PISTE
PRAGMATIC ISCHAEMIC STROKE THROMBECTOMY EVALUATION

PISTE NEWSLETTER

September 2014, Issue 02

PISTE is a prospective, randomised controlled multicentre parallel group trial comparing IV rtPA alone with IV rtPA and adjunctive mechanical thrombectomy in patients eligible for treatment with IV rtPA and who have a large vessel carotid territory arterial occlusion. Any approved device can be used. The trial uses a PROBE (Prospective Randomised Open Blinded End-point) design.

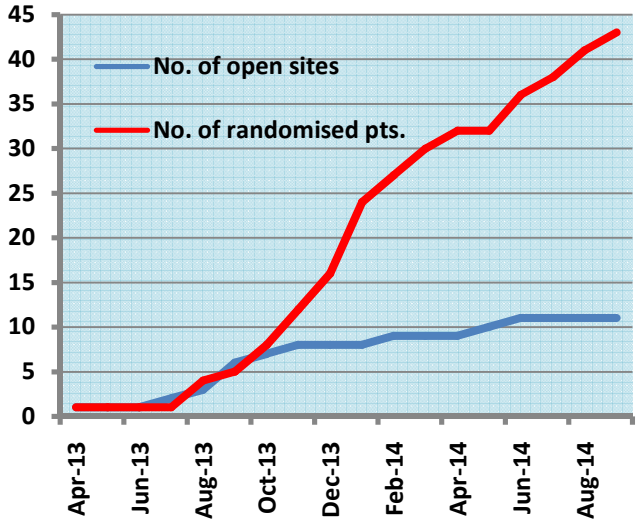
Dear PISTE colleagues,

Hello and welcome to the second edition of the PISTE trial newsletter. Its been a successful & busy period since the last edition, with multiple updates to the study. This important edition of the newsletter aims to provide you with essential guidance on running the trial.

Study status

Thank you for your hard work and support for the PISTE trial. At present we have 11 sites open to recruitment, and these sites have enrolled 43 patients to date.

Additional sites have been contacted regarding participation on the PISTE trial. These sites are collating the information required for the site qualification phase. We hope to be in a position to open these sites soon.



Important announcement

New study documents are live:
Protocol v1.5, 1st September 2014 & study workbook v3.0, 4th September 2014
Further details on page 3 of this newsletter.

Monday 6th October 2014 *(2pm-4pm)*: PISTE refresher training for site coordinators. (WebEx online training– further details to follow).

Thursday 4th December 2014: *PISTE investigator meeting*
We are pleased to announce that a PISTE investigator meeting will occur at the UKSF Conference in Harrogate.

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Site information

Congratulation to all sites who have recruited patients into the PISTE trial. Currently, the team at UCLH are leading the way with PISTE recruitment, having randomised 11 patients so far.

We would like to say thank you to the UCLH team for their efforts.

UCLH research team: A) Dr Fergus Robertson, B) Stroke researcher practitioners: Back row L-R: Laura Howaniec, Maria Brezitski, Ifan Jones, Luci Crook, Caroline Watchurst, Front L-R: Krishna Patel, Azra Banaras.

Site name	Site PI	'Green for go' date	No. recruited	Most recent randomisation date
Royal Victoria Infirmary, Newcastle	Dr A Dixit	06 Feb 13	8	20 Aug 2014
St George's Hospital, London	Dr G Cloud	16 May 13	7	23 Jul 2014
University College London Hospital	Dr F Robertson	03 Sep 13	11	05 Sep 2014
King's College Hospital, London	Dr N Kandasamy	25 Sep 13	2	01 Apr 2014
Charing Cross Hospital, London	Dr K Lobotesis	06 Aug 13	4	26 Jun 2014
University Hospital of North Staffordshire	Prof C Roffe	19 Sep 13	6	15 Sep 2014
Leeds General Infirmary	Dr A Goddard & Dr J Bamford	12 Jul 13	2	28 Apr 2014
Salford Royal Hospital	Dr C Smith	26 Jun 13	3	30 Jan 2014
Nottingham University Hospitals	Dr G Subramanian	22 May 14	0	N/A
Queen Elizabeth Hospital, Birmingham	Dr E Littleton	18 Feb 14	0	N/A
University Hospital of Wales	Dr S Ahmad	11 Jun 14	0	N/A

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Updated study documents

Protocol v1.5, 1st Sept 2014: The protocol has undergone a minor amendment. The key updates include:

1) Clarification on inclusion criteria and study eligibility.
2) Updates on the site qualification process for potential sites.

The following inclusion criteria are part of the PISTE protocol v1.5:

- ✓ Male or non-pregnant female ≥18 years of age.
- ✓ Eligible for IV rtPA according to standard guidelines and able to be commenced on IV treatment <4.5h after symptom onset (<3h after symptom onset for patients >80 years of age).

With this in mind the PISTE management team would like to provide the following guidance:

- NCGS 4th edition guidance on IVT for patients over 80 years is IVT must be given within 3h not 4.5h. Therefore when patients over 80 years are recruited to PISTE, the time windows are very tight indeed so please bear this in mind when considering recruitment.
- There is evidence of poorer IAT outcomes in patients over 75 years. Therefore, when considering recruiting patients over 75 years please ensure that the patient had both a good pre stroke functional status (e.g. Rankin 0-1) & does not have multiple co-morbidities that might be associated with an increased IAT risk.

Study workbooks v3.0, 4th Sept 2014: In association with the protocol amendment the updated version of the study workbook provides specific guidance on the data required at each study visit. The updated version is now live and should be used going forward.

An important guidance note included in the workbook regards thrombectomy patients. One of the data points collected during the procedure is 'total duration of procedure'. This is defined as the time from groin puncture to time of final recanalisation established by angiography.

Please review the data collected to date for this data point to ensure that the correct information is recorded.

Please insert a master copy of the updated version into your PI site file. Please remove all previous versions of study workbooks from your working site file and replace with the updated version. The updated version can also be found on the study web portal.

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Missing study data

On review of data collected to date, several recurring issues have been identified. Please review the following guidance regarding missing data.

Timely uploading of data onto the eCRF*:* The PISTE management team kindly requests that sites ensure that study data is uploaded from the study workbooks onto the eCRF within 48 hours of each study visit. This is not occurring routinely at all sites. It is imperative that all data is made available on the eCRF within a timely manner to allow patient safety to be monitored and to prevent unnecessary DCQs.

Missing laboratory results*:* Laboratory tests stipulated by the protocol are required for safety analysis, and are an essential component of the study. Please note that even if thrombolysis has started prior to laboratory results being available, the results should still be uploaded onto the CRF. Missing data will be requested by the team managing the eCRF. If laboratory tests are not performed, please complete a protocol deviation form (available on the study web portal & in your local site file) and forward to Alicia.Murray@ggc.scot.nhs.uk.

The independent data monitoring committee have emphasised the critical importance of such information to allow safety review, and have asked the trial monitoring team to ensure that sites enter protocol specified data in a timely manner.

Follow up visits not occurring as per protocol*:* It is expected that patients randomised into the PISTE trial will attend **ALL** protocol defined follow up visits (unless the patient has withdrawn from the study. Please see the patient withdrawal guidelines which were issued to all sites for details). If a patient is discharged prior to the 72 hour post treatment visit, and/or the day 7, day 30 or day 90 visit, it is expected that sites will schedule all subsequent follow up visits with the patient, and collect data as stipulated by the protocol.

Steps to be taken in the event that a patient does not attend a follow up visit within the protocol stipulated window:

a) If a patient cannot be seen within the protocol defined timescale, sites should complete a protocol deviation form and forward to the PISTE management team for review.

b) If a face to face visit cannot be conducted for visits 6 & 7, sites should try to conduct a telephone visit and record the mRS and (home time evaluation assessment – for visit 7).

c) If a visit window has already passed, the site should to call the patient/ next of kin/ GP etc. to request the details. Please then forward the data to the PISTE management team.

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Site payments

Site payments: In April all sites that had recruited patients were contacted regarding payments due. In order to process site payments, each site must provide certain details on headed site paper (fax number, email address, VAT registration number, bank name, address, sort code & account number). This is to allow a PO number to be generated (without which site payments cannot be made).

If your site randomised patients prior to April 2014, please confirm your site has submitted an invoice to Alicia.Murray@ggc.scot.nhs.uk before the end of August to ensure payment.

SAE reporting guidance

The current PISTE SAE form is version 2.0 (6th Nov 2013). Please complete all sections as instructed in the form and report as soon as practicable, and in any event within 24 hours of first becoming aware of an SAE.

If the event being reported is a consequence of the initial stroke which caused the patient to be included in the study, please make this clear in the diagnosis as well as in the narrative section of the form. (If the diagnosis is entered simply as "ischaemic stroke" it is unclear if this is the initial stroke, a new stroke or a consequence of the initial stroke).

Co-recruitment guidance

PISTE trial patients cannot be co-recruited into CTIMP trials within their 90 day involvement in the PISTE trial. However, after the patient's 90 day involvement they can be recruited into other studies. If sites are in any doubt, they should contact the PISTE management team in the first instance.

Recommendations from the monitoring team:

Consent forms: please update patient consent forms with subject numbers issued by the IVRS system following randomisation.

Laboratory results: To be compliant with GCP, please ensure all lab test results are printed, initialled and dated by a medically qualified member of the team and filed in the patient's records. Alternatively they can be kept in subject specific files as long as these files are stored in a confidential manner, and appropriately disposed of at the end of the trial.

Delegation logs: The 'study role' section should specify accurately what each member of the study team does in the context of the study (for example, neurointerventionalists should be recorded as such on the delegation log, therefore adding meaning to the responsibilities column).

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Study Contacts

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Additional contact information:

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Robertson Centre for Biostatistics (web portal, eCRF, IVRS): PISTEITSUPPORT@glasgowctu.org
SAE reporting: pharmacovig@glasgowctu.org ☎ 0141 330 4744

PISTE trial web portal (secure portal with links to essential study documents & eCRF)
www.glasgowctu.org/piste/

PISTE trial website (public access)
www.gla.ac.uk/piste

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