Preserve Your Patient's Future with

Brelor 90
Ticagrelor

- **Potent P2Y12 Inhibitor**
- **Rapid Onset Of Action**
- **Reversible Inhibition**

PLATO Trial:
Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

Study Design

- A multicenter, randomized, double-blind, double-dummy trial
- 18,624 patients from 862 centers in 43 countries from Oct 2006 to July 2008

Groups:

- **Ticagrelor:**
  - Loading dose: 180 mg
  - Maintenance dose: 90 mg twice daily
- **Clopidogrel:**
  - Loading dose: 300 to 600 mg
  - Maintenance dose: 75 mg daily

Objectives

- **Primary efficacy endpoint:**
  The time to the first occurrence of composite of death from vascular causes, myocardial infarction, or stroke
- **Secondary efficacy endpoint:**
  The composite of death from any cause, from vascular causes, MI, stroke, severe recurrent cardiac ischemia and transient ischemic attack
- **Tertiary efficacy endpoint:**
  Evaluation for stent thrombosis

The same basline characteristics of the patients in two groups

Characteristic	Ticagrelor Group	Clopidogrel Group
Cardiovascular risk factor — no./total no. (%)		
Habitual smoker	(36.0)	(35.7)
Hypertension	(65.8)	(65.1)
Dyslipidemia	(46.6)	(46.7)
Diabetes mellitus	(24.9)	(25.1)
Other medical history — no./total no. (%)		
MI	(20.4)	(20.7)
Percutaneous coronary intervention	(13.6)	(13.1)
Coronary-artery bypass grafting	(5.7)	(6.2)
Congestive heart failure	(5.5)	(5.8)
Nonhemorrhagic stroke	(3.8)	(4.0)
Peripheral arterial disease	(6.1)	(6.2)
Chronic renal disease	(4.1)	(4.4)
History of dyspnea	(15.1)	(14.6)
Chronic obstructive pulmonary disease	(5.9)	(5.7)
Asthma	(2.9)	(2.9)
Gout	(2.9)	(2.8)
ECG findings at study entry — no./total no. (%)		
Persistent ST-segment elevation	(37.5)	(37.8)
ST-segment depression	(50.7)	(51.2)
T-wave inversion	(31.8)	(32.0)
Positive troponin I test at study entry — no./total no. (%)	(85.3)	(86.1)
Final diagnosis of ACS — no./total no. (%)		
ST-elevation MI	(37.5)	(38.0)
Non–ST-elevation MI	(42.9)	(42.5)
Unstable angina	(16.6)	(16.8)
Other diagnosis or missing data	(3.0)	(2.7)
Risk factors for ST-elevation MI — no./total no. (%)		
Killip class >2	(0.7)	(1.2)
TIMI risk score ≥3	(45.3)	(44.0)
Risk factors for non–ST-elevation MI — no./total no. (%)		
Positive troponin I test	(79.5)	(80.8)
ST-segment depression >0.1 mV	(56.6)	(57.7)
TIMI risk score ≥5	(20.0)	(21.2)

Results

Primary efficacy
outcome at 12 months

Primary End Point	Ticagrelor Group	Clopidogrel Group	Hazard Ratio for Ticagrelor Group (95% CI)	P Value
Death from vascular causes, MI, or stroke — no./total no. (%)	(9.8)	(11.7)	0.84 (0.77-0.92)	<0.001

- The primary end point occurred significantly less often in the **Ticagrelor** group than in the Clopidogrel group.
- The difference in treatment effect was apparent within the first 30 days of therapy and persisted throughout the study period.

Secondary efficacy
outcome at 12 months

- The secondary end points showed significant reductions in **Ticagrelor** vs Clopidogrel, with respect to the rates of the composite end point of death from any cause, myocardial infarction, or stroke, the composite end point of death from vascular causes, myocardial infarction, stroke, severe recurrent ischemia, recurrent ischemia, transient ischemic attack, or other arterial thrombotic events alone.

Secondary End Point	Ticagrelor Group	Clopidogrel Group	Hazard Ratio for Ticagrelor Group (95% CI)	P Value
Secondary end points — no./total no. (%)				
Death from any cause, MI, or stroke	(10.2)	(12.3)	0.84 (0.77–0.92)	<0.001
Death from vascular causes, MI, stroke, severe recurrent ischemia, recurrent ischemia, TIA, or other arterial thrombotic event	(14.6)	(16.7)	0.88 (0.81–0.95)	<0.001
MI	(5.8)	(6.9)	0.84 (0.75–0.95)	0.005
Death from vascular causes	(4.0)	(5.1)	0.79 (0.69–0.91)	0.001
Stroke	(1.5)	(1.3)	1.17 (0.91–1.52)	0.22
Ischemic	(1.1)	(1.1)		0.74
Hemorrhagic	(0.2)	(0.1)		0.10
Unknown	(0.1)	(0.02)		0.04
Other events — no./total no. (%)				
Death from any cause	(4.5)	(5.9)	0.78 (0.69–0.89)	<0.001
Death from causes other than vascular causes	(0.5)	(0.8)	0.71 (0.49–1.04)	0.08
Severe recurrent ischemia	(3.5)	(4.0)	0.87 (0.74–1.01)	0.08
Recurrent ischemia	(5.8)	(6.2)	0.93 (0.82–1.05)	0.22
TIA	(0.2)	(0.3)	0.78 (0.42–1.44)	0.42
Other arterial thrombotic event	(0.2)	(0.4)	0.61 (0.34–1.08)	0.09
Death from vascular causes, MI, stroke — no./total no. (%)				
Invasive treatment planned	(8.9)	(10.6)	0.84 (0.75–0.94)	0.003
Event rate, days 1–30	(4.8)	(5.4)	0.88 (0.77–1.00)	0.045
Event rate, days 31–360	(5.3)	(6.6)	0.80 (0.70–0.91)	<0.001

Tertiary efficacy
outcome at 12 months

Tertiary End Point	Ticagrelor Group	Clopidogrel Group	Hazard Ratio for Ticagrelor Group (95% CI)	P Value
Stent thrombosis — no. of patients who received a stent/ total no. (%)				
Definite	(1.3)	(1.9)	0.67 (0.50–0.91)	0.009
Probable or definite	(2.2)	(2.9)	0.75 (0.59–0.95)	0.02
Possible, probable, or definite	(2.9)	(3.8)	0.77 (0.62–0.95)	0.01

Among patients who received a stent during the study, the rate of definite stent thrombosis was lower in **Ticagrelor** vs Clopidogrel.

Conclusion

1. Treatment with **Ticagrelor** as compared with clopidogrel in patients with acute coronary syndromes with or without ST-segment elevation significantly reduced the rate of death from vascular causes, myocardial infarction, or stroke and death from any other cause, resulting in an overall reduction of 22% in the mortality rate with **Ticagrelor** from any cause at 1 year.

2. The incremental reduction in the risk of coronary thrombotic events (i.e., myocardial infarction and stent thrombosis) and survival benefit through more-intense P2Y12 inhibition with **Ticagrelor**, regardless of whether invasive or noninvasive management was planned, is consistent; this issue has not been investigated with other P2Y12 inhibitors.

3. Since P2Y12 inhibition with **Ticagrelor** is reversible, the antiplatelet effect dissipates more rapidly than with the thienopyridines, which are irreversible P2Y12 inhibitors, therefore, less procedure related bleeding might be expected.

4. There was no increased risk of CABG-related bleeding with **Ticagrelor**.

5. The beneficial effects of **Ticagrelor** were achieved without a significant increase in the rate of major bleeding, as seen with other antithrombotic treatments in patients with an acute coronary syndrome.

Brelor 90 Ticagrelor

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Reference: Lars Wallentin, M.D., ph.D., et al, NEW ENGL J MED, 2009, 361;11,(1045_1057).