Effects of the P-Selectin Antagonist Inclacumab on Myocardial Damage After Percutaneous Coronary Intervention According to Timing of Infusion: Insights From the SELECT-ACS Trial

Barbara E. Stähli, MD, MBA; Catherine Gebhard, MD; Valérie Duchatay, MD; Daniel Cournoyer, MSc; Thibaut Petroni, MD; Jean-François Tanguay, MD; Stephen Robb, MD; Jessica Mann, MD, PhD; Marie-Claude Guertin, PhD; R. Scott Wright, MD; Philippe L.’Allier, MD; Jean-Claude Tardif, MD

Background—The Effects of the P-Selectin Antagonist Inclacumab on Myocardial Damage After Percutaneous Coronary Intervention for Non-ST-Segment Elevation Myocardial Infarction (SELECT-ACS) trial suggested beneficial effects of inclacumab, a monoclonal antibody directed against P-selectin, on periprocedural myocardial damage. This study evaluated the effect of inclacumab on myocardial damage according to varying time intervals between study drug infusion and percutaneous coronary intervention (PCI).

Methods and Results—Patients (n=544) enrolled in the SELECT-ACS trial and randomized to receive 1 infusion of placebo or inclacumab (5 or 20 mg/kg, administered between 1 and 24 hours before PCI) were divided according to the time interval between study drug infusion and PCI. The primary end point was the change in troponin I from baseline at 16 and 24 hours after PCI. In patients receiving inclacumab 20 mg/kg with a short (less than median) time interval between infusion and PCI, placebo-adjusted geometric mean percent changes in troponin I, creatine kinase–myocardial band, and peak troponin I at 24 hours were −45.6% (P=0.005), −30.7% (P=0.01), and −37.3% (P=0.02), respectively. No significant changes were observed in patients with a long (greater than median) time interval between infusion and PCI. Placebo-adjusted geometric mean percent changes in troponin I and creatine kinase–myocardial band were −43.5% (P=0.02) and −26.0% (P=0.07), respectively, when inclacumab 20 mg/kg was administered between 1 and 3 hours before PCI, whereas the drug had no effect with longer intervals.

Conclusions—Inclacumab 20 mg/kg significantly reduces myocardial damage after PCI in patients with non–ST-segment elevation myocardial infarction, and benefits are larger when the infusion is administered <3 hours before PCI.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01327183. (J Am Heart Assoc. 2016;5: e004255 doi: 10.1161/JAHA.116.004255)

Key Words: acute coronary syndrome • inflammation • myocardial infarction • percutaneous coronary intervention • thrombosis

Myocardial damage is frequently observed in patients undergoing percutaneous coronary intervention (PCI) and has been associated with worse outcomes.1,2 Although different treatment strategies have been developed to reduce myocardial injury after coronary revascularization,3–5 the high incidence highlights the need for novel therapeutic concepts. Pathophysiological mechanisms of periprocedural myocardial injury are incompletely understood, and activation of inflammation and platelets, along with distal embolization and microvascular obstruction, seem to play a pivotal role.6,7 P-selectin is a cell adhesion molecule that is expressed on activated endothelial cells and platelets, and known to mediate leukocyte recruitment and promote the formation of procoagulant microparticles.8–10 Recent research has indicated that P-selectin appears to be involved in the pathogenesis of myocardial damage in acute coronary syndromes and during PCI.11–13 The SELECT-ACS (Effects of the P-Selectin Antagonist Inclacumab on Myocardial Damage After Percutaneous Coronary Intervention for Non-ST-Segment Elevation Myocardial
Infarction) trial suggested beneficial effects of inclacumab, a monoclonal antibody directed against P-selectin, on myocardial damage after PCI in patients with non–ST-segment elevation myocardial infarction (NSTEMI). In this trial, inclacumab (5 and 20 mg/kg) was administered as a single intravenous infusion between 1 and 24 hours before PCI.

This study aimed to evaluate the effects of inclacumab on periprocedural myocardial damage according to varying time intervals between study drug infusion and PCI. Favorable effects of inclacumab in patients with NSTEMI would support the concept of targeting the P-selectin pathway for the reduction of myocardial damage during PCI and would contribute to the optimization of the study drug regimen.

Methods

The SELECT-ACS Study Design

Details of the SELECT-ACS trial were published previously. The SELECT-ACS study was a multicenter, randomized, double-blind, placebo-controlled trial (NCT01327183) evaluating the efficacy and safety of inclacumab (RO4905417; F. Hoffmann-La Roche) in patients with NSTEMI undergoing PCI. A total of 544 patients presenting with NSTEMI and scheduled for coronary angiography and PCI were enrolled at 66 centers located in Canada, the United States, Poland, and the Netherlands. Patients were randomized at a 1:1:1 ratio to receive inclacumab 5 mg/kg, inclacumab 20 mg/kg, or placebo. The study drug or placebo was administered as a single 1-hour infusion between 1 and 24 hours before PCI. Troponin I (TnI) and creatine kinase–myocardial band (CK-MB) levels were measured at baseline and at 8, 16, and 24 hours after PCI (or at discharge if patients were discharged before the last time point). The efficacy population (n=322) comprised patients who received the study drug or placebo, underwent PCI, and had TnI levels measured at both baseline and follow-up. The study was coordinated by the Montreal Health Innovations Coordinating Center, a division of the Montreal Heart Institute. The protocol was approved by the institutional review board at each participating center, and all participants enrolled in the study provided written informed consent.

Outcomes

The primary efficacy endpoint was the change in TnI from baseline at 16 and 24 hours after PCI (or at discharge if patients were discharged before the last time point). The secondary endpoints were the peak TnI, the area under the curve for TnI over 24 hours, the change in TnI from baseline at 8 hours, and the changes in CK-MB from baseline at 8, 16, and 24 hours after PCI. Data on the time interval between study drug infusion and PCI were available for 321 patients. Comparisons were made between patients with a short (less than median) and a long (greater than median) time interval between study drug infusion and PCI and between patients receiving the study drug or placebo 1 to 3, 3 to 4, and >4 hours before PCI.

Statistical Analysis

Continuous variables are presented as mean±SD or median and interquartile range. Categorical variables are given as frequencies. For inclacumab 5 and 20 mg/kg, treatment groups with varying time intervals between study drug infusion and PCI were compared with placebo using appropriate contrast and log transformation to account for the skewed distribution. Log transformation was performed for TnI, CK-MB, peak TnI, and area under the curve for TnI. The study end points were analyzed using an ANCOVA model including treatment group (placebo, inclacumab 5 mg/kg, and inclacumab 20 mg/kg) and time interval (categorized as short and long time interval or as 1–3, 3–4, and >4 hours) as main effects and adjusting for baseline biomarker levels, known diabetes mellitus (the stratification factor of the SELECT-ACS trial), and differences (P≤0.10) in procedural characteristics between the short and long time interval groups. The dataset was not split, and the ANCOVA models were not applied separately in the short and long time interval groups. The area under the curve for TnI over 24 hours was analyzed using an ANOVA model including treatment group (placebo, inclacumab 5 mg/kg, and inclacumab 20 mg/kg) and time interval (categorized as short and long time interval or as 1–3, 3–4, and >4 hours) as main effects and adjusting for known diabetes mellitus and differences in procedural characteristics. Differences between treatment and placebo groups were described through placebo-adjusted geometric mean percent change, and the geometric mean was obtained by the antilog of log-transformed data. A P value <0.05 was considered statistically significant. All statistical analyses were performed using SAS statistical software version 9.3 (SAS Institute).

Results

Patient Characteristics

Baseline clinical and procedural characteristics are summarized in Tables 1 and 2. Patients were mostly white (96.0%) and male (78.8%). In both the placebo and inclacumab 5 mg/kg groups, baseline characteristics did not differ between patients with short and long time intervals between study drug infusion and PCI. In the inclacumab 20 mg/kg group, the number of vessels treated per patient was slightly lower in patients with a short versus long time interval (1.1±0.2 versus 1.2±0.4, P=0.049). The median time interval between study drug infusion and PCI was 202 minutes (interquartile...
range 154–323 minutes) and was similar among treatment groups, with 205 minutes (interquartile range 160–300 minutes), 195 minutes (interquartile range 145–390 minutes), and 200 minutes (interquartile range 160–361 minutes) in the placebo, inclacumab 5 mg/kg, and inclacumab 20 mg/kg groups, respectively.

**Effects of Inclacumab 5 mg/kg on Myocardial Damage**

Inclacumab 5 mg/kg had no effect on periprocedural myocardial damage irrespective of the time interval between study drug infusion and PCI. Placebo-adjusted geometric mean percentage changes in TnI from baseline at 16 and 24 hours were 12.1% ($P=0.57$) and 0.6% ($P=0.98$), respectively, in patients with a short time interval and $-6.2\%$ ($P=0.68$) and $-9.6\%$ ($P=0.50$), respectively, in those with a long time interval. The placebo-adjusted geometric mean percent changes in peak TnI were 11.3% ($P=0.48$) and 17.8% ($P=0.36$), respectively, in patients with a short time interval and $-13.4\%$ ($P=0.03$) and $-17.8\%$ ($P=0.005$), respectively, in those with a long time interval. Corresponding changes in CK-MB at 16 and 24 hours were $-4.9\%$ ($P=0.75$) and $-8.0\%$ ($P=0.59$), respectively, in patients with a short time interval and $-6.2\%$ ($P=0.68$) and $-9.6\%$ ($P=0.50$), respectively, in those with a long time interval. The placebo-adjusted geometric mean percent changes in peak TnI were 11.3% ($P=0.60$) and $-11.6\%$ ($P=0.55$) in the short and long time interval groups, respectively, and corresponding changes in the area under the curve for TnI over 24 hours were $-39.6\%$ ($P=0.14$) and $-13.1\%$ ($P=0.68$), respectively.

**Effects of Inclacumab 20 mg/kg on Myocardial Damage**

Effects of inclacumab 20 mg/kg on periprocedural myocardial damage differed according to the time interval between study drug infusion and PCI. In patients with a short time interval (less than the median of 202 minutes), inclacumab resulted in significant placebo-adjusted geometric mean percent changes in TnI at 16 and at 24 hours of $-34.9\%$ ($P=0.03$) and $-45.6\%$ ($P=0.005$), respectively, whereas it had

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Table 1. Baseline Characteristics

|                          | Placebo | Inclacumab (5 mg/kg) | Inclacumab (20 mg/kg) |
|--------------------------|---------|----------------------|-----------------------|
|                          | Short Time Interval (n=56) | Long Time Interval (n=59) | Short Time Interval (n=48) | Long Time Interval (n=47) | Short Time Interval (n=56) | Long Time Interval (n=55) | P Value | P Value* |
| Age, y                   | 59.7 (54.2–66.6) | 61.4 (55.4–66.6) | 0.66 | 61.5 (56.7–69.4) | 65.4 (54.6–71.9) | 0.45 | 60.4 (53.8–68.4) | 59.0 (51.9–68.6) | 0.87 | 1.00 |
| Male                     | 76.8 | 81.4 | 0.54 | 75.0 | 80.9 | 0.49 | 85.7 | 72.7 | 0.10 | 0.22 |
| Race                     | White | 98.2 | 93.2 | 95.8 | 95.7 | 92.9 | 100.0 |
|                          | Asian | 0.0 | 0.0 | 0.0 | 0.0 | 1.7 | 0.0 |
|                          | Black or African American | 1.8 | 5.1 | 4.2 | 4.3 | 5.4 | 0.0 |
|                          | Other | 0.0 | 1.7 | 0.0 | 0.0 | 0.0 | 0.0 |
| Body mass index, kg/m²   | 29.3 (26.3–32.2) | 28.4 (25.8–31.5) | 0.38 | 27.4 (25.0–31.1) | 27.9 (24.8–31.3) | 0.66 | 29.0 (26.6–32.1) | 28.9 (25.5–32.1) | 0.78 | 0.92 |
| Diabetes mellitus        | 19.6 | 22.0 | 0.75 | 20.8 | 27.7 | 0.44 | 23.2 | 21.8 | 0.86 | 0.65 |
| P2Y12 antagonists before PCI | 76.8 | 82.8 | 0.43 | 74.5 | 82.6 | 0.34 | 83.6 | 80.0 | 0.62 | 0.37 |
| Glycoprotein IIb/IIIa antagonists | 16.1 | 18.6 | 0.72 | 20.8 | 12.8 | 0.29 | 19.6 | 20.0 | 0.96 | 0.63 |
| Aspirin                  | 94.6 | 94.9 | 0.95 | 93.8 | 89.4 | 0.44 | 92.9 | 87.3 | 0.33 | 0.69 |
| Statins                  | 94.6 | 96.6 | 0.61 | 95.8 | 95.7 | 0.98 | 96.4 | 94.6 | 0.64 | 0.65 |
| Angiotensin-converting enzyme inhibitors | 78.6 | 67.8 | 0.20 | 75.0 | 66.0 | 0.36 | 75.0 | 81.8 | 0.39 | 0.67 |
| Angiotensin II receptor antagonists | 12.5 | 18.6 | 0.39 | 20.8 | 14.9 | 0.37 | 12.5 | 5.5 | 0.21 | 0.95 |
| Beta blockers            | 89.3 | 93.2 | 0.46 | 93.8 | 85.1 | 0.18 | 85.7 | 96.4 | 0.07 | 0.57 |
| GRACE risk score, %      | 109 (93–121) | 111 (99–133) | 0.54 | 109 (93–121) | 112 (95–133) | 0.20 | 103 (96–119) | 105 (90–123) | 0.95 | 0.46 |

Values are median (interquartile range) or percentages. GRACE indicates Global Registry of Acute Coronary Events; PCI, percutaneous coronary intervention.

*For comparisons between the placebo and inclacumab 20 mg/kg short time interval groups.

DOI: 10.1161/JAHA.116.004255
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Table 2. Procedural Characteristics

| Placebo       | Inclacumab (5 mg/kg) | Inclacumab (20 mg/kg) | P Value | P Value |
|---------------|----------------------|-----------------------|---------|---------|
|               | Short Time Interval (n=56) | Long Time Interval (n=59) |         |         |
|               | Duration of PCI, minutes | 20.0 (12.5–35.5) | 0.22 |         |
|               | Number of vessels treated per patient | 1.1±0.4 | 0.94 |         |
|               | Reference vessel diameter, mm† | 3.0 (2.5–3.5) | 0.40 |         |
|               | Bifurcation lesion, % | 16.1 | 17.0 |         |
|               | Loss of side branch during the procedure, % | 3.6 | 3.4 |         |
|               | Transient no-reflow, % | 1.8 | 3.4 |         |
|               | Total stent length, mm | 23.0 (15.0–30.0) | 0.91 |         |
|               | Stent type, number of stents | n=71 | n=76 |         |
|               | Drug-eluting, % | 64.8 | 54.0 |         |
|               | Bare metal, % | 29.6 | 40.8 |         |
|               | None, % | 5.6 | 5.2 |         |

Values are median (interquartile range), mean±SD or percentages. PCI indicates percutaneous coronary intervention.
†For comparisons between the placebo and inclacumab 20 mg/kg short time interval groups.
*Reference vessel diameter was evaluated visually on coronary angiograms.

no effect in patients with a long time interval (Table 3). Corresponding changes in CK-MB at 16 and 24 hours were −26.0% (P=0.049) and −30.7% (P=0.01), respectively, in patients with a short time interval and −9.8% (P=0.49) and −15.7% (P=0.25), respectively, in those with a long time interval (Table 4). When adjusting for sex, use of P2Y12 antagonists, use of glycoprotein IIb/IIIa antagonists, and transient “no-reflow” phenomenon, the trends remained the same.

When dividing patients into 3 groups according to the time interval between study drug infusion and PCI, placebo-adjusted geometric mean percent changes in TnI and CK-MB at 24 hours were −43.5% (P=0.02) and −26.0% (P=0.07), respectively, when inclacumab 20 mg/kg was administered between 1 and 3 hours before PCI, whereas infusions between 3 and 4 hours and >4 hours before PCI had no effect (Table 5).

Inclacumab 20 mg/kg was associated with a significant placebo-adjusted geometric mean percent change in peak TnI levels (−37.3%, P=0.02) in patients with a short time interval (less than the median of 202 minutes), whereas it did not exert any effect on those with a long time interval (−15.6%, P=0.39). The placebo-adjusted geometric mean percent changes in the area under the curve for TnI over the 24-hour period after PCI were −48.2 (P=0.047) and −32.4% (P=0.23) in the short and the long time interval groups, respectively.

Discussion

This study showed that inclacumab 20 mg/kg significantly reduces periprocedural myocardial damage in patients with NSTEMI undergoing PCI, with benefits being larger when the study drug was administered between 1 and 3 hours before PCI. These results support therapeutic concepts targeting P-selectin–dependent pathways in patients with acute coronary syndromes.

P-Selectin and Myocardial Damage After PCI

Periprocedural myocardial injury is seen in up to 50% of coronary interventions and, being associated more with difficult PCI procedures, occurs mostly in patients with large plaque volumes, high thrombus burden, and complex coronary
anatomy. Although occurring mostly silently, even minor postprocedural elevations of cardiac biomarkers have been associated with adverse outcomes. Inflammation and platelet activation play a critical role in the pathogenesis of myocardial damage following coronary interventions. Inhibiting P-selectin–dependent functions such as platelet activation and leukocyte recruitment has initially emerged as a promising therapeutic approach in preventing neointimal formation. Based on encouraging results from animal models of myocardial ischemia–reperfusion injury and phase I clinical studies, the recent SELECT-ACS trial has then extended the concept of targeting P-selectin pathways to patients with acute coronary syndromes undergoing PCI and demonstrated the efficacy of the P-selectin antagonist inclacumab in reducing periprocedural myocardial damage. Inclacumab Effects on Myocardial Damage After PCI

Our study demonstrated that the largest benefits in reducing periprocedural myocardial damage were achieved when inclacumab was given between 1 and 3 hours before PCI. This observation may at least in part explain the modest statistical significance of inclacumab effects observed in the SELECT-ACS trial, in which the study drug was administered within 24 hours before PCI. Pathophysiological mechanisms linking the time point of drug administration to inclacumab effects are not yet known. Given the long half-life of inclacumab comparable to that of other human IgG antibodies and the persistent inhibition of platelet–leukocyte aggregates demonstrated after inclacumab administration, alternative signaling cascades involving rapidly activated pathways and short-term effects at maximum drug concentrations achieved at the end of the infusion may have accounted for these findings. Furthermore, cross-reactivity of inclacumab with other receptors, similar to the observations reported for different drugs including glycoprotein IIb/IIIa antagonists, may come into play. This raises the question of whether shorter (<1 hour) time intervals between study drug infusion and PCI or continuous infusions administered throughout the procedure, along with intracoronary infusion methods, would have caused an even larger effect. Further studies are needed to fully elucidate pharmacokinetic profiles of inclacumab in patients presenting with acute coronary syndromes and undergoing PCI and to prospectively compare different treatment regimens. In addition, one might speculate that a shorter time interval between study drug administration and PCI mirrors a shorter time interval between symptom onset

| Table 3. Change in Troponin I at 16 and 24 Hours After PCI in Patients With Short and Long Time Intervals Between Study Drug Infusion and PCI |

| Short (Less Than Median) Time Interval | Long (Greater Than Median) Time Interval |
|---------------------------------------|----------------------------------------|
| Placebo | Inclacumab (5 mg/kg) | Inclacumab (20 mg/kg) | Placebo | Inclacumab (5 mg/kg) | Inclacumab (20 mg/kg) |
| Baseline GM (IQR) | 1.12 (0.26–5.90) | 0.56 (0.11–2.99) | 0.91 (0.18–4.32) | 0.96 (0.22–4.23) | 0.89 (0.25, 4.18) | 0.71 (0.19–3.05) |
| 16 hours after PCI GM | 2.01 (n=56) | 1.35 (n=48) | 1.15 (n=54) | 1.51 (n=58) | 1.25 (n=46) | 1.01 (n=53) |
| Adjusted GM percentage change from baseline to 16 hours | 133.3 | 161.6 | 51.8 | 89.8 | 64.4 | 57.3 |
| Placebo-adjusted GM percentage change at 16 hours | 12.1 | –34.9 | –13.4 | –17.1 |
| 95% CI | –24.7 to 67.0 | –55.8 to –4.2 | –41.7 to 28.7 | –43.6 to 21.7 |
| P value | 0.57 | 0.03 | 0.48 | 0.34 |
| 24 hours after PCI GM | 2.23 (n=50) | 1.35 | 1.00 (n=52) | 1.41 (n=54) | 1.10 (n=47) | 0.95 (n=48) |
| Adjusted GM percentage change from baseline to 24 hours | 179.5 | 181.1 | 52.0 | 104.9 | 68.5 | 63.6 |
| Placebo-adjusted GM percentage change at 24 hours | 0.57 | –45.6 | –17.8 | –20.2 |
| 95% CI | –35.2 to 56.0 | –64.4 to –16.9 | –46.2 to 25.5 | –47.7 to 21.9 |
| P value | 0.98 | 0.005 | 0.36 | 0.30 |

GM indicates geometric mean; IQR, interquartile range; PCI, percutaneous coronary intervention.
Table 4. Change in Creatine Kinase–Myocardial Band at 16 and 24 Hours After PCI in Patients With Short and Long Time Intervals Between Study Drug Infusion and PCI

| Time Interval                        | Placebo | Inclacumab (5 mg/kg) | Inclacumab (20 mg/kg) | Placebo | Inclacumab (5 mg/kg) | Inclacumab (20 mg/kg) |
|-------------------------------------|---------|----------------------|-----------------------|---------|----------------------|-----------------------|
|                                     | GM (IQR)| GM (n)               | GM (n)                | GM (IQR)| GM (n)               | GM (n)                |
| Short (Less Than Median) Time Interval |         |                      |                       |         |                      |                       |
| Baseline GM                         | 10.76 (3.95–30.00) | 7.41 (2.40, 21.65) | 7.99 (2.75–17.85) | 8.37 (3.20–21.30) | 7.68 (3.30–12.90) | 7.71 (3.30–14.50) |
| 16 hours after PCI GM               | 10.96 (n=56) | 8.36 (n=48)          | 7.10 (n=54)          | 8.40 (n=58) | 7.50 (n=46)          | 7.33 (n=53)          |
| Adjusted GM percent change from baseline to 16 hours | 31.0 | 24.6 | –3.0 | 12.8 | 5.8 | 1.8 |
| Placebo-adjusted GM percent change at 16 hours | –4.9 | –26.0 | –6.2 | –9.8 | –30.9 to 27.3 | –33.0 to 21.3 |
| 95% CI                              | –30.0 to 29.2 | –45.1 to –0.2 | –30.9 to 27.3 | –33.0 to 21.3 | |
| P value                             | 0.75 | 0.049 | 0.68 | 0.49 | |
| Long (Greater Than Median) Time Interval |         |                      |                       |         |                      |                       |
| 24 hours after PCI GM               | 8.99 (n=50) | 6.96 (n=45)          | 5.56 (n=52)          | 7.30 (n=54) | 6.22 (n=47)          | 6.02 (n=49)          |
| Adjusted GM percent change from baseline to 24 hours | 26.6 | 16.5 | –12.3 | 12.2 | 1.4 | –5.4 |
| Placebo-adjusted GM percent change at 24 hours | –8.0 | –30.7 | –9.6 | –15.7 | –32.6 to 21.2 | –37.0 to 12.9 |
| 95% CI                              | –32.1 to 24.7 | –48.4 to –7.0 | –32.6 to 21.2 | –37.0 to 12.9 | |
| P value                             | 0.59 | 0.01 | 0.50 | 0.25 | |

GM indicates geometric mean; IQR, interquartile range; PCI, percutaneous coronary intervention.

Table 5. Changes in Troponin I and CK-MB at 24 Hours After PCI According to Different Time Intervals Between Study Drug Infusion and PCI

| Time Interval                        | Troponin I | CK-MB |
|-------------------------------------|------------|-------|
|                                     | <3 Hours   | 3–4 Hours | >4 Hours | <3 Hours | 3–4 Hours | >4 Hours |
| Inclacumab 5 mg/kg                  |            |        |    |            |         |       |
| Patients, n                         | 39         | 17     | 36 | 39         | 17      | 36      |
| Adjusted GM percent change from baseline to 24 hours | 174.5 | 119.5 | 67.4 | 13.7 | 17.4 | 0.8 |
| Placebo-adjusted GM percent change at 24 hours | 0.77 | –20.4 | –11.2 | –10.5 | –6.8 | –6.9 |
| 95% CI                              | –37.7 to 62.9 | –59.5 to 56.4 | –46.0 to 46.0 | –35.8 to 24.9 | –41.7 to 49.1 | –34.1 to 31.4 |
| P value                             | 0.97       | 0.51   | 0.64 | 0.51       | 0.77   | 0.68   |
| Inclacumab 20 mg/kg                 |            |        |    |            |         |       |
| Patients, n                         | 41         | 23     | 36 | 41         | 24      | 36      |
| Adjusted GM percent change from baseline to 24 hours | 54.0 | 63.6 | 58.6 | –6.0 | –12.9 | –8.4 |
| Placebo-adjusted GM percent change at 24 hours | –43.5 | –40.7 | –15.9 | –26.0 | –30.9 | –15.4 |
| 95% CI                              | –64.8 to –9.3 | –68.1 to 10.3 | –49.0 to 38.7 | –46.7 to 2.8 | –54.9 to 5.8 | –40.2 to 19.6 |
| P value                             | 0.02       | 0.10   | 0.50 | 0.07       | 0.09   | 0.34   |

CK-MB indicates creatine kinase-myocardial band; GM, geometric mean.
and PCI, and that patients with a longer time interval between infusion and PCI were those who presented at a later myocardial infarction stage when inclacumab may have exerted less pronounced effects. However, data on symptom duration were not collected in the SELECT-ACS trial. Although concomitant evidence-based therapies were balanced between treatment and placebo groups and between patients with a short and a long time interval between study drug infusion and PCI, drug interactions between inclacumab and standard of care medications cannot be ruled out completely.

Study Limitations
This study has the limitations of a post hoc analysis, and larger trials randomizing patients to different treatment regimens are needed to confirm these results. Although procedural complexity as reflected by the duration of PCI did not differ between groups, and adjustments for specific procedural characteristics including number of vessels treated and stent type implanted were performed, other aspects such as plaque burden and coronary dissection/perforation which might have affected the endpoints were not addressed. Further, as patients with NSTEMI undergoing interventional treatment were included in the SELECT-ACS trial, these findings cannot be extrapolated to patients presenting with stable coronary artery disease or ST-segment elevation myocardial infarction, and potential inclacumab effects in patients treated medically need to be assessed in future studies.

Conclusion
Inclacumab 20 mg/kg significantly reduces postprocedural myocardial damage in patients with NSTEMI, with the largest benefits observed when the drug is administered between 1 and 3 hours before PCI. The results of this study provide a strong rationale to further define the role of a P-selectin–based therapy in patients presenting with acute coronary syndromes.

Sources of Funding
The SELECT-ACS trial was funded by F. Hoffmann-La Roche, Basel, Switzerland. Stähli was supported by the Gottfried and Julia Bangerter-Rhyner Foundation, Berne, Switzerland, the Novartis Foundation for medical-biological research (13B067), Basel, Switzerland, and the Swiss Foundation for Medical-Biological Scholarships (SSMBS; No 142741).

Disclosures
Robb is an employee of F. Hoffmann-La Roche, Basel, Switzerland. Tardif holds the Canada Research Chair in translational and personalized medicine and the Université de Montréal Pfizer-endowed research chair in atherosclerosis, and has received honoraria from Roche. All other authors have no interests to declare.

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