Research Review
PRODUCT REVIEW

Ticagrelor (Brilinta™)

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He was chairman of the PRISM and HERO trials. He is a member of the Virtual Coordinating Centre for Global Collaborative Cardiovascular Research (VIGOUR) and Bleeding Academic Research Consortium (BARC) group and co-chairman of the Redefinition of MI ESC/ACC/AHA Consensus group and the STABILITY Trial. He has served on the steering committees of international trial groups including ISIS, GUSTO, LIPID and TIMI.

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This review discusses the evidence in support of the use of ticagrelor (Brilinta™), a reversible, selective $P2Y_{12}$-receptor antagonist that was recently approved by Medsafe New Zealand for the prevention of atherothrombotic events in patients aged ≥18 years with acute coronary syndrome (ACS), including patients managed medically, and those who are managed with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

The treatment of Acute Coronary Syndrome (ACS) in New Zealand

The term acute coronary syndrome (ACS) refers to any group of clinical symptoms compatible with acute myocardial ischaemia and includes unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI).[1,2] These high-risk manifestations of coronary atherosclerosis are important causes of the use of emergency medical care and hospitalisation. Systemic factors and inflammation contribute to plaque rupture or fissuring and alterations in haemostatic and coagulation pathways play a part in the initiation of the coronary artery thrombosis that is a characteristic of ACS.[3,4]

The treatment of ACS in New Zealand was audited in 2002 in a nationwide study, in which data were collected from all patients presenting with suspected or definite ACS to all 36 hospitals in the country accepting such admissions.[5] Over a 14-day period in May 2002, there were 721 patients with confirmed ACS (101 were diagnosed with STEMI, 287 with NSTEMI, and 333 with unstable angina); this translates to nearly 19,000 New Zealanders requiring treatment over one year. It is therefore imperative that this very common disease receives appropriate treatment to achieve favourable outcomes and minimise costs to patients, the health system, and society.

Notably, the audit results suggested low levels of appropriate investigations, evidence-based treatments and revascularisation of ACS in New Zealand hospitals, when compared with management recommendations in overseas registries and international guidelines.[6,7] Furthermore, treatments varied between regions and depended on whether the hospital had on-site cardiac catheterisation facilities.[5] When the Cardiac Society of New Zealand Acute Coronary Syndrome Audit Group conducted a second nationwide audit of the management of ACS patients in 2007, the main finding was that levels of investigations, evidence-based treatments and revascularisation had not changed substantially in 5 years.[8]

There is thus an urgent need to improve the management of ACS in New Zealand,[9] which has experienced a rapid rise in the incidence of this condition in recent years. In 2002/2003, more than twice as many New Zealanders had a heart attack than in 1989, and 9,000 more New Zealanders were admitted to hospital with ACS than in 1989.[10] While these data may be influenced by changes in coding systems since 1989, and do not distinguish repeat admissions from first admissions, observations suggest an epidemic in ACS is in progress.[5,8,10] Worryingly, ACS has increased more rapidly in Māori and Pacific Island peoples than in other New Zealand ethnic groups. Between 1995/96 and 2000/2001, ACS overall increased by 15% per year in Māori (15% in men and women), 25% per year in Pacific Islanders (26% in men and 24% in women), and 5% per year in other New Zealanders (4.1% in men and 6.4% in women).[10] While the ageing population is acknowledged to be a contributing factor to this epidemic, increases occurred in men and women of all age groups.[10]

Current treatment options for ACS

Antiplatelet and anticoagulant therapies play an important role in the management of ACS. These therapies include the oral antiplatelet agents aspirin, clopidogrel and ticlopidine, as well as intravenous antiplatelet agents abciximab, eptifibatide, and tirofiban.[11,12] Anticoagulant therapies include unfractionated heparin, bivalirudin, dalteparin, enoxaparin, and fondaparinux. Systemic anticoagulant therapy, typically with unfractionated heparin, has long been a mainstay in the management of ACS despite several limitations, including intravenous administration and unpredictable pharmacokinetics necessitating frequent monitoring.[11]

The current standard dual antiplatelet therapy for ACS consists of clopidogrel plus aspirin.[11] A disadvantage of this strategy is that clopidogrel, a thienopyridine, is a prodrug that undergoes hepatic conversion to its active metabolite, which leads to delayed onset of action and substantial variability between individuals in the levels of platelet inhibition. Up to a third of patients are low responders who have inadequate levels of platelet inhibition.[13] The variability in clopidogrel response has important effects on clinical outcomes; as many as 25% of STEMI patients undergoing primary PCI with stenting are resistant to clopidogrel and may therefore be at increased risk for recurrent cardiovascular (CV) events including stent thrombosis.[14]

Several newer, more potent antiplatelet agents are now available for therapeutic use, including prasugrel and ticagrelor. In phase 3 studies, prasugrel and ticagrelor have demonstrated significant reductions in CV events compared with clopidogrel.[15-17] Importantly, prasugrel and ticagrelor are not associated with the interindividual variability in bioactivation observed with clopidogrel. In addition, the use of these newer agents is not helped by platelet function testing or genotyping, which may be helpful prior to treatment initiation with clopidogrel.[18,19] Also, while prasugrel is associated with increased inhibition of platelet function and further reductions in the risk of MI and stent thrombosis compared with clopidogrel when started at the time of PCI, this agent is associated with an increased risk of bleeding.[16]

Advantages of ticagrelor

Ticagrelor, a reversible and direct-acting oral $P2Y_{12}$-receptor antagonist, provides greater and more consistent platelet inhibition than clopidogrel, with a more rapid onset and offset of action.[15]

Pharmacological properties of ticagrelor

- Ticagrelor, the first reversibly binding oral $P2Y_{12}$ receptor antagonist, provides faster, greater, and more consistent inhibition of platelet aggregation than clopidogrel.[20]
- In patients with stable coronary artery disease on aspirin, ticagrelor demonstrates a rapid onset of pharmacological effect as demonstrated by a mean Inhibition of Platelet Aggregation (IPA) for ticagrelor at 0.5 hours after a 180 mg loading dose of about 41%, with the maximum IPA effect of 89% achieved by 2–4 hours post dose, and maintained between 2–8 hours.[21] 90% of patients have an IPA >70% by 2 hours post dose.[21]
- Ticagrelor demonstrates linear pharmacokinetics and exposure to ticagrelor and the active metabolite (AR-C124910XX) are approximately dose proportional up to 1260 mg.[21]
- Absorption of ticagrelor occurs with a median t_{max} of approximately 1.5 hours. The formation of the metabolite AR-C124910XX from ticagrelor occurs with a median t_{max} of approximately 2.5 hours.[21]
- The mean absolute bioavailability of ticagrelor is about 36%. Ingestion of a high-fat meal had no effect on ticagrelor C_{max}, but resulted in a 21% increase in ticagrelor AUC.[21] The C_{max} of its major metabolite was decreased by 22% with no change in its AUC.[21] Ticagrelor can be taken with or without food.[21]
- The steady state volume of distribution of ticagrelor is 88.5 L. Ticagrelor and the active metabolite are extensively bound to human plasma protein (>99.7%).[21] CYP3A4 is the major hepatic enzyme responsible for ticagrelor metabolism and the formation of its major active metabolite. Ticagrelor is also a weak P-glycoprotein inhibitor. The systemic exposure to the active metabolite is approximately 30%–40% of that obtained for ticagrelor.[21]
- The primary route of ticagrelor elimination is via hepatic metabolism.[21] Recoveries of ticagrelor and the active metabolite in urine are both less than 1% of the dose.[21] The primary route of elimination for the major metabolite of ticagrelor is most likely to be biliary secretion.[21] The mean $t_{1/2}$ is approximately 7 hours for ticagrelor and 8.5 hours for the active metabolite.[21]
- No dose adjustments are required in patients with renal impairment or mild hepatic impairment.[21] Available pharmacodynamic/toxicological data in animals have shown excretion of ticagrelor and its active metabolites in milk.[21] A risk to newborns/infants cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from ticagrelor therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.[21]

- **Ticagrelor inhibits platelet aggregation by 41% at 30 minutes after ingestion.[21]**
- **No adjustments in dose are required for renal or hepatic impairment.[21]**
- **Ticagrelor provides faster, greater and more consistent inhibition of platelet aggregation than clopidogrel.[20]**

EFFICACY AND SAFETY OF TICAGRELOR IN MAJOR CLINICAL TRIALS

Ticagrelor versus clopidogrel in patients with acute coronary syndromes[15]

In the PLATelet inhibition and patient Outcomes (PLATO) study, 18,624 patients admitted to hospital with ACS, with or without ST-segment elevation (STE), were randomised to receive either ticagrelor (180-mg loading dose, 90 mg twice daily thereafter) or clopidogrel (300- to 600-mg loading dose, 75 mg thereafter) for one year. Patients also received aspirin (75 mg to 100 mg/day), unless contraindicated because of intolerability.

At 12 months, the primary end point – composite of death from vascular causes, MI, or stroke – had occurred in 9.8% of the ticagrelor group compared with 11.7% of the clopidogrel group (hazard ratio [HR] 0.84; p<0.001). Predefined secondary end points also revealed significant between-group differences in favour of ticagrelor, including MI alone (5.8% in the ticagrelor group vs 6.9% in the clopidogrel group; p=0.005) and death from vascular causes (4.0% vs 5.1%; p=0.001). However, there was no significant difference in the risk of stroke between the two groups (1.5% vs 1.3%; p=0.22). The rate of death from any cause was also reduced with ticagrelor (4.5% vs 5.9% with clopidogrel; p<0.001).

No significant difference in the rates of major bleeding as defined in the trial was observed between ticagrelor and clopidogrel (11.6% and 11.2%, respectively; p=0.43). There was also no significant difference in the rates of major bleeding according to the Thrombolysis in Myocardial Infarction (TIMI) criteria (7.9% with ticagrelor and 7.7% with clopidogrel; p=0.57) or fatal or life-threatening bleeding (5.8% in both groups; p=0.70). However, ticagrelor was associated with a higher rate of non-CABG-related major bleeding (4.5% vs 3.8%; p=0.03) by the PLATO definition of bleeding and the TIMI criteria (2.8% vs 2.2%; p=0.03). In addition, ticagrelor was associated with more instances of intracranial bleeding, including fatal intracranial bleeding, but fewer instances of fatal bleeding of other types.

The incidence of dyspnoea was higher with ticagrelor than with clopidogrel (in 13.8% of patients vs 7.8%; p<0.001). However, few patients discontinued the study drug because of dyspnoea (0.9% of patients in the ticagrelor group and 0.1% in the clopidogrel group). Holter monitoring during the study did detect more frequent ventricular pauses during the first week in the ticagrelor group than in the clopidogrel group, but such episodes were infrequent at 30 days and were rarely associated with symptoms.

Comment: Compared with clopidogrel, more intense $P2Y_{12}$ receptor inhibition with ticagrelor achieved clinically important reductions in ischaemic events and mortality, without increasing overall major bleeding. Most cases of dyspnoea resolved over one week.

These results have led the European Society of Cardiology (ESC) 2011 Guidelines to recommend ticagrelor for all patients at moderate-to-high risk of ischaemic events (e.g., elevated troponins), regardless of initial treatment strategy and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced).

Comparison of ticagrelor with clopidogrel in patients with a planned invasive strategy for acute coronary syndromes (PLATO): a randomised double-blind study[17]

At randomisation, an invasive strategy was planned for 13,408 (72.0%) of the 18,624 patients in the PLATO trial; 6,732 patients were assigned to ticagrelor and 6,676 to clopidogrel.

The primary composite endpoint of CV death, MI, or stroke occurred in fewer patients in the ticagrelor group than in the clopidogrel group (569 [event rate at 360 days 9.0%] vs 668 [10.7%], HR 0.84; p=0.0025). There was no difference between clopidogrel and ticagrelor groups in the rates of PLATO total major bleeding (691 [11.6%] vs 689 [11.5%]; p=0.8803) or severe bleeding, as defined according to the Global Use of Strategies To Open occluded coronary arteries (GUSTO) criteria (198 [3.2%] vs 185 [2.9%]; p=0.3785).

Rates of deaths resulting from cardiovascular causes (5.3% vs 6.6%; p=0.0023) and of MI (3.4% vs 4.3%; p=0.0250) were lower in the ticagrelor group than in the clopidogrel group, whereas rates of strokes did not differ between the groups; rates of ischaemic, haemorrhagic and unknown stroke were 0.9%, 0.2% and 0.07%, respectively, for the ticagrelor group versus 0.9%, 0.1% and 0.01%, respectively, in the clopidogrel group.

The total mortality rate was significantly reduced in the ticagrelor group versus the clopidogrel group (3.9% vs 5.0%; p=0.0103).

Although episodes of dyspnoea occurred significantly more often in the ticagrelor group than in the clopidogrel group (924 [event rate 13.9%] vs 527 [8.0%]; p<0.0001), only 51 (0.8%) patients in the ticagrelor group and 10 (0.2%) in the clopidogrel group permanently discontinued the study drug because of this adverse event. Rates of definite (1.6% vs 2.4%; p=0.03), definite or probable, and definite, probable, or possible stent thrombosis were all lower in the ticagrelor-treated patients, both within 30 days and at one year.

Comment: Ticagrelor appears to be a better option than clopidogrel for patients with acute coronary syndrome for whom an early invasive strategy is planned. This is probably related to the more rapid onset of ticagrelor. As a radial artery approach is now used predominantly in New Zealand for PCI, the rates of bleeding are likely to be lower than reported in the PLATO trial. Reduction in stent thrombosis is important, as approximately 15% of patients who have stent thrombosis die.

Ticagrelor versus clopidogrel in patients with acute coronary syndromes undergoing coronary artery bypass surgery: results from the PLATO (Platelet Inhibition and Patient Outcomes) trial[22]

This predefined PLATO analysis evaluated the outcomes of the 1,261 patients who underwent CABG post-randomisation and were receiving study drug treatment <7 days before surgery. At 12 months, the relative reduction of the primary composite end point (10.6% [66 of 629] with ticagrelor vs 13.1% [79 of 629] with clopidogrel; HR 0.84; p=0.29) was consistent with the results of the whole trial. No between-group differences were observed in the rates of MI (6.0% for ticagrelor vs 6.7% for clopidogrel; p=0.8193) or stroke (2.1% vs 2.1%, respectively; p=0.6967). Total mortality was reduced from 9.7% to 4.7% (HR 0.49; p<0.01), CV death from 7.9% (47 of 629) to 4.1% (25 of 629; HR 0.52; p<0.01), and non-CV death numerically from 2.0% to 0.7% (p=0.07). There was no significant difference in CABG-related major bleeding between the ticagrelor and clopidogrel groups (81.3% vs 80.1% of patients, respectively; HR 1.01; p=0.84). Also, the reoperation rates due to bleeding were similar between the groups (4.0% for ticagrelor-treated patients vs 3.3% for clopidogrel-treated patients; HR 1.19; p=0.6628).

Comment: In the PLATO trial it was recommended that ticagrelor/placebo be withheld for 24 to 72 hours prior to CABG and clopidogrel to be withheld for 5 days preoperatively. Ticagrelor was stopped in 30% of patients' ≤2 days prior to CABG. It is reassuring that in this study bleeding was not increased with ticagrelor.

The increased platelet inhibition achieved with ticagrelor decreases to less than that achieved with clopidogrel by 48 hours after drug cessation and the inhibition of platelet aggregation (IPA) for ticagrelor on day 5 after the last dose is comparable to clopidogrel on day 7 after the last dose.[23]

The 50% reduction in mortality is large. These data show that ticagrelor can be given prior to a coronary angiogram and that bleeding, if CABG is required urgently, won't be increased over that seen with stopping clopidogrel, and likely a shorter period (e.g.: 5 days instead of 7 days) would not expose the patients to a longer period of not being covered by a platelet $P2Y_{12}$ inhibitor to reduce the risk of MI.

Ticagrelor versus clopidogrel in acute coronary syndromes in relation to renal function: results from the Platelet Inhibition and Patient Outcomes (PLATO) trial[24]

This study investigated the main efficacy and bleeding effects of ticagrelor versus clopidogrel in relation to renal function at admission. Serum creatinine levels were available for 15,202 (81.9%) patients at baseline. In patients with chronic kidney disease (creatinine clearance <60 mL/min; n=3,237), ticagrelor significantly reduced the primary end point to 17.3% from 22.0% (HR 0.77) with an absolute risk reduction greater than that of patients with normal renal function (n=11,965): 7.9% versus 8.9% (HR 0.90). Ticagrelor also reduced total mortality (10.0% vs 14.0%; HR 0.72). Major bleeding rates, fatal bleeding and non-CABG-related major bleedings were not significantly different between the ticagrelor and clopidogrel groups (15.1% vs 14.3%; HR 1.07; 0.34% vs 0.77%; HR 0.48; and 8.5% vs 7.3%; HR 1.28). The interactions between creatinine clearance and randomised treatment on any of the outcome variables were nonsignificant.

Comment: ACS patients with any impairment of renal function do worse, with higher ischaemic events and also increased bleeding. In PLATO there was no exclusion for impaired renal function other than for patients with end-stage renal failure requiring dialysis.

Ticagrelor was more effective than clopidogrel regardless of renal function and the effect was larger with worse renal function without an increase in major bleeding. Ticagrelor represents a good choice for the large numbers (up to half of patients >60 years) of patients with ACS who have renal impairment. No adjustment in dose is required for decreased renal function.

Ticagrelor vs. clopidogrel in patients with acute coronary syndromes and diabetes: a substudy from the PLATelet inhibition and patient Outcomes (PLATO) trial[25]

This substudy of the PLATO trial investigated outcomes associated with ticagrelor versus clopidogrel in patients with diabetes or poor glycaemic control. Patients that were analysed included those with pre-existing diabetes (n=4,662), including 1,036 patients on insulin, those without diabetes (n=13,951), and subgroups based on admission levels of haemoglobin A1c (HbA1c; subgroups were defined according to whether HbA1c levels were above or below the median of 6%; n=7260 and n=7890, respectively). Diabetes and higher baseline serum levels of glucose and HbA1c were strongly associated with all ischaemic and bleeding endpoints and with higher risks of the primary outcome (primary composite endpoint of CV death, MI and stroke) and all-cause mortality in patients on insulin treatment. Compared with clopidogrel, ticagrelor reduced the primary composite endpoint and also all-cause mortality and stent thrombosis, without any significant increase in overall PLATO major bleeding. These effects were seen irrespective of diabetic status, insulin treatment, and glycaemic control.

Comment: While the combination of clopidogrel and aspirin prevents thrombotic events in patients with ACS, patients with diabetes mellitus have consistently been shown to have higher on-treatment platelet reactivity and worse clinical outcomes than patients without diabetes, and therefore have a large unmet need.[26-28]

Ticagrelor, when compared with clopidogrel, reduced ischaemic events in ACS patients irrespective of diabetic status and glycaemic control, without increasing major bleeding events.

Ticagrelor versus clopidogrel in patients with ST-elevation acute coronary syndromes intended for reperfusion with primary percutaneous coronary intervention: A Platelet Inhibition and Patient Outcomes (PLATO) trial subgroup analysis[29]

This report concerns the 7,544 ACS patients participating in the PLATO trial with STEMI or left bundle-branch block (LBBB) undergoing primary PCI. The reduction of the primary end point (MI, stroke, or CV death) with ticagrelor versus clopidogrel (10.8% vs 9.4%; HR 0.87; p=0.07) was consistent with the overall PLATO results. There was no interaction between presentation with STEMI/LBBB and randomised treatment (interaction p=0.29). Ticagrelor reduced several secondary end points, including MI alone (HR, 0.80; p=0.03), total mortality (HR 0.82; p=0.05), and definite stent thrombosis (HR 0.66; p=0.03). The risk of stroke was higher with ticagrelor (1.7% vs 1.0%; HR1.63; p=0.02). Ticagrelor did not affect PLATO major bleeding (HR 0.98; p=0.76).

Comment: In patients with STEMI and planned primary PCI, ticagrelor demonstrated effects that were consistent with those observed in the overall PLATO trial. Because of its rapid onset (~30 minutes), administration prehospital or in the Emergency Department (ED) would ensure that most patients undergoing primary PCI would have platelet inhibition at the time of stenting. There are no data with fibrinolytic therapy.

Effect of *CYP2C19* and *ABCB1* single nucleotide polymorphisms on outcomes of treatment with ticagrelor versus clopidogrel for acute coronary syndromes: a genetic substudy of the PLATO trial[30]

DNA samples obtained from 10,285 patients in the PLATO trial were genotyped for *CYP2C19* loss-of-function alleles, the *CYP2C19* gain-of-function allele, and the *ABCB1* single nucleotide polymorphism 3435C→T. The superiority of ticagrelor over clopidogrel in reducing major CV events was not significantly affected by patient *CYP2C19* or *ABCB1* genotype. Similar to the overall PLATO study, rates of total major bleeding events did not differ between ticagrelor and clopidogrel, regardless of *CYP2C19* or *ABCB1* genotype. In a post-hoc analysis that combined data for *CYP2C19* and *ABCB1* polymorphisms, Kaplan-Meier estimates of events of the primary efficacy outcome among patients with either any loss-of-function *CYP2C19* allele or the predicted high-expression *ABCB1* phenotype were significantly lower in the ticagrelor group versus the clopidogrel group (8.6% vs 11.2%; p=0.004). Corresponding event rates in patients without these alleles, were 8.9% and 9.5%, respectively (p=0.39). However, this genetic grouping did not have a significant interaction with the overall effects of ticagrelor versus clopidogrel (p=0.13).

Comment: Ticagrelor was a more efficacious treatment for ACS in reducing cardiovascular death than was clopidogrel, irrespective of *CYP2C19* and *ABCB1* gene polymorphisms. Use of ticagrelor instead of clopidogrel eliminates any possible advantages for genetic testing before dual antiplatelet treatment.

Ticagrelor versus clopidogrel in patients with acute coronary syndromes intended for non-invasive management: substudy from prospective randomised PLATelet inhibition and patient Outcomes (PLATO) trial[31]

5,216 (28%) of 18,624 patients admitted to hospital for ACS who were specified as planned for non-invasive management were randomised to treatment with ticagrelor (n=2,601) or clopidogrel (2,615). By the end of follow-up, 3,143 (60.3%) of 5,216 patients had been managed non-invasively. In this patient population, the incidence of the primary composite end point of CV death, MI, and stroke was lower with ticagrelor than with clopidogrel (12.0% [n=295] vs 14.3% [n=346]; p=0.04). Overall mortality was also lower (6.1% [n=147] vs 8.2% [n=195]; p=0.01). Compared with clopidogrel, ticagrelor was associated with a numerically higher incidence of total PLATO defined major bleeding (11.9% [n=272] vs 10.3% [n=238]; p=0.08) and also non-CABG-related major bleeding (4.0% [n=90] vs 3.1% [n=71]; p=0.10).

Comment: In patients with ACS initially intended for non-invasive management, the benefits of ticagrelor over clopidogrel were consistent with those from the overall PLATO results. Of importance, the absolute reduction in ischaemic events is large, i.e.: for CVD, MI and stroke 23 per 1,000 patients randomised and 21 deaths per 1,000 patients randomised. The NNT to save one life is 48.

CONCLUSION

PLATO investigated the efficacy of ticagrelor and clopidogrel for the prevention of ischaemic events in ACS patients, including those intended for invasive procedures or medical management. Ticagrelor was associated with a 16% reduction in events (CV death, MI, stroke) vs clopidogrel (p<0.001). This was largely related to a statistically significant reduction in both CV death and MI, with no statistically significant difference in stroke compared with clopidogrel.

The reduction in risk of CV events with ticagrelor vs clopidogrel occurred early and this benefit was sustained over the 12 months studied.

As expected with a more potent antiplatelet therapy, there was an increase in non-CABG major bleeding with ticagrelor. Importantly, ticagrelor had no increase in overall major or fatal bleeding compared with clopidogrel.

Treating 1,000 ACS patients over 12 months with ticagrelor instead of clopidogrel results in 14 fewer deaths and 11 fewer MIs, 6–8 fewer cases with stent thrombosis, 6 more major non-CABG bleeds but no increase in fatal or life-threatening bleeds.

Nine patients per 1,000 may stop ticagrelor because of symptoms of dyspnoea.

For the metric, numbers needed to treat (NNT), treatment of 54 patients with ticagrelor instead of with clopidogrel for one year will prevent one CV death, MI or stroke.

Higher risk patients including those with STEMI, high risk non-STEMI patients, those with impaired renal function, patients likely to undergo CABG, patients being treated medically, patients with stent thrombosis, and patients with clopidogrel resistance have considerable treatment benefits from ticagrelor, as assessed by reduction in the combined risk of CV death, MI or stroke.

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