ROCKET AF

PHASE III

The Pivotal, Phase III ROCKET AF Study Proves 'Xarelto' Provides Effective Protection against Potentially Devastating Strokes in One Tablet, Once Daily in Patients with Atrial Fibrillation (AF)

Oral, Once-daily 'Xarelto' as Effective as Warfarin

'Xarelto' Lowers the Rate of Most Feared ICH and Fatal Bleeds

'Xarelto' Demonstrates a Reassuring Cardiovascular Profile

For patients with atrial fibrillation (AF), stroke prevention is critical as AF-related strokes are more severe than non AF-related strokes. AF-related strokes cause disability in more than half of patients and are associated with a 50% likelihood of death within one year[1,2,3]. Anticoagulation reduces the risk of stroke, however, it is consistently under-utilised in patients with AF[4].

The ROCKET AF study explored the efficacy and safety of the adjusted-dose Factor Xa inhibitor oral, once-daily 'Xarelto' compared with adjusted-dose warfarin.

ROCKET AF was presented at the American Heart Association (AHA) Congress in 2010 and published in the New England Journal of Medicine (NEJM) in September 2011[5].

The study is the basis of the approval of 'Xarelto' for the prevention of stroke and systemic embolism in adult patients with non-valvular AF with one or more risk factors.

Efficacy Results

'Xarelto' was shown to be non-inferior to warfarin[5].

Safety Results

Overall bleeding rates were comparable to warfarin[5].

'Xarelto' demonstrated a reassuring bleeding profile with similar overall bleeding rates and a significant reduction in intracranial haemorrhages (ICH) and fatal bleeds. Major gastrointestinal (GI) bleeds were more common with rivaroxaban than warfarin[5].

Results were achieved with an oral, once-daily, fixed dosing regimen unique to 'Xarelto'[6] (this included a reduced fixed 15 mg dose for patients with moderate renal impairment) and showed consistent results in all patient groups, including those with multiple co-morbidities who are considered more difficult to protect.

The extensive evaluation of rivaroxaban to protect different patient populations at risk of venous and arterial thromboembolism (VAT), makes it the most studied novel OAC in the world. Rivaroxaban (Xarelto®) is already approved for five indications in seven areas of use and its investigation - both completed and ongoing - will include more than 275,000 patients in clinical trials and real world settings.

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Patient Study Insights

About the ROCKET AF Patient Population

- 14,264 patients with non-valvular AF
- Moderate-to-high risk of stroke or non-CNS systemic embolism (SE) with multiple co-morbidities including:
  - Prior stroke or transient ischaemic attack (TIA) or SE; or
  - At least two of the following risk factors: congestive heart failure (LVEF <=35%), hypertension, age ≥75 years, diabetes mellitus (i.e., a $CHADS_2$ score of two or more)
- Approximately 50% of study patients had a history of stroke, TIA or SE
- Mean age greater than other trials in this disease area (average 73.1 years)
- A quarter of patients were 78 years or older

Atrial Fibrillation (AF)

AF is the most common sustained cardiac rhythm disorder and occurs when the upper chambers (atria) of the heart beat irregularly[7]. As a result, the atria do not empty completely and blood does not flow properly, potentially allowing blood clots to form. These blood clots can break loose and travel to the brain, resulting in a stroke[8].

Sub-Analyses: Exploring Specific AF Patient Groups

Patients with AF with Prior Stroke or TIA (n=7,468)

'Xarelto' provides consistent stroke prevention both in patients with AF who have and have not had a prior stroke or TIA, supporting the use of 'Xarelto' as an alternative to warfarin in primary and secondary stroke prevention[9].

Patients with AF over the age of 75 (n=6,229)

'Xarelto' showed consistent efficacy and safety benefits in these higher risk patients who are considered to be more difficult to manage, reflecting the overall ROCKET AF findings. Importantly, elderly patients treated with 'Xarelto' showed lower rates of ICH compared to patients receiving warfarin[10].

Patients with AF with Moderate Renal Impairment (n=2,950)

'Xarelto' can prevent stroke in patients with moderate renal insufficiency, without elevating the risk of critical bleeding events such as ICH. The 15 mg dose adjustment for renally impaired patients showed consistent results with the overall ROCKET AF findings[11].

References

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