

## Supplementary material

### Evaluation of the prognostic value of GDF-15 and ABC-AF scores in different geographical areas

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## Contents

<b>Supplementary Figure 1</b> .....	2
<b>Supplementary Table 1</b> .....	3
<b>Supplementary Table 2</b> .....	5

**Supplementary Figure 1.**

List of all included countries from both the ARISTOTLE and the RE-LY trial.

<u>ARISTOTLE</u>	<u>RELY</u>
<b>ASIA/PACIFIC</b>	<b>ASIA</b>
Australia	China
China	Hong Kong
Hong Kong	India
India	Japan
Japan	Malaysia
Malaysia	Philippines
Philippines	Singapore
Singapore	South Korea
South Korea	Taiwan
Taiwan	Thailand
<b>EUROPE</b>	<b>EUROPE</b>
Austria	Austria
Belgium	Belgium
Czech	Bulgaria
Denmark	Czech
Finland	Denmark
France	Finland
Germany	France
Hungary	Germany
Israel	Greece
Italy	Hungary
Netherlands	Italy
Norway	Netherlands
Poland	Norway
Romania	Poland
Russia	Portugal
South Africa	Romania
Spain	Russia
Sweden	Slovakia
Turkey	Spain
UK	Sweden
Ukraine	Switzerland
<b>LATIN AMERICA</b>	<b>LATIN AMERICA</b>
Argentina	Turkey
Brazil	Ukraine
Chile	UK
Colombia	<b>LATIN AMERICA</b>
Mexico	Argentina
Peru	Brazil
Puerto Rico	Colombia
<b>NORTH AMERICA</b>	Mexico
Canada	Peru
USA	<b>NORTH AMERICA</b>
<b>OTHER</b>	<b>NORTH AMERICA</b>
	Canada
	USA
	<b>OTHER</b>
	Australia
	Israel
	South Africa

**Supplementary Table 1.** Baseline characteristics of the 14949 patients in the ARISTOTLE cohort according to study region.

	<b>ASIA/PACIFIC</b> <i>N</i> = 2389	<b>EUROPE</b> <i>N</i> = 6027	<b>LATIN AMERICA</b> <i>N</i> = 2959	<b>NORTH AMERICA</b> <i>N</i> = 3574
Age, Median (Q1 - Q3)	69.0 (61.0 - 75.0)	69.0 (62.0 - 75.0)	70.0 (64.0 - 77.0)	72.0 (65.0 - 78.0)
Female	35.7% (853)	37.1% (2235)	38.0% (1125)	31.0% (1109)
BMI, Median (Q1 - Q3)	25.1 (22.6 - 28.0) [7]	29.1 (26.1 - 32.8) [21]	28.7 (25.4 - 32.6) [24]	30.2 (26.5 - 35.0) [19]
Systolic blood pressure Median (Q1 - Q3)	130.0 (120.0 - 140.0) [8]	133.0 (123.0 - 143.0) [12]	130.0 (120.0 - 140.0) [2]	128.0 (117.0 - 138.0) [10]
Diabetes	24.7% (589)	22.7% (1370)	20.1% (595)	31.7% (1133)
Hypertension	81.0% (1936)	89.8% (5414)	88.8% (2629)	86.9% (3105)
Smoker	8.4% (200) [1]	9.9% (593) [9]	5.6% (166) [4]	7.2% (258) [0]
Permanent or persistent AF	89.6% (2141) [0]	80.8% (4867) [1]	91.5% (2706) [1]	83.2% (2973) [1]
Stroke/TIA	26.7% (637)	19.0% (1148)	15.3% (454)	15.8% (565)
Prior bleeding	15.8% (377)	12.1% (732)	13.2% (392)	26.1% (932)
Prior anemia	3.8% (90) [0]	4.9% (298) [3]	3.5% (104) [6]	14.4% (514) [2]
Congestive heart failure	24.9% (596)	40.8% (2458)	33.4% (989)	16.8% (601)

Myocardial infarction	8.2% (196) [0]	15.0% (906) [0]	9.5% (280) [1]	15.2% (542) [0]
Peripheral arterial disease	2.5% (59) [0]	5.3% (317) [0]	3.7% (109) [1]	6.8% (244) [0]
CKD-EPI (mL/min/1.73m <sup>2</sup> ), Median (Q1 - Q3)	59.0 (47.2 - 72.8) [1]	56.5 (46.4 - 67.8) [7]	57.0 (45.5 - 70.5) [0]	52.4 (42.1 - 63.2) [0]
GDF-15 (ng/L), Median (Q1 - Q3)	1476.5 (1049.8 - 2167.5) [29]	1263.0 (919.5 - 1865.0) [88]	1362.0 (973.0 - 2012.0) [34]	1559.0 (1074.5 - 2297.5) [31]
Haemoglobin (g/dL), Median (Q1 - Q3)	14.1 (13.0 - 15.3) [13]	14.3 (13.3 - 15.3) [13]	14.4 (13.4 - 15.5) [26]	14.1 (13.0 - 15.0) [18]
NT-proBNP (ng/L), Median (Q1 - Q3)	725.0 (377.8 - 1220.2) [13]	695.0 (339.2 - 1244.0) [57]	751.0 (397.0 - 1325.0) [10]	706.0 (370.0 - 1217.8) [8]
hs-cTnI (ng/L), Median (Q1 - Q3)	5.1 (3.0 - 10.4) [26]	5.3 (3.3 - 9.7) [91]	6.6 (3.8 - 12.8) [16]	4.9 (2.9 - 8.7) [26]
hs-cTnT (ng/L), Median (Q1 - Q3)	9.8 (7.0 - 14.7) [12]	10.8 (7.4 - 16.3) [53]	11.4 (7.9 - 17.6) [9]	11.7 (7.9 - 17.6) [9]
<b>Outcomes</b>				
Death	152 (6%)	330 (5%)	332 (11%)	245 (7%)
Major bleeding	130 (5%)	206 (3%)	138 (5%)	195 (5%)
Missing GDF-15	28 (1%)	88 (1%)	34 (1%)	31 (1%)

AF indicates atrial fibrillation; BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration equation; Interleukin-6;

Q, quartile; TIA, transient ischemic attack and number in brackets represents number of missings.

**Supplementary Table 2.** Baseline characteristics of the 9369 patients in the RE-LY cohort according to study region.

	<b>ASIA</b> N = 891	<b>EUROPE</b> N = 5024	<b>LATIN AMERICA</b> N = 629	<b>NORTH AMERICA</b> N = 2082	<b>OTHER</b> N = 743
Age, Median (Q1 - Q3)	69.0 (63.0 - 75.0)	72.0 (66.0 - 77.0)	73.0 (67.0 - 78.0)	74.0 (68.0 - 79.0)	74.0 (69.0 - 79.0)
Female	32.9% (293)	36.9% (1855)	40.1% (252)	34.1% (711)	40.0% (297)
BMI, Median (Q1 - Q3)	24.3 (22.0 - 27.0) [3]	28.1 (25.4 - 31.4) [1]	27.9 (25.3 - 31.6) [0]	29.0 (25.7 - 33.3) [3]	28.4 (25.3 - 31.6) [0]
Systolic blood pressure, Median (Q1 - Q3)	130.0 (120.0 - 140.0) [2]	132.0 (120.0 - 145.0) [8]	131.0 (120.0 - 144.0) [0]	128.0 (118.0 - 140.0) [2]	130.0 (120.0 - 143.8) [1]
Diabetes	25.3% (225)	20.4% (1024)	16.2% (102)	24.4% (509)	29.5% (219)
Hypertension	71.6% (638)	78.7% (3954)	82.0% (516)	81.4% (1694)	79.3% (589)
Smoker	8.4% (75)	8.6% (432)	4.8% (30)	6.3% (132)	7.0% (52)
Permanent or persistent AF	69.7% (621) [0]	71.3% (3580) [0]	87.3% (549) [0]	55.2% (1147) [4]	58.7% (436) [0]
Stroke/TIA	29.4% (262)	18.8% (944)	14.9% (94)	16.8% (349)	23.4% (174)
Anemia	22.2% (198)	10.2% (513)	7.5% (47)	14.0% (291)	18.0% (134)
Congestive heart failure	34.9% (311) [0]	33.8% (1696) [0]	33.9% (213) [0]	16.0% (334) [1]	21.1% (157) [0]
Myocardial infarction	10.2% (91)	17.2% (864)	7.5% (47)	19.6% (408)	24.1% (179)

Peripheral arterial disease	0.4% (4) [0]	3.8% (193) [0]	2.2% (14) [0]	5.0% (105) [0]	3.9% (29) [1]
CKD-EPI (mL/min/1.73m <sup>2</sup> ), Median (Q1 - Q3)	70.7 (58.5 - 85.4) [0]	65.5 (54.5 - 76.9) [75]	57.9 (47.5 - 68.3) [0]	64.2 (53.3 - 76.4) [8]	63.1 (52.2 - 75.2) [8]
GDF-15 (ng/L), Median (Q1 - Q3)	1606.0 (1181.5 - 2407.5) [76]	1436.0 (1060.0 - 2067.0) [365]	1545.0 (1142.2 - 2081.2) [19]	1608.0 (1182.0 - 2332.0) [171]	1744.5 (1231.5 - 2605.8) [87]
Hemoglobin (g/dL), Median (Q1 - Q3)	13.9 (12.7 - 15.1) [3]	14.4 (13.4 - 15.4) [103]	14.4 (13.4 - 15.5) [4]	14.1 (13.1 - 15.1) [29]	14.0 (12.8 - 15.0) [20]
NT-proBNP (ng/L), Median (Q1 - Q3)	807.0 (400.5 - 1576.5) [3]	837.0 (396.0 - 1477.0) [35]	819.0 (453.0 - 1410.0) [8]	748.0 (368.5 - 1354.0) [19]	854.0 (372.5 - 1406.5) [8]
hs-cTnI (ng/L), Median (Q1 - Q3)	6.8 (4.2 - 14.8) [33]	7.2 (4.7 - 13.0) [290]	7.3 (4.4 - 14.0) [18]	5.6 (3.5 - 10.0) [102]	7.4 (4.5 - 15.0) [11]
hs-cTnT (ng/L), Median (Q1 - Q3)	10.8 (7.1 - 18.0) [39]	12.2 (7.7 - 19.5) [385]	12.9 (8.3 - 20.0) [21]	12.0 (7.6 - 19.0) [121]	13.8 (8.5 - 22.8) [84]
<b>Outcomes</b>					
Death	66 (7%)	341 (7%)	54 (9%)	104 (5%)	42 (6%)
Major bleeding	38 (4%)	210 (4%)	29 (5%)	151 (7%)	46 (6%)
Missing GDF-15	76 (9%)	365 (7%)	19 (3%)	171 (8%)	87 (12%)

AF indicates atrial fibrillation; BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration equation; Q, quartile; TIA, transient ischemic attack and number in brackets represents number of missings.