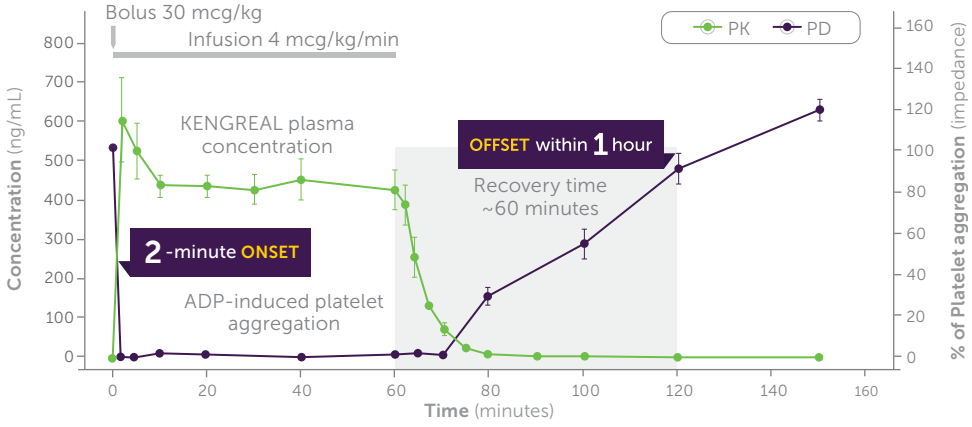
For confidence during high-risk PCI cases.*

KENGREAL® (cangrelor) for injection

IV KENGREAL® (cangrelor) is the only parenteral $P2Y_{12}$ inhibitor

- >98% INHIBITION OF PLATELET AGGREGATION[1]
- Rapid onset within **2 MINUTES**[2]
- Quick offset within **1 HOUR** after discontinuation[2]
- Average elimination half-life of **3–6 MINUTES**[2]

KENGREAL pharmacology[2,3]



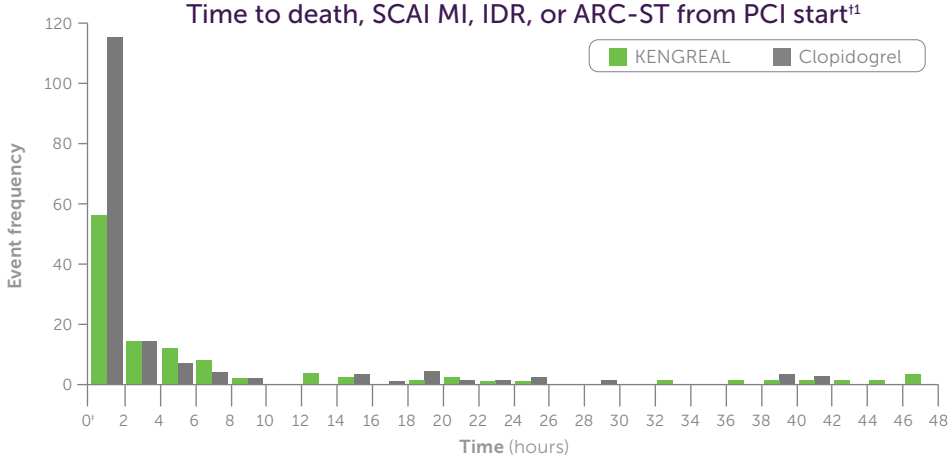
- >98% inhibition of platelet aggregation in whole blood impedance aggregometry[1]
- Clearance is independent of renal or hepatic function[2]
- No dosage adjustment required for renal impairment[2]

Phase I study in healthy volunteers (n=9); dose: 30 mcg/kg IV bolus + 4 mcg/kg/min IV infusion. KENGREAL blood levels and platelet activity were assessed over 150 minutes by whole blood impedance aggregometry in response to 20 µM of ADP.[3]

KENGREAL significantly reduced MACE (death, MI, IDR, stent thrombosis) at 48 hours compared to clopidogrel (22% relative risk reduction)[2,4]

CHAMPION PHOENIX was a randomized, double-blind, placebo-controlled, phase III trial in 11,145 patients who were undergoing either urgent or elective PCI and were receiving guideline-recommended therapy. Patients received a bolus and infusion of KENGREAL or a loading dose of 600 mg or 300 mg of clopidogrel.[4]

CHAMPION PHOENIX post hoc analysis of thrombotic event timing: Time to death, SCAI MI, IDR, or ARC-ST from PCI start[†1]



†Data derived represents a post hoc supplemental analysis in which the study was powered for superiority at the 48-hour time frame. SCAI MI: CK-MB ≥10X ULN, or CK-MB ≥5X ULN with new Q waves or new LBBB. ARC-ST defined according to the ARC definition.

‡Time 0 represents the start of PCI. KENGREAL for Injection was administered at the time of PCI. Clopidogrel oral 300 mg or 600 mg was administered shortly before PCI or shortly afterward in patients randomized to clopidogrel.

ARC=Academic Research Consortium; CK-MB=creatine kinase MB isoenzyme; GUSTO=Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Arteries; IDR=ischemia-driven revascularization; MI=myocardial infarction; SCAI=Society for Cardiovascular Angiography and Interventions; ST=stent thrombosis; ULN=upper limit of normal.

Bleeding events in CHAMPION PHOENIX

- Patients receiving KENGREAL had no statistically significant increase in either GUSTO-defined severe bleeding (P=0.23) or need for transfusion (P=0.22)[4,5]
- Bleeding events of all severities were more common with KENGREAL than with clopidogrel[2]

*In a post hoc analysis of CHAMPION PHOENIX, the absolute benefit of KENGREAL increased progressively with the number of high-risk lesion features treated and was greatest for patients with ≥3.[6]

Important Safety Information

KENGREAL® (cangrelor) for Injection is contraindicated in patients with significant active bleeding.

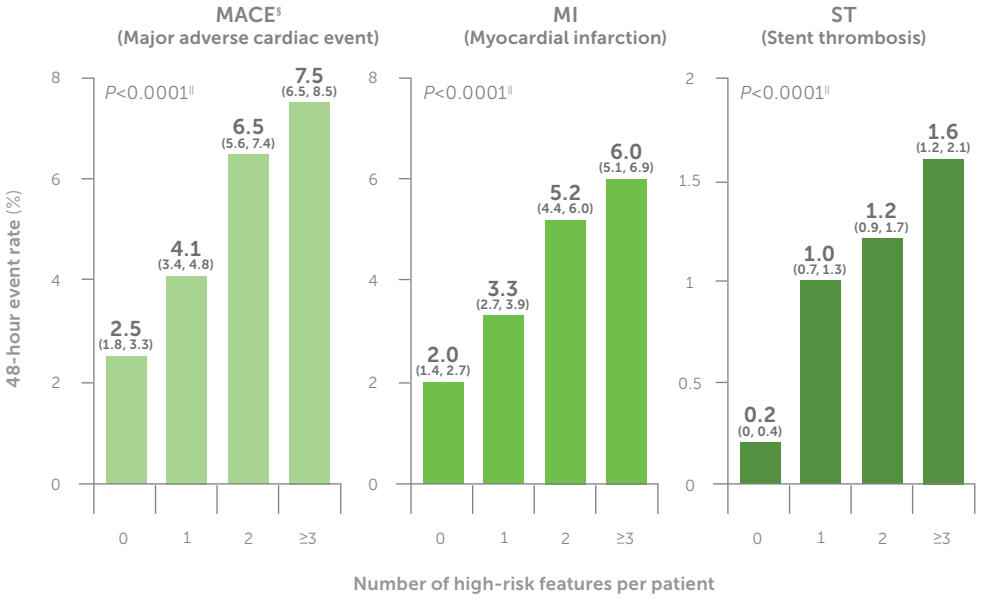
Please see Full Important Safety Information and accompanying Full Prescribing Information.

Platelet inhibition when you need it most

Patients at higher risk for periprocedural thrombotic events benefited from KENGREAL® (cangrelor)

KENGREAL® (cangrelor) for injection

A post hoc analysis of CHAMPION PHOENIX: 48-hour event rates by number of angiographic high-risk features treated[6]



- Nearly 25% of patients had ≥3 high-risk lesion features treated[6]
- The absolute benefit of KENGREAL increased progressively with the number of high-risk lesion features treated and was greatest for patients with ≥3[6]

95% confidence intervals appear under each rate estimate in parentheses.

§MACE is the measure of death, MI, IDR, or ST.
‖Comparison between 0 and ≥3 high-risk features.

It is important to note that PCI patients with high-risk characteristics can differ in disease severity and comorbidities, and not all high-risk lesion characteristics were accounted for in the present analysis. Treatment protocols should account for individualization of care as KENGREAL may not be appropriate for some patients.

Consider KENGREAL for these types of PCI cases

- ☑ Acute coronary syndrome (STEMI and NSTEMI)
- ☑ Fentanyl and/or morphine coadministration
  - Opioids are known to interfere with the absorption of oral $P2Y_{12}$ inhibitors
- ☑ High angiographic risk or complex anatomy
- ☑ Known or potential need for surgery soon after PCI
- ☑ Inability to administer or reliably absorb oral medication
- ☑ High-risk comorbidities (e.g., diabetes)
- ☑ Renal or hepatic impairment, or unknown renal status

Indication

KENGREAL® (cangrelor) for Injection is a $P2Y_{12}$ platelet inhibitor indicated as an adjunct to percutaneous coronary intervention (PCI) to reduce the risk of periprocedural myocardial infarction (MI), repeat coronary revascularization, and stent thrombosis (ST) in patients who have not been treated with a $P2Y_{12}$ platelet inhibitor and are not being given a glycoprotein IIb/IIIa inhibitor.

Important Safety Information

KENGREAL® (cangrelor) for Injection is contraindicated in patients with significant active bleeding.

KENGREAL® is contraindicated in patients with known hypersensitivity (e.g., anaphylaxis) to cangrelor or any component of the product.

Drugs that inhibit platelet $P2Y_{12}$ function, including KENGREAL®, increase the risk of bleeding. In CHAMPION PHOENIX, bleeding events of all severities were more common with KENGREAL® than with clopidogrel. Bleeding complications with KENGREAL® were consistent across a variety of clinically important subgroups. Once KENGREAL® is discontinued, there is no antiplatelet effect after an hour.

The most common adverse reaction is bleeding.

Please see accompanying Full Prescribing Information.

References: 1. Data on file. Chiesi USA, Inc. **2.** KENGREAL® (cangrelor) Prescribing Information. 2016. **3.** Akers WS, Oh JJ, Oestreich JH, Ferraris S, Wethington M, Steinhubl SR. Pharmacokinetics and pharmacodynamics of a bolus and infusion of cangrelor: a direct, parenteral $P2Y_{12}$ receptor antagonist. *J Clin Pharmacol.* 2010;50(1):27-35. **4.** Bhatt DL, Stone GW, Mahaffey KW, et al; CHAMPION PHOENIX Investigators. Effect of platelet inhibition with cangrelor during PCI on ischemic events. *N Engl J Med.* 2013;368(14):1303-1313. **5.** Bhatt DL, Jatene T, Harrington RA, et al. Investigator-reported bleeding versus post hoc adjudication of bleeding. *J Am Coll Cardiol.* 2016;67(5):596-598. **6.** Stone GW, Généreux P, Harrington RA, et al. Impact of lesion complexity on peri-procedural adverse events and the benefit of potent intravenous platelet adenosine diphosphate receptor inhibition after percutaneous coronary intervention: core laboratory analysis from 10,854 patients from the CHAMPION PHOENIX trial. *Eur Heart J.* 2018;39(46):4112-4121.

For more information, please visit **KENGREAL.com**

Chiesi
People and ideas for innovation in healthcare