

Karen Sanders

From: CT Submission [ct.Submission@mhra.gsi.gov.uk]
Sent: 10 February 2010 15:45
To: Trial - STAMPEDE
Subject: Letter for EudraCT 2004-000193-31
Follow Up Flag: Follow up
Flag Status: Red

Dear Applicant,

Thank you for your letter dated 3rd Feb 2010, in regards to pre-planned changes. As these pre-planned changes had already been approved in the protocol, there is no requirement for you to inform us of the changes.

Kind Regards
CT Submissions

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03 Feb 2010

Ms Anne McCullough
West Midlands Main REC
Osprey House
Albert Street
Redditch
Worcestershire
B97 4DE

Dear Ms McCullough,

Re: STAMPEDE: Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy

MRC PR08

ISRCTN number: ISRCTN78818544

NCT number: NCT00268476

EUDRACT number: 2004-000193-31

CTA number: 00316/0026/001-0001

STAMPEDE is an ongoing, nationwide randomised controlled trial that is assessing the effectiveness of a number of agents, alone or in combination in patients with high-risk prostate cancer. We are writing to you now to give you further information ahead of the forthcoming interim analysis as this may require some pre-planned changes to the trial being activated promptly.

Background to STAMPEDE

As documented in section 9 of the STAMPEDE protocol the trial is using multi-arm, multi-stage (MAMS) methods. It is assessing 5 research arms against a common control arm and is being conducted in a number of stages: Pilot Stage, Activity Stages I, II and III and, finally, Efficacy Stage IV. We are currently in Activity Stage I and anticipate having sufficient data to assess the current trial arms in a pre-planned intermediate activity analysis by March this year. At this point the Independent Data Monitoring Committee (IDMC) will meet to review the data and make a recommendation to the Trial Steering Committee (TSC), the trial's executive body. The recommendation will be on whether recruitment (and treatment) should continue to each of the trial arms. The TSC will then decide whether recruitment to any of the arms of the trial should be discontinued at this point. There are two main reasons why a trial arm could be dropped:

1. Safety – if the data from an arm is showing an unacceptable toxicity profile
2. Lack of activity – if the data from the arm are not showing a *sufficient* activity compared with the control arm. This is the focus of the MAMS design: the evidence required to continue recruiting to a particular arm becomes more stringent as the trial goes on. Therefore, an arm may stop recruitment despite showing some evidence of a small advantage in terms of activity, but that this is unlikely to translate into a worthwhile benefit.

Relevance to centres

If the TSC reach a decision to stop recruitment or treatment in one or more arms, we shall aim to implement this as soon as possible and all participating centres will be informed as soon as possible, by phone and in writing. The MRC CTU team will make the necessary changes to the trial documentation (including patient information documentation), submit these for information to the ethics and regulatory bodies and distribute the updated documents to centres to pass through local processes.

Further information

The principle of stopping one or more arms in this trial is fully described in the current, approved protocol (version 6.0, 09 Jul-2009) and does not constitute a substantial amendment to the trial. Clearly, some trial documentation will need to be amended following any decision to drop arms and this will be done as soon as possible afterwards.

For more information in regard to the design of the STAMPEDE study, please refer to section 9 of the STAMPEDE protocol. In addition, the reference, below, which is freely available on-line gives information about MAMS trials in general.

If you require any further information or clarification then please do not hesitate to contact us

Kind Regards



Nick James Karen Sanders
Chief Investigator Trial Manager

On behalf of the STAMPEDE Trial Management Group

Reference

Issues in applying multi-arm multi-stage methodology to a clinical trial in prostate cancer: the MRC STAMPEDE trial. Sydes MR, Parmar MKB, James ND, Clarke NW, Dearnaley DP, Mason MD, Morgan RC, Sanders K, Royston P *Trials* 2009, 10:39

03 Feb 2010

Dr Martyn Ward
Medicines and Healthcare products regulatory Agency
Regulatory Agency
Market Towers
1 Nine Elms Lane
London
SW8 5NQ

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