Background and Importance

- Rituximab (RTX) is widely used in the treatment of several B-cell-derived haematological malignancies and non-oncology indications such as autoimmune diseases1,2
- Sandoz biosimilar of RTX (SDZ-RTX), Rixathon® or Riximyo®, is available as a concentrate solution for infusion as a single-dose vial3
- For any short-term temperature excursion outside the intended storage conditions, it is recommended to discard SDZ-RTX unless the excision is permitted according to the provided patient leaflet
- There is a limited evidence on the effect of short-term temperature excursions on the quality of an unopened SDZ-RTX vial stored in the original outer box at caregiver level

Materials and Methods

- The OOF stability study was performed with three SDZ-RTX batches of 39–43 months age: one batch of 100 mg (10-mL vials) and two batches of 500 mg (50-mL vials)
- The study was designed to simulate temperature excursion outside the intended storage conditions of 2–8°C, with a duration of up to 21 days. The OOF study was performed at OOF condition I (25 ± 2°C / 60 ± 5% RH) and OOF condition II (30 ± 2°C / 60 ± 5% RH) (Figure 1) - SDZ-RTX samples with the OOF duration of 21, 14 and 7 days were transferred from the intended conditions (2°-8°C) into stability chambers of OOF conditions I or II on Day 0, 7 and 14, respectively

Results

- The study also comprised SDZ-RTX reference sample, which was not exposed to the OOF conditions, based on which the effect of temperature excursion was evaluated
- On Day 21, all samples including reference samples were pulled from stability chambers and subjected to analyses, thus, allowing direct head-to-head comparison and reducing potential variability of the analytical method
- Identity was assessed with cation exchange chromatography (CEX) and liquid chromatography-ultraviolet (LC-UV) peptide mapping
- Purity was assessed using CEX, size exclusion chromatography (SEC), and non-reducing capillary electrophoresis-sodium dodecyl sulphate (nrCE-SDS)
- Complement-dependent cytotoxicity (CDC)-biactivity was utilized to assess potency
- Pharmacopeia test methods were utilized to assess clarity, presence of visible and subvisible particles, container appearance, degree of coloration, pH, osmolality, extractable volume. Microbiological parameters assessed were sterility and bacterial endotoxins
- Integrity of container was evaluated with the container closure integrity testing
- Protein content was assessed with the ultraviolet (UV)/visible absorbance spectrometry

- The analysis of SDZ-RTX purity with CEX revealed decrease in percentage of the main peak (Figure 2a), contaminant change in sum of acidic peaks (increase, see Figure 2b) and sum of basic peaks (decrease, see Figure 2c) was observed in all three SDZ-RTX batches after 21 days of OOF study

- For potency, which was measured with CDC-bioactivity, no common trend in stability behaviour could be determined for all three tested SDZ-RTX batches. At OOF condition I (25 ± 2°C / 60 ± 5% RH) changes within the range of method variability can be seen for all three tested batches. At OOF condition II (30 ± 2°C / 60 ± 5% RH), decrease in potency was observed only in one of the three tested SDZ-RTX batches; however, variation in data was observed in other two SDZ-RTX batches (Figure 2)

- No notable changes were observed across all batches in clarity (6 NTU [nephelometric turbidity unit] in all batches), visible and subvisible particles, container appearance, degree of coloration, pH, osmolality, extractable volume, and container closure integrity testing, protein content by UV spectrometry
- For microbiological tests, no notable changes were observed. All three batches meet the specification limits

Conclusions

- Findings of this study support single-time OOF temperature excursion in an unopened vial of SDZ-RTX stored in original outer box
- SDZ-RTX samples with the actual age even beyond the claimed shelf-life were shown as safe and fit for use even under worst-case conditions e.g., after subjecting for up to 21 days to the OOF conditions

References


Disclosures

All authors are employees of Novartis. All authors participated in the development of the poster and approved the final poster for presentation.

Acknowledgments

The authors thank Ankit Koushik, MS, and Saikat Keshri Gokari, Ph.D. (Novartis, India) for medical writing support and Saketh Vellanki for graphical design support.

Funding

The study was funded by Sandoz.