AggreDYNE A-100 Platelet Aggregation Test

ADP Assay

INTENDED USE
The AggreGuide A-100 ADP Assay is used with the AggreGuide A-100 instrument in non-CLIA waived physician's office or clinical laboratory for the detection of platelet dysfunction in patients age 22 or older receiving P2Y12 antiplatelet drugs, prasugrel and ticagrelor, using 3.2% sodium citrated whole blood. The AggreGuide A-100 ADP Assay is a semi-quantitative assay. The level of platelet aggregation is determined by the platelet activity index (PAI) where values < 4.7 PAI suggest that platelet dysfunction is due to the presence of P2Y12 antiplatelet drugs, prasugrel and ticagrelor. The test results should be interpreted in conjunction with all other clinical and laboratory data available to the clinician.

PRODUCT DESCRIPTION
The AggreGuide A-100 ADP Assay is an individual use, disposable assay cartridge for use with the AggreGuide A-100 instrument. The cartridge contains preloaded freeze-dried agonist. The level of platelet aggregation induced by the adenosine diphosphate (ADP) agonist in a sample of whole blood is detected within the cartridge. The amount of platelet aggregation is measured by detecting and quantifying the laser light scattering caused by platelet aggregates. P2Y12 inhibitor drugs e.g. clopidogrel, prasugrel, and ticagrelor are known to inhibit the level of platelet aggregation, causing platelet dysfunction.

PRINCIPLE OF THE ASSAY
The AggreGuide A-100 ADP Assay is designed to measure platelet aggregation when a patient's whole blood is mixed with adenosine diphosphate (ADP), which activates platelets by binding to the ADP receptors on the platelet surface, resulting in platelet aggregation. P2Y12 inhibitors inhibit ADP-induced platelet aggregation by blocking the P2Y12 ADP receptor on the platelet surface.

MATERIALS PROVIDED
AggreGuide ADP assay cartridges come individually sealed in Mylar® pouches. Each cartridge contains a lyophilized mixture of 10 µM adenosine diphosphate and excipients to facilitate freeze drying.

REAGENT STORAGE AND HANDLING
When receiving or opening a box of reagent cartridges, check the temperature indicator located on the outside of the box. If the indicator spot has turned black, this indicates exposure to elevated temperatures and should not be used. Call customer support for a replacement.

- Store cartridges at room temperature, per the instructions on the box and pouches.
- Reagent cartridges should remain sealed in their Mylar pouch until ready for use to prevent damage by humidity.

MATERIALS REQUIRED BUT NOT PROVIDED
- Blood collection tubes containing 3.2% sodium citrate.
- AggreGuide A-100 Instrument.
- Pipettor.

PRECAUTIONS
- For *in-vitro* diagnostic use.
- The AggreGuide and its components should only be used as directed in the AggreGuide A-100 User's Manual.
- Do not use the AggreGuide ADP assay cartridge beyond the expiration date indicated on the case and the individual cartridge pouch.
- Cartridges should remain sealed in the Mylar pouch until ready for use.
- All patient blood samples should be handled as if capable of transmitting disease.
- Samples and used cartridges should be treated as bio-hazardous material and handled according to the institution's policies.

SAMPLE COLLECTION AND HANDLING
- All whole blood samples must be assayed from vacuum collection tubes containing sodium citrate (3.2%).
- Blood should be tested within 10 minutes - 4 hours of the blood draw.

Instructions for Sample Collection Directly Into Vacuum Collection Tubes:
1. Whole blood may be collected from venous sites using a 19 or 21 gauge needle in 3.2% citrate vacuum collection tubes. Blood samples should be obtained from an extremity free of peripheral venous infusions.
2. Gently invert the sample tube at least 5 times to ensure complete mixing of the contents.

Special Instructions if blood is obtained from an indwelling catheter:
1. Whole blood samples that are obtained from an indwelling catheter should be collected after sufficient discard (approximately 5 mL) has been drawn to clear the line. Ensure indwelling catheter is free of clots.
2. When using a syringe, transfer blood to the appropriate blood collection tube immediately after collection.
3. Gently invert the sample tube 5 times to ensure complete mixing of the contents.

SAMPLE COLLECTION PRECAUTIONS
- Improper blood collection techniques may cause erroneous results. If unexpected or questionable results are reported, repeat the test with a new sample and a new cartridge.
- Fresh whole blood samples in the appropriate collection device are required for use with the AggreGuide A-100.
- Do not freeze or refrigerate sample. Samples should be stored at room temperature.
- Collection of the blood sample should be performed with care to avoid hemolysis or contamination by tissue factors. Samples with any evidence of clotting should not be used.
- Thorough but gentle mixing of the collected blood sample with the anticoagulant is required. Five repetitions of gentle inversion of each tube is appropriate.
- Do not shake or agitate samples. Hand carrying of samples is preferred. Pneumatic tube systems and rockers should be avoided.
- Always ensure collection tubes are filled to the indicated fill volumes. At altitudes greater than 2500 feet (760 meters) above sea level, blood collection tubes may not fill to the specified volume, which results in an incorrect ratio of blood to anticoagulant. Users at these elevations should refer to their facility's blood collection protocols for instructions to properly fill blood collection tubes.
- Samples should be collected and handled according to the institution's policies and procedures pertaining to bio hazardous material.
- The cap of the collection tube should be replaced promptly after blood has been sampled to avoid pH changes in the blood sample.

TEST PROCEDURE
1. Refer to the AggreGuide A-100 User's Manual for complete operating instructions.
2. Prior to starting the Assay, select ADP Assay from the drop down menu.
3. Open the Mylar® pouch and remove the cartridge.
4. Insert the cartridge into the AggreGuide A-100 sample chamber.
5. The AggreGuide will prompt user to prepare to pipette blood and press the READY button. Gently and slowly invert the sample tube 3 - 5 times before opening the tube and aspirating blood with pipettor.
6. The AggreGuide will prompt user to introduce the blood sample into the cartridge with the pipettor, and then press the RUN button.
7. The AggreGuide will begin the assay run. The platelet activity index (PAI) will be displayed once the test has completed.
8. Remove the cartridge and check for any visible bubbles larger than 1 mm. If bubbles greater than 1 mm are present, abort the test and repeat with a new cartridge.
9. If the cartridge shows no evidence of bubbles larger than 1 mm, press SAVE.

REPORTED RESULTS
Results are reported as Platelet Activity Index (PAI). The PAI represents the degree of ADP induced platelet aggregation in whole blood.

The PAI is related to the number of ADP-induced platelet aggregates in the blood sample. The PAI represents the level of platelet aggregation. Higher PAI values represent higher levels of platelet aggregation and lower PAI values represent lower levels of platelet aggregation (such low levels are referred to as platelet dysfunction). With the AggreGuide A-100 ADP Assay, results with PAI values less than 4.7 indicate platelet dysfunction due to P2Y12 inhibitor drugs.

The Limit of Blank (LOB) is 0.8 PAI, however any result below 2.1 PAI is reported simply as "LOW". Similarly, any result above 12.0 PAI is reported as "HIGH".

ERROR MESSAGES
If the instrument displays an error message or there is a technical error while running a test, the assay run may be aborted by selecting "abort" during or after running a test. Please refer to the AggreGuide A-100 User's Manual for a detailed explanation of errors and troubleshooting.

CALIBRATION
The AggreGuide is calibrated at the factory. There are no user calibrations.

QUALITY CONTROL
The manufacturer recommends that laboratory quality control testing be performed by the user to verify the assay reagent is performing to expectation, as part of a regular quality control program including those that the user may be required to perform to comply with any local and state regulations, or other accrediting bodies' requirements.

Certificates of Conformance are provided for each lot of ADP Assay Cartridges which certify that lot release testing for precision and accuracy of the cartridges have met the release criteria.

Internal Controls: The AggreGuide A-100 system utilizes controls that are internal to the instrument and act in connection to the AggreGuide A-100 ADP Assay cartridges. These internal controls are checked at instrument start up, on an ongoing basis when the instrument is waiting for an assay to be performed, and during the beginning and ongoing portions of the actual assay.

External Controls: The "QC2" quality control cartridge and included software features allow the user to test for any gross changes to the system that might diminish quality of the AggreGuide A-100 measurements. Using a special quality control device called the "QC2 Cartridge" the A-100 tests the system that detects platelet aggregates. The QC2 quality control test is not a replacement for clinical laboratory validation, but does serve as a method of detecting gross failures of the A-100 system. The A-100 system software requires that the QC2 test is performed every thirty days, or every 200 assays, whichever occurs first. Additional A-100 assays cannot be performed unless a QC2 test has been successfully performed. The laboratory can elect to perform the QC2 test more frequently, for example, daily, as part of its laboratory quality control program.

The manufacturer recommends that laboratory quality control testing be performed by the user to verify the ADP Assay cartridge is performing to expectation. This is recommended each time a new lot or shipment of assay cartridges is received, or every thirty days.

Since there are no commercially available standard control materials for platelet aggregation testing, it is recommended that the laboratory establish their quality control program using suitable elements from these approaches.

1. Aggredyne provides a liquid quality control kit, the **AggreGuide A-100 Liquid Quality Control (LQC) Kit**. It is suggested that each laboratory establish a testing program that utilizes this product as part of its quality control program. This LQC Kit is used without blood, and permits the User to verify correct operation of the AggreGuide A-100 ADP Assay cartridges in the AggreGuide A-100. The LQC Kit contains both negative control and positive control liquid samples. When pipetted into Assay cartridges the negative control shows behavior that is representative of aggregation of platelets, indicative of the absence of platelet dysfunction due to anti-platelet medications. The positive control shows behavior representative of the absence of platelet aggregates, indicative of the presence of platelet dysfunction due to anti-platelet medications.
2. Blood drawn from healthy adult donors may be used for normal controls. It is suggested that each laboratory establish a control donor group. Such donors must not have taken any medication that is known to affect platelet function for at least 5 days and should have prior platelet aggregation tests that have fallen within the normal reference range established by the laboratory. The manufacturer recommends using donors whose PAI value is > 6.7. If the results do not fall within the expected range, a second donor should be tested. If the second control donor's results are also considered outside the reference range, the assay should be considered out of control and no further clinical testing should be performed. Please call technical support for assistance.

It is the responsibility of the laboratory director to develop an appropriate laboratory quality control program.

Please call technical support for assistance.

ASSAY LIMITATIONS
The lyophilized reagent in the cartridge is hygroscopic and may degrade after prolonged exposure to room air. Therefore, the cartridge should be used shortly after removal from the Mylar pouch, a process that should only take a few minutes. Testing indicates that cartridges removed from the pouch operate properly when loaded with the blood sample up to 12 minutes after opening the pouch.

When results are not within the expected limits, the possibility of improper specimen collection or handling should be investigated. Repeat the test using a new cartridge and specimen.

Patients with inherited platelet disorders such as Von Willebrand Factor Deficiency, Glanzmann Thrombasthenia and Bernard-Soulier Syndrome have not been studied with the AggreGuide.

The potential for non-platelet blood cell pathologies and/or abnormalities such as dysmorphic RBCs, RBC agglutination or WBC clumping to cause false high readings of background is assessed as infrequent and of low impact because the clinical instances that might give rise to these sorts of cellular assemblies are rare, and because the device design's fluid dynamics, optics and algorithm favor rejection of signals from any such interfering cell assembly.

Patients with a known history of platelet counts < 150,000/µL have not been studied.

The AggreGuide A-100 has been tested in subjects with hematocrit values ranging from 29.3% to 51.9%.

Many medications or compounds (prescription and non-prescription) are thought to affect platelet aggregation. Some of these materials have been tested for interference with the Assay, as reported in the section on Interferents, below. Therefore a thorough medication history of the patient should be taken and reviewed.

ADP-induced platelet aggregation operates on a different and independent biochemical pathway than the arachidonic acid (AA) pathway. Platelet dysfunction can exist with either pathway, both pathways, or neither pathway. This A-100 ADP assay should not be used for testing for aspirin-induced platelet dysfunction. Instead the AggreGuide A-100 AA Assay should be used to test for platelet dysfunction due to aspirin ingestion.

Ticagrelor is a potent inhibitor of platelet function, but reversible and relatively short-acting. "Full-Effect" is achieved within 3 - 6 hours after the ingestion of the loading dose, but in contrast to other anti-platelet therapeutics, only 60% of this effect remains at 24 hours post-ingestion[2,3] ("Not-Full-Effect").

Clinicians using the test to evaluate on-therapy residual platelet activity are advised to make observations within 3 - 6 hours of the most recent dose of ticagrelor.

AggreGuide test results should be interpreted in conjunction with other clinical and laboratory data available to the clinician.

INTERFERING SUBSTANCES
- Assay performance is not affected by hemolysis up to 600 mg/dL plasma free hemoglobin.
- No interference was observed with blood samples spiked with bilirubin up to 10 mg/dL.
- Assay performance was not affected by triglyceride levels between 66 and 361 mg/dL.
- Assay performance is not affected by the presence or absence of aspirin. Aspirin is known to inhibit platelet function by a different and independent mechanism (COX-1) than the P2Y12 pathway. Platelet dysfunction due to aspirin should not be evaluated with the ADP assay but by another assay such as the AggreGuide A-100 AA Assay
- Other potential interfering substances were screened to ascertain whether the Assay is effected by the presence or absence of the substance.
- The difference between the control mean and the interferent mean was tested using a Student's t-test. If the farthest limit of the 95% confidence interval of the estimate of the difference did not exceed 1.5 PAI (the d_{max} per protocol), then the substance was judged to not interfere with the assay.
- These substances appear in the following table.

Interferent Testing Table:
Those substances tested for interference with effect limited to less than 1.5 PAI:

Interferent	Test Concentration	Units
Acetominophen	15.7	mg/dL
Aminocaproic acid	0.90	mg/dL
Caffeine	11.0	mg/dL
Captopril	0.276	mg/dL
Catechin	2.54	mg/dL
Chlorpromazine	0.303	mg/dL
Cilostazol	2.22	mg/dL
Cimetidine	2.99	mg/dL
Dextran 40	2,425	mg/dL
Diltiazem	0.0090	mg/dL
Dipyridamole	1.01	mg/dL
Fish Oil	32.0	mg/dL
Gabapentin	2.7	mg/dL
Glipizide	0.30	mg/dL
Glucosamine HCl	0.203	mg/dL
Heparin	340.5	U/dL
Ibuprofen	21.8	mg/dL
Insulin	0.00053	mg/dL
Liraglutide	0.0168	mg/dL
L-Thyroxine	5.00	mg/dL
Metformin	1.20	mg/dL
Norfluoxitine	0.0695	mg/dL
Norverapamil	0.056	mg/dL
Omeprazole	0.755	mg/dL
Oxypurinol	1.36	mg/dL
Pravastatin	0.0207	mg/dL
Prednisone	0.121	mg/dL
Propranolol	0.102	mg/dL
Salicylic Acid	2.87	mg/dL
Sitagliptin	0.12	mg/dL
Streptokinase	40200	U/dL
Theophylline	5.70	mg/dL
Valsartan	1.17	mg/dL
Warfarin sodium	7.50	mg/dL

In the case of three potentially interfering substances, the farthest limit of the 95% CI did exceed the 1.5 PAI value of d_{max}.

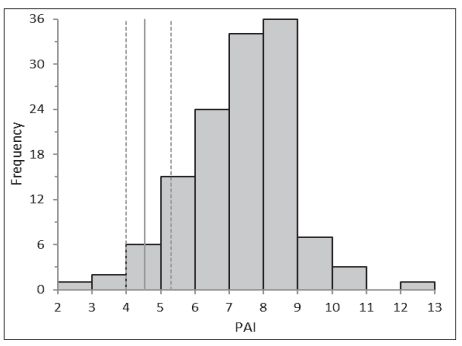
t-Test Estimates, PAI				
Interferent	Test Concentration	Units	Difference Of The Means (PAI)	Difference to 95% CI Limit (PAI)
Amlodipine	0.0075	mg/dL	-0.7	-1.6
Daunorubicin	5.625	mg/dL	-1.2	-1.9
Nitroglycerin	10	mg/dL	-2.6	-2.9

SERVICE
The AggreGuide is not intended to be serviced by the user. Instruments in need of service must be returned to Aggredyne, Inc. If there are problems related to the AggreGuide, contact your distributor or call Aggredyne Customer Support. Customer/Technical Support by emailing to Support@aggredyne.com or calling 866-800-1955.

PERFORMANCE CHARACTERISTICS

Reference Range
The reference limit was calculated from AggreGuide A-100 ADP Assay Platelet Activity Index (PAI) measurements of blood samples collected at baseline, prior to administration of a P2Y12 inhibitor, in 129 subjects between 22 and 75 years of age.

The 95% one-sided reference limit (with 95% at higher PAI) was determined by finding the nonparametric 5th percentile limit (solid line) and its associated 90% confidence interval (dashed line) as reported below.



One-Sided 95% Reference Limit (N=129)

Lower Limit	4.54 PAI	(4.00 to 5.30) 90% CI

It is recommended that each laboratory should establish its own reference ranges.

Expected Baseline Values In the Intended Use Population:
Table of Baseline PAI Values (absence of P2Y12 inhibitor treatment) in the intended use population:

Baseline Off-Therapy	N=280	PAI
PAI Value	Mean	7.16
	Median	7.4
	10% Quantile	4.7
	1st Quartile	5.9
	3rd Quartile	8.4
	90% Quantile	9.5

For the purposes of this study, operational definitions were established to describe the nominally expected effect of the P2Y12 drugs on platelet function.

"Full-Effect" describes those drugs that are both potent and observed at times of full pharmacological effect.

"Not-Full-Effect" describes those drugs that were not expected to reach full inhibition of platelet function at the package-insert specified doses used in the study (clopidogrel), or a drug that had reached a waning pharmacological time point in which full inhibition had subsided (ticagrelor at 24-hours post-loading).

"Clinical Truth" describes the expectation that no subjects that are off-treatment with P2Y12 inhibitors will exhibit platelet dysfunction, and that all subjects that are on-treatment at Full-Effect will exhibit platelet dysfunction.

CONFIRMATION OF PRE-DETERMINED 4.7 PAI CUT OFF

The cut off of 4.7 was confirmed with the absence and presence of anti-platelet drugs that are potent, exhibit little inter-individual variability and are tested at a pharmacodynamics state of peak anti-platelet effect using prasugrel and ticagrelor. The use of these specific clinical states acting as "clinical truth" allowed evaluation of, predominantly, the performance of the AggreGuide A-100 ADP Assay device, as opposed to that device performance convolved with the clinical state created by less-than-potent or less-than-fully-active drugs.

The ROC J-Statistic (Youden) analysis of the 2018 clinical truth data set shows a 4.7 PAI cut off value, consistent with that of the pre-determined cut off from the 2014 clinical study, also 4.7 PAI.

METHOD COMPARISON

The AggreGuide A-100 ADP Assay was validated by means of a clinical trial studying ADP-induced platelet aggregation in the presence of the P2Y12 inhibitor drugs prasugrel, ticagrelor and clopidogrel. The AggreGuide A-100 Assay performance evaluation was based on detection of platelet dysfunction response to drug from the prasugrel and ticagrelor arms of the study because these potent P2Y12 inhibitors can elicit more consistent, substantial and identifiable pharmacological response which enables cut-off-point based assay device sensitivity determinations.

Clopidogrel is a less potent P2Y12 inhibitor that is known to exhibit substantial variability in pharmacological response, especially with the loading dose of 300 mg recommended by the manufacturer [see drug prescribing Information].

Thus, a cut-point based assessment of the device sensitivity to clopidogrel at the manufacturer recommended loading dose was not suitable for determining assay device performance.

With ticagrelor, the sensitivities (95% CI) of this device that were evaluated at Full-Effect clinical status, within 3 - 6 hrs of loading-dose and after 7-days of maintenance-dose, were found have respective sensitivities of 0.906 (0.825, 0.952) and 0.839 (0.770, 0.890), whereas at 24-hrs post-loading, with a Not-Full-Effect clinical status, the sensitivity was found to be 0.571 (0.491, 0.652). Clinicians must be aware of the clinical status of the antiplatelet therapeutic with respect to dose timing and pharmacodynamics of the P2Y12 inhibitor in use, especially in connection to ticagrelor.

Each drug's individual effect may be dependent on dosage and timing of measurement after the most recent dose. See clinical trial performance data that follows in this Package Insert. Also see the prescribing information for each respective anti-platelet medication.

QUALITATIVE AGREEMENT

Qualitative Agreement of the AggreGuide A-100 ADP Assay (PAI), the VerifyNow PRU Test, and Clinical Truth (CT).

Table of Negative and, Positive Percent Agreement (NPA, PPA) and Total Percent Agreement (Total PA). Clinical truth data set is the Full-Effect data set using ticagrelor and prasugrel. Cut off for VN PRU Test used was 184 PRU.

		Agreement:		
		NPA	PPA	Total PA
AggreGuide A-100 ADP Assay PAI versus VerifyNow PRU Test	**Proportion**	**91%**	**88%**	**89%**
	Exact 95% CI -	86%	84%	86%
	Exact 95% CI +	95%	91%	91%
AggreGuide A-100 ADP Assay PAI versus Clinical Truth	**Proportion**	**92%**	**89%**	**90%**
	Exact 95% CI -	87%	85%	87%
	Exact 95% CI +	95%	92%	92%
VerifyNow PRU Test versus Clinical Truth	**Proportion**	**97%**	**99%**	**98%**
	Exact 95% CI -	93%	97%	96%
	Exact 95% CI +	99%	100%	99%

SPECIFICITY:

A-100 PAI Specificity		
Arm at Baseline	**N**	**Specificity (95% CI Limits)**
All	280	0.907 (0.867 – 0.936)
prasugrel & ticagrelor subjects	186	0.919 (0.871 – 0.951)
prasugrel subjects	43	0.907 (0.774 – 0.973)
ticagrelor subjects	143	0.924 (0.867 – 0.961)
clopidogrel subjects	94	0.883 (0.802 – 0.933)

Subjects were tested for platelet function at baseline clinical status (post-81 mg aspirin, but pre-P2Y12 drug) to assess specificity against Clinical Truth. All subjects are in the identical clinical truth status baseline and are reported in the aggregate (All) as well as study arm.

SENSITIVITY:

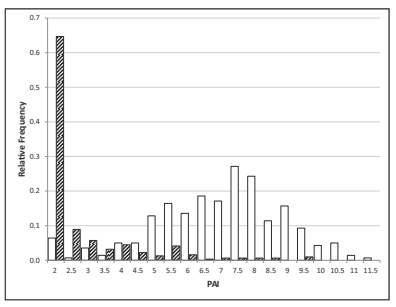
Subjects were tested for platelet function after administration of P2Y12 anti-platelet drug to assess sensitivity against Clinical Truth.

Sensitivity Stratified by Dose Status with Exact Confidence Intervals					
High Potency Anti-Platelet Therapeutics at Full-Effect					
Anti-Platelet Drug	**N**	**Clinical Status**	**Timing** (time from dose)	**A-100 PAI (95% CI Limits)**	**VerifyNow PRU† (95% CI Limits)**
Prasugrel	43	**Full-Effect**	**Post-Loading** (24 hours)	1.000 (0.918 – 1.000)	0.977 (0.877 – 0.996)
	43		**Post-Maintenance** (7 days)	0.907 (0.784 – 0.963)	0.977 (0.877 – 0.996)
Ticagrelor	85		**Post-Loading** (3 - 6 hours)	0.906 (0.825 – 0.952)	1.000 (0.957– 1.000)
Ticagrelor	143		**Post-Maintenance** (7 days)	0.839 (0.770 – 0.890)	0.968 (0.951 – 0.998)
Anti-Platelet Therapeutics at Not-Full-Effect or of Low Potency					
Ticagrelor	143	**Not-Full-Effect**	**Post-Loading** (24 hours)	0.571 (0.491 – 0.652)	0.860 (0.794 – 0.908)
Clopidogrel	94	**Low Potency**	**Post-Loading*** (24 hours)	0.319* (0.234 – 0.419)	0.372* (0.281 – 0.473)
			Post-Maintenance (7 days)	0.511 (0.411 – 0.609)	0.628 (0.527 – 0.719)

† Cut off of 183 PRU

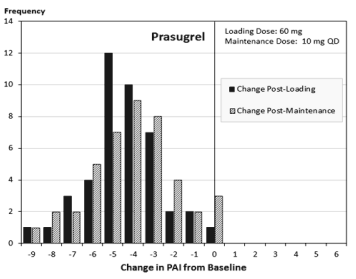
* Loading dose of clopidogrel was 300 mg per manufacturer's prescribing information. Current guidance for loading dose may vary.

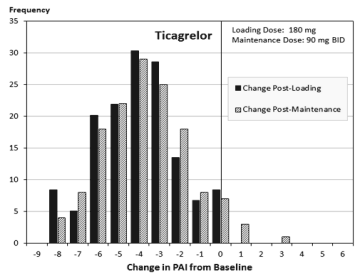
Histogram Of PAI Values At Baseline (solid white bars) and After Administration Of Potent P2Y12 Inhibitors At Full-Effect (filled bars).

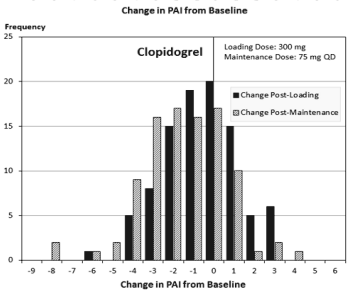


Difference in PAI Value from Baseline to On-Treatment Observations.
Frequency vs. Change in PAI from Baseline at Post-Loading and Post-Maintenance time points for each of the three P2Y12 inhibitor medicines tested. Baseline PAI observation, established "0" per subject. Changes in PAI after Administration of P2Y12-inhibitor Medications:

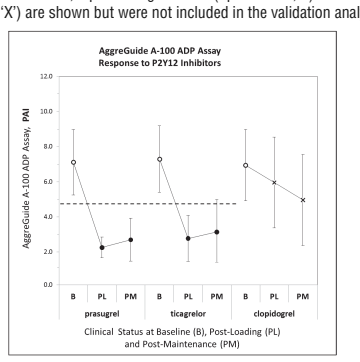
Medication	Clinical State	Mean PAI Change
Prasugrel	Baseline	0.0 PAI
	Post-Loading	-4.9 PAI
	Post-Maintenance	-4.4 PAI
Ticagrelor	Baseline	0.0 PAI
	Post-Loading	-4.5 PAI
	Post-Maintenance	-4.2 PAI
Clopidogrel	Baseline	0.0 PAI
	Post-Loading	-1.0 PAI
	Post-Maintenance	-2.0 PAI







Average of AggreGuide A-100 ADP Assay PAI values in various clinical states of P2Y12-inhibitor treatment. Clinical truth points used in the device validation are shown as circles, representing Baseline (open circles, B) or Full-Effect clinical states (filled circles). Clopidogrel points at Not-Full-Effect ('X') are shown but were not included in the validation analysis.



Expected Values in the Intended Use Population:
Off-Therapy (Baseline, **B**)
On-Therapy with P2Y12 Inhibitors (**PL**, post-loading; **PM**, post-maintenance).

Clinical truth data set utilized P2Y12 inhibitors in clinical states of high potency and at full-effect to establish sensitivity, marked in **UNDERLINED BOLD** font.

81 mg aspirin prior to baseline and each morning daily.

					PAI Values				
P2Y12 Inhibitor	**Clinical Status**	**Loading Dose**	**Maintenance Dose**	**N**	**Mean**	**SD**	**1st Quartile**	**Median**	**3rd Quartile**
PRASUGREL	**B**	-	-	43	**7.1**	**1.8**	**6.0**	**7.2**	**8.0**
	PL	60 mg	-	43	**2.2**	**0.6**	**2.0**	**2.0**	**2.3**
	PM	-	10 mg QD	43	**2.7**	**1.2**	**2.0**	**2.0**	**2.9**
TICAGRELOR	**B**	-	-	143	**7.3**	**1.9**	**6.0**	**7.5**	**8.5**
	PL*	180 mg	-	85	**2.8**	**1.3**	**2.0**	**2.0**	**3.1**
	PM	-	90 mg BID	143	**3.1**	**1.8**	**2.0**	**2.0**	**3.5**
CLOPIDOGREL	**B**	-	-	94	**6.9**	**2.0**	**5.5**	**7.0**	**8.6**
	PL	300 mg	-	94	6.0	2.6	3.6	6.3	8.0
	PM	-	75 mg QD	94	5.0	2.6	2.0	4.6	6.8

* Observations made 3 - 6 hours after the loading dose was administered.

PRECISION

Quality Control with the QC2 Device

The "QC2" quality control device is used to make an evaluation of the electro-optical behavior of the AggreGuide A-100 to ensure that gross changes in the system have not occurred. This test is performed by inserting the QC2 device into the A-100 and starting the test that is performed automatically by the system software. No user interpretation is needed for the test. See the AggreGuide A-100 User's Manual for details.

Whole Blood Precision Testing

Testing was conducted at three levels of PAI. Each of the Within-Date imprecision standard deviation values are < 0.5 PAI, the acceptance criterion for the levels of PAI tested. (Between-Date and Within-Laboratory imprecision may include variability due to changing platelet biology within each donor, and therefore should not be evaluated against the acceptance criterion. Also, the use of %CV in cases where the measure and value approaches zero is not appropriate because the %CV expression becomes arbitrarily large.)

PAI Level	**Mean PAI**	**Repeatability**	**Between Run**	**Within Date**
High-Level: (PAI > 6.7)	3 Date x 11 Run x 3 Observations			
	8.5	0.46	0.15	**0.48**
		5.4%	1.8%	5.6%
Mid-Level: (3.7 < PAI < 5.7)	3 Date x 9 Run x 3 Observations			
	4.6	0.47	0	**0.47**
		10.2%	0.0%	10.2%
Low Level: (PAI < 3.7)	3 Date x 7 Run x 3 Observations			
	0.62*	0.27	0.12	**0.30**
		43.5%*	19.4%*	48.4%*

* Values lower than 2.1 PAI are reported simply as "Low." The %CV at the lowest reported numerical value of 2.1 PAI is approximately 20%.

STABILITY

Shelf-Life Stability: Reagent cartridges are shipped with labeling indicating shelf-life expiration. Do not use reagent cartridges that have expired. In addition, reagent cartridge boxes (carton of 20 pouched cartridges) have a thermally-sensitive indicator which turns black in the event that the box has been exposed to high temperatures. If this indicator is black, do not use the cartridges within that box.

Blood Sample Stability: Bench testing indicates that the AggreGuide A-100 ADP Assay should be conducted on blood samples that are between 10 minutes and four hours of having been collected.

In-Use (Open Pouch) Stability: Reagent cartridges are shipped and stored in a sealed Mylar® pouch until the time to perform an assay. Immediately prior to running the assay, open the pouch and perform the steps necessary for the assay. These steps should not take more than a few minutes from the time the pouch is opened until the blood is successfully loaded into the cartridge. Testing indicates that these cartridges are stable for at least 12 minutes after the pouch is opened.

REFERENCES

1. Tantry US, Bonello L, Aradi D, Price MJ, Jeong YH, Angiolillo DJ, Stone GW, Curzen N, Geisler T, Ten Berg J, Kirtane A, Siller-Matula J, Mahla E, Becker RC, Bhatt DL, Waksman R, Rao SV, Alexopoulos D, Marcucci R, Reny JL, Trenk D, Sibbing D, Gurbel PA; Working Group on On-Treatment Platelet Reactivity. J Am Coll Cardiol. 2013 Dec 17;62(24):2261-73.
2. Package Insert, Brilinta®
3. Teng et al., 2012 Eur J. Clin Pharmacol DOI 10.1007/s000228-012-1227-4.

AggreDYNE GUIDING PLATELET THERAPY™ ADP Assay
US Patents 6,043,871, 7,393,690 B2, 7,262,059 B2

IVD

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