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 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 κ 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 solution 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:

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.

- 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: