Optimizing Sampling Designs for Apixaban Phase III Studies Using Trial Simulation

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METHODS

A compartmental model of apixaban was used for trial simulation. Optimal sparse sampling designs were explored using TrialSim simulator, a web-based tool for evaluating trial designs (1). Simulation was performed using 500 simulated trials for each sampling design at baseline, and 300 for each design at Month 3 and Month 6. Optimal sparse sampling designs were compared to a baseline design (Design #5) for estimation of population parameters. Optimal sparse sampling designs were compared to a design with the same number of samples obtained on a single day at a fixed time point.

RESULTS

Table 1. Apixaban Population Exposure Parameters

<table>
<thead>
<tr>
<th>Parameter (Units)</th>
<th>Value (CV%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CL/F</td>
<td>2.84 (1.79)</td>
</tr>
<tr>
<td>V/F</td>
<td>0.311 (4.28)</td>
</tr>
<tr>
<td>CL</td>
<td>0.170 (6.82)</td>
</tr>
<tr>
<td>V</td>
<td>0.90 (16.64)</td>
</tr>
</tbody>
</table>

Table 2. Design Sampling Criteria for Study Type I

Table 3. Design Sampling Criteria for Study Type II

Table 4. Mean Bias and MACE

Table 5. Population PK Profiles from 500 simulated trials

Figure 1. Factor Xa and Thrombin

Figure 2. Apixaban Phase III Studies Using Trial Simulation

Figure 3. Number of Patients and Parameter Precision

Figure 4. Summary of the Quality of PK Information that is Retrieved from Different Sampling Designs

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REFERENCES

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ABSTRACT

Introduction

Optimizing sparse sampling designs is critical in obtaining knowledge of drug exposure in diverse patient populations, while limiting cost and maintaining compatibility with study logistics. Appropriate sparse sampling design is essential for the deep vein thrombosis (DVT) and post-operative venous thromboembolism (VTE) prevention trials and for secondary prevention in patients with atrial fibrillation (AFib), and for secondary prevention in patients with acute coronary syndrome (ACS).

Methods

A compartmental model of apixaban was used for trial simulation. Optimal sparse sampling designs were compared to a baseline design (Design #5) for estimation of population parameters. Optimal sparse sampling designs were compared to a design with the same number of samples obtained on a single day at a fixed time point. Optimal sparse sampling designs were compared to a design with the same number of samples obtained on a single day at a fixed time point.

RESULTS

Optimal sparse sampling designs were selected for Study Types I (Day 1, Month 3, and Month 6) and II (Day 1, Month 3, and Month 6). Optimal sparse sampling designs were compared to a baseline design (Design #5) for estimation of population parameters. Optimal sparse sampling designs were compared to a design with the same number of samples obtained on a single day at a fixed time point. Optimal sparse sampling designs were compared to a design with the same number of samples obtained on a single day at a fixed time point. Optimal sparse sampling designs were compared to a design with the same number of samples obtained on a single day at a fixed time point.