Interventional Procedure

Patients with inadequate response to their antiplatelet medications may be at significantly greater risk of myocardial infarction, stent thrombosis and death. Patients with hyper response to their antiplatelet medications may be at risk of bleeding.¹-³

Up to 40% of patients on antiplatelet medications may not receive the expected platelet inhibiting effect.⁴

Numerous factors may cause inadequate response,⁵ including:

- Drug Interactions (e.g. proton pump inhibitors)
- Genetic differences
- Pre-existing health conditions (e.g. diabetes)
- Non-compliance

### Decrease in Drug Effect Over Time⁶

<table>
<thead>
<tr>
<th>Washout Day</th>
<th>% of Subjects Returning to Baseline PRU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30.8%</td>
</tr>
<tr>
<td>3</td>
<td>53.8%</td>
</tr>
<tr>
<td>5</td>
<td>37%</td>
</tr>
<tr>
<td>6</td>
<td>80.8%</td>
</tr>
<tr>
<td>7</td>
<td>88.5%</td>
</tr>
<tr>
<td>9</td>
<td>96.2%</td>
</tr>
</tbody>
</table>

- Red Bar: Clopidogrel
- Gray Bar: Prasugrel
How It Works: Activates Specific Drug Receptor Sites

Receptor Blockade

• Measures the P2Y12 platelet receptor blockade. Assesses patient response to antiplatelet therapy including clopidogrel (Plavix®), prasugrel (Effient®) and ticagrelor (Brilinta®).

• Measures the platelet response to aspirin by an arachidonic acid initiated reaction.

• Measures the patient response to IIb/IIIa inhibitors such as eptifibatide (Integrilin®) and abciximab (ReoPro®).

Blood Sample Showing Inhibition of Platelet Function

- Low Light Transmittance
  - Agonist
  - Red Blood Cells
  - Fibrinogen-Coated Beads
  - Platelets

Blood Sample Showing Normal Platelet Function

- Increased Light Transmittance
  - Platelet-Bead Aggregates
VerifyNow Aspirin or PRU Test Sample Collection Procedure*

Direct Venipuncture
Sample collection directly into vacuum collection tubes

1. Use 2 mL Greiner Bio-One partial-fill vacuette tubes with 3.2% sodium citrate (blue top). Greiner #454322.

2. Collect 2 tubes of whole blood using a 21 gauge or larger needle. First, collect a discard tube (at least 2 mL) making sure the discard tube does not contain any platelet inhibiting substance (e.g. EDTA). Butterfly (21 gauge) is OK to use.

3. Fill the second tube (sample tube) to the black line (1/2 tube). Do not under fill. Discard the first tube. Keep the second tube for testing.

4. If drawing blood for a CBC at the same time, fill the CBC tube last.

5. Gently invert the tube at least 5 times to ensure complete mixing of the contents. Samples with evidence of clotting should not be used. Do not shake, as that may give incorrect results.

6. Label the tube with the patient ID, date and time it was drawn. Do not refrigerate. Do not put in pneumatic tube system.

Indwelling Catheter

1. Discard the first 5 mL from an indwelling catheter to clear the line. Ensure the catheter is free of clots.

2. Immediately transfer blood to a 2 mL Greiner Bio-One partial-fill vacuette tube with 3.2% sodium citrate (blue top). Greiner #454322. Fill to the black line (1/2 tube). Do not under fill.

3. If drawing blood for a CBC at the same time, fill the CBC tube last.

4. Gently invert the tube at least 5 times to ensure complete mixing of the contents. Samples with evidence of clotting should not be used. Do not shake, as that may give incorrect results.

5. Label the tube with the patient ID, date and time it was drawn. Do not refrigerate. Do not put in pneumatic tube system.

*Refer to the Instructions for Use for VerifyNow IIb/IIIa Test sample collection
VerifyNow PRU Test Results: What is Reported?

The lab report may look similar to the following:

**********************************************************
**********************************************************

**Patient Example PRU Test Results**

<table>
<thead>
<tr>
<th>Patient A</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>132</td>
<td>PRU</td>
</tr>
</tbody>
</table>

Reference Range (off drug):

180–376

Values less than 180 PRU suggest evidence of a P2Y12 inhibitor effect.

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**Patient Response to Antiplatelet Therapy**

- **NO DRUG EFFECT**
  - Normal platelet reactivity due to low P2Y12 inhibition response

- **200 ± 10%**

- **DRUG EFFECT**
  - Decreased platelet reactivity due to the effect of a P2Y12 inhibitor
VerifyNow PRUTest:
Platelet response to P2Y12 inhibitors (e.g clopidogrel, prasugrel, and ticagrelor).

PRU (P2Y12 Reaction Units)
• ADP induced aggregation—extent of platelet aggregation in the presence of P2Y12 inhibitors.
• Measures the On-Treatment Platelet Reactivity (OTPR) of ADP P2Y12 receptor.

Pre-Surgical Application
• Studies show that there is patient variability in response to P2Y12 inhibitors.\(^8\)
• Patients that have been administered P2Y12 inhibitors such as clopidogrel and prasugrel are at risk of perioperative bleeding due to platelet dysfunction from drug effect.
• It has been recommended to discontinue P2Y12 inhibitors for 5 – 7 days prior to surgery\(^9\) for platelet function to be restored\(^10\), however, 2012 STS Guidelines\(^11\) recommend using platelet function testing to aid in timing of surgery, instead of arbitrarily waiting a pre-specified period of time.

Conditions that May Affect Test Results
• Patient’s exposure to GP IIb/IIIa inhibitors within 48 hours of eptifibatide (Integrilin\(^®\)) or tirofiban (Aggrastat\(^®\)), or 14 days of abciximab (ReoPro\(^®\)).
• Improper sample collection.

To Order This Test:
VerifyNow Aspirin Test:
Platelet response to aspirin.

Result Interpretation:
\( \leq 549 \): Evidence of platelet dysfunction due to aspirin.
\( > 550 \): No evidence of aspirin-induced platelet dysfunction.

ARU (Aspirin Reaction Units)
Arachidonic acid induced aggregation.
VerifyNow IIb/IIIa Test Results

Platelet response to GP IIb/IIIa inhibitors, e.g. abciximab (ReoPro), eptifibatide (Integrilin).

PAU (Platelet Aggregation Units)
- Thrombin receptor induced platelet aggregation.

Reference Ranges
- abciximab:
  - Baseline: 125-330 PAU
  - >80% inhibition: 0-44 PAU
  - >95% inhibition: 0-13 PAU
- eptifibatide:
  - Baseline: 136-288 PAU
  - >80% inhibition: 0-31 PAU
  - >95% inhibition: 0-10 PAU

% Inhibition
- Calculated by measuring pre-drug PAU and 10 minutes post start of IIb/IIIa inhibitor.

When to Test
- Prior to GP IIb/IIIa administration for baseline result (needed to calculate % inhibition).
- 10 minutes post GP IIb/IIIa administration for post drug result.
- If no baseline sample was collected, refer to abciximab and eptifibatide reference ranges.

Conditions that May Affect Test Results
- Test must be run within 15 minutes after drawing blood sample.
- Improper sample collection (platelet activation).
<table>
<thead>
<tr>
<th>VerifyNow Test</th>
<th>Medication(s) Tested</th>
<th>Dose Given</th>
<th>Suggested Test Timing</th>
<th>Sample Incubation (Minutes)</th>
<th>Run Time (Minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRU Test</td>
<td>Clopidogrel (Plavix®)</td>
<td>75 mg</td>
<td>≥ 7 days on maintenance¹</td>
<td>10</td>
<td>~3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>300 mg</td>
<td>≥ 8 hours post bolus²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>600 mg</td>
<td>≥ 6 hours post bolus³</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prasugrel (Effient®)</td>
<td>5 mg</td>
<td>≥ 5 days on maintenance¹³</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 mg</td>
<td>≥ 5 days on maintenance¹³</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>60 mg</td>
<td>≥ 45 minutes post bolus⁸</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ticagrelor (Brilinta®)</td>
<td>90 mg (bid)</td>
<td>≥ 1 day on maintenance⁹ (within 8 hours of last dose for maximal effect)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>180 mg</td>
<td>≥ 2 hours post bolus⁹ (within 8 hours for maximal effect)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>Aspirin</td>
<td>0.25 mg/kg</td>
<td>≥ 2 hours post dose</td>
<td>30</td>
<td>~5</td>
</tr>
<tr>
<td>IIb/IIIa</td>
<td>Abciximab (ReoPro®) Eptifibatide (Integrilin®)</td>
<td>0.25 mg/kg</td>
<td>≤ 10 minutes post bolus¹⁴</td>
<td>No incubation required (run within 15 minutes)</td>
<td>&lt;2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>180 mcg/kg</td>
<td>≤ 10 minutes post bolus¹⁵</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
For more details, see the VerifyNow Test package insert.