Inclusion Criteria

track
Treatment of CVD with low dose Rivaroxaban in Advanced CKD

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1. ***≥18 years***

2.

ESKD 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 for at least 90 days/ 3 months, ***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,
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 109/L,
14. Significant liver disease 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,
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

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

» All 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/ESKD and associated conditions

» Planned hospitalisations (for example, surgery, respite care, etc)
» SAEs (including unplanned hospitalisations) that are expected to occur in 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/ESKD 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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