The Effects of Freeze-Thaw Cycling on the Stability of the Adalimumab Biosimilar SB5

3PC-204

Ebbers HC[1], Kim JH[2], Yun JH[2], Park DK[2], Hwang SJ[2], Park SJ[2]

[1]Biogen International GmbH, Baar, Switzerland; [2]Samsung Bioepis, Incheon, South Korea

https://www.eahp.eu/25-3PC-024

Conclusions

- SB5 was stable in the immediate pack (nude pre-filled syringe) when exposed to multiple freeze-thaw cycles.
- These results may help hospital pharmacists to assess the impact of temperature excursions during shipment or storage on the product quality of SB5.

Introduction

- Temperature excursions may occur during manufacturing, storage, distribution and clinical trials.
- Limited data are available to hospital pharmacists to support decision making following temperature excursions.

Objectives

- The purpose of this stability study was to evaluate the impact of high and low temperature conditions over a short period on the adalimumab biosimilar SB5.

Methods

Temperature exposure

- SB5 drug product (DP) was exposed to extreme temperature cycling conditions with a total of three cycles equating to 144 hours at 30 ± 2ºC/65 ± 5% relative humidity and 144 hours at –5 ± 3ºC (Table 1).

Table 1. Short-term temperature cycling stability study design for SB5 DP

	Storage conditions	Storage time
Cycle 1		
	30 ± 2°C/65 ± 5% RH	48 hours
	–5 ± 3°C	48 hours
Cycle 2		
	30 ± 2°C/65 ± 5% RH	48 hours
	–5 ± 3°C	48 hours
Cycle 3		
	30 ± 2°C/65 ± 5% RH	48 hours
	–5 ± 3°C	48 hours

RH, relative humidity

Assessments

- Samples were analyzed using a variety of validated methods for appearance, pH, protein concentration, container closure integrity, impurities, charge variants, oxidation, endotoxin, particulates and biological activity.

Results

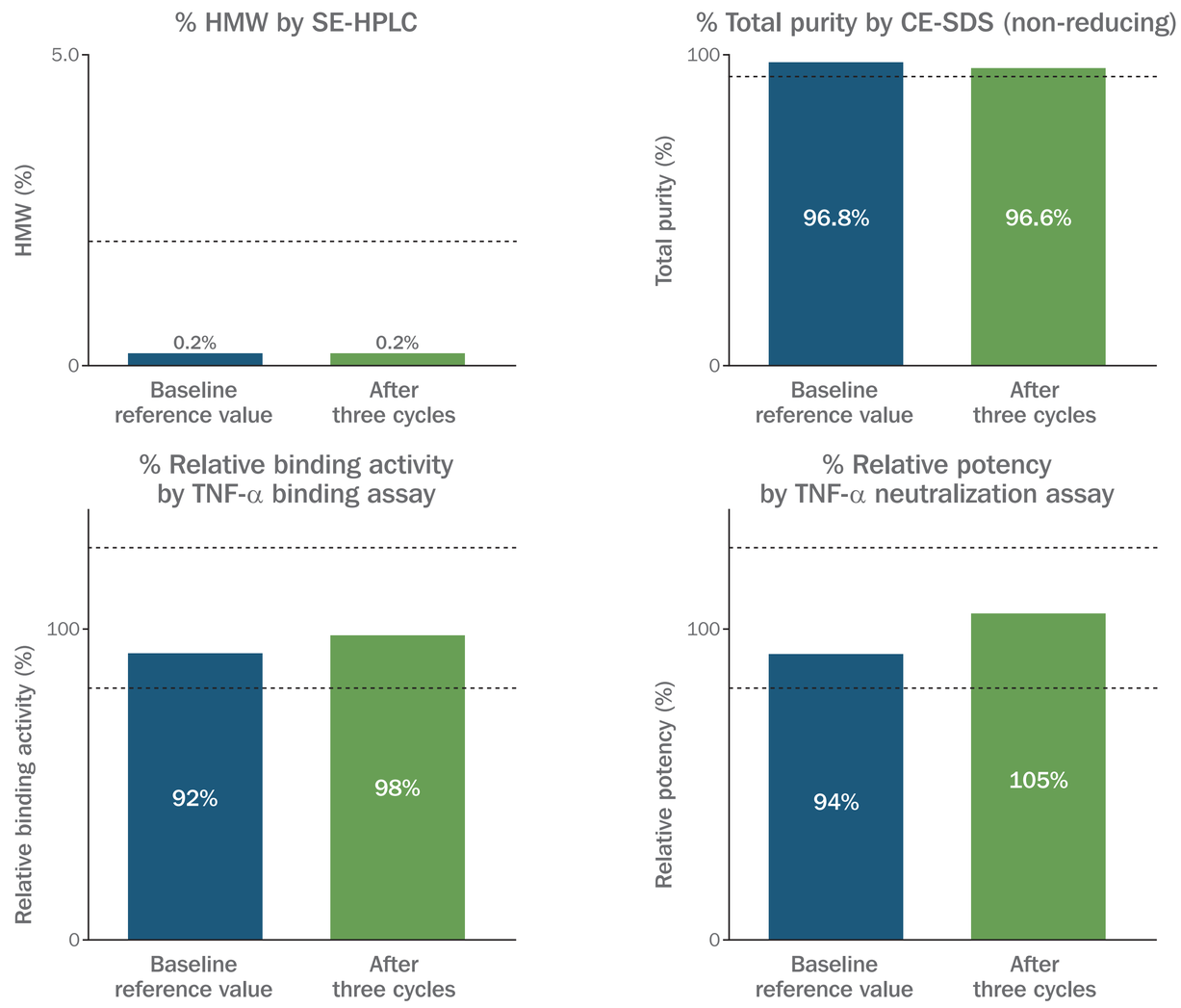
Critical quality attributes

- There were no apparent changes in critical quality attributes between baseline and following three temperature cycles (Figure 1).
- All results met the stability acceptance criteria for the four critical quality attributes.

Other

- Table 2 shows appearance, including colour, clarity, visible particle, pH, protein concentration, oxidation level, charge variant, endotoxin, container closure integrity and particulates, after three temperature cycles versus baseline.
  - The results showed no apparent changes and/or met the stability acceptance criteria for each product quality attribute over the three temperature cycles.

Figure 1. Short-term temperature cycling result of SB5 DP across four critical quality attributes



-------- Stability acceptance criteria.
CE-SDS: capillary electrophoresis-sodium dodecyl sulfate; HMW: high-molecular-weight species; SE-HPLC, size exclusion-high performance liquid chromatography; TNF-α, tumour necrosis factor-α

Table 2. Test results of SB5 drug product at baseline and following three temperature cycles

Category	Test item		Baseline reference value	Temperature cycle 3
General test	Appearance: Colour		Colourless	B8 ≤ Sample < B7
	Appearance: Clarity		18 NTU	17 NTU
	Appearance: Visual particulates		Practically free from particles	Practically free from particles
	pH		5.3	5.3
Quantity test	Protein concentration (A_{280})	(mg/mL)	51.6	49.7
Purity and impurities	SE-HPLC	% HMW impurities	0.2	0.2
	CE-SDS (non-reducing)	% Total purity	96.8	96.6
		% Single highest impurity	2.1	2.0
	icIEF	% Isoelectric point of main peak	8.6	8.6
		% Acidic	21.8	25.0
		% Main	67.1	64.5
		% Basic	11.2	10.5
Biological activity	Competitive binding assay to TNF-α by FRET	% Binding activity relative to reference standard	92	98
	TNF-α neutralization assay by NF-κB reporter gene	% Potency relative to reference standard	94	105
Safety	Particulates[a]	Particle ≥10 µm: particles/syringe	1521	1494
		Particle ≥25 µm: particles/syringe	15	18
	Endotoxin	(EU/mL)	<5	<5
	Container closure integrity		NS	All sample syringes tested negative for visible signs of dye incursion
Additional tests	CEX-HPLC	% Acidic	23.5	24.0
		% Main	67.2	65.2
		% Basic	9.3	10.9
	Oxidation	% Heavy chain Met34	0.6	0.6
		% Heavy chain Met83	0.3	0.4
		% Heavy chain Met256	5.8	4.7
		% Heavy chain Met432	ND	ND
		% Light chain Met4	0.2	0.5
	Particulates	Particle ≥2 µm: particles/syringe	12217	13111
		Particle ≥5 µm: particles/syringe	6257	6882
		Particle ≥8 µm: particles/syringe	2476	2579

[a]The acceptance criteria of particulate matter are 'Particle ≥10 µm: ≤6000/syringe' and 'Particle ≥25 µm: ≤600/syringe' according to Ph. Eur. 2.9.19/<USP 788>
CE-SDS, capillary electrophoresis-sodium dodecyl sulfate; CEX-HPLC, cation exchange-high performance liquid chromatography; DP, drug product; EU/mL, endotoxin units per millilitre; FRET, fluorescence resonance energy transfer; HMW, high-molecular-weight species; HPLC, high performance liquid chromatography; icIEF, imaged capillary isoelectric focusing; ND, not detected; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; NS, not scheduled; NTU, nephelometric turbidity unit; SE-HPLC, size exclusion-high performance liquid chromatography; TNF-α, tumour necrosis factor-α

Disclosures Biogen International GmbH (Baar, Switzerland) funded and sponsored this study. Ebbers HC is an employee of Biogen and may hold stock in Biogen. Kim JH, Yun JH, Park DK, Hwang SJ and Park SJ are employees of Samsung Bioepis.
Acknowledgements Editorial support for the preparation of this poster was provided by Springer Healthcare (London, UK); funding was provided by Biogen International GmbH.