Inclusion Criteria

track
Treatment of CVD with low dose Rivaroxaban in Advanced CKD

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1. ***≥18 years***

2.

Kidney failure on haemodialysis or peritoneal dialysis	*or*	***CKD stage 4 or 5 (eGFR ≤29 mL/min/ 1.73 m²) not receiving renal replacement therapy***
• Receiving maintenance haemodialysis or peritoneal dialysis ***and*** • Irreversible kidney failure (opinion of the treating nephrologist).		• eGFR ≤29 mL/min/1.73 m² for >3 months, ***and*** • Not currently receiving maintenance haemodialysis or peritoneal dialysis, ***and*** • Not have a functioning kidney allograft in a kidney transplant recipient.

3.

Elevated CV risk, defined by at least one of :					
History of CAD *or*	***One or more of:*** • Myocardial infarction, ***or*** • Multi-vessel PCI or CABG surgery, ***or*** • Single-vessel PCI or CABG surgery and stenosis of greater than or equal to 50% in at least one other coronary artery, confirmed by invasive coronary angiography, or non-invasive imaging or stress studies (e.g. exercise or pharmacologic) suggestive of significant ischemia, ***or*** • Medically managed multi-vessel coronary disease with symptoms or with history of stable or unstable angina.	*or*	*Diabetes mellitus*	*or*	*≥65 years*
PAD *or*	***One or more of :*** • Previous aorto-femoral bypass surgery, limb bypass surgery, or percutaneous transluminal angioplasty revascularization of the iliac, or infra-inguinal arteries, ***or*** • Previous limb or foot amputation for arterial vascular disease, ***or*** • History of intermittent claudication ***and*** one or more of the following: 1. An ankle/arm BP ratio <0.90, or 2. Significant peripheral artery stenosis (≥50%) documented by angiography, or by duplex ultrasound, ***or*** • Previous carotid revascularization or asymptomatic carotid artery stenosis ≥50% as diagnosed by duplex ultrasound or angiography				
Non-haemorrhagic non-lacunar stroke	***One or more of:*** • Non-haemorrhagic non-lacunar stroke more than one month prior to study enrolment, ***or*** • Diffusion-weighted imaging (DWI) positive TIA on magnetic resonance imaging more than one month prior to study enrolment.				

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1. Heart valve, (does not include bioprosthetic valves that do not require therapeutic anticoagulation)
2. Indication/contraindication to anticoagulant therapy,
3. High bleeding risk/coagulopathy,
4. Lesion/condition of significant risk of major bleeding*,
5. Major bleeding episode within 30 days prior to study enrolment, or active and clinically significant bleeding,
6. P2Y12 inhibitors/adenosine diphosphate (ADP) receptor inhibitors or phosphodiesterase inhibitors, physician/patient does not wish to stop medications,
7. Strong inhibitors of combined CYP3A4 and P-glycoprotein; or strong inducers of CYP3A4,
8. Stroke within 1 month,
9. History of a haemorrhagic or lacunar stroke,
10. Severe heart failure with ejection fraction <30% or NYHA class III or IV symptoms,
11. Hypersensitivity or contraindication to rivaroxaban,
12. Uncontrolled hypertension (≥180/110 mm Hg) at screening,
13. Haemoglobin <90g/L, or platelet count <100 x 10^9/L,
14. Significant liver disease (defined as Child-Pugh Class B or C) or ALT >3 times upper normal limit,
15. Kidney transplant recipients with a functioning allograft, or scheduled for living-donor kidney transplant surgery,
16. Pregnancy/ intention to become pregnant/ breast-feeding, Europe only: Women who are not in a postmenopausal state, where postmenopausal is defined as no menses for 12 months without alternative medical causes.
17. Inability to understand or comply with the requirements of the study.

Examples for risk of major bleeding

- *gastrointestinal ulceration,*
- *malignant neoplasms at high risk of bleeding,*
- *brain or spinal injury,*
- *brain or spinal or ophthalmic surgery,*
- *intracranial haemorrhage,*
- *oesophageal varices,*
- *arteriovenous malformations (excluding AV fistula or AV graft for dialysis vascular access),*
- *vascular aneurysms or major intraspinal or intracerebral vascular abnormalities,*
- *bronchiectasis or pulmonary bleeding,*
- *congenital or acquired bleeding disorder.*

List of prohibited medications for TRACK eligibility

- ***Oral or parenteral anticoagulant treatment***
  except for regional anticoagulation for haemodialysis
- ***P2Y12 inhibitors/ADP receptor inhibitors:***
  clopidogrel, prasugrel, ticagrelor, cangrelor
- ***Phosphodiesterase inhibitor:*** dipyridamole
- ***Strong inhibitors of combined CYP3A4 and P-glycoprotein:***
  - » synthetic azole antimycotics, eg. ketoconazole, fluconazole, itraconazole, voriconazole, or posaconazole, if used systemically
  - » HIV-protease inhibitors, eg. ritonavir
  - » clarithromycin, erythromycin.
- ***Strong inducers of CYP3A4:***
  - » rifampicin, rifabutin, phenobarbital, phenytoin, carbamazepine, St John's wort.

SAE reporting

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★ ***Contact National Lead or Chief Investigators if SUSAR is suspected***

SAEs that are study outcomes

(study outcomes will not be considered to be SUSARs for regulatory reporting purposes.)

Primary efficacy outcomes

» cardiovascular death
» non-fatal myocardial infarction
» stroke
» peripheral artery disease event

Secondary and tertiary efficacy outcomes

» All-cause death (including non-cardiovascular death and death due to undetermined cause)
» venous thromboembolism
» thrombosis of dialysis vascular access among participants with an AV fistula/graft

Safety outcomes

» Modified ISTH major bleeding events, including fatal bleeding, symptomatic bleeding in a critical area or organ, bleeding leading to hospitalization
» Gastrointestinal bleeding

SAEs that are consistent with the natural history of advanced CKD/Kidney failure and associated conditions

» Planned hospitalisations (for example, surgery, respite care, etc)
» SAEs (including unplanned hospitalisations) that are expected to occur at high frequency in the study population.

Event	*Report on*	*Timelines*
SAEs that are study outcomes	*Outcome eCRF*	*Within* ***7 days of discharge from hospital***
SAEs consistent with natural history of advanced CKD/Kidney failure and associated conditions; planned admissions	*SAE eCRF*	*Within* ***7 days of discharge from hospital***
Suspected unexpected serious adverse reactions (SUSARs)	*SAE eCRF*	*Within* ***24 hours***
Any event of particular concern to the investigator*	*SAE eCRF*	*Within* ***24 hours***
SAEs that are none of the above	*SAE eCRF*	*Within* ***7 days of discharge from hospital***

✱ *Includes pregnancies*

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