



THE IST-3 TIMES

April 2011



RECRUITMENT AT 7th April 2011

NUMBER OF PATIENTS RECRUITED

UK	1314
Poland	341
Italy	303
Sweden	270
Norway	196
Australia	176
Belgium	73
Portugal	71
Austria	41
Switzerland	20
Canada	8
Mexico	3

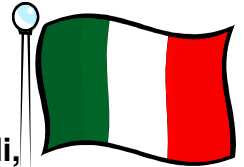
TOTAL NUMBER OF PATIENTS RECRUITED

2816

**ONLY
3 MONTHS LEFT
TO RECRUIT!**



GUEST EDITORIAL



Guest Editorial by the IST-3 National co-ordinator for Italy, Dr Stefano Ricci and colleagues: **Silvia Cenciarelli, Tatiana Mazzoli, Laura Maria Greco, Elisabetta Gallinella, Alessia Mattioni, Chiara Menichetti, Rosaria Conduro**

“With the pessimism of reason and the optimism of will” (Antonio Gramsci, 1891-1937)

As at the end of a long journey, thoughts concerning our work are coming over more than ever. During these years we have strongly defended our ideas and our work against “foreign” attacks. We have always done it with the same enthusiasm and with a strong belief in our ‘cause’, being conscious and proud to be the actors in a great and unforgettable play.

At the very beginning, we had been considered to be “against progress” in the worst case, or “the usual exaggerated critics” in the best, because we were not satisfied by the available data on rtPA, and tried to show something better if it existed. Today, thanks to the work of all the IST 3 groups (including the constant updating of the Cochrane review and its diffusion in all the meetings we had the chance to make presentations at); our forthcoming results are waited with interest even by those who were strongly against us when the trial started.

As a scenario will open on the stage, we are going to show answers on the main questions about acute treatment of ischaemic stroke:

- First of all, we are going to give an answer about what to do in patients older than 80: a great improvement in clinical practice if you consider that these are the largest proportion of stroke patients.
- We are going to know how to deal with patients within 3 hours who do not exactly meet the current licensed indication for treatment and with patients between 3 and 6 hours: we know rt-PA has a track record in an “effective but not useful” time window and we need to know if it is possible to extend the number of patients who can benefit from thrombolysis.
- We are going to know what to do with different severity of stroke and if there is a particular kind of stroke that will get the best from thrombolysis.
- We are going to know what it means to have subtle, early change on CT: it will provide uniquely useful data on the impact of clinical and CT findings on response to rt-PA.

Our trial will help to address a ‘real world’ intervention and will therefore make a huge contribution to the world evidence base. It is going to change our behaviour in front of a stroke patient and the treatment choice will be established by guidelines on the basis of that evidence. This will reduce inequalities in patient access to treatment in routine practice.

Editorial continued;

We think everyone of us involved in the trial should be aware of the importance of his or her work. Everyone should therefore make every effort to recruit all eligible patients to achieve our target of 3,100 subjects. It is important to keep randomising to make it all worthwhile. There are only 84 days and 284 patients to go before 30th June. Even if we cannot reach 3,100, what we are going to add to the whole randomised evidence will strongly increase the power of the Cochrane review, and we could heavily rely on it for future decisions.

In Italy, all active centres are doing their best. Recruitment has increased during the last year and new centres have come into the trial. At the beginning, IST 3 involved only few centres, but the enthusiasm of those got other centres participating in the trial. So now we have 21 centres for a number of 303 patients. We are really satisfied with the job. The enthusiasm of Italy was our first goal but still we are continuing in the last rush to reach the finishing line.

In the new Stroke Units of Città di Castello and Branca the enthusiasm is alive because we know the importance of what we are doing and we have realized in every day clinical practice how many stroke patients would miss thrombolysis if we had not the possibility to randomise in the trial. These patients are the grey area about which we want to know more. Benefit in Italy will be even more because at the moment many of us still don't have the permission for treatment within 4.5 hours from the Health Authorities.

This sentence (guess who wrote it!) actually applies to our situation. "Philosophers have hitherto only interpreted the world in different ways, now we have to change it". And this applies to stroke doctors as well.



IST-3 Team at Ospedale Citta di Castello



**Dr.ssa Laura Greco e Tatiana Mazzoli,
Stroke Unit Gubbio e Gualdo Hospital**

Thank you to the following Italian Centres who have randomised into IST-3: A.O. Niguarda Ca' Granda, Milano; S.C. Neurologia Universitaria, Azienda Ospedaliero, Foggia; Clinica Dr Pederzoli Spa, Peschiera sul Garda; Mater Salutis Hospital, Legnago; Nuovo Ospedale Civile, Modena; Ospedale Beato Giacomo Villa, Citta Della Pieve; Ospedale Civile San Matteo Degli Infermi, Spoleto; Ospedale Civile S.Andrea, La Spezia; Ospedale di Branca, Gubbio; Ospedale Guglielmo da Saliceto, Piacenza; Ospedale Maggiore, Bologna; Ospedale Regionale della Valle d'Aosta, Aosta; Ospedale S.Giovanni Battista, Foligno; Ospedale Sacro Cuore, Negrar; Ospedale Silvestrini, Perugia; Ospedale Valduce di Como, Como; Ospedale Citta di Castello, Citta; Ospedale a Vibo Valentia, Vibo Valentia; Ospedale di Cattinara, Trieste; R.Guzzardi Hospital, Vittoria; Universita degli Studi di Genova, Genova

Plans for the Closeout of IST-3 Centres

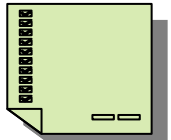
Once recruitment in the Trial closes on the 30th June 2011 centres will be closed down. This process will start in your centre only after all of the data, queries and scans have been collected. Whether you have recruited or not, you will be required to follow a Sponsor approved procedure to close down your centre in accordance with regulatory requirements. It will be the responsibility of each Principal Investigator to ensure that all the patient related data, regulatory and trial correspondence and patient records in their centre are archived appropriately.

Our Sponsors have agreed that we can close down IST-3 centres without visiting each site. However, if we identify problems in a centre we may need to arrange a monitoring visit. We are in the process of finalising the details of the process with our Sponsor.

As soon as the procedure has been agreed, we would like to begin to close some of our inactive centres before the 30th June 2011. Alison will co-ordinate this process and will contact all of the centres that have already informed us that they can no longer participate in the trial. Alison will then contact the centres that have not recruited in the past 6 months to request an update on their current position and, following agreement with the Principal Investigator, will then close those centres. All other centres will be closed after 30th June 2011.



Timelines for Data and Scans: An appeal for your help!



All of the team at the trial co-ordinating centre are very busy cleaning up the data we have received so far. If recruitment is maintained, we may well reach our target of 3100 or be very close to it, which is an excellent achievement. However, we still have a lot of data and scans to process and clean before the database can be locked and the analysis can begin.

We must receive all the patient data and brain images, process them and make sure the data is clean by the end of August 2011. Therefore it is vitally important that we receive the data from you as soon as possible after randomisation (ideally within two weeks of the randomisation) to ensure that we achieve this target.

If we don't meet our target, this will affect the ongoing clean up and analysis of the data which may jeopardise the plan to announce the all important final results prior to the European Stroke Conference in May 2012.

If you have received requests for outstanding data, scans or queries about data please, please send these without delay! If you are unsure if you have anything outstanding, or have any problems providing the data or images, please contact us as soon as possible to discuss this. From now until the end of recruitment please complete and send the data and images for any new patients within two weeks of randomisation. The data we need to receive for each patient is: Patient Treatment & Monitoring Record; Hospital Treatment Follow-up Form (to be completed at 7 days, discharge or death, whichever occurs first; Pre and Post randomisation scans and any additional scans confirming a cerebral event within 7 days; Scan Transfer Forms for each scan sent.

Thank you

AN INVITATION TO ALL IST-3 COLLABORATORS ATTENDING THE ESC IN HAMBURG

If you are attending the ESC Hamburg you are invited to join us for the

IST-3 and ENOS Collaborators Meeting

On

Wednesday 25th May 2011

At

18.00 – 19.00 Meeting

19.00 – 20.00 Drinks & Canapés

In

Room 7, Congress Centre Hamburg



**ENOS will start off the meeting at 18.00 followed by IST-3 at 18.30.
The meeting will be followed by drinks and canapés for all.**

**We expect this to be a busy meeting, so please book your place
by emailing Karen Innes at karen.innes@ed.ac.uk**

We look forward to seeing you there.

FIRST RANDOMISATIONS

Our thanks and congratulations go to the following centres on randomising their first patient to the Trial:

- Dr Giles Durward and the Team at Southampton General Hospital, Southampton, UK
- Dr Rajesh Saksena and the Team at Colchester Hospital University Foundation Trust, Colchester, UK

Special congratulations go to Dr Vera Cvoro and the Team at Victoria Hospital, Kirkcaldy, UK. The Team at this centre successfully randomised their first patient into the Trial **3 days** after receiving their manual! **Well Done!**



NEW CENTRES

Our thanks and congratulations go to the following centres for all their hard work in getting through the start-up procedures and are now ready to start randomising:

- Dr Johan Sanner and the Team at Karlstad Central Hospital, Karlstad, Sweden
- Dr Vera Cvoro and the Team at Victoria Hospital, Kirkcaldy, UK
- Professor Andreas Luft and the Team at Universitätsspital Zürich, Switzerland
- Dr Claudio Gobbi and the Team at Ospedale Civico, Lugano, Switzerland

Informed Consent Options in the UK

Following several recent issues that have arisen with the consent process in the UK, we would like to clarify the types of informed consent approved for use in the UK for the trial:

Only the patient or their personal legal representative (e.g. a relative) can give consent for IST-3. In England, the Clinical Trials Regulations state that 'A professional legal representative (PrLR) may be approached if no suitable personal legal representative is available' The regulations define a PrLR as 'A person not connected with the conduct of the trial who is: (a) The doctor primarily responsible for the adults' medical treatment, or, (b) A person nominated by the relevant health care provider (e.g. an acute NHS Trust or Health Board)'.

Section 1 of The NHS R & D Research Governance Working Group guidance document (v2 November 2008) on who can be identified as a PrLR, clarifies that in most cases the Principal Investigator is also the doctor primarily responsible for the adult's medical treatment and would therefore **not** be suitable to act as the PrLR.

We would also like to clarify that we do not have ethics approval in the UK to cover consent in an 'emergency situation' (formerly known as waiver of consent).

You must ensure that informed consent has been obtained and the consent form completed and signed before you randomise a patient. Never assume consent has been obtained until you have the written confirmation. Careful documentation of the consent process must also be made in the patients medical records. Only persons trained in consent procedures, hold a current GCP certificate and have been delegated this responsibility by the Principal Investigator (and recorded on the Delegation Log) can obtain consent. Inability to obtain fully informed consent or provide documentation of the consent process is a protocol violation and requires expedited reporting to the trial Sponsors.

If you have recently added new research staff to the team, please ensure that they have an update in the trial protocol particularly trial consent procedures and regulations for the last 3 months of recruitment. We would like to maintain the high standards of ethical conduct for the trial that you have all achieved so far.