INTRODUCTION

• ABP 215 (MVASTM) is the first US marketed biosimilar to Avastin® (bevacizumab reference product, RR)
• ABP 215 is approved in the US and EU for the following indications:
  - Metastatic colorectal cancer
  - Metastatic breast cancer
  - Recurrent or metastatic non-squamous non-small cell lung cancer
  - Renal cell carcinoma
  - Mantle cell lymphoma
  - Ependymoma, medulloblastoma, or other pediatric solid tumors

• ABP 215 drug product is supplied commercially as a liquid single-use solution in a single-use vial containing 25 mg/mL. ABP 215 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 physiochemical 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

1. Infusion preparation
2. Extended storage conditions
3. Infusion simulation

ABP 215, 1.4 mg/mL
ABP 215, 16.5 mg/mL
Control Formulation

Low-dose and high-dose solutions of ABP 215 using 2 commercial drug product lots were prepared in 2 IV bag systems (polyolefin and PVC) with the aim to evaluate physiochemical stability under worst-case handling conditions.

Table 1. Assay (Method) Summary and Objectives

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

RESULTS

Table 2. Summary of Results

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Assay (method)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purity</td>
<td>SE-HPLC</td>
<td>- No meaningful changes were seen for all 3 purity assays as illustrated in Figures 2 - 4</td>
</tr>
<tr>
<td>Quantity</td>
<td>Protein concentration</td>
<td>- All results indicated no protein loss throughout the duration of exposure to IV bag and infusion system materials (Figure 5)</td>
</tr>
<tr>
<td>Potency</td>
<td>Proliferation inhibition bioassay</td>
<td>- All results indicated no practically significant loss in potency over the study duration (Figure 6)</td>
</tr>
<tr>
<td>General</td>
<td>HIAC</td>
<td>- No potentially proteinaceous particles were observed throughout the study</td>
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</tbody>
</table>

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 diuret 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


DISCLOSURES

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

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