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Physicochemical stability of durvalumab (Imfinzi®) concentrate for solution in original vials after first opening

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Abstract

Objectives: Durvalumab (Imfinzi®), a PD-L1 monoclonal antibody (mAb) medication is available as concentrate (50 mg/mL) for solution for infusion. The summary of product characteristics provides information about the physicochemical stability of ready-to-administer durvalumab preparations (vehicle solution 0.9 % NaCl, G5%), but not about the concentrate after first opening. The objective of this study was to determine the physicochemical stability of durvalumab concentrate for solution after first opening over a period of 28 days.

Methods: Imfinzi® vials were punctured and stored refrigerated (2–8 °C) or at room temperature (20–25 °C) light protected. At predefined time points (day 0, 7, 14, 21, 28) the physicochemical stability of the concentrated solution was determined by ion-exchange/size-exclusion high-performance liquid chromatography (IE-/SE-HPLC) with photodiode array detection and pH measurement. Vials were inspected with regard to changes of color, clarity, and visible particles at any time point.

Results: Regardless of the storage temperature, durvalumab 50 mg/mL solutions remained physiochemically stable for 28 days in punctured vials. The concentrations of durvalumab monomer remained unchanged and no secondary peaks (fragments, aggregates) were observed in any of the SE-HPLC chromatograms. The IE-HPLC test results showed no substantial changes of the peak areas of the main peak and of the acidic and basic charge variants during the whole storage period. Appearance and pH of the test solutions remained unchanged until the end of the study.

Conclusions: Regardless of storage conditions none of the analytical methods indicated physicochemical instability of the intact durvalumab monomer over the 28 days of the study. To avoid microbiological instability storage under refrigeration is recommended.

Keywords: concentrate for solution; durvalumab; IE-HPLC; physicochemical stability; SE-HPLC; temperature

Introduction

Durvalumab is a fully humanized immunoglobulin G1-kappa (IgG1κ) monoclonal antibody (mAb) approved or under clinical investigation in various solid tumors. The checkpoint inhibitor specifically binds to programmed cell death ligand 1 (PD-L1), selectively blocking the interaction of PD-L1/PD-1 as well as PD-L1/CD80, resulting in increased T-cell activation and improved antitumor immune response [1]. Antibodies are large glycoproteins consisting of four polypeptide chains (2 large, 2 short) with two antigen binding sites. Due to their high complexity, antibodies can be subject to a variety of degradation reactions. Instabilities can occur simultaneously on various structures and are influenced by different factors, such as light, temperature, hydrophobic surfaces, and shear stress [2–8].

Durvalumab (Imfinzi®) is marketed as concentrate for solution for infusion (50 mg/mL) and available in 120 mg (2.4 mL) and 500 mg (10 mL) vials. The finished medicinal product consists of 26 mM histidine/histidine-HCL (buffer), 275 mM trehalose dihydrate (isotonization), 0.02 % (w/v) polysorbate 80 (nonionic surfactant stabilizer) and water for injection as excipients. Recommended durvalumab doses are fixed doses of 1,500 mg administered every 3 or 4 weeks or body weight adjusted doses of 10 mg/kg given every 2 weeks or 20 mg/kg given every 3 or 4 weeks. In the first version of the SmPC was given that chemical and physical in-use stability of the diluted solutions have been demonstrated for up to 24 h at 2–8 °C and for up to 4 h at room temperature (up to 25 °C) from the time of preparation [9]. In October 2021 [10], physicochemical in-use stability has been extended to 30 days at 2–8 °C and to 24 h when stored at 25 °C [1].

However, in-use stability was not enlarged for the concentrated solution. Therefore, any residues of the concentrate left in the original vial must be discarded [1, 9].

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Additional data on the physicochemical stability and biological activity of concentrated durvalumab solutions are only available as non-peer-reviewed poster presentations [11, 12]. Since weight-based doses result in residues in the original vials, the objective of our study was to determine physicochemical in-use-stability of the punctured concentrate in order to allow vial sharing and to avoid wasting. We determined the physicochemical stability of durvalumab concentrate for solution via size-exclusion high-performance liquid chromatography (SE-HPLC), ion-exchange high-performance liquid chromatography (IE-HPLC), pH analyses, and visible inspection.

Materials and methods

Reagents

Disodium hydrogen phosphate, sodium sulfate, hydrochloric acid were purchased from Merck (Darmstadt, Germany); Sodium hydroxide solution, water HPLC Grade from AppliChem (Darmstadt, Germany); sodium dihydrogen phosphate, 2-(N-morpholine)ethanesulfonic acid (MES), isopropanol from Carl Roth (Karlsruhe, Germany); hydrogen peroxide, sodium chloride from Caelo (Hilden, Germany); acetonitrile HPLC Grade from Honeywell (Offenbach, Germany). All reagents used were of analytical grade.

Test solutions

Stability tests were performed with durvalumab (Imfinzi®) 50 mg/mL concentrate for solution for infusion provided by AstraZeneca GmbH (batch AADS, AARM). Fourteen vials were punctured with a Codan microspike (CODAN GmbH & Co KG, Lensahn, Germany) and stored. Seven vials each were stored refrigerated (2–8 °C) and at room temperature (20–25 °C) protected from light. Out of these, three vials each were assayed by SE-HPLC and IE-HPLC. One vial each was used for pH measurements. Samples were withdrawn on day 0, 7, 14, 21, 28 via the spike continuously inserted into the rubber stopper of each vial.

Sample preparation for SE-HPLC

200 µL samples of the test solutions were diluted with 9.8 mL 0.9 % NaCl infusion solution (Fresenius Kabi, Bad Homburg, Germany) and homogenized. Afterwards, 400 µL were diluted with 600 µL 0.9 % NaCl solution in HPLC vials (final concentration 0.4 mg/mL), to fit the calibration curve. 20 µL aliquots were injected by an autosampler in triplicate.

Sample preparation for IE-HPLC

100 µL samples of the test solutions were diluted with 900 µL buffer A (see Table 1) in HPLC vials (final concentration 5 mg/mL). 25 µL aliquots were injected by an autosampler in triplicate.

pH measurement

400 µL aliquots of undiluted solution were used for pH measurement.

HPLC assay

The HPLC system consisted of a Waters Alliance 2,695 pump connected to a Waters photodiode array detector 2,990 (Waters, Eschborn, Germany). Waters Empower Pro, Empower 2 Software, Version 6.10.01.00 was used for instrument operation, data collection and processing. For IE-HPLC, individual peak areas were calculated as a percentage of the total peak area.

Size-exclusion high-performance liquid chromatography (SE-HPLC), ion-exchange high-performance liquid chromatography (IE-HPLC)

Acceptance criteria were set to a 5 % maximum loss in active protein and maximum increase of secondary species of 2 % [8]. Detailed information on the SE-HPLC assay and the IE-HPLC assay is given in Table 1.

Method validation

To prove the stability indicating nature of the SE-HPLC assay and the IE-HPLC assay forced degradation experiments were performed by subjecting durvalumab solutions to heat, oxidant, acidic, and alkaline solution. In addition, accuracy, intra- and inter-day precision, and linearity were determined. Because a chemical reference substance (CRS) was not available when the tests were performed, the finished medicinal product (Imfinzi® (durvalumab) 50 mg/mL concentrate for solution for infusion, AstraZeneca GmbH, Germany) was used as reference.

SE-HPLC

For linearity testing, durvalumab concentrate was diluted with 0.9 % NaCl infusion solution (freeflex®, Fresenius Kabi, Germany) to achieve seven calibration standards (0.20 mg/mL, 0.32 mg/mL, 0.36 mg/mL, 0.40 mg/mL, 0.44 mg/mL, 0.48 mg/mL, 0.60 mg/mL). Aliquots of these standards were injected in triplicate. The calibration curve was constructed by plotting the peak area vs. the nominal concentration of durvalumab. Accuracy, inter-day and intra-day precision of the method were validated by preparing and analyzing 1 mg/mL and 5 mg/mL durvalumab standard solutions. Prior to measurement, durvalumab standard solutions were diluted with 0.9 % NaCl to a concentration of 0.4 mg/mL to fit the calibration curve. To determine accuracy, standard solutions were prepared onefold, diluted and aliquots were injected tenfold (per concentration). For inter-day precision, duplicate standard solutions were prepared on five consecutive days, diluted and aliquots were injected onefold each. To determine intra-day precision, ten standard solutions each were prepared on the same day, diluted and aliquots were injected onefold each.

Table 1: Characteristics of the SE-HPLC assay and the IE-HPLC assay.

	SE-HPLC assay (based on Vats et al. [13])	IE-HPLC assay (based on Vieillard et al. [14])
Column	TSKgel® G3000SW$_{XL}$, 7,8 × 300 mm (Tosoh Bioscience, Japan)	ProPac™ WCX-10, 4 × 250 mm (Thermo Fisher Scientific, USA)
Guard column	TSKgel® SW$_{XL}$ Guard column, 6 × 40 mm (Tosoh Bioscience, Japan)	ProPac™ WCX-10G, 4 × 50 mm (Thermo Fisher Scientific, USA)
Column temperature	25 °C	35 °C
Sample temperature	5 °C	5 °C
Flow rate	1.0 mL/min	0.8 mL/min
Injection volume	20 µL	25 µL
Injections per vial	3	3
Runtime	15 min	50 min
Detection wavelength	280 nm	280 nm
Mobile phase	0.1 M Na_2SO_4 + 0.1 M phosphate buffer solution R (pH 6.7)	Buffer A: 20 mM MES (2-(N-morpholino)ethanesulfonic acid) + 60 mM NaCl (adjusted to pH 6) Buffer B: 20 mM MES + 180 mM NaCl (adjusted to pH 6)
Gradient profile	Isocratic	Gradient 0 min → 30 min: starting with 100 % buffer A, 0 % buffer B linearly decreasing/ increasing to 40 % buffer A, 60 % buffer B 30 min → 40 min: 0 % buffer A, 100 % buffer B (purge) 40 min → 50 min: 100 % buffer A, 0 % buffer B (equilibrium period)
Retention time	About 8 min	About 22 min

SE-HPLC, size-exclusion high-performance liquid chromatography; IE-HPLC, ion-exchange high-performance liquid chromatography.

IE-HPLC

Inter- and intra-day accuracy and precision of the method were validated by preparing and analyzing 5 mg/mL durvalumab standard solutions. Ten standard solutions were prepared per day by diluting durvalumab concentrate with buffer A (see Table 1) on five consecutive days. Aliquots of standard solutions 1 and 10 were injected in triplicate and aliquots of standard solution 2–9 were injected onefold.

Appearance

Durvalumab concentrate is a clear to opalescent, colorless to slightly yellow solution, free from visible particles [1]. At each sampling time point, the test solutions were checked for any changes with the unaided eye. Test solutions without any changes were characterized as physicochemically stable.

pH

The pH measurements were carried out with a pH 210 Microprocessor pH meter (Hanna Instruments, Kehl am Rhein, Germany) equipped with an InLab Micro pH glass electrode (Mettler Toledo, Greifensee, Germany). The pH meter was calibrated with a five-point calibration (pH 2.00, 4.01, 7.00, 9.21, 11.00) with standard buffer solutions (Technical Buffer Solution, Mettler-Toledo AG) at each time point of measurement. Each sample was measured once. According to SmPC, specification was pH 6.0.

Results

Validation of the SE-HPLC assay

Figure 1 shows a representative chromatogram of durvalumab concentrate immediately after puncturing the vial with a microspike. In Figure 2a–d the resulting chromatograms of the forced degradation tests are given. Acidic and alkaline forced degradation led to major changes in the chromatograms (Figure 2a, b), e.g. broadening of the monomer peak, appearance of secondary peaks, total loss of the monomer peak. Moderate heating and oxidant use (Figure 2c, d) resulted in less significant changes. The lack of secondary peaks resulting from forced degradation and interfering with the durvalumab monomer peak indicates the suitability of the method.

The correlation coefficient of the assay amounted to R^2=0.999 and proved linearity over the concentration range. The accuracy was 98.2 % ± 0.50 standard deviation (SD) for 1 mg/mL and 99.1 % ± 0.37 SD for 5 mg/mL solutions. The mean durvalumab concentration of the inter-day precision test was 0.987 mg/mL (98.7 % ± 0.01) for 1 mg/mL and 4.895 mg/mL (97.9 % ± 0.12) for 5 mg/mL solutions. The intra-day precision tests revealed a mean durvalumab concentration of 0.981 mg/mL (98.1 % ± 0.01) for 1 mg/mL and 4.971 mg/mL (99.4 % ± 0.10) for 5 mg/mL solutions.

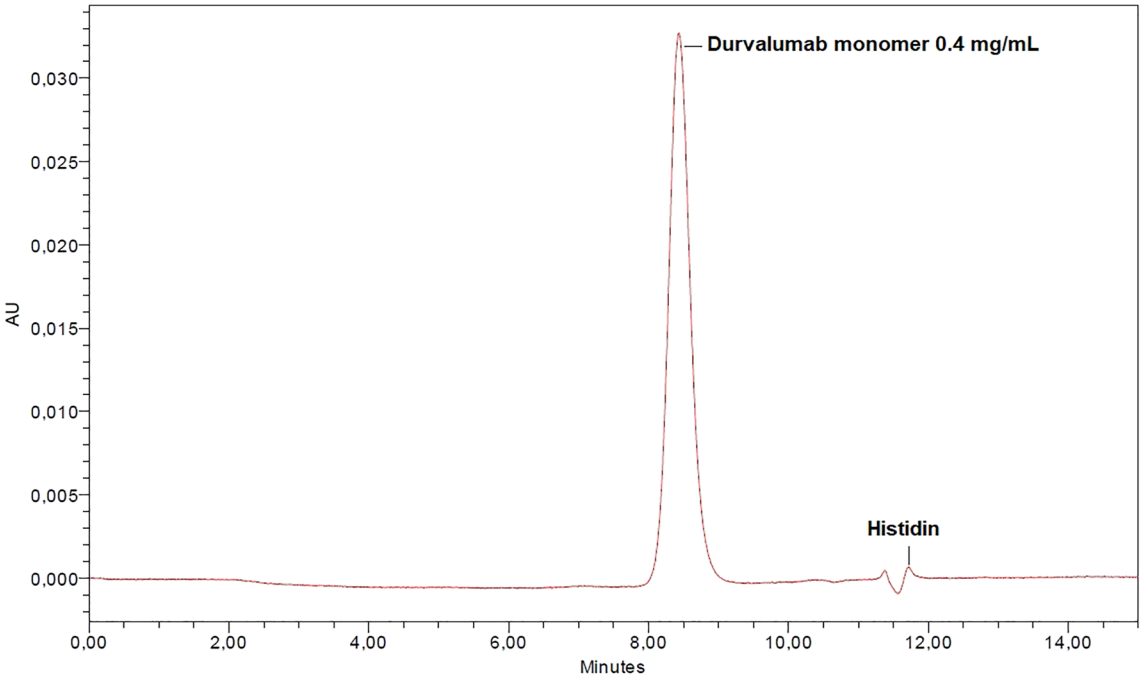

Figure 1: Representative SE-HPLC chromatogram of freshly prepared 0.4 mg/mL durvalumab solution (Imfinzi®); detection wavelength 280 nm.

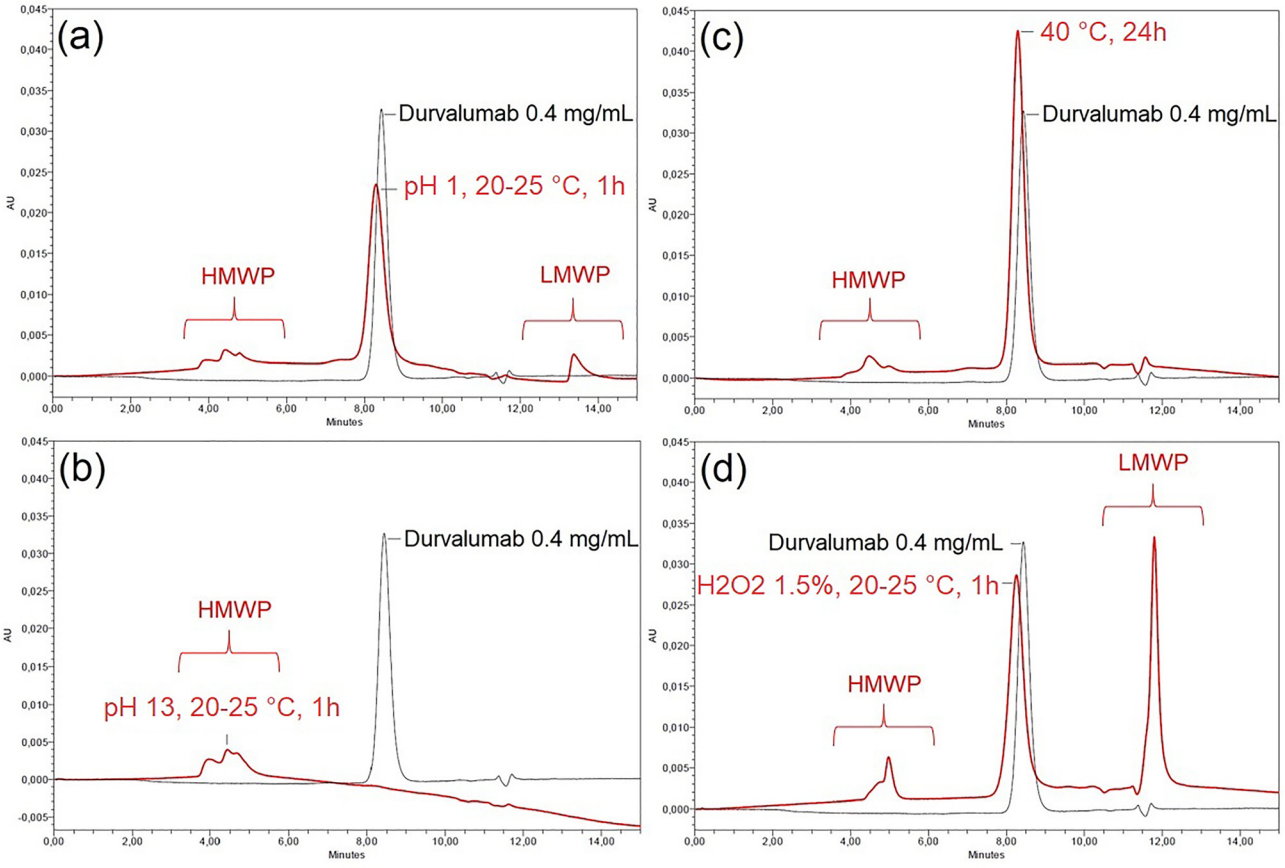

Figure 2: a–d: Overlay of SE-HPLC chromatograms of freshly prepared 0.4 mg/mL (black line) and degraded durvalumab (red line) samples; a: pH 1, 20–25 °C, 1 h; b: pH 13, 20–25 °C, 1 h; c: 40 °C, 24 h; d: H_2O_2 1.5%, 20–25 °C, 1 h; HMWP: high molecular weight protein, LMWP: low molecular weight protein.

Validation of the IE-HPLC assay

Figure 3 shows a representative chromatogram of durvalumab concentrate immediately after puncturing the vial with a microspike. In Figure 4a–d the resulting chromatograms of the forced degradation tests are given. Acidic conditions (Figure 4a) led to minor changes of the peak areas representing basic charge variants, whereas alkaline conditions (Figure 4b) resulted in total loss of the main peak. Pure heat (Figure 4c) caused minor changes of the peak pattern and oxidation (Figure 4d) induced major changes in the peak pattern and decrease of the main peak areas. Secondary peaks resulting from forced degradation conditions did not interfere with the durvalumab main peak and thereby demonstrate the suitability of the assay.

Results of interday- and intraday-precision tests are summarized in Table 2. Subsequent injections resulted in incremental overlapping of peak 2 and the main peak (see Figure 5). Therefore, the standard deviation of the percentage peak area of peak 2 is higher for inter-day precision than for intra-day precision (see Table 2). The decrease of the ratio of peak 2 corresponds to the increase of the ratio of the main peak, confirming the increasing overlap of peak 2 and the main peak.

Durvalumab 50 mg/mL analyzed by SE-HPLC

All chromatograms were checked for secondary peaks (e.g., high molecular weight (HMW) protein forms, low molecular weight (LMW) protein forms) or changes of the monomer peak area. In none of the test solutions stored either refrigerated or at room temperature, systematic or substantial changes got obvious over time. Besides the durvalumab monomer peak (retention time (R_t) approximately 8.5 min) only one second peak (relative retention time (rR_t) about 1.4) referring to histidine (identification by assaying pure histidine; data not shown) was present in the SE-HPLC chromatogram. Detailed results of the quantitative analyses of the durvalumab monomer peak area are shown in Table 3. When stored at 2–8 °C durvalumab monomer concentration remained unchanged over the 28 day-period. The slight increase of the durvalumab monomer concentration in test solutions stored at room temperature lies within the 5 % acceptance limit.

Durvalumab 50 mg/mL analyzed by IE-HPLC

The assay resulted in five durvalumab peaks, with peak 1 and 2 corresponding to the acidic charge variants and peak 4 and 5 corresponding to the basic charge variants of the main peak 3 (see Figure 3). Peak areas of the main peak and charge variants are given in Table 4 as percentage rates of the total peak area. Similar to the validation measurements, peak 2 increasingly overlapped with the main peak as the number of injections increased. Resulting from the overlap, the peak 2 area decreased about the same amount as the main peak area increased, indicating declining column performance. For verification, day 28

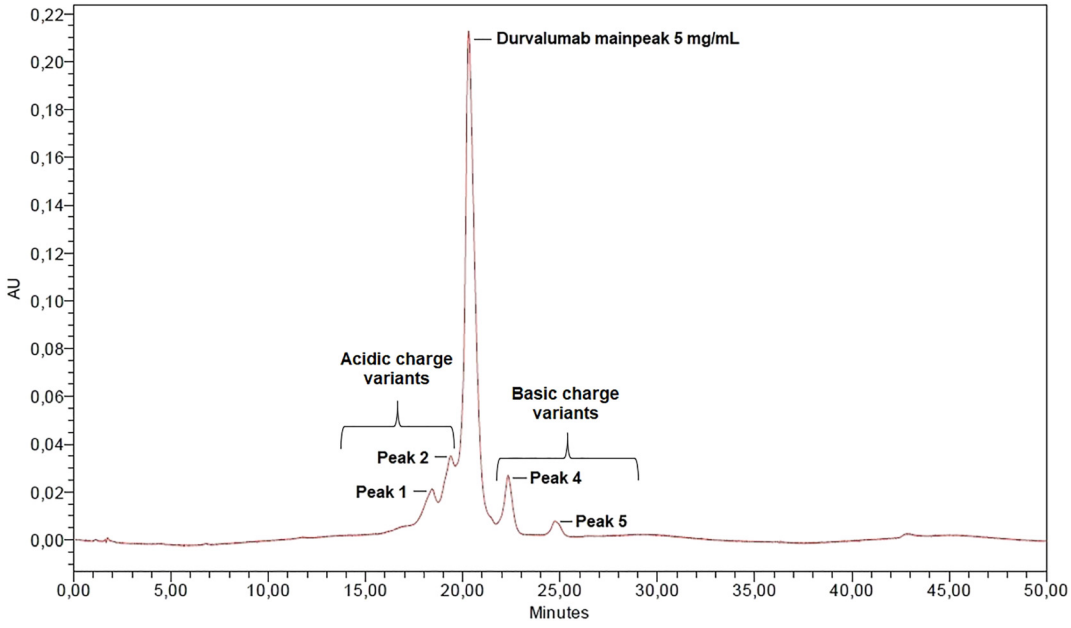

Figure 3: Representative IE-HPLC chromatogram of freshly prepared 5 mg/mL durvalumab solution (Imfinzi®); detection wavelength 280 nm.

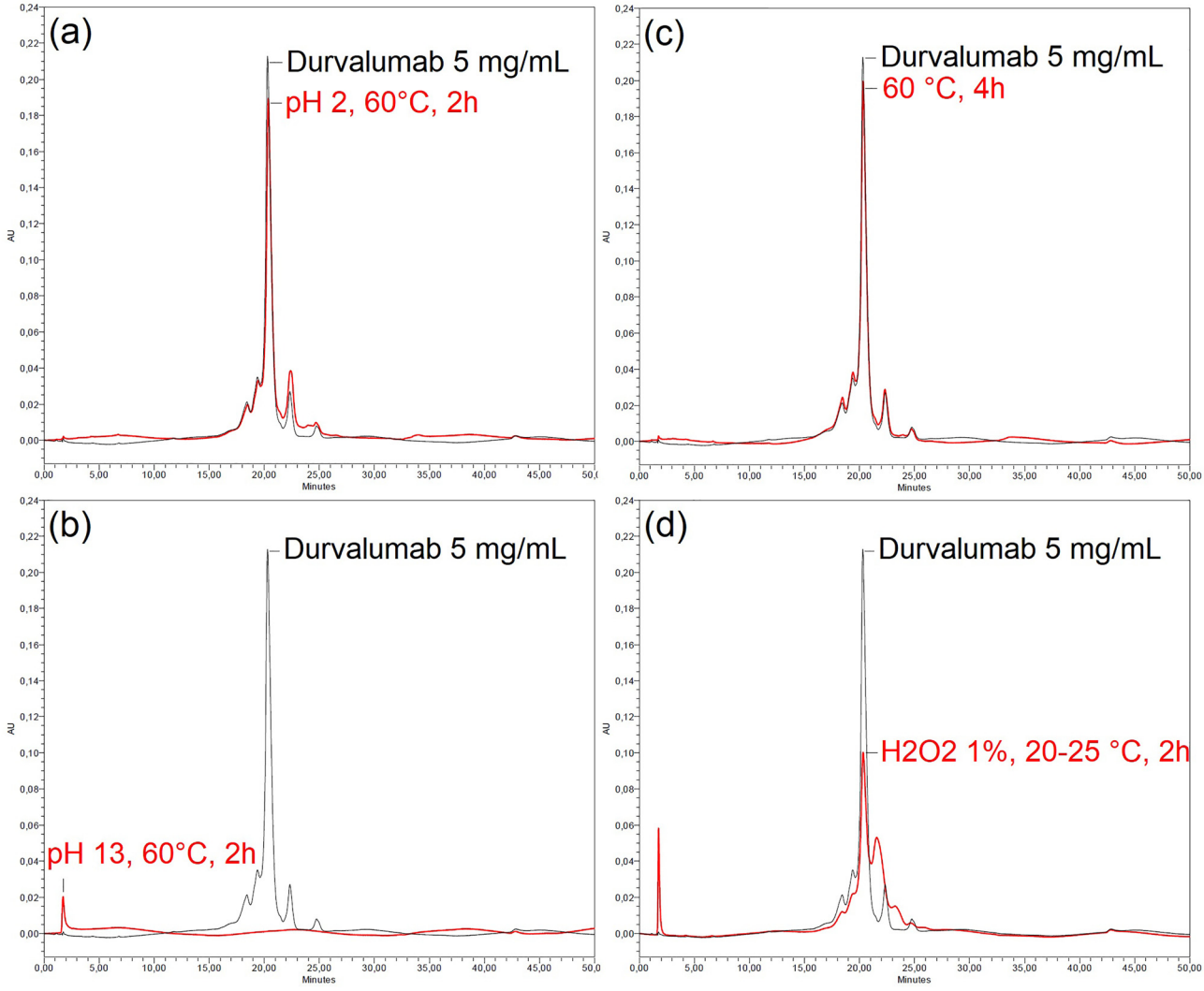

Figure 4: a–d: Overlay of IE-HPLC chromatograms of freshly prepared 5 mg/mL (black line) and degraded durvalumab (red line) samples; a: pH 2, 60 °C, 2 h; b: pH 13, 60 °C, 2 h; c: 60 °C, 4 h; d: H_2O_2 1%, 20–25 °C, 2 h

Table 2: Inter-day- and intra-day-precision of the IE-HPLC assay; peak areas calculated as percentage rate of the total peak area expressed as mean ± SD.

	IE-HPLC assay				
	% peak 1 ± SD	**% peak 2 ± SD**	**% Main peak ± SD**	**% peak 4 ± SD**	**% peak 5 ± SD**
Intra-day precision[a]	3.29 ± 0.02	2.75 ± 0.03	83.97 ± 0.04	7.68 ± 0.02	2.30 ± 0.01
Inter-day precision[b]	3.28 ± 0.02	2.58 ± 0.24	84.14 ± 0.23	7.70 ± 0.03	2.30 ± 0.02

[a]10 individual durvalumab 5 mg/mL standard solutions assayed on the same day, [b]10 individual durvalumab 5 mg/mL standard solutions assayed on 5 consecutive days. IE-HPLC, ion-exchange high-performance liquid chromatography; SD, standard deviation.

samples were re-measured with a new column on the same day resulting in values similar to the initial values (compare Table 4). Overall, peak area ratios met the acceptance criteria (main peak deviation ≤5 %) regardless of storage conditions.

Durvalumab 50 mg/mL appearance and pH

The appearance of durvalumab test solutions remained unchanged during the observation period. There was no formation of visible particles, cloudiness or discoloration.

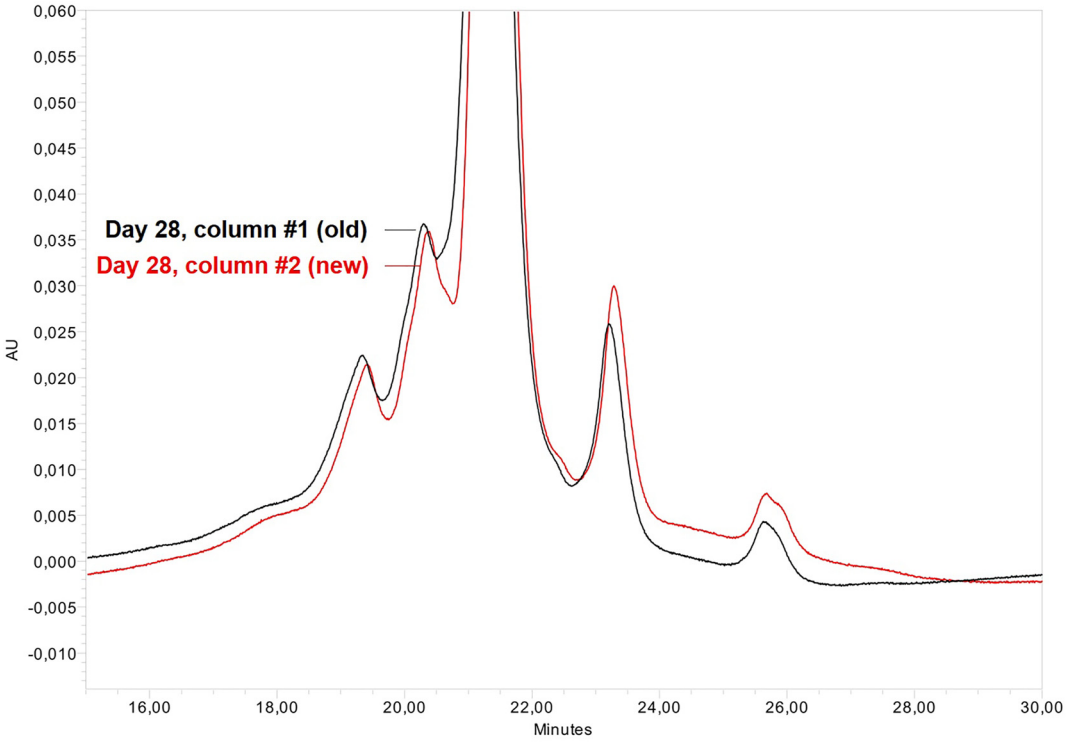

Figure 5: Overlay of IE-HPLC chromatograms of the same 5 mg/mL durvalumab samples on day 28, obtained with the new (red) or old (black) column.

Table 3: Stability of 50 mg/mL durvalumab concentrate in the punctured vial when stored light protected for 28 days at 2–8 °C or 20–25 °C. Results of the SE-HPLC assay are given in percent of the initial concentration (mean ± SD; n=9); one pH measurement per time point (n=1).

		Initial durvalumab monomer concentration [mg/mL] ± SD		Durvalumab monomer concentration remaining ± SD; measured concentration day 0=100 %			
	Storage temperature	Nominal	Measured (day 0)	Day 7	Day 14	Day 21	Day 28
SE-HPLC assay	2–8 °C	50.0	49.38 (±2.52)	100.4 (±1.02)	100.6 (±0.98)	100.3 (±1.21)	100.0 (±0.71)
	20–25 °C	50.0	50.39 (±1.12)	99.5 (±0.62)	99.9 (±0.55)	101.1 (±1.39)	101.1 (±1.55)
pH	2–8 °C	6.0	6.0	6.0	6.0	6.0	6.0
	20–25 °C	6.0	6.0	6.0	6.0	6.0	6.0

SE-HPLC, size-exclusion high-performance liquid chromatography; SD, standard deviation.

Table 4: Stability of 50 mg/mL durvalumab concentrate in the punctured vial determined by IE-HPLC stored for 28 days at 2–8 °C or 20–25 °C, protected from light. Peak areas calculated as percentage rates of the total peak area expressed as mean ± SD of nine measurements per time point (n=9).

		IE-HPLC assay				
Storage temperature	Days	% peak 1 ± SD	% peak 2 ± SD	% main peak ± SD	% peak 4 ± SD	% peak 5 ± SD
2–8 °C	0	3.32 (±0.05)	4.02 (±0.05)	81.77 (±0.09)	8.24 (±0.03)	2.65 (±0.02)
	7	3.32 (±0.01)	3.56 (±0.14)	82.31 (±0.13)	8.16 (±0.02)	2.65 (±0.01)
	14	3.32 (±0.02)	3.05 (±0.05)	82.85 (±0.07)	8.13 (±0.03)	2.66 (±0.01)
	21	3.32 (±0.02)	2.71 (±0.10)	83.31 (±0.11)	8.01 (±0.03)	2.65 (±0.01)
	28	3.31 (±0.04)	2.46 (±0.03)	83.61 (±0.07)	7.98 (±0.02)	2.65 (±0.03)
	28[a]	3.53 (±0.10)	4.60 (±0.08)	80.99 (±0.22)	8.24 (±0.04)	2.64 (±0.02)
20–25 °C	0	3.33 (±0.02)	3.94 (±0.05)	81.83 (±0.05)	8.25 (±0.01)	2.65 (±0.01)
	7	3.42 (±0.04)	3.50 (±0.05)	82.27 (±0.06)	8.16 (±0.01)	2.65 (±0.01)
	14	3.48 (±0.04)	3.06 (±0.03)	82.69 (±0.06)	8.13 (±0.01)	2.65 (±0.01)
	21	3.61 (±0.04)	2.72 (±0.04)	82.98 (±0.05)	8.04 (±0.02)	2.65 (±0.01)
	28	3.62 (±0.03)	2.48 (±0.05)	83.24 (±0.08)	8.02 (±0.01)	2.64 (±0.02)
	28[a]	3.97 (±0.03)	4.98 (±0.04)	80.16 (±0.05)	8.25 (±0.02)	2.64 (±0.03)

[a]Results obtained with new column. IE-HPLC, ion-exchange high-performance liquid chromatography; SD, standard deviation.

The pH values of the concentrate remained unchanged at pH 6, regardless of the storage conditions (see Table 3).

Discussion

The physicochemical stability of durvalumab (Imfinzi®) concentrate was analyzed by orthogonal methods over a prolonged period of 28 days, in order to demonstrate extended in-use stability of the original vials after first opening. Overall the study demonstrated that durvalumab was physicochemically stable in punctured vials regardless of storage conditions. Appearance and pH remained unchanged, impurities and degradation products were not detected.

The analytical methods used were selected according to the recommendations of a European consensus group [15]. Within the recommended methods, SE-HPLC and IE-HPLC are considered to be the most stability indicating assays [16]. By SE-HPLC chain fragmentation and the formation of aggregates and oligomers are assessed qualitatively and quantitatively [8]. By IE-HPLC different charge related variants of monoclonal antibodies are separated according to their isoelectric points (pI) [2] and chemical degradation, like deamidation of asparagine residues, is visualized.

The shelf-life of unopened Imfinzi® vials is set to three years [1]. Since the concentration of the stabilizing excipients as well as the adjusted pH were not changed by dilution with vehicle solution, a strong impairment of the stability of the finished medicinal product appears unlikely. Therefore, additional investigations of the higher order structures and physical stability (e.g. measurement of subvisible particles over time, turbidity measurement) were not applied. The sample numbers, sampling time points, and temperature conditions were chosen according to the specifications of the NHS Pharmaceutical Quality Assurance Committee [8] while the sampling technique (via syringes and spikes) was chosen according to clinical practice.

In SE-HPLC chromatograms, no secondary peaks were found at any time point, indicating the absence of fragmentation or aggregation. A decrease in peak height, increase in peak width, and increasing system pressure over the operating life of the HPLC column was observed and can be explained by the deleterious interaction of the surfactant (polysorbate 80) and the column packing [17]. To minimize the polysorbate 80 load and thereby the deterioration, we injected highly diluted samples and retrogradely rinsed the column with 20 % isopropanol.

The chromatographic profile of the IE-HPLC assay revealed minor changes over the assay period. Peak heights of acidic and basic variants did not increase over time proving no formation of more acidic variants (e.g. by deamidation) and more basic variants (e.g. by oxidation) regardless of the storage temperature. The observed changes are related to the deteriorated column performance, as shown by the results of re-measurement at day 28.

The results of our stability study regarding durvalumab concentrate are in accordance with extended stability data given in the Imfinzi® SmPC for diluted solutions [1]. Moreover, physicochemical stability of diluted durvalumab solutions and durvalumab concentrate for 3 weeks at 4 °C following 3 days at 25 °C, was reported by Bros et al. [11]. Acramel et al. demonstrated the unchanged biological activity of diluted durvalumab solutions and durvalumab concentrate for 28 days at 4 °C and for 7 days at room temperature [12]. Study results and the prolonged stability data given in the SmPC consistently indicate high physicochemical stability of durvalumab solutions, regardless of concentration.

Moreover, several other studies have demonstrated the stability of various mAbs inhibiting the PD-1/PD-L1 signaling pathway. For instance, Hui et al. investigated the PD-L1 inhibitor atezolizumab and demonstrated stability of various concentrations stored for 24 h at 30 °C followed by 3 months at 2–8 °C [18]. Le Guyader et al. studied diluted and undiluted solutions of the PD-1 inhibitor nivolumab and demonstrated stability for one month and for seven days at 2–8 °C and at 40 °C, respectively. Slight changes occurred after an observation period of three months at 2–8 °C [19]. Furthermore, Sundaramurthi et al. demonstrated physicochemical stability of diluted solutions of the PD-1 inhibitor pembrolizumab at 5 °C and room temperature for a period of at least one week [20].

All these studies indicate a physicochemical stability of mAb solutions exceeding the stability information provided in the respective SmPCs, demonstrating a tremendous progress in the field of protein stabilization [5].

In a recent study, microbiological stability of durvalumab solutions was tested by intended contamination with various facultative pathogenic microorganisms [21]. Tested strains remained viable in diluted durvalumab solutions, but pronounced growth supporting activity was not given. To inhibit growth of any contaminating mesophilic microorganisms, refrigerated storage is recommended for durvalumab residues. However, if cold chain interruption of unpunctured vials occurs for a few days, physicochemical stability is assured and wasting can be avoided.

Conclusions

Physicochemical stability of Durvalumab 50 mg/mL concentrate for solution for infusion in punctured vials was

demonstrated by stability-indicating assays. During the observation period of 28 days, no substantial changes were observed by any analytical method, regardless of the storage temperature. Therefore, leftovers can be used for up to 28 days after first opening. From a microbiological point of view, refrigerated storage is recommended. Results are appropriate to gain economic and ecological benefit by vial sharing.

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Competing interests: Authors state no conflict of interest.
Informed consent: Not applicable.
Ethical approval: Not applicable.

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