

IN USE PHYSICOCHEMICAL STABILITY OF PEMBROLIZUMAB UNDER THE DILUTION CONDITION REQUIRED FOR USE IN A DAY HOSPITAL

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BACKGROUND AND IMPORTANCE

Pembrolizumab is a monoclonal antibody widely used in the oncology field at a fixed dose of 200 mg.

The stability of pembrolizumab diluted in 0.9% sodium chloride solution, is 96 h stored between 2-8 °C, as reported in the Summary of Product Characteristics [1].

AIM AND OBJECTIVES

The purpose of this study was to evaluate the in-use stability of pembrolizumab diluted at clinically relevant concentration and stored in polyolefin infusion bags over a 14-day period.

It could have a practical implication in the possibility to compound these solutions in advance, with a view to a strategic reorganization and optimization of work in an antineoplastic drug preparation laboratory integrated in a Day Hospital system.

MATERIALS AND METHODS

Analysis was performed on 3 samples of pembrolizumab at a concentration of 2 mg/ml stored at 2-8 °C, on days 0, 1, 4, 7, 11 and 14. Analyses included pH, osmolality, turbidimetry, dynamic light scattering (DLS), size-exclusion chromatography (SEC-HPLC) and nanoparticle tracking analysis (NTA). These methods were selected on the basis of a preliminary study on samples subjected to mechanical and thermal stresses.

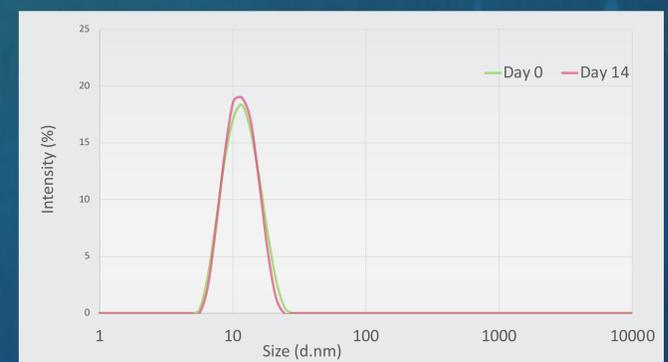
RESULTS

All samples were clear, without particulate or precipitates, turbidity-free. pH and osmolality did not reveal different results at day 14 compared with day 0. Using SEC-HPLC, only one peak was found corresponding to the monomer of pembrolizumab with a retention time (Rt) at 16.27±0.02 and 16.41±0.08 at day 0 and day 14, respectively. No signs of aggregates or fragmentations were detected since Rt and AUC of peaks remained constant over time. At all-time points, DLS showed a monomodal sample with a hydrodynamic diameter around 11 nm. These results were in agreement with NTA data.

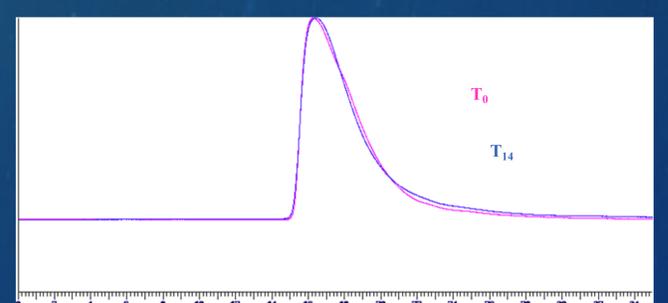
CONCLUSION AND RELEVANCE

No physicochemical instability of pembrolizumab solutions was observed in the considered period of time. Therefore, the preparation in advance of pembrolizumab might be considered in a perspective of dose banding for a cost-saving strategy, for reducing the patient's waiting time between the evaluation and the beginning of a treatment, for avoiding the waste of drugs.

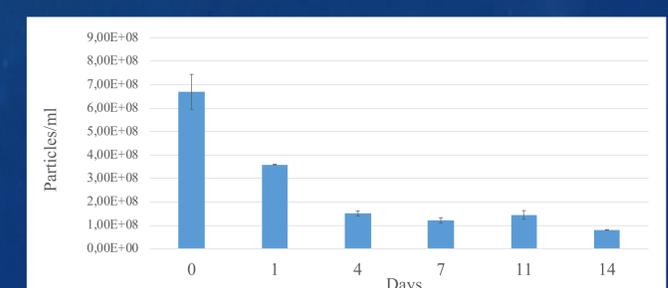
Maintenance of biological activity and lack of immunogenicity should be investigated to confirm these studies.



Dynamic light scattering analysis



SEC-HPLC analysis



Nanoparticle tracking analysis