COMMANDER HF

PHASE III

COMMANDER HF Will Provide Insights on How Best to Protect Patients with Chronic Heart Failure (HF) and Coronary Artery Disease (CAD) against Long-term Clot Formation

First Novel OAC Study in Patients with HF and CAD

5,000 Patients >12 Countries

FDA Fast Track Designation

Despite many recent advances in HF treatment, these patients remain at high risk of complications and death following hospitalisation for exacerbation of their HF[1,2]. Additionally, the admissions for worsening HF represent a significant healthcare burden[1,3,4,5,6] that has a major impact on patient quality of life and increasing short-term and long-term mortality[7].

Antiplatelets and rivaroxaban have complementary mechanisms of action that together address the dual pathway of clot formation[8]. In a sub-group of acute coronary syndrome (ACS) patients with HF in the ATLAS ACS 2-TIMI 51 Study, treatment with rivaroxaban 2.5 mg twice daily plus antiplatelet therapy demonstrated decreased rates of cardiovascular (CV) events and death compared with antiplatelet therapy alone[8]. In a similar way, COMMANDER HF will evaluate the potential of this combination to provide more complete protection against long-term clot formation compared to each therapy alone.

COMMANDER HF Study Design[9]

First patient was enrolled in September 2013

Randomised, double-blind Phase III global pivotal study in ~5,000 patients with chronic HF and CAD following recent hospitalisation

Rivaroxaban 2.5 mg BID + Single or Dual Antiplatelet Therapy

Single or Dual Antiplatelet Therapy

Average 16-month study duration with 6–30 months treatment phase followed by 15–45 day follow-up phase

Primary efficacy endpoint: all cause death, heart attack, stroke
Primary safety endpoint: fatal bleeding or critical bleeding with potential for permanent disability

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.

COMMANDER HF

BAYER

PHASE III

About the COMMANDER HF Study Patients

The number of patients with chronic HF and CAD is increasing[4,10,11] and is expected to continue to rise dramatically due to ageing of the global population[3,4,6,12,13,14].

Fast Facts: HF and CAD

- CAD is universally identified as the leading cause of HF[1,3,15,16,17]
- Nearly 65% of HF patients have diagnosed CAD as the underlying cause[16]
- 30-50% of all middle-aged adults in the western world are at risk of developing CAD during their lifetime[18]
- CAD is the most common cause of heart disease, leading to 7.4 million deaths worldwide in 2012[19]
- By 2020, the global burden of CAD will account for an estimated 11.1 million deaths worldwide[20]

The Relationship Between HF and CAD

HF is a serious medical condition where the heart doesn't pump blood around the body as well as it should[21], which means the blood can't deliver enough oxygen and nutrients to the body to allow it to work normally. HF often develops due to a medical condition such as CAD, heart attack or high blood pressure that has damaged or put extra workload on the heart[3,15,22,23].

CAD is the build-up of plaque inside the artery walls that decreases blood flow to the heart and can cause arterial blood clots[22,24]. CAD can act to weaken or damage the heart muscle over time, resulting in HF[21,22]. The presence of CAD has also been shown to be independently associated with worsening long-term prognosis for HF patients[1,3,16].

References

1) Flaherty JD, Bax JJ, De Luca L, et al. Acute heart failure syndromes in patients with coronary artery disease. Early assessment and treatment. Journal of the American College of Cardiology. 2009; 53(3): 254-263. **2)** Weintraub NL, Collins SP, Pang PS, et al. Acute heart failure syndromes: emergency department presentation, treatment, and disposition: current approaches and future aims: a scientific statement from the American Heart Association. Circulation. 2010: 122: 1975-1996. **3)** Cowie MR, Mosterd A, Wood DA, et al. The epidemiology of heart failure. European Heart Journal. 1997; 18: 208-225. **4)** McMurray JJV, Stewart S. The burden of heart failure. European Heart Journal Supplements. 2002; 4 (Supplement D): D50-D58. **5)** Cleland JGF, Swedberg K, Follath F, et al. The EuroHeart Failure survey programme – a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. European Heart Journal. 2003; 24: 442-463. **6)** Davis RC, Hobbs FDR, Lip GYH. ABC of heart failure. History and epidemiology. BMJ. 2000; 320: 39-42. **7)** Spoletini I, Vitale C, Volterrani M. Day-to-day management of patients with heart failure. Medicographia. 2011; 33: 401-408. **8)** Mega JL, Braunwald E, Wiviott SD, et al. Rivaroxaban in Patients with a Recent Acute Coronary Syndrome. N Engl J Med 2012; 366: 9-19. 9) ClinicalTrials.gov. A Study to Assess the Effectiveness and Safety of Rivaroxaban in Reducing the Risk of Death, Myocardial Infarction or Stroke in Participants With Heart Failure and Coronary Artery Disease Following Hospitalization for Heart Failure (COMMANDER HF). Available at: http://clinicaltrials.gov/ct2/show/NCT01877915?term=commander+hf&rank=1. Accessed January 2015. 10) Cleland JGF, Gemmell I, Khand A, et al. Is the prognosis of heart failure improving? European Journal of Heart Failure. 1999; 1: 229-24. 11) Gheorghiade M, Zannad F. Modern management of acute heart failure syndromes. European Heart Journal Supplements. 2005; 7 (Supplement B): B3–B7. 12) Cowie MR, Fox KF, Wood DA, et al. Hospitalization of patients with heart failure. A population-based study. European Heart Journal. 2002; 23: 877-885. 13) López-Sendón J. The heart failure epidemic. Medicographia. 2011; 33: 363-369. **14)** Tendera M. Epidemiology, treatment, and guidelines for the treatment of heart failure in Europe. European Heart Journal Supplements. 2005; 7 (Supplement J): J5-J9. **15)** Cowie MR, Wood DA, Coats AJS, et al. Incidence and aetiology of heart failure. A population-based study. European Heart Journal. 1999; 20: 421-428. **16)** Gheorghiade M, Sopko G, De Luca L, et al. Navigating the crossroads of coronary artery disease and heart failure. Circulation. 2006; 114:1202-1213. **17)** Fox KF, Cowie MR, Wood DA, et al. Coronary artery disease as the cause of incident heart failure in the population. European Heart Journal. 2001; 22: 228-236. **18)** Roeters van Lennep JE, Westerveld T, Erkelens DW, et al. Risk factors for coronary heart disease: implications of gender. Cardiovascular Research. 2002; 53: 538–549. **19)** WHO. The top 10 causes of death. Available at: http://www.who.int/mediacentre/factsheets/fs310/en/index2.html Accessed January 2015. **20)** Tardif J-C. Coronary artery disease in 2010. European Heart Journal Supplements. 2010; 12 (Supplement C): C2-C10. **21)** Centers for Disease Control and Prevention. Coronary Artery Disease (CAD). Available at: http://www.cdc.gov/heartdisease/coronary_ad.htm. Accessed July 2014. **22)** American Heart Association. Understand Your Risk for Heart Failure. Available at: http://www.heart.org/HEARTORG/Conditions/HeartFailure/UnderstandYourRiskforHeartFailure/Understand-Your-Risk-for-Heart-Failure_UCM_002046_Article.jsp. Accessed January 2015. **23)** Heart Failure Matters. Understanding Heart Failure. Available at: http://www.heartfailurematters.org/EN/Understanding-heart-failure/What-is-heart-failure. Accessed January 2015. **24)** American Heart Association. Coronary Artery Disease - The ABCs of CAD. Available at: http://www.heart.org/HEARTORG/Conditions/More/MyHeartandStrokeNews/Coronary-Artery-Disease---The-ABCs-of-CAD_UCM_436416_Article.jsp. Accessed January 2015.