PRAETORIAN
S-ICD vs TV-ICD

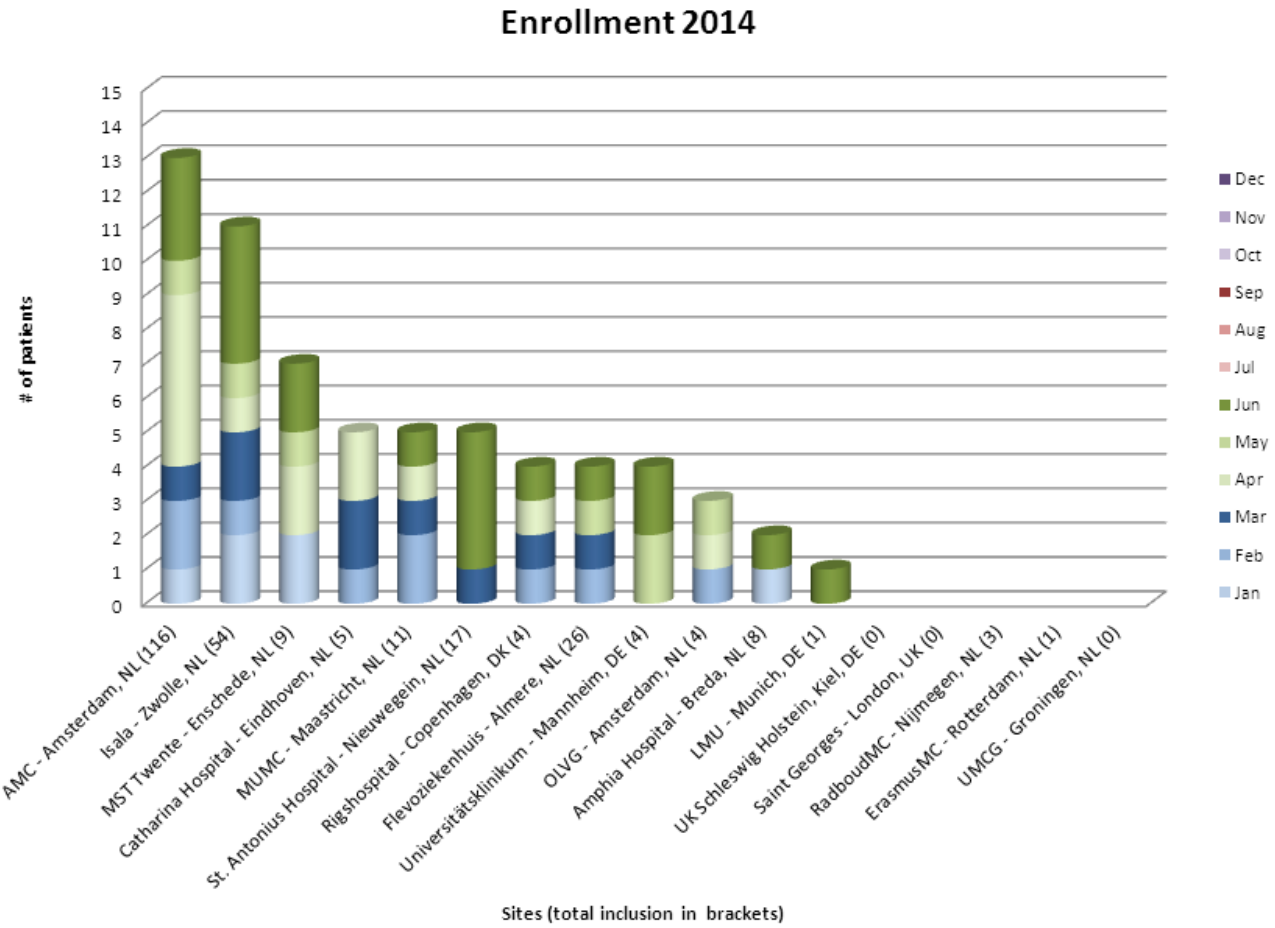
Newsletter d.d. 30 June 2014

In this newsletter

Last June 23, the Steering Committee has held a teleconference during which several topics were discussed. One of these issues involved the addition of two exclusion criteria, namely previous ICD implant and the presence or expected need for a cardiac contractility modulator. Please read more about this in this newsletter. Furthermore, a summary of the Investigator Meeting at HRS can be found in this newsletter.

Enrollment

At this moment 263 patients are enrolled. An overview of enrollments in 2014 can be found below. The total number of enrollments per site is shown in brackets. We would like to thank all participating centers for their enrollments.



Enrollment 250th patient

The 250th patient was enrolled by the Flevoziekenhuis in Almere. Congratulations!

Initiation new Praetorian sites

On May 22, 2014 the University Hospital in Mannheim, Germany was initiated. PI here is Dr. Jürgen Kuschyk. Currently already 4 patients are enrolled at this site! On June 26, 2014 the University Hospital Schleswig Holstein in Kiel, Germany, with Prof. Dr. Hendrik Bonnemeier as PI, was initiated. Initiation in the Heart and Chest Hospital in Liverpool, is scheduled for July 1st, 2014. PI will be Dr. Jay Wright. Also initiation visits in the Heart Centre in Leipzig, Germany and Queen Elizabeth Hospital, Birmingham UK are currently being scheduled.

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Expansion to the US

We are very excited to announce that Boston Scientific has granted us budget to expand the Praetorian Trial to the US. Following an Investigator meeting for US physicians at HRS, nine sites have indicated their wish to participate. Dr. Suneet Mittal from The Valley Hospital, NY/NJ has agreed to act as national coordinator for the Praetorian Trial in the US.

Introduction Tom Brouwer

This June, Tom Brouwer, MD has started as coordinating research physician of the Praetorian Trial. He will take over the daily Praetorian activities of Louise Olde Nordkamp, as she will start her residency soon. Louise Olde Nordkamp will remain co-PI of the study and member of the Steering Committee.

Additional exclusion criteria

The following exclusion criteria are added to the current criteria.

- *Previous ICD implant.* Only first implant patients can be included in the trial. Therefore, also patients who have had a complete removal of a previous system are excluded. If second implant patients are already enrolled, they can continue participation, but a comment must be added to the eCRF.
- *The presence or expected indication of a cardiac contractility modulator (CCM).* As treatment with a CCM involves transvenous leads, patients who currently have, or are expected to need a CCM are excluded from the trial. Patients who are already enrolled and develop an indication for CCM treatment during the trial can be treated, without discontinuation of participation in the trial.

New variables in eCRF:

During the execution of the trial, it turned out that it may be necessary to add some extra variables to the eCRF as this may give more insight in the treatment patients received. As it would be preferred that these data will be entered retrospectively for currently enrolled patients as well, the steering committee discussed which variables would give sufficient scientific benefit considering the extra work load. It was decided to add variables regarding baseline characteristics, the (change of) settings, rhythm prior to an arrhythmia episode and the end of study. When these changes are implemented, this will be communicated further.

Experience with S-ICD prior to participation

A growing number of physicians is enthusiastic to participate with Praetorian. Amongst them are physicians who are just starting to build experience with the S-ICD. It is discussed with the steering committee that, although the enthusiasm is appreciated, a minimum of 10 S-ICD implants is absolutely required to participate in the trial. Since the primary endpoint is the composite of inappropriate shocks and ICD-related complications, it should be avoided to include the learning curve of individual physicians in the trial.

FAQ eCRF

During the conduct of the trial, we learned there were some uncertainties about how to enter some data in the eCRF. We have therefore made a FAQ for the Praetorian eCRF. This FAQ is added to the eCRF user manual which can be found at the Praetorian site (www.praetorian-trial.org, clinical links). Moreover, the FAQ is sent along with this newsletter.

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Investigator Meeting, 8 May 2014, San Francisco, USA

At HRS in San Francisco an Investigator meeting was held. During this meeting an update on the current status as well as some practical aspects of the conduct of the trial was given. The meeting was held in a family-style restaurant, which created a very informal atmosphere. We hope all attendees look back at a nice meeting; we certainly do! We would like to thank all attendees for their presence and helping to make this meeting a success.

During this meeting several issues were discussed: The interest for the S-ICD and the Praetorian Trial is massively increasing. The number of publications on the S-ICD is growing, and the publication of the trial design has been cited 20 times as of now. Furthermore, the first data of the S-ICD registry Effortless were recently published, such that the results of a randomized trial is the next information that people are now looking for. Therefore, the time to enroll in Praetorian is now!

Praetorian Expansion

Last year at HRS was the Kick off meeting of the expansion of Praetorian in Europe. Since then, the sites of the national coordinators in Denmark, UK and Germany were opened *(NB. current status of site opening can be found in this newsletter)*. Also multiple sites are almost ready to open. Moreover, 4 extra sites in the Netherlands started enrollment.

Next to the expansion in Europe, Boston Scientific has granted budget for expansion of the Praetorian Trial to the US. Ten sites in the US were invited to participate in the Trial. Prior to the Investigator meeting, a US Investigator meeting was held, in which the background, rationale and design of the trial was explained. All investigators showed great enthusiasm, and it was therefore a very positive meeting. Several hurdles need to be taken before the trial can start in the US, but we hope to be able to work these out and create a nice enrollment in the US as well.

Praetorian vs Effortless

Now that the first Effortless data are published, the interest is shifting towards Praetorian. As there are several centers that are enrolling in both Praetorian and Effortless, we hope these centers will first consider a patient for participation in Praetorian. Enrollment in Effortless can be considered if the patient does not meet Praetorian criteria. In the Academic Medical Center Amsterdam this strategy is resulting in proper enrollment in both studies.

Study Counselling

It can sometimes be difficult to counsel patients on this study. It is our experience, that it is best to keep the study counselling simple and to explain that we do not know which device is best for the patient, and that this is the reason we perform the study. Also it appears important to explain that benefits of the S-ICD may be expected, but are not yet proven.

End of study

If a patient wants to stop participation If a patient want to stop the participation in the trial, it is important to talk with the patient to ask why (s)he wants to quit. Specifically since the study creates no burden to the patient, there may be another issue which can be solved. If a patient insist on quitting, the data that are collected so far will remain in the database.

Please note that in this case the patient has decided to quit follow-up, but has NOT withdrawn consent. In the eCRF a specific option will be made on the End of Study form. All efforts should be made to prevent the complete withdrawal of consent. As the latter would require the removal of all collected data from the database, this would severely harm the study.

Death of participant As already mentioned in the previous newsletter, it is very important to obtain read-outs of the ICD if a patient has died. Read outs of the ICD after death may reveal arrhythmia episodes between the last follow up and death. Moreover, it can shed light on the cause of death. If a patient has died because of an untreated or not-successful treated arrhythmia episode, this is very important for the trial. Therefore maximal efforts must be made to obtain a final read-out the ICD.

During the meeting it turned out that there are different rules about ICD retrieval after death. In the Netherlands, the ICD is always removed after death. In that case the family or the morgue can be called to localize the ICD. In other countries, this is not standard practice. For these countries, it is extra important to inform all medical staff about the participation of the patient in trial. The staff as well as the participant's relatives should be aware to contact the site immediately if a patient has passed away. Representatives of the device manufacturer or the Praetorian Trial Bureau may be contacted to help to obtain this final read out.

Announcements of the Steering Committee

In the previous Investigator Meeting in January 2014, several topics were discussed, for which follow up action of the steering committee was required.

The following announcements were made during the Investigator Meeting at HRS:

- Our biostatistician, Prof. J.G.P. Tijssen has checked the current event rate, and based on this he has decided that at this moment no adjustment of the sample size is required.
- A request was made to create a more international DSMB and CEC. The search for new CEC members is ongoing. It is planned to invite three international members. The DSMB is expanded; Dr. Bruce Wilkoff and Dr. Johannes Sperzel have kindly accepted the invitation to take place in the DSMB.
- The publication policy, as was agreed upon in the latest investigator meeting, is presented, and attached to this newsletter.

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