Cardiac

ichroma™ ST2

INTENDED USE

ichroma™ ST2 is a fluorescence Immunoassay (FIA) for the quantitative soluble Suppressor of Tumorigenicity 2 (ST2) level in human whole blood/serum/plasma. It is useful as an aid in management and assessing the prognosis of patients diagnosed with chronic heart failure (CHF).

For *in vitro* diagnostic use only.

INTRODUCTION

Soluble ST2 (sST2) is a member of the interleukin-1 (IL-1) receptor family and it can be found in a transmembrane form (ST2 ligand or ST2L) and a soluble, circulating form (sST2)

When soluble ST2 levels are low, ST2's ligand, IL-33, is available to bind to ST2L and has a cardioprotective effect resulting in preserved cardiac function. However, when soluble ST2 levels are high, soluble ST2 competitively binds to IL-33, making IL-33 less likely to bind to ST2L and thereby making IL-33 unavailable for cardioprotective signaling. This higher concentration of soluble ST2 is associated with increased myocardial fibrosis, adverse cardiac remodeling, worse cardiovascular outcomes and an increase in the rate of disease progression.

Studies shows that the changes in sST2 level during follow up patients admitted with acute HF represent a strong, independent predictor of the composite endpoint of all-cause mortality or readmission for HF over at least 1 year follow-up.

ichroma™ ST2 Assay quantitatively measures the concentration of soluble ST2, providing a physician with an accurate tool to assess prognosis in patients with chronic heart failure.

PRINCIPLE

The test uses a sandwich immunodetection method; the detector antibodies in buffer binds to antigens in the sample, forming antigen-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized-antibodies on test strip.

More antigens in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by instrument for ichroma™ tests to show ST2 concentration in the sample.

COMPONENTS

ichroma™ ST2 consists of 'cartridges', 'detector tubes', and 'detector diluent.'

- The cartridge contains the membrane called a test strip which has anti-ST2 at the test line, and chicken IgY at the control line. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant in a box.
- The detector tube has a granule containing anti human ST2- fluorescence conjugator, anti-chicken IgY-fluorescence conjugator and sodium azide as a preservative in phosphate buffered saline. All detector tubes are packed in a pouch.
- The detector diluent contains sodium azide as a preservative in phosphate buffered saline, and it is pre-dispensed in a vial. The detector diluent is packed in a box.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instruction For Use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, detector tube, detector diluent, and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect test result(s).
- Do not reuse cartridges or detector tube. A cartridge should be for testing one sample only. A detector tube should be used for processing one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use the cartridge, if pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- Allow cartridge, detector tube, detector diluent and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for ichroma™ tests may generate slight vibration during use.
- Used cartridges, detector tubes, detector diluent and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The detector tube and the detector diluent contain sodium azide (NaN_3), and they may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- **ichroma™ ST2** will provide accurate and reliable results subject to the below conditions.

- **ichroma™ ST2** should be used only in conjunction with instrument for ichroma™ tests.
- Have to use recommended anticoagulant sample.

Recommended anticoagulant
K_2EDTA, K_3EDTA, Sodium heparin, Lithium heparin

STORAGE AND STABILITY

Storage condition			
Component	Storage Temperature	Shelf life	Note
Cartridge	2 - 30 °C.	20 months	Disposable
Detector tube	2 - 30 °C.	20 months	Disposable
Detector diluent	2 - 30 °C.	20 months	Unopened
	2 - 30 °C.	20 months	Opened

- After the cartridge pouch is opened, the test should be performed immediately.

LIMITATION OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the antigen to the antibodies which is most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the antigen with time and/or temperature may also cause false negative result as it makes antigen unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician in conjunction with clinical symptoms and other relevant test results.

MATERIALS SUPPLIED

REF CFPC-100

Components of **ichroma™ ST2**

- Cartridge Box:
  - Cartridge 25
  - Detector tube 25
  - Detector diluent 1
  - ID chip 1
  - Instruction for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ ST2**.

Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™-50** REF FPRR022
  - **ichroma™-50 Plus** REF FPRR036
  - **ichroma™ M3** REF FPRR035
  - **Boditech ST2 Control** REF CFPO-289

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ ST2** is human whole blood/serum/plasma.

- It is recommended to test the sample within 24 hours after collection.
- The serum or plasma should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- Samples may be stored for up to 7 days at 2 ~ 8 °C prior to being tested. If testing will be delayed more than 7 days, serum and plasma should be frozen at - 20 °C.
- Samples stored frozen at -20 °C for 12 months showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.

TEST SETUP

- Check the contents of **ichroma™ ST2**: Sealed Cartridges, Detector tubes, Detector diluent, ID Chip and an Instruction for use.
- Ensure that the lot number of the cartridges matches that of the detector tube, detector diluent as well as an ID chip.
- If the sealed cartridge, the detector tube and detector diluent have been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.
- Turn on the instrument for ichroma™ tests.
  (Please refer to the 'Instrument for ichroma™ tests Operation Manual' for complete information and operating instructions.)

TEST PROCEDURE

▶ ichroma™ II, ichroma™ M3

Multi test mode

1) Take 150 µL of detector diluent using a pipette and dispense it to the detector tube containing a granule. When the granule form is completely dissolved in the tube, it becomes detection buffer.
   (The detection buffer must be used immediately. Do not exceed 30 seconds.)
2) Take 75 µL of sample (whole blood/serum/ plasma /control) using a pipette and dispense it to the detector tube.
3) Close the lid of the detector tube and mix the sample thoroughly by shaking it about 20 times
   (The sample mixture must be used immediately. Do not exceed 30 seconds.)
4) Take 75 µL of the sample mixture and dispense it into the sample well of the cartridge.
5) Leave the cartridge at room temperature for 12 minutes.

⚠ Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.

6) To scan the sample-loaded cartridge, insert it into the cartridge holder of the instrument for ichroma™ tests.

Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
7) Press the 'Select' or tap the 'Start' button on the instrument for ichroma™ tests to start the scanning process.
(ichroma™ M3 is tested automatically after inserting.)
8) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
9) Read the test result on the display screen of the instrument for ichroma™ tests.

Single test mode

1) The test procedure is same with the 'Multi test mode 1) – 4)'.
2) Insert the sample-loaded cartridge into the holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
3) Press the 'Select' or tap the 'Start' button on the instrument for ichroma™ tests.
(ichroma™ M3 is tested automatically after inserting.)
4) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 12 minutes.
5) Read the test result on the display screen of the instrument for ichroma™ tests.

▶ichroma™ III

1) The test procedure is same with "Single test mode".

▶ ichroma™-50, ichroma™-50 Plus

1) Insert the tip array in the tip station.
2) Insert the detector tube in the reagent station and cover the reagent station to hold the detector tubes in place.
3) Open the lid of the detector diluent and insert the detector diluent in the diluent station.
4) Insert the cartridge magazine with the cartridges into the magazine station.
5) Insert the sample tube into the blood collection tube rack and load the blood collection tube rack into the sampling station (loading part).
6) Tap the button located in the upper side of the No. of test cartridge region to select the ID chip that you want to use.
7) When the selected cartridge slot is activated, set the number of the detector tube by tapping.
8) Set the number of pipette tips by tapping.
9) Tap the 'START' button on the left upper of the main screen to start test.

INTERPRETATION OF TEST RESULT

- Instrument for ichroma™ tests calculates the test result automatically and displays ST2 concentration of the test sample in terms of ng/mL.
- Reference value : 35 ng/mL
- Working range : 3.1 - 200.0 ng/mL

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with **ichroma™ ST2**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
(Please refer to the instructions for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**
  - Limit of Blank (LoB) 1.20 ng/mL
  - Limit of Detection (LoD) 2.80 ng/mL
  - Limit of Quantification (LoQ) 3.10 ng/mL
- **Analytical specificity**
  - **Cross-reactivity**
    Biomolecules such as below the ones in the table were added to the test sample(s) at concentrations much higher than their normal physiological levels in the blood. **ichroma™ ST2** test results did not show any significant cross-reactivity with these biomolecules.

Materials	Concetration (%)
Human IL-1 sR-1	2 ug/mL
Recombinant human IL-1α	2 ug/mL
Recombinant human IL-1β	2 ug/mL

  - **Interference**
    Interferents listed in the following table were added to the test sample at the concentration mentioned below. **ichroma™ ST2** test results did not show any significant interference with these materials.

Interference materials	Concentration
D-glucose	60 mM/L
L-Ascorbic acid	0.2 mM/L
Bilirubin	0.4 mM/L
Hemoglobin	2 g/L
Cholesterol	13 mM/L
Triglyceride	10 mg/ml
Heparin	100 U/ml
EDTA	2 mg/ml

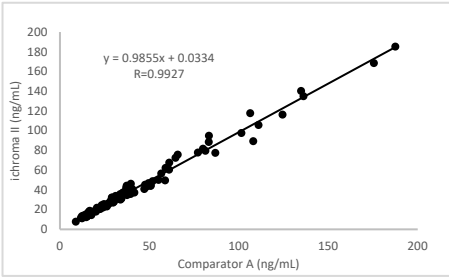
- **Precision**
  - Repeatability (within-run precision)
    Repeatability of **ichroma™ ST2** was evaluated with results of 1 Lot.
  - Total precision (within-laboratory precision)
    Total precision of **ichroma™ ST2** was evaluated with results of 1 Lot.
  - Lot to lot precision
    Lot to lot precision of **ichroma™ ST2** was evaluated with results of 3 Lots.

- Between person
  Three different persons tested **ichroma™ ST2**; ten times at each concentration of the control standard.
- Between site
  One person tested **ichroma™ ST2** at three different sites; ten times at each concentration of the control standard.

conc. (ng/mL)	Repeatability		Total precision		Lot to Lot	
	AVG	CV (%)	AVG	CV (%)	AVG	CV (%)
6.25	6.33	5.8	6.28	5.5	6.28	5.4
25.00	24.62	5.8	24.81	6.1	24.92	6.2
100.0	99.70	5.8	99.61	5.4	99.73	5.6

conc.	Between person		Between site	
(ng/mL	AVG	CV(%)	AVG	CV(%)
6.25	6.25	6.0	6.36	5.4
25.00	25.03	5.5	25.35	5.1
100.00	100.42	5.5	97.62	5.4

- **Comparability**
  ST2 concentrations of 100 samples were quantified independently with **ichroma™ ST2 (ichroma™ II)** and Comparator A as per prescribed test procedures. Test results were compared and their comparability was investigated with linear regression and correlation coefficient (R). The regression equation and correlation coefficient are as follows.



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Note: Please refer to the table below to identify various symbols

	Sufficient for <n> tests
	Read instruction for use
	Use by Date
LOT	Batch code
REF	Catalog number
	Caution
	Manufacturer
EC REP	Authorized representative of the European Community
IVD	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
CE	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

For technical assistance, please contact:
Boditech Med Inc.'s Technical Services
Tel: +(82) -33-243-1400
E-mail: sales@boditech.co.kr

Boditech Med Inc.
43, Geodudanji 1-gil, Dongnae-myeon, Chuncheon-si, Gang-won-do, 24398, Republic of Korea
Tel: +(82) -33-243-1400
Fax: +(82) -33-243-9373
www.boditech.co.kr

EC REP **Obelis s.a**
Bd. Général Wahis 53, 1030 Brussels, Belgium
Tel: +(32) -2-732-59-54
Fax: +(32) -2-732-60-03
E-Mail: mail@obelis.net

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