

Volume 6

December 2010



AUSTRALASIAN
**KIDNEY
TRIALS
NETWORK**

AUSTRALASIAN KIDNEY TRIALS NETWORK

FAVOURED Newsletter

Have a Happy Festive Season

from FAVOURED Study

2010 has again been a very busy year for the FAVOURED Study with 2011 looking even busier.

All members of the Trial Management Committee and myself would like to thank everybody involved in the study, including all staff involved in the study at sites, the representatives from Abbott and Bayer for their assistance with organising the study medication and everybody involved in the introduction of the study at our new overseas sites in Malaysia and the United Kingdom.

I hope that everybody has a Joyous Christmas and an Abundant New Year.

Cheers

FAVOURED Project Officer

Peta-Anne Paul-Brent



New Version of Study Protocol – V9



One of major focuses of the latter part of 2010 has been the development and release of Version 9 of the Study Protocol.

It has been an incredibly complex and intense process requiring a huge amount of time and energy from everybody involved. Thanks to everyone for their hard work and good cheer throughout this long process.

Included within this newsletter is further information about the various aspects of the new protocol and what these changes mean to progress of the study.



Inside this issue:

Protocol Change—Aspirin	2	Questions from Sites	4
Protocol Change—Outcome Measures	2	Monitoring	4
ANZ Site Status	3	Fishy Laws	4
Other changes to study	3		

Key Change to Protocol - Inclusion of Patients taking Aspirin

One of the major changes introduced in Version 9 of the Protocol was the inclusion of patients taking open-label aspirin. There are a number of reasons for this change including:



Recruitment Rate

From the enrolment of the first patient in August 2008, patient recruitment for the study has been much lower than expected. As of June 2010, 154 patients were randomised to the study which was a recruitment rate of about one-ninth of expected. Analysis of screening logs showed that there was a high rate of screening failure. Out of 1,619 patients screened, 1,180 (73%) were excluded with the most common cause of exclusion from the trial being aspirin in 37% patients.

With the inclusion of these open-label aspirin patients, enrolment rates should increase signifi-

Patient Population

An analysis of the baseline characteristics of the enrolled patients showed that the study population was relatively young and healthy, with a mean age of 55 years and an ischaemic heart disease rate of only 4%. This current study cohort is not representative of contemporary renal population and this disparity is attributed to the exclusion of patients taking aspirin i.e. patients

more likely to be older with higher rates of significant cardiovascular disease.

Opening the study to open-label aspirin taking patients will significantly increase the possibility that the results will have wide applicability to the general renal population.

Event Rate

An analysis of rate of failure of Primary Patency at 12 weeks (primary outcome) was found the rate to be much lower than expected (5% instead of 25%). This can largely be explained by the fact that the study cohort is relatively young and healthy compared with the general renal population. This analysis was performed with only a small number of participants so it may be premature to conclude the study would be under powered. However, if this trend were to continue and study was under-powered due to low event rates, the study would require a much larger number of patients than anticipated 1200.

Studies have shown that patients taking aspirin are more likely to experience vascular events, possibly due to their increased age and cardiovascular burden. Thus the inclusion of these patients should increase the vascular event rates and in turn improve study power.

Key Change to Protocol - New Outcome Measures

In 2008, the results of a study examining the effect of the anti-platelet agent Clopidogrel on early thrombosis in AVF were published. This study found that, although Clopidogrel reduced the rate of early thrombosis in new AVF, the ability to actually use the access for haemodialysis was not improved. This demonstrated that the rate of thrombosis (which in the case of the FAVOURED is reported as primary patency) was not a valid surrogate for usability of AV fistula.

With this conclusion the Trial Management Committee went back to basics and considered what the renal community would most like to learn from this study. After much thought and discussion, the new primary outcome AVF Access Failure was decided upon.

AVF Access Failure is a combination of the following questions assessed up to 12 months after surgery:

- Did the patient's AVF have a clot or require any intervention to remove a clot?
- Was the patient's AVF abandoned (never to be used again)?
- Was the patient able to use the AVF during at least 8 out of the first 12 HD sessions after the Week 12 visit?

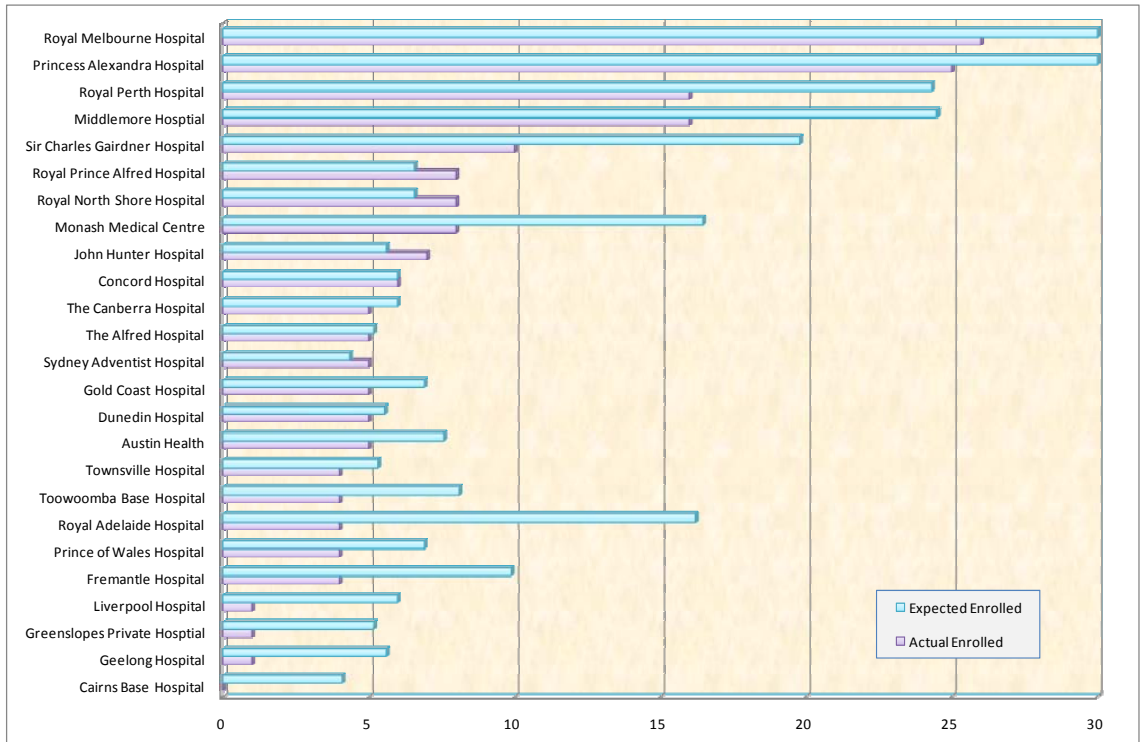
Along with the revision of the primary outcome, the secondary and tertiary outcomes were also reviewed. All of the previous outcomes have been retained, with the addition of a number of outcomes relating to the use of Central Venous Catheters (CVC) at various times during the 12 months after surgery. These outcomes were considered important to add because of the significant increase in risk to patients of infection, thrombosis and death associated with CVC use.

Australian and New Zealand Site Status

We now have 25 sites actively recruiting; 24 of those which have enrolled at least one patient. We have two new sites, Western and Royal Darwin Hospitals, undergoing ethical approval. The total number of patients enrolled is 183.

Royal Melbourne and Princess Alexandra Hospitals still have the highest number of patients enrolled, with 26 and 25 patients respectively. Special mention also goes to Middlemore Hospital with the highest rate of recruitment at over 1 patient recruited per month.

Concord, John Hunter, Royal North Shore, Royal Prince Alfred and Sydney Adventist Hospitals have the best percentage of what they expected with all sites at over 100% recruitment.



Other Changes to Study with New Protocol

There have been some lead on adjustments to the study as a consequence of the Protocol Changes, including:

Enrolment Target

The protocol amendments are likely to have an important effect of on the sample size calculation for the study.

A brief review of the event rate in the current study population of the new primary outcome of AVF Access Failure was estimated of 30%. Using this rate to calculate the new sample size, the Enrolment target has been reduced from 1200 patients to 954 patients.

When considered in combination with the inclusion of aspirin patients, with their tendency to be a older and sicker population, the event rate of 30% is considered to be quite conservative. This means that the enrolment target may drop further with event rate of 40% needing 634 patients and 50% needing only 442.

This will also have a significant effect on the timeline for the study with current estimate of December 2012 for the end of recruitment.

Flexetrial - Randomisation System

The major change to Flexetrial will be the ability to randomise patients taking open label aspirin to fish oil or placebo only. The changes required to the system are currently underway and should be made available when the fish oil-only medication packs are available to sites.



InForm - Electronic Case Report Forms

With the revision of the outcome measures, the data being collected has also needed to be reevaluated. The key additional information will include the use of Central Venous Catheters, date and reason for AVF Abandonments and the details of the first 12 HD sessions after the Week 12 visit.



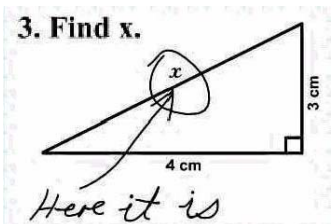
Questions from Sites

Q: The current study medication has expired, When will we receive new packs?

A: Due to a delay to aspirin delivery, we will not have any medication packs containing aspirin until end of January. We are however currently packing the fish oil only medication packs which should be ready to delivery to sites in the New Year. We are advising sites to submit the new protocol for ethical approval at the next available submission date and once received, sites will be able to start recruiting aspirin taking patients.

Q: How are Monitoring Visits scheduled?

A: All sites are monitored at least annually. The frequency of the visit may be increased based on a number of factors including the number of patient recruited at a site, the rate of staff turnover and whether that staff is experienced with clinical trials and the location of the site (for example, it is easier to perform frequent visit to Princess Alexandra Hospital than it is to Royal Perth Hospital). Sites can also request a monitoring visit if the site has a specific issue to address i.e. a new study coordinator coming on board.



For Further Information :

Peta-Anne Paul-Brent
FAVOURÉD Project Officer

Australasian Kidney Trials Network
School of Medicine Health, University of Queensland
Ground Level, Building 33,
Princess Alexandra Hospital
Ipswich Rd, Woolloongabba QLD 4102,

Phone: +61 7 3176 5817
Fax: +61 7 3176 5112
E-mail: p.kerr@uq.edu.au

Monitoring

All sites with patients have now had at least one monitoring visit. There have been 33 visits to sites over the last 12 months to a total of 24 sites.

There have been no major issues that have arisen during monitoring with all sites having done a great job. For remaining sites, monitoring will be organised as soon as sites have recruited one or two patients.

There are plans to organise a series of meetings for site coordinators to act as an introduction to V9 of the Protocol with associated amendments to the electronic systems. These meetings will be scheduled for the New Year.



Fishy Laws

Did you know...

In **California** it is a misdemeanor to shoot at any kind of game from a moving vehicle, unless your target is a whale.

Idaho residents cannot fish from a giraffe's or camel's back.

It is illegal in **Ohio** to get a fish drunk.

In **Oklahoma** and **Seattle, Washington** it is illegal to carry a fishbowl or aquarium onto a public bus because the sound of the splashing water may disturb other passengers.

It is illegal to catch a fish in **Kansas** with your bare hands.

You may not catch a fish in **Pennsylvania** with any body part except your mouth. Also dynamite cannot be used to catch fish.

Tennessee law says it is illegal to catch fish by lasso.

In **Muncie, Indiana** it's a crime to carry fishing tackle into a cemetery.

It is illegal in **Vermont** to whistle underwater.

In **Liverpool, England**, it is illegal for a woman to be topless in public except as a clerk in a tropical fish store.

Montana wins the prize in my opinion for stupid laws. It's illegal for married women to go fishing alone on Sundays, and illegal for unmarried women to fish alone at all. It is also against the law for a man to knit during fishing season. This one is not fish related but definitely worth a mention... It is illegal to have a sheep in the cab of your truck without a chaperone.

