Purpose

The purpose of this estimation is to evaluate any change in the **drug-related adverse (ADR) events** and any additional costs after the transition to the **FLAT-DOSE**.

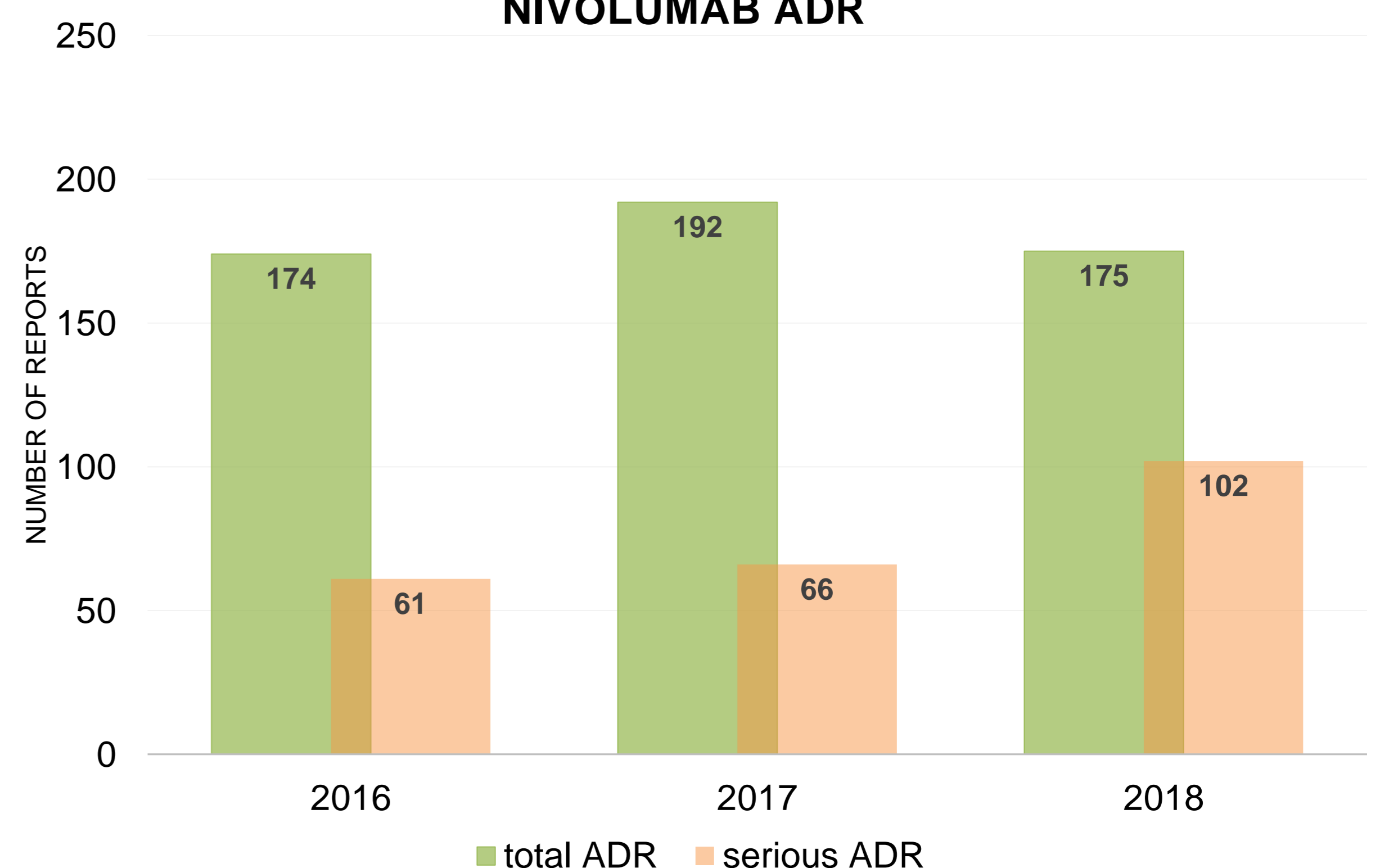
## Materials & methods

We collected data from the National Pharmacovigilance Network (NPN) from the 2<sup>nd</sup> of May to 15th October in the years **2016, 2017** and **2018**. The number of reported ADRs and the percentage of severe ADR has been compared (deaths were not considered). For the estimation of costs we considered all patients who received nivolumab treatment from 2016. For the naive patients after the 2<sup>nd</sup> of May, the dose was calculated with the old scheme of **3 mg/kg**. For patients who have already discontinued therapy the dose difference was calculated with the flat-dose. The price ex-factory per mg was **€ 13,44**.

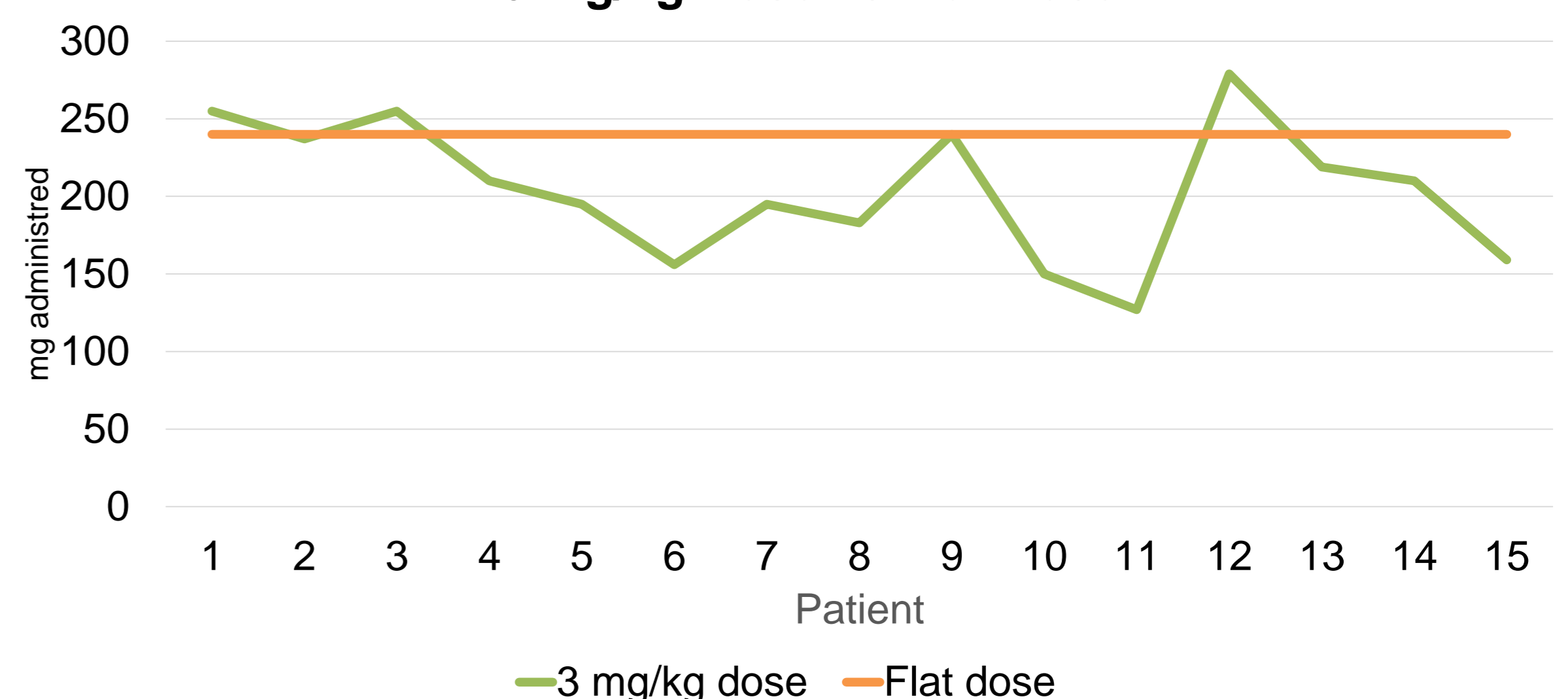
## Results

The reported ADRs in NPN were respectively: **174 (35,1% serious)**, **192 (34,4% serious)** and **175 (58,3% serious)**. For the estimation of costs, was measured an average increase of **35,3 mg** for a single administration, corresponding to an increase of **€ 474,43**.

## NIVOLUMAB ADR



## 3 mg/kg Dose vs Flat Dose



## Conclusion

Since the flat-dose was calculated on a hypothetical patient weighing of **80kg**, it was easy to view a rapid increase in direct costs related to the drug (**11 out of 15 of the patients considered had lower weight**). Despite the bias related to the applied methodology, it is possible to think that the costs associated with nivolumab will increase. Furthermore, **it is not clear why the 3 mg/kg dosage is to be considered off label**. Furthermore, it is interesting to note that the number of serious ADRs has increased. However, pharmacovigilance monitoring is required to evaluate changes in the safety profile.

