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National registry and DNA-bank of adults with congenital heart disease

Number of included patients: 11,500

Project group: BJM Mulder, AMC Amsterdam; ET van der Velde, LUMC Leiden; J Vis, ICIN; CJM Engelfriet-Rijk, ICIN; I Harms, ICIN; S Mantels, ICIN

Steering committee: BJM Mulder, chairman, ICIN; ET van der Velde, LUMC Leiden; ECM Mariman, AZM Maastricht; FJ Meijboom, UMC Utrecht; HW Vliegen, LUMC Leiden; G Veen, VUMC Amsterdam; PG Pieper, UMC Groningen; HWM Plokker, St Antonius Hospital Nieuwegein; APJ van Dijk, Radboud UMC Nijmegen; JLM Stappers, AZM Maastricht; JW Roos-Hesselink, EMC Rotterdam; JGP Tijssen, AMC Amsterdam; RMF Berger, UMC Groningen; GJ Sieswerda, UMC Utrecht

Results: New gene identified: mutations in ALK2 may be causative for AVSD.

Smith KA, Joziasse IC et al. Circulation 2009;119:3062-9.
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Figure 1. Schematic representation of the ALK2 protein and structural domains: signal peptide (SP), ligand binding domain (LBD), transmembrane domain (TM), GS domain (GS), and kinase domain (KD).

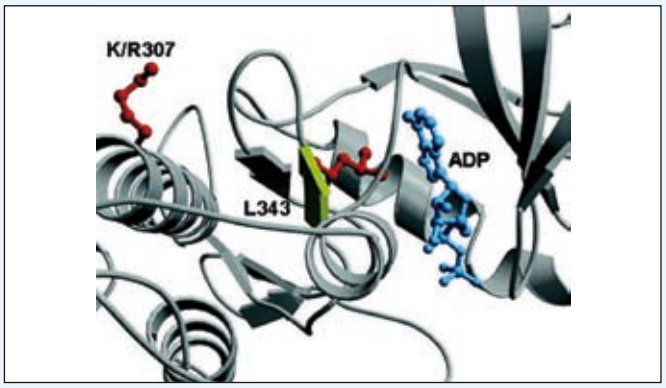

Figure 2. Model of ALK2 protein (TGFβ receptor I), showing mutations R307 and L343 in red.

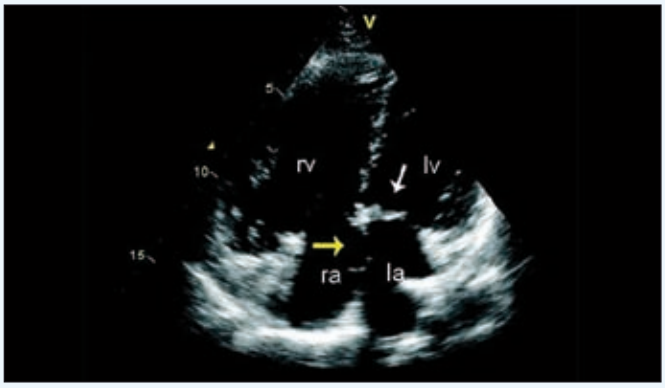

Figure 3. Echocardiogram of a corrected AVSD and pulmonary arterial hypertension in a patient with ALK2 mutation (R307L).

ZAHARA II

Pregnancy in adult congenital heart disease

A prospective, international multi-centre cohort study to examine the cardio-uterine interaction in pregnancy of women with congenital heart disease (CHD). Women with CHD presenting <20 weeks of pregnancy duration can be included.

Start of study: 1 March 2008
Planned inclusion: Minimum of 160 pregnant women with CHD and 60 healthy pregnant women
Number of included patients: 160 (expanded with 40 additional patients)
Number of included healthy controls: 35
15 December 2009

Study coordination: A Balci, ICIN, Utrecht; Department of Cardiology, UMCG, Groningen, the Netherlands.
Project leaders: PG Pieper, Department of Cardiology, UMCG, Groningen
JG Aarnoudse, Department of Obstetrics & Gynaecology UMCG, Groningen
Principal investigators: The Netherlands: Department of Cardiology: PG Pieper, UMCG, Groningen; BJM Mulder, AMC, Amsterdam; JW Roos-Hesselink, Erasmus MC, Rotterdam; APJ van Dijk, UMCN St. Radboud, Nijmegen; HW Vliegen, LUMC, Leiden; E Wajon, MST, Enschede; JLM Stappers, AZM, Maastricht; GJ Sieswerda, UMCU, Utrecht; G Veen, VUMC, Amsterdam. Department of Obstetrics & Gynaecology: JG Aarnoudse, KM Sollie, UMCG, Groningen.
Belgium: Department of Cardiology: W Budts, UZL, Leuven, Department of Obstetrics & Gynaecology: M. Hanssens, UZL, Leuven

For information or inclusion of patients, please contact us at: a.balci@thorax.umcg.nl

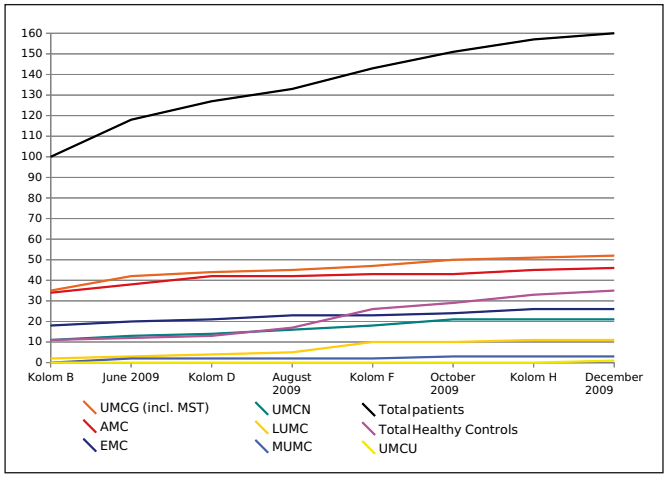

Figure 1. Distribution of included patients and healthy controls in ZAHARA II.

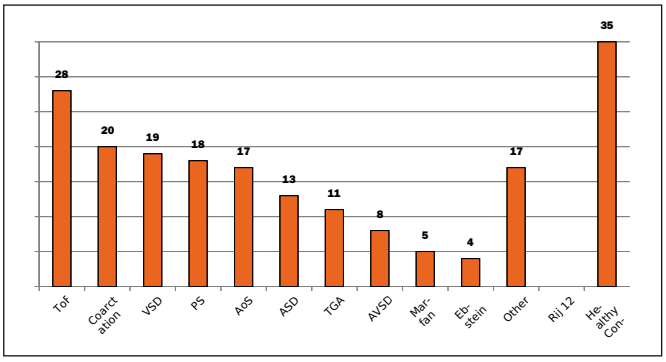

Figure 2. Distribution of main CHD diagnoses in ZAHARA II.

ESC/AEPC

In cooperation with the ESC and the AEPC

Total inclusion Europe: 617
Total inclusion Netherlands: 115
January 2010

International Expert Committee: Jörg Stein, Austria; Roger Hall, UK; Jolien Roos-Hesselink, the Netherlands
National coordinators for the Netherlands: Jolien Roos-Hesselink, Department of Cardiology, ErasmusMC, Rotterdam; Els Pieper, Department of Cardiology, UMCG, Groningen

At the moment the enrolment is increasing with centres from all over Europe and also from the USA and Canada. Nearly 800 patients have been enrolled so far. The first analysis will be performed after the first 1000 patients have been followed until six months after delivery. Heart disease is a major cause of mortality in pregnant patients. This registry will focus on complications during pregnancy, method of delivery and medication during pregnancy.

Table 1. Inclusion of patients in the Netherlands.

City	Hospital	Included
Rotterdam	Erasmus University Medical Center	72
Lelystad	IJsselmeer Hospitals	1
The Hague	MCHaaglanden	8
Groningen	University Medical Center Groningen	26
Utrecht	Wilhelmina Children's Hospital Utrecht	7
Leiden	Leiden University Medical Center	1

Please join the Registry!
Contact the EuroHeartSurvey: ehs@escardio.org or contact us at: j.roos@erasmusmc.nl or p.g.pieper@thorax.umcg.nl. ■

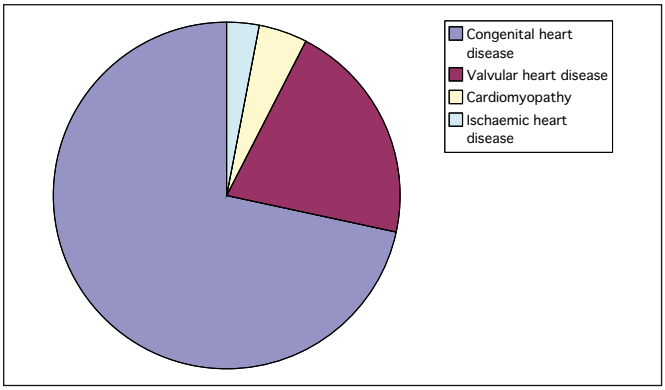

Figure 1. The diagnosis of the pregnant patients per type of diagnosis.

HEBE III

A prospective, randomised, clinical study to examine the effects of a single bolus of erythropoietin on left ventricular function in patients with a myocardial infarction

Number of included patients: 529
1 June 2009

Funded by the Netherlands Heart Foundation

Study coordination: A. Belonje, UMC Groningen

Principal investigators: A.A. Voors, F. Zijlstra, D.J. van Veldhuisen, UMC Groningen

Participating centres: University Medical Center Groningen, University Medical Center Leiden, Medical Centre Alkmaar, Isala Clinics Zwolle, Amphia Hospital Breda, Academic Medical Center Amsterdam, St. Antonius Hospital Nieuwegein

Erythropoietin and left ventricular function

In the previous edition of the Netherlands Heart Journal, we mentioned the safety issues concerning erythropoietin treatment. In this issue we would like to share some information about the possible effects of erythropoietin on left ventricular function.

Erythropoietin is a protein produced by the kidney in a reaction to low oxygen tension. Besides regulating haemoglobin concentrations, erythropoietin has antiapoptotic properties and is known to stimulate new vessel formation through the action of vascular endothelial growth factor. In patients with heart failure, erythropoietin levels are raised and related to poor outcome. These elevated levels may be caused by the lower renal function often found in patients with heart failure. Another explanation may be that the chronic inflammatory state in heart failure causes bone-marrow resistance to the effects of erythropoietin. As a result, erythropoietin levels rise. The elevated erythropoietin levels in patients with a decreased left ventricular function may be a reaction to disease severity, but may also be beneficial for the heart by stimulating neovascularisation and decreasing the amount of apoptotic cells.

Patients who suffer a myocardial infarction also have raised erythropoietin levels. This increase can be protective in the acute phase by reducing apoptosis and thus decreasing infarct size and in the early follow-up phase by promoting vasculogenesis. Administration of exogenous erythropoietin, therefore, may add to these cardioprotective properties. ■

RACE 3

Number of included patients: 17
16 December 2009

This study is supported by: Biotronik, Boehringer Ingelheim, Boston Scientific, Medtronic, Sanofi Aventis, St. Jude Medical and Astra Zeneca.

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Study coordination: Marcelle D. Smit, UMC Groningen
PhD Student: Ismaël D. Achekar, UMC Groningen

In November 2009, the Race 3 steering committee submitted a protocol amendment to the central Medical Ethics Committee (MEC). An important change made to the protocol concerns the definition of heart failure (HF) used for the inclusion criteria, distinguishing diastolic from systolic HF and increasing the minimum NT-proBNP elevation to 400 ng/l. 'Mild to moderate early heart failure' is now defined as:

1. Total HF history <1 year, and
2. One of the following:
   - LVEF >40% and NYHA class II-III, and
     - Previously documented HF-related NT-proBNP elevation (>400 ng/l (=48 pmol/l)), or
     - Previous admission for HF, or
     - Evidence of diastolic dysfunction on echocardiography
   - LVEF 25-40% and NYHA class I-III

Another important change is that clear guidelines have now been added to the protocol with regard to the treatment of diastolic and systolic heart failure and to the treatment of the upstream group and the conventional group. This was recently approved by the MEC. ■