Safety and efficacy of dabigatran-reversing idarucizumab in Japanese patients

Dabigatran is an oral anticoagulant approved for preventing stroke in patients with nonvalvular atrial fibrillation.

Reversing the effects of anticoagulants is central to the management of uncontrolled bleeding, and the prevention of serious bleeding during emergency surgery or other invasive procedures in patients on anticoagulants.

Idarucizumab is a humanized monoclonal antibody fragment that specifically binds to dabigatran and reverses its anticoagulant effect. Idarucizumab has been approved in Japan since 2016 based on interim results of the REVERSE-AD study, a global phase 3 clinical trial; however, the trial treated only a limited number of Japanese patients. Therefore, an all-case post-marketing surveillance is in progress to collect data from Japanese patients treated with idarucizumab.

In the current analysis, we report the preliminary results from the post-marketing surveillance study regarding the safety and effectiveness of idarucizumab in reversing the effects of dabigtran in Japanese patients.

In the current study, patients administered idarucizumab were categorized into two groups according to the reason for using idarucizumab. Group A had uncontrolled or life-threatening bleeding, and B required an urgent procedure. Patients were followed-up for 4 weeks. The primary endpoint was safety, and the secondary endpoint was effectiveness.

This interim analysis included 262 patients treated with idarucizumab. Among 262 patients, 18 experienced adverse drug reactions within 4 weeks. By MedDRA System Organ Class, those most frequently reported were “Nervous system disorders” in six patients, followed by "Infections and infestations" and “Injury, poisoning and procedural complications” in three patients each. The majority of these events appeared to be a worsening of the index event or were associated with coexisting conditions. No new safety concerns have been identified thus far.

The median maximum reversal effect evaluated by activated partial thromboplastin time was 100%. The median time to bleeding cessation in Group A (excluding patients with intracranial bleeding) was 3.3 hours, and normal intraoperative hemostasis in Group B was reported in 72% of patients.

Among the reasons for using idarucizumab, the most common bleeding event in Group A was intracranial hemorrhage in 47% of patients, followed by

gastrointestinal bleeding in 28% of patients and Intra-pericardial bleeding in 9% of patients.

In Group A, approximately 30% of cases were caused by trauma such as a fall or injury. In addition, some patients experienced life-threatening bleeding during or after invasive surgeries or procedures such as catheter ablation for atrial fibrillation.

Among patients in Group B, the most common emergency surgery or urgent intervention, reported in 56% of patients, was a neurological procedure such as reperfusion for stroke or craniotomy. Next were abdominal procedures, reported in 21% patients for conditions such as cholecystitis, and cardiovascular procedures, which were reported in 17% of patients for conditions such as aortic dissection.

In conclusion, these interim results suggest that idarucizumab is safe and effective for the reversal of dabigatran in Japanese patients in a real-world setting, and they support the continued use of idarucizumab.