

SHORT-TERM STABILITY OF DILUTED SOLUTIONS OF THE MONOCLONAL ANTIBODY DARATUMUMAB

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Background and Importance

Monoclonal antibodies (mAb) are biotechnological products mostly used as therapeutic agents. Because of their nature, mAb may go through a variety of chemical and physical degradation processes upon handling. For this reason, extended in-use conditions are not included in stability assessment prior to regulatory approval. Daratumumab, a CD38-targeting, human IgG1 K mAb, is largely used in the treatment of multiple myeloma. After dilution in saline (0.9% sodium chloride) solution using the appropriate aseptic technique, it is reported to be physically and chemically stable for 24 h at refrigerated conditions (2-8 °C) protected from light [1]



Aim and Objectives

To evaluate the physicochemical stability of daratumumab diluted at clinically relevant concentration over a 14-d period

Materials and Methods

Daratumumab (Darzalex®, Jassen Biotech, B) was diluted to concentrations of 1.2 and 2.0 mg/mL in low-density polyethylene (LDPE) infusion bag in saline solution for intravenous injection (B. Braun, Italy). To determine changes in physicochemical properties over a 14-day period, various methods were used: size-exclusion chromatography (SEC-HPLC), dynamic light scattering (DLS), nano-particle tracking analysis (NTA), turbidimetry, pH and osmolality. They were selected based on the preliminary results of a forced degradation study [2].

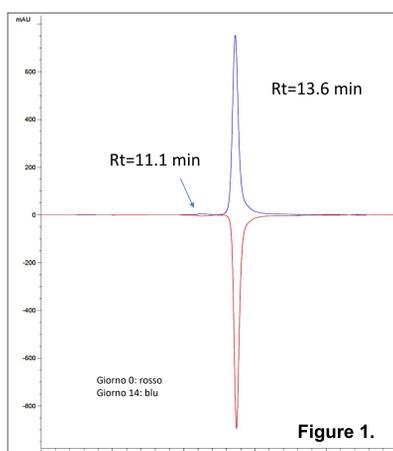
Results

All samples remained clear with no precipitates or particulate matter detected with the naked eye.

- **TURBIDITY:** No change was observed
- **PH:** range 5,53-5,85,
- **OSMOLALITY:** range 296-313 mOsm/Kg,
- **SEC-HPLC:**



No changes, No instability



SEC-HPLC did not show the formation of aggregates or fragmentations. The ratio between the major peak (Rt=13 min) and a minor signal (Rt=11 min) remained constant over time

●- DLS

No clear trend in the presence of sub-visible particles was observed by DLS. Indeed, the main peak of daratumumab was detected at about 13 nm which accounted for up 98% and 95% for 1.2 mg/mL and 2.4 mg/mL solution, respectively.

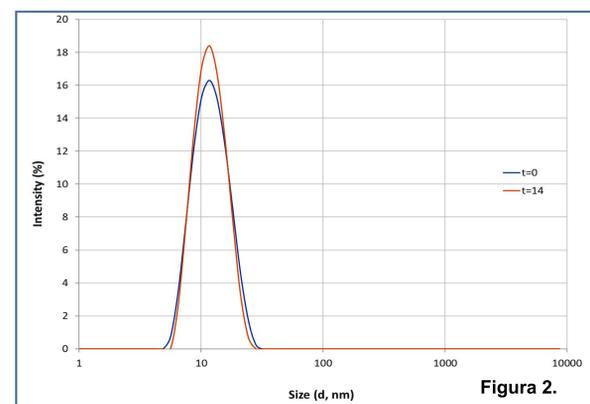


Figure 2. 1.2 mg/ml day 0 (blue) and day 14 (red).

●- NTA

NTA revealed a particle level of about 60X10⁶ particles/mL for the physiologic solution used as reference.

Conclusions

No physico-chemical variations were evident in daratumumab solution at 1.2 mg/ml and 2 mg/ml stored in LDPE infusion bag at 2-8 °C. The evaluation of biological activity is required to confirm the extended in-use stability.