3PC-038

PHYSICOCHEMICAL STABILITY OF THE BEVACIZUMAB BIOSIMILAR, ABP 215, IN INTRAVENOUS BAGS AFTER PREPARATION AND STORAGE

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INTRODUCTION

- ABP 215 (MVASI™) is the first US marketed biosimilar to Avastin® (bevacizumab reference product, RP)[1]
- ABP 215 is approved in the US and EU for the following indications:[1,2]

Indication	US[1]	EU[2]
Metastatic colorectal cancer	√	√
Metastatic breast cancer	-	√
Recurrent or metastatic non-squamous non-small cell lung cancer	√	√
Recurrent glioblastoma	√	-
Advanced and/or metastatic renal cell carcinoma	√	√
Persistent, recurrent, or metastatic cervical cancer	√	√
Epithelial ovarian, fallopian tube, or primary peritoneal cancer	√	√

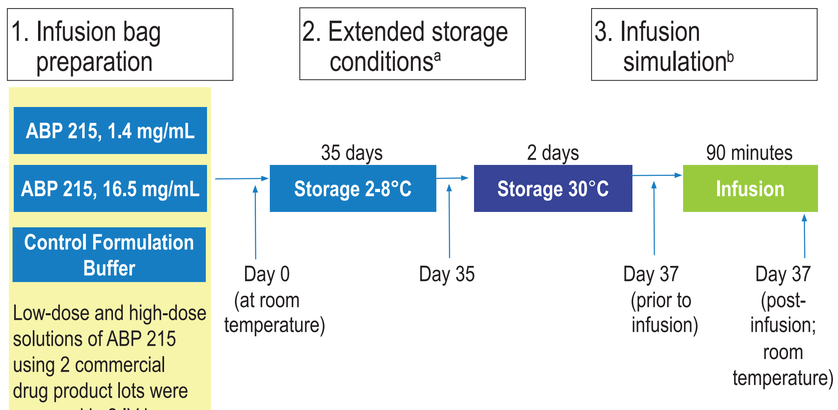
- ABP 215 drug product is supplied commercially as a liquid single-use solution in a single-use vial containing 25 mg/mL ABP 215. It is administered intravenously after dilution in an infusion bag, with the recommended intravenous (IV) bag concentration range of 1.4 mg/mL to 16.5 mg/mL
- In other regions, IV bags may be routinely prepared at centralized pharmacy locations and then distributed to clinical oncology sites for patient administration

Rationale

- Extended physicochemical stability under in-use conditions is valuable to enable administration flexibility by ensuring efficacy during handling conditions not covered by standard stability studies
- Results of an extended IV bag stability study that was performed to evaluate the chemical and physical stability of ABP 215 upon dilution into IV bags, extended storage (2°C to 8°C for 35 days followed by storage at 30°C for 48 hours), and infusion are presented here

METHODS

Figure 1. Sample Plan



[a]The bags were stored at 2-8°C for 35 days, followed by 2 days at 30°C to simulate worst-case storage conditions at the patient administration site.
[b]Simulation involved a 100 mL bag volume infusion (infusion rate was 67 mL/hour) over 90 minutes using an infusion pump to collect pre- and post-infusion samples.

Table 1. Assay (Methods) Summary and Objectives

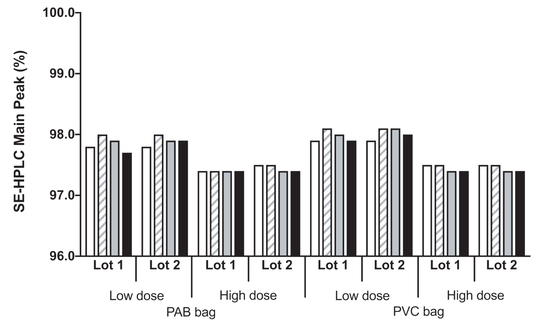
Assessment	Assay (method)	Objectives
Purity	SE-HPLC	• To assess size heterogeneity by resolving HMW species from the monomer main peak
	CEX-HPLC	• To assess charge heterogeneity by resolving the main, acidic, and basic peak regions
	rCE-SDS	• To assess the relative amount of HC, LC, and other size variants based on the protein hydrodynamic size
Quantity	Protein concentration	• To assess protein loss due to surface contact binding • Protein recovery was calculated from the concentration rssults as the ratio of the final 37-day post-infusion protein concentration measurement over the initial time 0 measurement
Potency	Proliferation inhibition bioassay	• To quantify the biological activity
General	Visual inspection	• To assess the presence and trends in protein-aceous particles
	HIAC	• To assess subvisible particulate matter trends

CEX-HPLC = cation-exchange high performance liquid chromatography;
HC = heavy chain; HMW = high molecular weight; HIAC = high-accuracy light obscuration;
LC = light chain; rCE-SDS = reduced capillary electrophoresis-sodium dodecyl sulphate;
SE-HPLC = size-exclusion high-performance liquid chromatography.

RESULTS

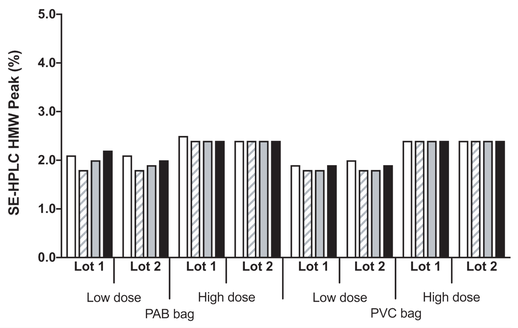
Figure 2. SE-HPLC Results: Main and HMW Peaks

a. SE-HPLC Main Peak



Od	97.8	97.8	97.4	97.5	97.9	97.9	97.5	97.5
35d	98.0	98.0	97.4	97.5	98.1	98.1	97.5	97.5
37d bag	97.9	97.9	97.4	97.4	98.0	98.1	97.4	97.4
37d final	97.9	97.9	97.4	97.4	97.9	98.0	97.4	97.4

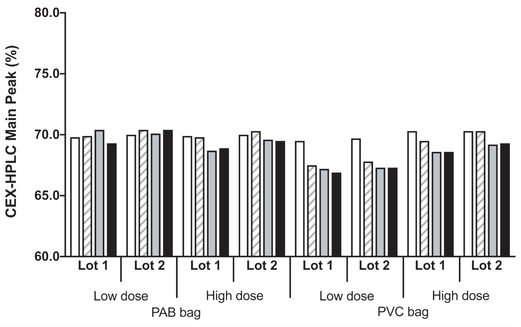
b. SE-HPLC HMW Peak



Od	2.1	2.1	2.5	2.4	1.9	2.0	2.4	2.4
35d	1.8	1.8	2.4	2.4	1.8	1.8	2.4	2.4
37d bag	2.0	1.9	2.4	2.4	1.8	1.8	2.4	2.4
37d final	2.2	2.0	2.4	2.4	1.9	1.9	2.4	2.4

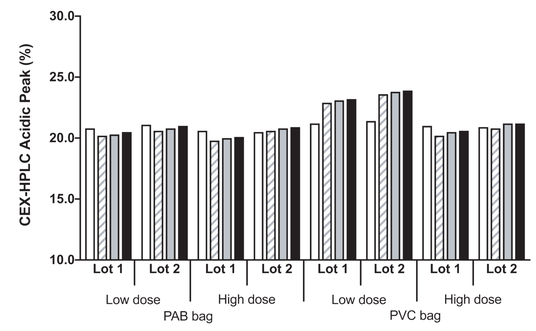
Figure 3. CEX-HPLC Results: Main, Acidic, Basic Peaks

a. CEX-HPLC Main Peak



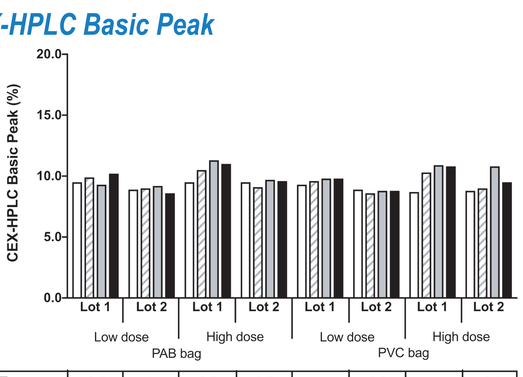
Od	69.8	70.0	69.9	70.0	69.5	69.7	70.3	70.3
35d	69.9	70.4	69.8	70.3	67.5	67.8	69.5	70.3
37d bag	70.4	70.1	68.7	69.6	67.2	67.3	68.6	69.2
37d final	69.3	70.4	68.9	69.5	66.9	67.3	68.6	69.3

b. CEX-HPLC Acidic Peak



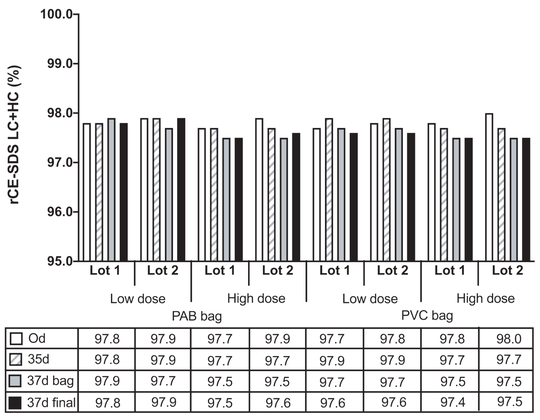
Od	20.8	21.1	20.6	20.5	21.2	21.4	21.0	20.9
35d	20.2	20.6	19.8	20.6	22.9	23.6	20.2	20.8
37d bag	20.3	20.8	20.0	20.8	23.1	23.8	20.5	21.2
37d final	20.5	21.0	20.1	20.9	23.2	23.9	20.6	21.2

c. CEX-HPLC Basic Peak



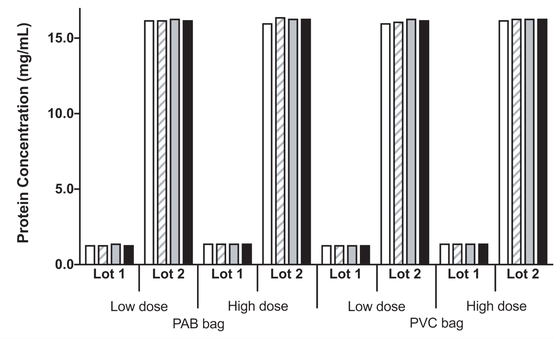
Od	9.5	8.9	9.5	9.5	9.2	8.9	8.7	8.8
35d	9.9	9.0	10.5	9.1	9.6	8.6	10.3	9.0
37d bag	9.3	9.2	11.3	9.7	9.8	8.8	10.9	9.6
37d final	10.2	8.6	11.0	9.6	9.8	8.8	10.8	9.5

Figure 4. rCE-SDS Heavy and Light Chain Results



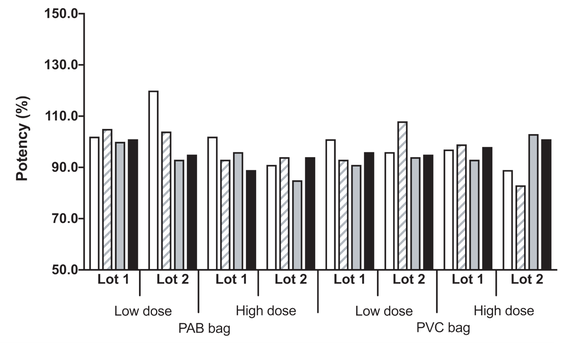
Od	97.8	97.9	97.7	97.9	97.7	97.8	97.8	98.0
35d	97.8	97.9	97.7	97.7	97.9	97.9	97.7	97.7
37d bag	97.9	97.7	97.5	97.5	97.7	97.7	97.5	97.5
37d final	97.8	97.9	97.5	97.6	97.6	97.6	97.4	97.5

Figure 5. Protein Concentration Results



Od	1.3	16.2	1.4	16.0	1.3	16.0	1.4	16.2
35d	1.3	16.2	1.4	16.4	1.3	16.1	1.4	16.3
37d bag	1.4	16.2	1.4	16.3	1.3	16.3	1.4	16.3
37d final	1.3	16.2	1.4	16.3	1.3	16.2	1.4	16.3

Figure 6. Potency Results: Proliferation Inhibition Bioassay



Od	102.0	120.0	102.0	91.0	101.0	96.0	97.0	89.0
35d	105.0	104.0	93.0	94.0	93.0	108.0	99.0	83.0
37d bag	100.0	93.0	96.0	85.0	91.0	94.0	93.0	103.0
37d final	101.0	95.0	89.0	94.0	96.0	95.0	98.0	101.0

Table 2. Summary of Results

Assessment	Assay (method)	Results
Purity	SE-HPLC CEX-HPLC rCE-SDS	• No meaningful changes were seen for all 3 purity assays as illustrated in **Figures 2 - 4**
Quantity	Protein concentration	• All results indicated no protein loss throughout the duration of exposure to IV bag and infusion system materials (**Figure 5**) • Protein recovery ranged from 99.4% to 101.7%
Potency	Proliferation inhibition bioassay	• All results indicated no practically significant loss in potency over the study duration (**Figure 6**)
General	Visual inspection	• No potentially proteinaceous particles were observed throughout the study
	HIAC	• No consistent trends over time were noted in any IV bag material in the dosed drug product and control formulation buffer

CEX-HPLC = cation-exchange high-performance liquid chromatography;
HIAC = high-accuracy light obscuration; rCE-SDS = reduced capillary electrophoresis-sodium dodecyl sulphate; SE-HPLC = size-exclusion high-performance liquid chromatography.

SUMMARY AND CONCLUSIONS

- Under different dilution, storage and infusion conditions, ABP 215 demonstrated consistent product quality and stability for all attributes tested including size variants or charge variants, fragmentation, particulate formation, protein concentration, and potency
- The results of this study demonstrate that ABP 215 drug product is physically and chemically stable in 0.9% saline diluent for IV administration for up to 35 days at 2°C to 8°C followed by 2 days at 30°C storage and is compatible with commonly used IV bags and tubing assembly materials
- Across the evaluated worst-case handling conditions, a robust set of stability-indicating assays showed that ABP 215 product quality and activity is maintained with no significant degradation

REFERENCES

1. MVASI™ (bevacizumab) prescribing information. Thousand Oaks, CA: Amgen, Inc.; June 2019.
2. MVASI™ 25 mg/mL concentrate for solution for infusion. Summary of Product Characteristics. The Netherlands: Amgen Europe B.V.; Jan 2018.

DISCLOSURES

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