Please note that the uses described in the following page(s) have not been approved or cleared by FDA, with respect to the described assay or test.

In the US, the product is intended For Research Use Only. Not for Use in Diagnostic Procedures.
Thrombin Inhibitors: general information

- Increasing curative or preventive applications of DTIs in severe clinical situations at high risk context (eg VTE, orthopedic (total hip or knee replacement, ...), which are candidates for substituting to long term oral anticoagulant therapies with VKA. Laboratory methods are required for drug efficacy adjustment and avoiding overdosage, with the most limited impact to other plasma factors: ECT, TT and aPTT are used but too sensitive and less reliable at high DTI therapeutic levels, and patient coagulation factors may interfere.

- Hirudin (Refudran®; Bayer HealthCare Pharmaceuticals): Intravenous injection, individual dosing, and frequent laboratory monitoring required. Irreversible binding to thrombin. More effective than heparin but associated with increased bleeding.

- Other DTIs: Bivalirudin (Angiox®; The Medicines Company, eg for PCI) and Argatroban (Argatra®; Mitsubishi Pharma, eg for HIT): Intravenous administration, more favorable safety profile than hirudin, reversible binding to thrombin (inhibit both free and clot-bound thrombin), individual dosing and laboratory monitoring still required.

- Dabigatran Etxilale (Pradaxa®; Boehringer Ingelheim): oral fixed-dose “once or twice daily” as a prodrug of its active moiety dabigatran, specific and reversible DTI inhibiting both free and clot-bound thrombin, no food interference, limited drug interaction, mainly renal excretion, no antidote available (possible dialysis), no need for monitoring claimed except in case of suspicion of excess of anticoagulant activity.

Thrombin Inhibitors: key publications

- Landmarks in Anti-Thrombin drug development: the Argatroban study; Seminars in Thrombosis and Hemostasis; Vol 34, Suppl 1, Oct 2008.
HEMOCLOT THROMBIN INHIBITORS (#ACK002K/L)  INTENDED USE AND PRINCIPLE

IVD (CE mark) : as an aid for the quantitative measurement of hirudin and other DTIs in plasma (eg dabigatran when required, in case of suspicion of excess of anticoagulant activity, or Argatroban®) with a clotting method.

The diluted tested plasma is mixed with a normal human plasma pool (R1). Clotting is then initiated by adding a constant and in excess amount of highly purified human α-thrombin (R2). The clotting time (CT) measured is directly related to the concentration of assayed DTI in plasma.

R1: normal plasma pool, lyophilised
R2 : purified human calcium thrombin, lyophilised.

CHARACTERISTICS AND ADVANTAGES

• Rapid (< 3 min), Fully automatable or easy to use with basic equipment
(=3x10 (ACK002K) or 3x25 (ACK002L) tests/kit)

• Standardized calibrators and controls for Hirudin (Lepirudin), Argatroban®, Dabigatran

• Covers usual levels in treated patients’ plasma:
  Up to 2µg/ml Hirudin or Argatroban , or 0.50 µg/ml Dabigatran (low range, 1:8 dilution)
  Extended range up to 5 µg/ml Hirudin (eg ECC) (high range, 1:20 dilution)

Possible research use with other DTIs, by specifically adjusting the calibration and protocol, or by alternative expression of inhibition as “hirudin equivalent”.

• Reproducible, sensitive, no impact of other plasma factors, highly stable
  (24h2-8 C, 8hRT, frozen)

• Purified (h)Thrombin tested for viral safety.

• Reflects the “true anti-lla” potential: presence of heparin or other antithrombin substances may interfere in the assay and prolong CT, to avoid any underestimation of an existing hypocoagulability.

DOSE RESPONSE CURVES TO 3 DTIs, AND REPRODUCIBILITY (STAR)

Untreated patients <0.05 µg/ml

Excellent linearity in the usual therapeutic range for the tested DTIs

INTER LOTS CORRELATION ON STAR

Good recovery, with no significant effect of other coagulation factors deficiency in the tested samples (eg AT, FII, Fibrinogen...).

RELATED PRODUCTS

1. Hirudin Standard Low (#ASC020K) or High (#ASC020L), Hirudin Plasma Control (#ASC025K),
2. Argatroban Plasma Calibrator (#ASC030K) and Control Plasma (#ASC035K)
3. Dabigatran Plasma Calibrator (#A222801) and Control Plasma (#A2274801).
4. Biophen DTI (#A227202)(chromogenic assay, not suitable for Argatroban®)