POSNOC SWAT proposal

SWAT Title

Addition of a pictorial aid to the patient information leaflet (PIL) to improve recruitment within a randomised trial.

Background

Recruitment remains to be one of the most important challenges for multi-centre trials. Various techniques have been developed and tested over the years and new methodologies are continuing to be developed. Enhanced PIL may help patients understand the trial and therefore boost recruitment.

Objective

To determine whether the addition of a pictorial aid to the patient information leaflet (PIL) will improve recruitment in the POSNOC trial.

The host trial

Adjuvant therapy alone versus adjuvant therapy plus clearance or axillary radiotherapy: A randomised controlled trial of axillary treatment in women with early stage breast cancer who have metastases in one or two sentinel nodes (POSNOC).

POSNOC is a pragmatic, randomised, multicentre, non-inferiority trial for women with early stage breast cancer and one or two sentinel node macrometastases. The aim is to assess whether adjuvant therapy alone is no worse than adjuvant therapy plus axillary treatment, in terms of axillary recurrence within 5 years.

SWAT Methods

Participants

Women approached about participation in the POSNOC trial.

Intervention

Enhanced PIL: A clearly illustrated pictorial aid at the end of the current approved PIL to depict the randomisation process and crucial information about the two treatment arms in the POSNOC trial.

Comparator

The current approved POSNOC PIL without the pictorial aid.

Outcomes

Primary: The proportion of women randomised to the POSNOC trial.

Randomisation

The SWAT will use a cluster randomised design, and the unit of allocation will be UK sites that are participating in POSNOC. All women at a site who are identified as potentially eligible and are approached about the POSNOC trial will be provided with either the standard PIL or an enhanced PIL with the pictorial aid, dependent upon the random allocation of the site. Allocation of sites will be stratified by recruitment to POSNOC in the last 12 months.

Statistical considerations

Because data regarding numbers of women approached and screened for POSNOC are reported at aggregate rather than individual level, data analysis for the SWAT will also be at aggregate level. This means that the number of observations in the analysis will equal the number of sites in the trial i.e. one observation per site. The relevant data for analysis will be the number of women screened, the number of women randomised, and hence the recruitment fraction, at each site during the period of the SWAT.

Data analysis for the SWAT will firstly describe number and proportion of women randomised in enhanced PIL and standard PIL arms. The distribution of recruitment fraction among participating sites is expected to be approximately log-normal (see sample size below). We will compare mean log-recruitment fraction between the arms using a multivariable regression model that will include stratification variables and be weighted according to number of women screened. The exponential of the difference in mean log-recruitment fraction represents the ratio of geometric means, which we will present with 95% confidence interval and exact p-value. No interim analyses are planned.

During the period Mar-2018 to Feb-2019, mean recruitment fraction was 0.33 and standard deviation 0.31 from a total 104 sites in POSNOC. Following log-transformation of the data, mean log-transformed recruitment fraction is -1.38 and standard deviation of 0.67. A sample size of 50 sites per arm enables a standardised difference of 0.66 SDs to be detected with 90% power and 5% two-sided alpha, equivalent to a ratio of geometric means of 1.56 (=exp(0.67*0.66)). Geometric mean recruitment fraction is assumed to be 0.25 (=exp(-1.38)) in the standard PIL arm, and therefore an effect size (ratio of geometric means) of 1.56 requires the recruitment fraction to be 0.39 (=exp(-1.38+0.67*0.66)) in the enhanced PIL arm.

An absolute increase of 14% in recruitment fraction is unlikely for this pictorial aid intervention. However, testing the effect of this intervention in a randomised evaluation will provide data that can be meta-analysed with other similar SWATs in systematic reviews in the future.

Current trial status

The POSNOC trial opened to recruitment in July 2014 and to date has recruited 1440 of the planned 1900 participants. Recruitment is due to end at the end of August 2021. It is expected that once started, the SWAT will continue until the target sample size of 1900 for POSNOC is reached.

Costs

We estimate a total 5 days of trial manager time for updating the trial protocol and other study documentation, applying for approvals, and providing additional training to site staff, costing £1,188. We estimate a total of a total of 2 days of statistician time for dataset preparation and analysis, costing £475. We estimate an additional £538 for professional printing of the pictorial aid. Adding the £750 standard payment to the CTU to be used for SWAT dissemination/staff training, the total amount requested is £2,951.

Possible problems associated with implementing this SWAT

The current version of the PIL will need to be updated with the pictorial aid and submitted for approval as a substantial amendment. Some additional training on the use of the pictorial aid will need to be provided to those sites that are randomised to use the enhanced PIL, however this is expected to be minimal. We do not foresee any additional problems.

Authors of this SWAT

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Expertise in team

The Nottingham Clinical Trials Unit (NCTU) is a registered UKCRC Clinical Trials Unit with experience of designing and conducting SWATs. **Montgomery** is Director of the NCTU and Professor of Medical Statistics and Clinical Trials. **Brittain** is the senior trial manager. POSNOC trial manager is **Khan,** and trial statistician is **Tan**. **Goyal** is Chief Investigator of the POSNOC Trial. The SWAT will be led by **Montgomery** and **Brittain** within NCTU.

POSNOC study / SWAT timelines

Activity	**Start date (approx.)**	**End date (approx.)**
SWAT set-up (document preparation, obtaining approvals, randomisation set-up)	01 Sep 2019	31 Oct 2019
Dissemination of SWAT materials and providing training to sites	01 Nov 2019	30 Nov 2019
Commencement of SWAT	01 Dec 2019	--
Current trial recruitment end date	--	31 August 2021
Analysis of SWAT data	01 Sep 2021	20 Dec 2021

Relevant SWATs registered on SWAT STORE

SWAT 23: Systematic Techniques for Assisting Recruitment to Trials (MRC START)
SWAT 32: Effects of a re-designed Participant Information Sheet