

ADVANCE *Affaires*

Issue 26 | October 2006

Welcome to the 26th edition of ADVANCE Affaires!

Firstly we would like to thank each and every one of you, as the integral part of the ADVANCE Study, for your dedication, enthusiasm and ongoing efforts with the study and patient care.

DATA BLITZ!

As you are aware we will be closing out the Blood Pressure arm of the ADVANCE Study by June 2007 and the Glucose arm by December 2007. In order to achieve these significant study milestones we have scheduled an interim data base lock for all study visit data up to and inclusive of L42 and for all primary outcome events reported up to and inclusive of the 1st October 2006.

What the database lock means is that all the above-mentioned data must be completed with all queries resolved, and submitted to the ICC by close of business on the 1st of December 2006.

To facilitate the 'interim data base lock' timeline you will need to fully focus on and prioritise the completion and resolution of the following issues up to L42 and Form X;

- 'Missing' forms from overdue forms list
- 'Event' documentation for primary outcomes
- Outstanding queries
- Rejected queries
- Vital status of all patients who are not attending study visits

A big thank you for your assistance with helping us achieve what we know will be a successful study!

STUDY EXTENSION – ETHICS APPROVAL AND PATIENT CONSENT

All sites should follow up with their ethics committees if ethics approval for the study extension has not been received. There are still outstanding study extension contracts. Please sign and return these to the ICC as soon as possible, along with the signed

protocol signature page. If you have any questions regarding the study extension or contract amendments, please contact your study monitor.

All patients should be re-consented for the study extension.

In the situation where a patient no longer wishes to attend study visits, written consent should be obtained detailing what level of contact the patient is happy to have with the LCC. Eg. Does the patient consent to be contacted by phone and/or does the patient consent to having the family doctor contacted to obtain information? The vital status of every patient randomised to the study is required. If a patient cannot physically attend the clinic, please mail a consent form to the patient and document that this has occurred.

KEY STUDY MILESTONES

Interim database lock for all forms up to and including L42 and Form X	1 December 2006
Final M48 visit conducted	31 December 2006
Final BP visit conducted	30 April 2007
ADREM final visit conducted (must occur before optional take-up of open label perindopril-indapamide)	30 April 2007
Echocardiography final visit conducted (must occur before optional take-up of open label perindopril-indapamide)	30 April 2007
BP database lock	1 June 2007
Presentation of BP results to investigators and coordinators	September 2007
Presentation of BP results at European Society of Cardiology Meeting	September 2007
Final glucose visit conducted	31 December 2007



ENDPOINT TIMELINES – INTERIM DATA BASE LOCK

As you are all well aware, endpoints comprise the key efficacy measure of the entire study. As such, it is imperative that all primary outcomes encountered by patients, are included in the analysis. All primary outcomes should be entered on a Form X as soon as you become aware of the event and appropriate documentation sent to the ICC within 1 month. In 2007 as we get closer to the close out of the study, documentation will need to be sent to the ICC within 2 weeks of the LCC becoming aware of an event.

In preparation for the interim database lock, all documentation for primary outcomes reported up until 1st October 2006 should be sent to the ICC by 1st December 2006. All queries on Form X's associated with these primary outcomes should also be resolved before this time. Documents requiring translation are due at the ICC by 1st November.

TIPS FOR IMPROVING ENDPOINT TIMELINES

General

- If no further documentation is available for an event, the investigator should confirm this in a file note. The file note should include a summary of what information is known, as well as the steps that have been taken to obtain further information.
- A formal admission or discharge summary is not always required to adjudicate events as long as there are clinical notes that outline the necessary information.

Death

- If a death has occurred, please remember that both the proximate and underlying causes of death need to be specified on a form X. If you are unsure of either the proximate or underlying cause, please enter "unknown".
- If a death has occurred, a death certificate alone is not sufficient documentation for adjudication. Please also provide any available clinical notes, a summary of the symptoms leading up to the death (even from family or GP), an autopsy report if available, or any other relevant documentation that supports the diagnoses of the proximate and underlying causes of death. If a patient dies at home, please send information about past medical history as well as information about the patient's health in the days leading up to their death.

Myocardial Infarction

- To adjudicate a MI, a description of the clinical symptoms, ECG and cardiac enzyme results (Troponin, CK or CKMB) are needed. An autopsy report of MI is also sufficient.

Stroke

- To adjudicate a stroke, it is very important to have a description of the presenting clinical symptoms. In particular, whether these symptoms lasted longer than 24 hours or not (to differentiate between a Transient Ischaemic Attack). CT or MRI results are also needed. An autopsy report is also sufficient.

Eye Outcomes

- To adjudicate proliferative retinopathy, please ensure documents specify "proliferative" retinopathy or the stage of the retinopathy (e.g. Stage 1-6) so it can be coded accurately. Background (non-proliferative) retinopathy is not a primary outcome for the study. All cases of the development of vitreous haemorrhage and macular oedema since baseline should be reported on Form X.
- To adjudicate the primary outcome 'diabetes related blindness' we must have the visual acuity and information from the Ophthalmologist about the cause of blindness. E.g. Fundoscopic examination results.

Renal Outcomes

- All events where by the patient develops macroalbuminuria (>33.9mg/mmol or >300µg/mg confirmed by 2 positive results) during the study follow up period should be reported on a Form X. If the patient had already developed macroalbuminuria at the 2 yr visit (and this has been reported on Form X), then it does not need to be reported on a Form X again at the 4 yr visit.
- The confirmatory test for macroalbuminuria or microalbuminuria should be done within 2 weeks of the first positive test. If the 2nd test (confirmatory) is negative, then a third test should be done.
- The date of event for macroalbuminuria on Form X should be the date of the 1st high positive result.
- Microalbuminuria is a secondary outcome. It does not need to be reported on a Form X (unless the patient was hospitalized for >24 hours in relation to this).
- To adjudicate the primary outcome 'doubling of serum creatinine (to a value of at least 200µmol/l, 0.2mmol/l or 2.26mg/dl), the result must have doubled and be at least to the values described here.

ALBUMIN: CREATININE RATIO – QUERY RESOLUTION FUNCTION

As you are well aware, if the A:C ratio result is not available at the time of entering the CRF, a query will be raised against that question on the CRF. The missing A:C ratio ends up on the query resolution page. The A:C field on the query resolution page is automatically set to mg/mg and so the result is automatically stored in the unit of mg/mg. To ensure that the A:C value is entered with the correct unit of measurement, it is recommended that you enter the A:C ratio directly onto the CRF. That is, you need to go into the CRF to enter the A:C ratio in either the mg/mg field or the mg/mmol field.

UPCOMING REGIONAL MEETINGS

The following regional meetings are scheduled:

- ▶ Continental Europe: 24th October- Budapest, 26th October - Warsaw, 27th October - Bratislava, 30th October – Paris, 8th November Amsterdam
- ▶ Northern Europe: 10th November – London
- ▶ ANZ/SEA: 24th November– Melbourne
- ▶ Canada: 12th November – Montreal
- ▶ China: January 2007 – Shandong Province

The focus of these meetings will be the BP close out, endpoints, data quality and improving glucose control.

Please note that it is a contractual requirement to send at least one LCC representative to the regional meeting.

GLUCOSE CONTROL INITIATIVES

Sue Quirk started working on the ADVANCE study in April this year as a diabetes nurse educator and is very enthusiastically supporting the Australian and New Zealand sites to improve glucose control in their intensive group patients. Sue has the following suggestions for initiatives for the new glucose contracts distributed in September.



GLUCOSE INITIATIVE IDEAS

By Sue Quirk, Diabetes Nurse Educator ANZ

As everyone knows, additional funding was made available for centres to use specifically to improve glucose control in the Intensive group patients. Throughout the past few months I have been visiting centres and one of the most commonly asked questions has been “How can we use our funding?” In answer to this I have listed below some suggestions for ways in which to use your funding to assist your patients to achieve optimal glucose control. Please let me know if you can add to my list:

- ▶ Additional visits – it is essential to maintain regular contact with all intensive group patients, in particular those above target HbA1c. Aim to perform an additional visit every month for patients above target.
- ▶ Medications – to support triple oral therapy and insulin use
- ▶ Appointments to external dieticians and diabetes educators
- ▶ Appointments to external physiotherapists or exercise physiologists
- ▶ Reimbursement of travel costs (if patient is unable to attend due to finances)
- ▶ Weight loss program enrolment and meeting fees
- ▶ Gym memberships
- ▶ Community exercise program enrolment fees
- ▶ Pedometers and exercise videos etc.
- ▶ Group outing that incorporates exercise i.e city walking tours
- ▶ Activities organised by some diabetes associations such as supermarket shopping tours
- ▶ Cookbooks, i.e. low G.I, low fat , shopping guides, carbohydrate counters etc.
- ▶ Educational resource materials, i.e cds, videos, books etc.

This list is limited only by your imagination! I encourage you to discuss your ideas with any member of the glucose control team and with your monitor.

REMEMBER MOTIVATION IS THE KEY TO SUCCESS!