GERMANY UPDATE

INTERNATIONAL STUDY OF COMPARATIVE HEALTH EFFECTIVENESS WITH MEDICAL AND INVASIVE APPROACHES

NYU Cardiovascular Clinical Research Center — Autumn 2016

Study Updates as of 12 Sep 2016

Global Enrollments: 5695
Global Randomizations: 3382
CKD Randomizations: 341

A Message from Dr. Doerr

Dear Colleagues,

With only 1% of all randomizations in the world **Germany is still considerably underrepresented in the ISCHEMIA Trial and far behind its potential!**

If you are interested in participating in the trial, please email ischemia@nyumc.org or doerr@praxisklinik-dresden.de.

With kind regards,

Rolf Doerr, MD

Country Leader

Dr. Rolf Doerr

Country Lead Nephrologists

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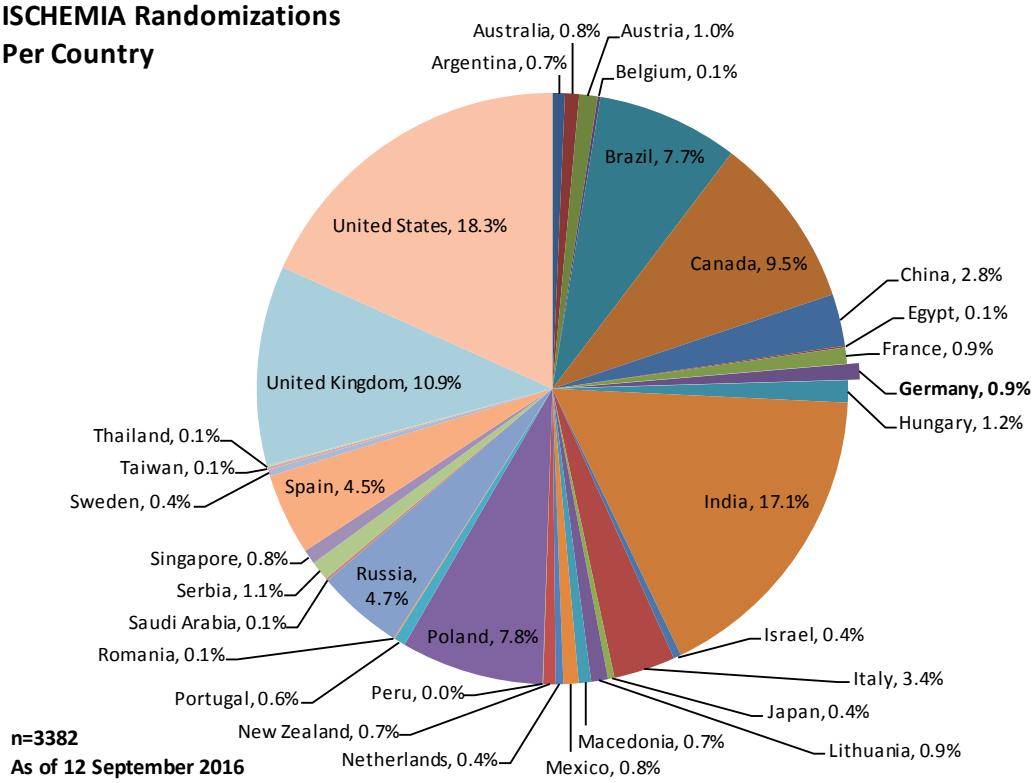
ALMAC Clinical Helpline

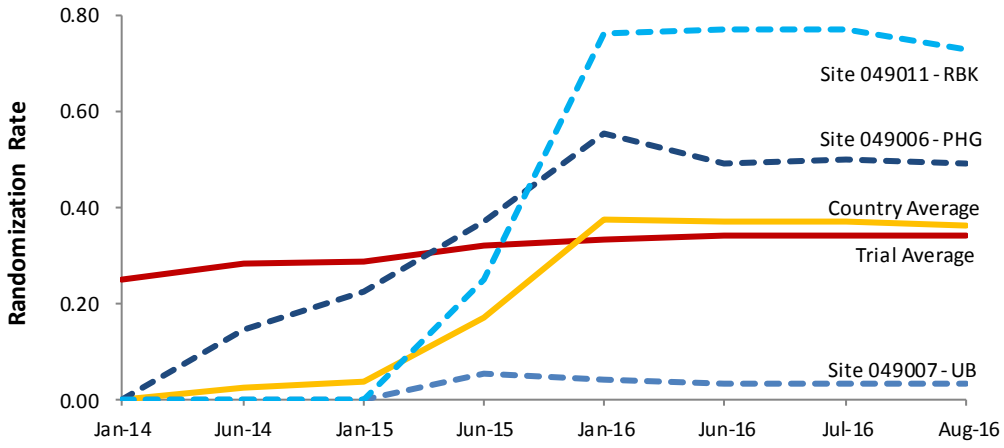
06950985571

ISCHEMIA Randomizations Per Country



n=3382
As of 12 September 2016

RANDOMIZATION RATE OVER TIME



Enrolling Sites in Germany	Main Trial Randomizations	CIAO-ISCHEMIA Enrollments
Site 049006—Praxisklinik Herz und Gefaesse, Dresden Dr. Rolf Doerr, Dr. Juergen Stumpf, Prof. Gregor Simonis, Dr. Clemens T. Kadalie, Franziska Günther, Kerstin Bonin, Dorit Grahl	**16**	-
Site 049011—Robert-Bosch-Krankenhaus, Stuttgart Prof. Udo Sechtem, Susanne Gruensfelder, Ina Wenzelburger	**13**	**1**
Site 049007—Universitaetsklinikum Bonn, Bonn Prof. Georg Nickenig, Dr. Nikos Werner, Dr. Marcel Weber	**1**	-

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Engage your Colleagues

How can I optimize recruitment?

- ✓ Speak with imaging physicians—remind them to contact you if there is an eligible patient
- ✓ Ask imaging labs to remind referring physicians about ISCHEMIA if they find patients with at least moderate ischemia
- ✓ Identify other cardiologists or primary care physicians who are willing to screen and refer their own patients to your site

How can I convince interventional cardiologists to support the study?

- ✓ Including high risk patients will reduce the impact of referral bias on the outcome of ISCHEMIA
- ✓ Results of this trial will have a long-lasting impact on interventional practice, including reimbursement
- ✓ Impact on cath lab volumes will be minimal as half of the participants are randomized to INV

What can I tell other colleagues at my site who do not support the trial?

- ✓ A Data and Safety Monitoring Board (DSMB) monitors the safety of the trial on a regular basis and has recommended the continuation of the trial.
- ✓ Evidence suggests that it is ethical to randomize stable patients with moderate or severe ischemia to an initial conservative strategy, with cath as needed
- ✓ CON participants are closely monitored in follow-up and can be sent to cath if necessary
- ✓ CCTA (performed in majority of participants) excludes participants with left main disease prior to randomization
- ✓ If your site is participating in the device donation program, stents (Xience or Resolute) are available at no charge for INV participants

Contact the ISCHEMIA CCC team for physician materials or support for a local meeting at your site.

Let's Work Together!

If sites in Germany continue to randomize **at least 1 participant per month**, Germany will surpass its randomization goal for the ISCHEMIA trial for the year!

What if I am not sure about the level of ischemia?

All sites may enroll patients based on their local core lab finding of moderate ischemia as long as all other eligibility criteria are met. If you would like to confirm that your site's interpretation of the amount of ischemia matches the core lab interpretation prior to enrollment, you may send anonymized stress images for core lab verification before trial consent or enrollment, if permissible by your local IRBs/ECs and privacy boards.

Stress images (NUC/ECHO/CMR) may be submitted via BioClinica. For pre-enrollment verification of an ETT, please send the technical worksheet and de-identified tracings to the ISCHEMIA CCC in a SendSafe email. Please see Section 9.1.1 of the **MOO** for additional details.

Assign a temporary participant ID number with the six-digit site ID and a three digit "-800" or "900" number (for example, 049001-801)

If transmitting stress images via BioClinica, select "Pre-enrollment ISCHEMIA" or "Pre-Enrollment CKD ISCHEMIA" as the Timepoint. Select "Expedited" reading

The CCC will email your site with the core lab interpretation. If all eligibility criteria are met, proceed with consenting and enrolling the participant

Notify the CCC of the participant ID assigned by ALMAC IXRS. The CCC will re-label the stress images (or ETT) with the new ID