SHORT-TERM STABILITY OF DILUTED SOLUTIONS OF THE MONOCLO-NAL ANTIBODY DARATUMUMAB

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Background and Importance

Monoclonal antibodies (mAb) are biotechnological products mostly used as ther-apeutic agents. Because of their nature, mAb may go through a variety of chemi-cal and physical degradation processes upon handling. For this reason, ex-tended in-use conditions are not included in stability assessment prior to regula-tory approval. Daratumumab, a CD38-targeting, human IgG1κ 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) pro-tected 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 so-lution for intravenous injection (B. Braun, Italy). To determine changes in phys-ico-chemical 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 se-lected 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

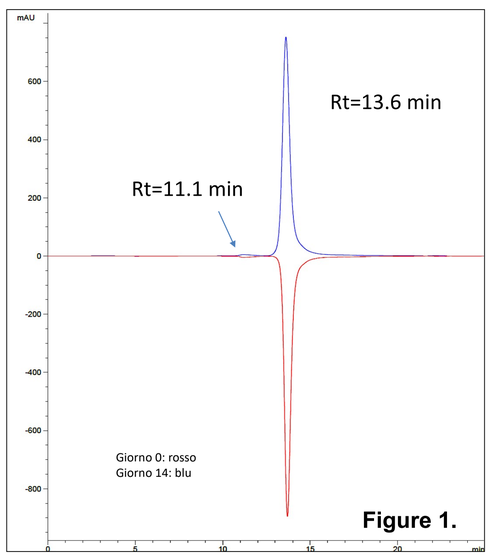

Figure 1.

SEC-HPLC did not show the formation of aggregates or frag-mentations. 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.

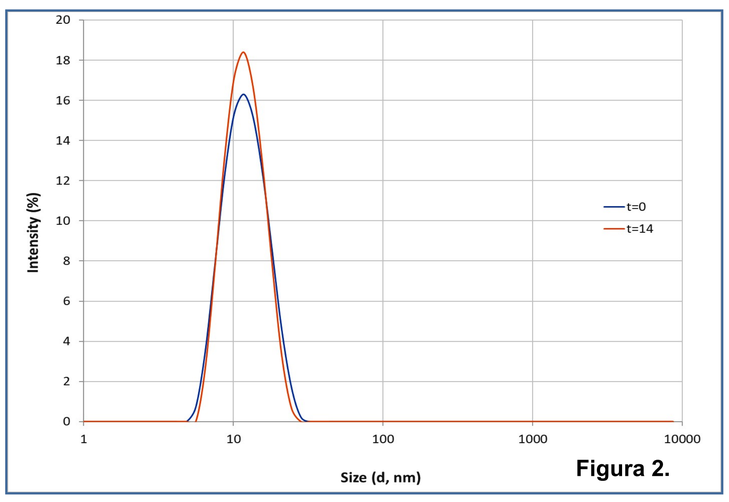

Figura 2.

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 bio-logical activity is required to confirm the extended in-use stability.

References and/or acknowledgements:
[1] Darzalex Summary of product characteristics. https://ec.eu-ropa.eu/health/documents/community-regis- ter/2017/20170428137394/anx_137394_en.pdf [2] Joubert M.K. et al., J Biological Chemestry 267(30): 25266-25279.