The CERC Chronicle

European Cardiovascular Research Center

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EDITORIAL

How can CERC support and optimize your Investigator-Initiated Trials?

Over the past few years, we have observed that an increasing number of physicians have been seeking financial support to initiate their own trials. If appropriately conducted, such trials can provide robust clinical data as well as invaluable insight into the performance of medical devices already in use.

Manufacturers of medical devices have always maintained a close collaboration with practitioners in order to obtain accurate outcome assessment and identify further potential enhancements to maximize the efficacy of their products.

In parallel, several device companies are now setting up dedicated departments or business units in charge of managing these IITs. However, before being successfully implemented, this centralized approach requires a clearly defined corporate strategy.

Thanks to its extensive experience in coordinating IITs, CERC is able to anticipate potential pitfalls and provide valid solutions to both physicians and manufacturers.

IITs are costly undertakings which sometimes put substantial strain on manufacturing companies as investigators may request additional support and funds to bring their research work to fruition. The challenge for the industry is to strike an optimal balance between their need to maximize the outcomes of research programs, while minimizing both risks and costs.

Based on its experience, CERC can generate realistic financial models and ensure budget control throughout the duration of the trial. CERC can also guarantee compliance with regulatory requirements and Good Clinical Practice as well as adherence to timelines.

CERC can act as the cornerstone, assisting both parties in establishing a clear and specific legal agreement with precisely defined data and research ownership.

CERC can help build up and preserve a sound relationship between physicians and manufacturers and manage all operational issues so that investigators may focus exclusively on their research work.

CERC is a group of KOL with unparalleled experience in clinical research and publication.

We provide expert guidance for abstract submission to international scientific sessions and publication of articles in prominent peer-review journals.

Marie-Claude Morice & Valérie Gombau Delavoipierre

Interview with Dr Keith Dawkins, *Global Chief Medical Officer & Executive Vice President, Boston Scientific Corporation*

Who are you?

My name is Keith Dawkins, Global Chief Medical Officer & Executive Vice President, Boston Scientific Corporation. Prior to joining the company six years ago, I was a Consultant Cardiologist at Southampton University Hospital, UK. I am an interventional cardiologist by training and have been active in clinical trials for the last 25 years!

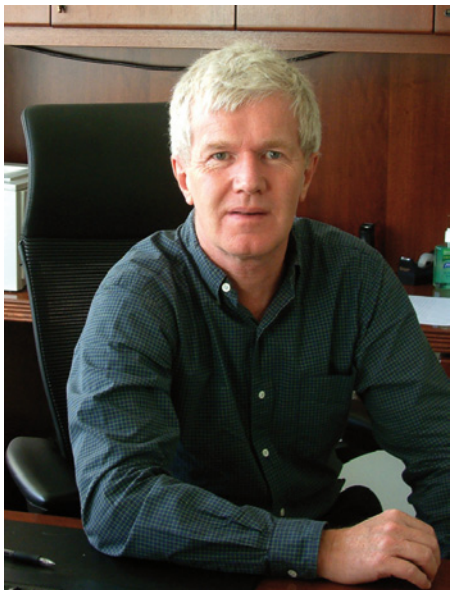
You are leading a very important research program for a major device company. How do you select the priorities for clinical trials; which ones are run internally; which ones are subcontracted to CRO's, and what is the role of Investigator Sponsored trials?

Boston Scientific has a very active internal clinical trial portfolio. Right now we have 135,529 patients under planned investigation in 113 trials across our seven businesses. Most are in the cardiovascular area (interventional cardiology, peripheral intervention, and cardiac rhythm management). Typically, our internal trials are run for product regulatory approval (CE-Mark, FDA, PMDA etc) prior to commercialization, or as mandated post-approval trials. Pivotal trials are usually randomized against an approved product using a non-inferiority design. Formally, frequentist statistics were usual, but more recently the application of a Bayesian statistical approach has allowed a reduction in sample size. Other internal trials are used for indication or label expansion. We also pride ourselves in funding trials asking important scientific questions (e.g. SYNTAX, HORIZONS, and the MADIT trials).

Over the last few years Boston Scientific has deliberately increased the focus and investment in Investigator Sponsored Research (ISR). These studies have a number of benefits. The company funds research at arm's length with the advantage that the investigator and the trial data are viewed as independent by other investigators and scientific journals. 'Real-world' patients can be recruited to explore off-label applications of the device, which are often more relevant than highly selected data gleaned from pivotal trials. Investigators have ownership of their data and enjoy the opportunity of increasing their podium presence and research profile. By funding the trial outside the Boston Scientific quality and regulatory systems, ISRs are cost-effective and an efficient approach to clinical and pre-clinical research. Recently, some regulators have accepted ISR trials in support of a product approval which is an important step forward.

As trials have become larger and more complex the principal investigator often needs the help of an independent CRO to execute the trial. Since the inception of CERC in 2008 we have enjoyed a close relationship with the organization which has included collaboration on a number of trials including PLATINUM Plus, ACTIVATION, CELTIC and SENIOR. Selecting a collaborative CRO, run by physicians with a deep knowledge of the space is a distinct advantage that ultimately leads to more effective and timely trial completion.

Of course, Europe has the advantage of a 3 – 5 year new device approval advantage over many other countries including the US and Japan. Although the European regulatory bar is increasing, the requirements remain less stringent. Europe is the obvious arena to investigate novel devices, and Investigator Sponsored Research coordinated by a CRO is a very cost-effective model. It is likely that Boston Scientific will rely on this research paradigm more frequently in the future.



Keith Dawkins

Publication center

Following requests from several of our partners, we are happy to announce that we are in the process of setting up our **Publication Centre**, a new service offered by CERC.

All too often, great efforts are made to collect, analyze and validate data in the field of clinical cardiovascular medicine, and abstracts are then submitted and presented at meetings, but final publications are delayed because the PI's are too busy, in-house resources are lacking and, sometimes, expertise in "fine-tuning" a manuscript is insufficient.

Such problems are perhaps not frequent for large, well-designed randomized trials, but more specifically plague large post-market registries. In the fast-moving field of interventional cardiology, each month that is lost leads to diminishing value of the data when they are eventually published.

We believe that CERC can be of significant help, by offering a full range of options to assist both authors and sponsors:

- Data management and analysis
- Statistical assistance
- Medical writing and referencing
- Group writing sessions
- Choice of target journal
- Definition of the timetable leading to submission

For further information, please contact:
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Philip Urban

Catherine Dupic, Medical Writer

Primary Endpoint of GIANT trial presented @ TCT Hotline

- CYP2C19 genetic profiling for thienopyridine management after primary percutaneous coronary intervention:

The results of the GIANT study will be presented during the TCT hotline session dedicated to first investigation reports on Thursday Oct 31st 2:07 pm in the Coronary Theater - Moscone Center, San Francisco.

It is not known whether on-line adjustment of thienopyridine therapy in genetically slow-responders to clopidogrel may counteract the previously described higher one-year risk of major ischemic events in such patients when treated with PCI for acute myocardial infarction.

Fifty-three centers enrolled 1,499 patients in the "GIANT" prospective, multicenter, single-arm study at the time of primary PCI (onset of chest pain < 24 hrs). Genetic profiling was performed within 48 hrs after intervention to detect a loss of function of CYP2C19 in order to identify resistance to clopidogrel. A strong recommendation for treatment adjustment (prasugrel or double dose of clopidogrel if prasugrel contraindication) was sent to the investigators in case the slow responder variant(s) was identified.

DAPT was prescribed for 12 months after PCI. The primary endpoint was the composite of death, myocardial infarction and stent thrombosis at one year follow-up. The secondary endpoints analysed the impact of compliance on the one-year outcomes and tertiary analyses evaluated the role of genetic profile on bleeding complications as well as on the different components of the composite endpoint.

The study was sponsored by Biotronik, conducted under the guidance of a coordination committee involving Dr Bernard Chevalier, Pr Gilles Montalescot, Dr Loic Belle and Dr Guillaume Cayla and was fully managed by the CERC. Dr Jean-Sebastien Hulot and his team carried out genetic analyses of this first large-scale trial evaluating the practical role of genomics in acute myocardial infarction management.

Bernard Chevalier

CERC Advisory Board

- The third CERC advisory board meeting took place on the Monday before EuroPCR 2013. The CERC medical council met the representatives of four companies based in Europe, Asia, and the USA in order to interact in both the development process and clinical validation phase of their leading products.

The format of these meetings is dynamic and concise in order to stimulate interactivity and to allow straightforward discussions covering all aspects of technical developments, clinical validation, market access and reimbursement.

According to the feedback that we received from the participants on both sides, the discussion was fruitful in that it provided food for thought in terms of validation of innovative projects and development of strategic approaches to future clinical studies.

Whatever the size of your company, if you are interested in taking part in this process, do not hesitate to get in touch with one of the CERC's directors.

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CERC present at PCR London Valves

- The PCR London Valves'2013 edition was held from September 15th to 17th.

All the valve manufacturing companies and physicians involved in TAVI attended this very successful event which gathered more than 1,500 participants.

The visibility of CERC was enhanced by the presentation of several studies managed by our company:

The MAVERIC trial (FIM evaluation of a device used in the treatment of mitral insufficiency) was presented, Martyn Thomas and Andrej Erglis are the study's PI's; a presentation of the ACTIVATION trial (should coronary lesions be treated prior to TAVI ?) by Martyn Thomas, PI of the study and several lectures regarding the EDWARDS studies (CENTERA, SAPIENS 3 and PROTAVI) for which CERC is in charge of coordinating the CEC and DSMB meetings.

Our team was kept very busy and welcomed many investigators who came to visit us on our booth.

Marie-Claude Morice

TCT2013

PCR london valves

European Cardiovascular Research Center

visit our app

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CERC map & sites of council members

France - Germany - Israël - Italy - Latvia - New Zealand

Spain - Switzerland - United Kingdom