

# Potential impact of prolonged dual antiplatelet therapy with ticagrelor in “real world” stable patients after acute myocardial infarction versus randomized controlled trial populations



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## BACKGROUND & OBJECTIVES

Long-term treatment with ticagrelor 60 mg bid added to aspirin (ASA) reduced cardiovascular (CV) events but increased major bleeding in stable patients after acute myocardial infarction (AMI). (<sup>1</sup>PEGASUS-TIMI 54 trial)

<sup>1</sup>Bonaca MP, *et al.* N Engl J Med. 2015;372:1791-800.

We aimed to estimate potential benefits of prolonged dual-antiplatelet therapy (DAPT) in “real-world” patients after AMI similar to those in PEGASUS-TIMI 54 trial.

## METHODS

**Study population** Retrospective analysis of 6,258 consecutive patients who survived ≥1 year after AMI from 3 public hospitals in Hong Kong between January 2005 and June 2018 (median follow-up 56 [IQR 26-95] months).

PEGASUS-like (PL) Chinese patients were identified based on PEGASUS-TIMI 54 (PT54) trial inclusion and exclusion criteria.

| PT54                                                                         |                                                                    | N=6,258                         |
|------------------------------------------------------------------------------|--------------------------------------------------------------------|---------------------------------|
| Key Inclusion Criteria <sup>1</sup>                                          |                                                                    |                                 |
| Age ≥50 years & Prior MI 1-3 years prior with ≥1 additional risk factors:    |                                                                    | 4,497 (71.8%)                   |
| • Age ≥65 years                                                              |                                                                    | patients met inclusion criteria |
| • Diabetes mellitus requiring medication                                     |                                                                    |                                 |
| • Second prior MI                                                            |                                                                    |                                 |
| • Multivessel coronary artery disease                                        |                                                                    |                                 |
| • Chronic kidney disease (non-ESRF, eGFR <60mL/min)                          |                                                                    |                                 |
| PT54                                                                         | PL Chinese                                                         | N=6,258                         |
| Key Exclusion Criteria <sup>1</sup>                                          | Exclusion Criteria                                                 |                                 |
| Age <50 years                                                                |                                                                    | 631 (10.1)                      |
| Planned use of P2Y12/ dipyridamole/ cilostazol/ anticoagulant                |                                                                    | 455 (7.3)                       |
| Increased risk of bleeding                                                   | Prior intracranial bleed/ gastrointestinal bleed in prior 6 months | 75 (1.2)                        |
| Prior ischemic stroke                                                        |                                                                    | 242 (3.9)                       |
| Coronary-artery bypass grafting in prior 5 years                             |                                                                    | 259 (4.1)                       |
| Known severe liver disease                                                   | Liver cirrhosis                                                    | 14 (0.2)                        |
| Renal failure requiring dialysis                                             | End stage renal failure                                            | 189 (3.0)                       |
| PL Chinese patients who met PT54 trial inclusion & exclusion criteria, N (%) |                                                                    | 3,513 (56.1)                    |

Subgroup analysis was performed in patients with high ischemic (≥2 ischemic risk factors) and low bleeding risk (non-anemia, no prior hospitalization for bleeding).

## Primary outcome measures

Estimated absolute risk reduction (eARR) with estimated number-needed-to-treat (eNNT) and estimated absolute risk increase (eARI) with estimated number-needed-to-harm (eNNH) in 3-year event rates in PL Chinese patients based on results from the PT54 trial:

- Major adverse cardiovascular events (MACE, including MI, CV death and stroke)
- TIMI major bleeding events

## RESULTS

Of 6,258 patients, 3,513 (56.1%) PL Chinese patients were identified. Our PL Chinese patients were older with more women compared to placebo-patients in PT54 trial.

Table 1. Characteristics of patients.

|                                        | PL Chinese patients<br>N=3,513 | PT54 patients on ASA<br>N=7,067 |
|----------------------------------------|--------------------------------|---------------------------------|
| Age, years, mean±SD                    | 82.2±11.3                      | 65.4±8.3                        |
| Age ≥65 years, %                       | 72.5                           | -                               |
| Female, %                              | 30.7                           | 24.3                            |
| History of STEMI, %                    | 55.5                           | 54.0                            |
| Diabetes mellitus, %                   | 39.6                           | 31.9                            |
| Multivessel coronary artery disease, % | 32.6                           | 59.6                            |
| Chronic renal dysfunction, %           | 32.9                           | 23.6                            |
| Peripheral artery disease, %           | 1.5                            | 5.7                             |

STEMI indicates ST-segment elevation myocardial infarction.

Table 2. Three-year outcomes and application of relative-risk reduction/increase from PT54 trial (ticagrelor 60mg bid daily group) to our PL patients. MACE and major bleeding rates were comparable. The eARR of 1.5% (95% CI 0.7-2.3) with eNNT of 66 (CI 43-138) to avoid one MACE; and eARI of 1.3% (CI 0.9-1.7) with eNNH of 78 (CI 60-106) to cause one major bleeding.

|                     | PT54 Overall on ASA <sup>1</sup> |      |     | PL Chinese Overall |      |      |
|---------------------|----------------------------------|------|-----|--------------------|------|------|
|                     | %                                | ARR  | NNT | %                  | eARR | eNNT |
| MACE                | 9.0                              | 1.3% | 79  | 9.4                | 1.5% | 66   |
| CV death            | 3.4                              | 0.5% | 189 | 4.1                | 0.7% | 143  |
| Stroke              | 1.9                              | 0.5% | 213 | 2.5                | 0.6% | 160  |
| MI                  | 5.3                              | 0.7% | 139 | 4.4                | 0.7% | 142  |
|                     | %                                | ARI  | NNH | %                  | eARI | eNNH |
| TIMI major bleeding | 1.1                              | 1.2% | 81  | 1.1                | 1.3% | 78   |

Table 3. N=1,373 patients were identified for subgroup analysis.

|                                                                                   | PL Chinese patients<br>N=3,513 |
|-----------------------------------------------------------------------------------|--------------------------------|
| Low bleeding risk, %                                                              | 76.3                           |
| ≥2 Ischemic risk factors, %                                                       | 52.1                           |
| High ischemic and low bleeding risk patients included in subgroup analysis, N (%) | 1,373/3,513 (39.0)             |

Table 4. Subgroup analysis in 1,373 patients with high ischemic and low bleeding risk. 3-year MACE and major bleeding rates were lower with eNNT of 63 (CI 42-115) and a more favorable NNH of 111 (CI 82-172), respectively.

|                     | PT54 Overall on ASA <sup>2</sup> |      |     | PL Chinese Overall |      |      |
|---------------------|----------------------------------|------|-----|--------------------|------|------|
|                     | %                                | ARR  | NNT | %                  | eARR | eNNT |
| MACE                | 9.9                              | 1.9% | 53  | 8.4                | 1.6% | 63   |
|                     | %                                | ARI  | NNH | %                  | eARI | eNNH |
| TIMI major bleeding | 1.0                              | 1.0% | 100 | 0.9                | 0.9% | 111  |

<sup>2</sup>Bonaca MP, *et al.* Circulation. 2018;138(suppl 1):A16658.

## CONCLUSIONS

- About 50% of patients a year or more after AMI are eligible for prolonged DAPT with ticagrelor.
- Estimated benefits of prolonged DAPT in “real-world” patients are similar to that observed in the PT54 trial and is likely to be greatest in patients with high ischemic and low bleeding risk.