Elecsys GDF-15

cobas®

			SYSTEM
			cobas e 411
08946779119	08946779500	100	**cobas e** 601
			cobas e 602

English

System information

For **cobas e** 411 analyzer: test number 1100
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 206

Intended use

Immunoassay for the in vitro quantitative determination of Growth Differentiation Factor-15 (GDF-15) in human serum and plasma.

The Elecsys GDF-15 assay is intended as an aid in risk stratification of patients with Non-ST Elevation (NSTE) Acute Coronary Syndrome (ACS) or Chronic Heart Failure (CHF). The Elecsys GDF-15 assay is intended as an aid in risk prediction of major bleeding events of patients with Atrial Fibrillation (AF).

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on Elecsys and **cobas e** immunoassay analyzers.

Note: Please note that the catalogue number appearing on the package insert retains only the first 8 digits of the licensed 11-digit Catalogue Number: 08946779190 for the Elecsys GDF-15 assay. The last 3 digits-190 have been replaced by -119 for logistic purposes.

Summary

GDF-15 is a member of the transforming growth factor β (TGF-β) cytokine superfamily.

GDF-15 levels increase sharply in response to pathological or physiological stress associated with inflammation, hypoxia, tissue injury and remodelling as observed in cardiovascular diseases, as well as in some tumors and pregnancy.[1,2]

Levels of GDF-15 increase with the severity of cardiovascular diseases: elevated serum levels are found in stable coronary artery disease, ACS and heart failure (HF).[2]

Increasing evidence indicates that GDF-15 levels predict adverse outcomes of cardiovascular disease, independently from traditional risk factors such as previous myocardial infarction (MI), age, elevated levels of cardiac troponin T, N-terminal pro B-type natriuretic peptide, or high-sensitivity C-reactive protein. Increased GDF-15 levels are indicative of high mortality in patients with ST-segment elevation ACS (STE-ACS),[3] non-ST-elevation ACS (NSTE-ACS)[4,5,6] and HF.[7,8] Higher levels of GDF-15 also identify NSTE-ACS patients at an elevated risk of recurrent MI[4] and bleeding.[6]

Adding GDF-15 levels to the Global Registry of Acute Coronary Events (GRACE) score further improves the prediction of 6-month all-cause mortality and non-fatal MI in patients with NSTE-ACS.[9] High levels of GDF-15 are also associated with increased risk of developing HF following an episode of ACS.[10] Therefore GDF-15 levels potentially allow identifying which ACS patients will benefit from more aggressive therapies aimed at reducing HF-related admissions.

AF is highly associated with major risk for stroke and death. The development and risk of stroke can be mitigated by control of risk factors and oral anticoagulation therapy. However, anticoagulant therapy is strongly associated with a risk of major bleeding. Clinical practice points to the benefit of oral anticoagulation in AF on a balance between reduction in ischemic stroke and increase in major bleeding events. In clinical practice the risk of bleeding can be assessed by e.g. the HAS-BLED[11] score and more recently by the ORBIT[12] score, which are based on clinical risk factors only. However, several new biomarkers have now been shown to provide incremental information about the risk of bleeding in AF patients. The recently introduced risk modelling score termed "ABC-bleeding risk score" taking into account age, biomarkers (GDF-15, cTNT-hs, and hemoglobin) and clinical history was shown to significantly improve the prediction of bleeding events of AF patients.[13] The ABC-bleeding risk score could therefore be a valuable decision support tool regarding indications for and selection of treatment with oral anticoagulants in patients with AF.

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: Antigen in the sample (35 µL), a biotinylated monoclonal GDF-15-specific antibody, and a monoclonal GDF-15-specific antibody labeled with a ruthenium complex[a)] form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode or e-barcode.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The reagent rackpack is labeled as GDF-15.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-GDF-15-Ab~biotin (gray cap), 1 bottle, 8 mL: Biotinylated monoclonal anti-GDF-15 antibody (mouse) 1.5 µg/mL; phosphate buffer 95 mmol/L, pH 6.0; preservative.

R2 Anti-GDF-15-Ab~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 8 mL: Monoclonal anti-GDF-15 antibody (mouse) labeled with ruthenium complex 2.0 µg/mL; phosphate buffer 95 mmol/L, pH 6.0; preservative.

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

2-methyl-2H-isothiazol-3-one hydrochloride

EUH 208 May produce an allergic reaction.

Warning

H319 Causes serious eye irritation.

Prevention:

P264 Wash skin thoroughly after handling.

P280 Wear eye protection/ face protection.

Response:

P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

P337 + P313 If eye irritation persists: Get medical advice/attention.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

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Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). The following results were obtained:

cobas e 411 analyzer					
		Repeatability		**Intermediate precision**	
Sample	Mean pg/mL	SD pg/mL	CV %	SD pg/mL	CV %
Human serum 1	608	10.2	1.7	27.8	4.6
Human serum 2	1119	25.8	2.3	53.8	4.8
Human serum 3	1290	26.3	2.0	59.4	4.6
Human serum 4	1896	27.1	1.4	86.9	4.6
Human serum 5	10601	158	1.5	510	4.8
Human serum 6	18766	292	1.6	869	4.6
PC[b)] Cardiac II 1	1428	22.6	1.6	66.0	4.6
PC Cardiac II 2	7655	90.1	1.2	328	4.3

b) PC = PreciControl

cobas e 601 and **cobas e** 602 analyzers					
		Repeatability		**Intermediate precision**	
Sample	Mean pg/mL	SD pg/mL	CV %	SD pg/mL	CV %
Human serum 1	574	5.62	1.0	10.1	1.8
Human serum 2	1062	16.1	1.5	19.6	1.8
Human serum 3	1229	13.6	1.1	18.4	1.5
Human serum 4	1813	18.6	1.0	26.0	1.4
Human serum 5	10496	128	1.2	188	1.8
Human serum 6	18838	224	1.2	297	1.6
PC Cardiac II 1	1373	12.4	0.9	19.6	1.4
PC Cardiac II 2	7574	70.4	0.9	104	1.4

Method comparison

A comparison of the Elecsys GDF-15 assay, REF 08946779190 (**cobas e** 601 analyzer; y) with the Elecsys GDF-15 assay, REF 07125933190 (**cobas e** 601 analyzer; x), using clinical samples gave the following correlations (pg/mL):

Number of samples measured: 136

Passing/Bablok[27]	Linear regression
y = 1.02x − 88.1	y = 1.03x – 99.4
τ = 0.993	r = 1.00

The sample concentrations were between 403 and 19493 pg/mL.

Analytical specificity

No significant cross-reactivity was found for Tumor necrosis factor-β (< 0.2 %; tested concentration 100 ng/mL) and C-reactive protein (< 0.001 %; tested concentration 200 mg/L).

References

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For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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