STABILITY OF NIVOLUMAB SOLUTIONS AFTER TRANSPORT THROUGH PNEUMATIC TUBE SYSTEMS

Francesca Selmin; Laura Camuffo; Francesca Vasile; Greta Mangoni; Mariantonietta Piccoli; Melania Rivano; Luca Cancanelli; Paola Minghetti

1 Dept. Pharmaceutical Sciences, University of Milan, Via G. Colombo 71, Milan (I) 2 School in Hospital Pharmacy, University of Milan, Via G. Colombo 71, Milan (I) 3 Dept. Chemistry, University of Milan, Via Golgi 19, Milan (I) - Corresponding Author: paola.minghetti@unimi.it

Abstract number: 25PD-029

PNEUMATIC TUBE SYSTEM in HOSPITALS...

... not recommended for active substances that could undergo physical alterations [1].

... could promote plasticizer nanodroplets extraction in saline polyvinyl chloride bags, with activation of the complement system in vitro assay [2].

... could produce signs of aggregation in diluted solution of rituximab in presence of air into the bag, probably due to the air-liquid interface [3].

This work AIMS to investigate:
- the stability of diluted solutions of nivolumab after PTS delivery;
- the effect of residual air inside the bag upon storage.

With residual air

Nivolumab

2.4 mg/mL in physiologic solution (bags: 100 mL pre-filled polyolefin infusion bag)

Without residual air

Control sample

Single pass in PTS

Two-station, bidirectional, STRAIN MC2/160 system

With residual air

Larger aggregates (i.e. > 5 μm) were not observed upon 7 days

Osmolality did not undergo to variation ranging from 283 to 297 mOsm/Kg during storage.

In all solutions pH ranged from 5.8-6.0 over time, in agreement to manufacturer’s pH range.

With residual air

Without residual air

Larger aggregates (i.e. > 5 μm) were not observed upon 7 days

Osmolality did not undergo to variation ranging from 283 to 297 mOsm/Kg during storage.

In all solutions pH ranged from 5.8-6.0 over time, in agreement to manufacturer’s pH range.

Characterization of compounded mAb

Quality attributes target Justification Is it critical? Methods

Appearance Limpid Indicative of formation of visual aggregates YES Turbidimetry

pH 5.5-6.0 The buffer system assure the stability, solubility and tolerability of the mAb. YES pHmeter

Dosimetry 30 μm (m/kg) Variation in dosimetry can induce physical instability and pain at the injection site YES Dosimetry

Aggregation No aggregates Low levels of aggregates potentially can cause immunogenicity in patients. YES DLS, NTA, SEC-HPLC

Higher order structure Native folded structure Higher order structure (HOS) comprises the 3D structure necessary for function. Changes in HOS can affect safety, efficacy and pharmacokinetics YES DOS-PAGE, IMAC, CO

Stability indicating methods were applied based on results of a forced degradation study consisting of different stress conditions (i.e. high temperature, shear and mechanical stress)

REFERENCES:

CONCLUSIONS

• No differences in the main physical and chemical properties were observed in compounded nivolumab solutions after a single pass in PTS for at least 7 days of storage.
• The presence of air-liquid interface inside the bag was not risk determining for protein stability.
• These results support the possible use of PTS to deliver bags to clinical services.