SAFETY PROFILE OF PEMBROLIZUMAB MONOTHERAPY VERSUS PEMBROLIZUMAB WITH COMBINED TREATMENTS: ANALYSIS OF FRENCH PHARMACOVIGILANCE DATABASE

Samy Babai*, Axelle Histe, Laure Thomas. Mondor Hospital, Creteil, France

Background The adverse drug reactions (ADRs) of cancer immunotherapies are mainly immuno-mediated with a first-line treatment which is essentially based on the use of corticosteroids. A favorable evolution of these toxicities after exposure to corticosteroids reinforces the imputability of immunotherapies in the occurrence of these ADRs. Furthermore, since pembrolizumab is eliminated from the circulation by catabolism, no metabolic drug interaction is expected. However, chronic or acute treatments associated with immunotherapies can influence the occurrence of ADRs. The aim of the study is to analyse and compare ADRs occurring with pembrolizumab alone versus ADRs occurring with pembrolizumab and combined treatment.

Methods The French Pharmacovigilance Database (FPD) has registered all adverse drug reactions (ADRs) spontaneously reported by health professionals in France since 1985. The safety profile of 2 cohorts patients was compared. The 1st cohort concerns patients exposed to pembrolizumab and having experienced at least one ADR. The 2nd cohort concerns patients exposed to permbrolizumab with acute or chronic treatment.

Results From January 2016 to January 2020, a total of 1000 reports of Pembrolizumab induced ADR were recorded in the FPD. Among these 1000 observations, 500 cases were registred with pembrolizumab associated with associated treatment (acute and chronic) and 500 were registred with pembrolizumab alone.

The comparison of the 2 cohorts regarding the average number of ADRs per patient (1.7 vs 1.6), the time to onset of ADRs (4.3 months vs 4.2) and the most frequent organ injury (5% of liver injury for the both cohorts) were quite similar. (table 1)

Cases of positive rechallenge occurre in 52% (13/25) for patients exposed to pembrolizumab alone versus 4% (13/331) for patients treated with pembrolizumab and associated treatment.

In 11% of cases of colitis after exposure to pembrolizumab, the patient was exposed to esomeprazole as chronic treatment. In 11% of cases of colitis after exposure to pembrolizumab, the patient was exposed to esomeprazole as chronic treatment.

Conclusions The cases of positive rechallenge during readministration of immunotherapy are different between the 2 cohorts. It could be a protective role of associated treatments or a dubious imputability of pembrolizumab.

The use of antacid drugs negatively impacts the survival of cancer patients treated with anticancer drugs. Moreover, this study showed an increased risk of colitis when esomeprazole is associated with pembrolizumab. Identifying predictive factors could contribute to improve patient selection for ICI treatment and is currently the topic of many ongoing research projects worldwide. Epidemiological studies are necessary to confirm these first results of tolerance of treatments associated with pembrolizumab.

Acknowledgements The authors wish to thank the French network of Pharmacovigilance centres.

REFERENCES
