UK DCTN Steering Group Meeting Minutes

Edinburgh

4 July 2018

Attendees: H Williams (Chair), M McPhee, C Layfield, N Levell, J Ingram, H Bell, S George, S Walton, M Wittmann, S Jones, A Wernham, J Thomson, T Burton, P Fairbrother, A Martin-Clavijo, C Smith, C Charman, K Thomas, J Chalmers, D Maslin, S Hill, A Macbeth, J Kassim, R Abbott, R Simpson, D Veitch.

Guests: D Koch, K Jackson.

Apologies: A Nunn, F Cowdell, F Hashmi, M Santer, S Ersser, K Radley.

Actions

	Action/ Resolution	*Owner*	*Date due*
	Outline proposal (KA) – review proposal in light of discussion and go to full vignette stage	D Koch	n/a
	Eczema Education study – bring to next UK DCTN meeting and make contact with recommended Health Economics expert T Sachs	K Jackson	16 Oct 2018

Minutes

1. Welcome and introductions

H Williams welcomed all those in attendance and thanked everyone for taking the time to attend our AGM within the busy conference schedule.

2. Minutes of February 2018 UK DCTN Steering Group meeting and matters arising

APRICOT Study - anakinra in acral pustular psoriasis. Currently recruiting at 12 sites – issues with getting some new sites set up and running. NEED MORE PARTCIPANTS AND INVESTIGATORS. Study highlighted again at this meeting - please contact the study team if you want to get involved. Email: dermatologytrials@gstt.nhs.uk

ALPHA Study –RCT investigating best treatment for hand eczema –alitretinoin vs PUVA (21 sites). Recruitment has also been a challenge and M Wittmann asked the group to continue looking for suitable patients to approach. Study highlighted again at this meeting - please contact the study team if you want to get involved. Email: ctru-alpha@leeds.ac.uk

New UK DCTN video – Agreed at the previous meeting that a video was needed to help promote the role of the UK DCTN. This has been actioned and was viewed at the meeting – please see http://www.ukdctn.org/about/index.aspx .

3. AGM Business

H Williams and C Layfield presented the treasurers report outlining income and spend for the previous 12 months. S Walton was thanked for her much continued donations from lectures. It was emphasised that funding allocations from UK DCTN supported clinical trials are a vital income source for the continuation of the Network with regards to supporting

activities such as Themed Calls and UK DCTN Awards. Full details of the treasurers' report can be found in the embedded AGM presentation.

H Williams finally drew everyone's attention to the UK DCTN annual reportsubmitted for the BAD AGM which provides a succinct summary of projects and activities during 2017/2018.

4. Main agenda items

Full vignette research proposal: Methotrexate vs Dupilumab for atopic dermatitis.

C Smith presented this proposal which has an experienced research team behind it with J Chalmers (UK DCTN Trial Development Manager) providing advice on behalf of the UK DCTN. Full details of the study can be found in the embedded presentation.

In summary this is a randomised, parallel group, multi-centre active comparator controlled trial which will be participant and assessor blinded. Planned as a 48 week trial (number and frequency of study visits tbc) with a non-inferiority design

The research question will look at the effectiveness and cost effectiveness of the drugs. It is currently planned as a 'non-inferiority' trial ie the effectiveness of methotrexate (MTX) is not inferior to dupilumab within a given non-inferiority margin (to be determined) but is lower cost than dupilumab.

Adult patients will be recruited from groups needing systemic therapy. MTX is widely used but with little data and dupilumab has recently been made available but there are no comparative studies with methotrexate or any other active systemic comparators. The study design needs to be acceptable to patients to encourage good recruitment and so a placebo arm is not appropriate.

There is also the potential for the study design to be adapted to a 'platform' type design such as the STAMPEDE trial in prostate cancer. This will allow further new biologic treatments for severe atopic eczema to be added as additional arms to the trial.

The team is planning a survey to gauge interest and feasibility in the trial – this will address the following issues:

- Extent of routine use of subcutaneous MTX
- Dosing schedule for MTX
- Use of MTX as a comparator
- Feasibility estimates of patient population
- Eliciting the non-inferiority margin
- Assuming cost of MTX = £X, Dupilimab = £X and the safety profile is X, give a range of efficacy values for MTX and Dupilimab to establish what is acceptable
- Willingness to randomise
- Would a non-inferiority design influence clinical practice?
- If results are XXX would you change your practice?

The main discussion points raised about the study were:

- Excess treatment costs will be high. Sanofi is not interested in providing dupilumab for this trial and are unsurprisingly not planning similar studies.
- Need to align with NICE guidance. Newly licensed drug and guidance – can use dupilumab if first line systemic treatment failed for moderate and severe eczema.
- Are patients likely to be willing to participate in a trial of dupilumab versus MTX once dupilumab widely available?
- Would a trial of largely systemic naïve patients be useful?
- Should we include patients with moderate disease? Greatest need is for those with severe disease but NICE approved dupilumab for moderate to severe disease

- Is non-inferiority the right trial design? For this to be a non-inferiority trial there must be a potential explicit 'gain' for patients as well as commissioners. The study would need to be bigger to show benefits.
- Should we be looking at superiority of dupilumab over MTX to justify the additional cost of dupilumab?
- Is the dosing schedule for MTX acceptable / too complicated? Cannot be too low – prescriptions often at an over-cautionary low level.
- Why subcutaneous MTX rather than oral? Explained due to increased bioavailability, probably faster onset of action, may have better GI tolerability, comparable to delivery of dupilumab for blinding purposes.
- Discounted cost of dupilumab to the NHS is confidential – will impact on health economic calculations.
- Patient view – good comparison because ciclosporine cannot be taken over a long period of time. Most patients would try either MTX or dupilumab. They need to know the benefits and potential side effects (some side effects more bothersome than others). Acceptibility of injections rather than tablets needs exploring.
- Liver fibrosis/ avoiding alcohol while taking MTX maybe a drawback. Although recent evidence from the psoriasis population suggests other factors (eg: obesity) major driver of liver fibrosis
- Doctors more familiar with MTX – side effects etc, need to know more about dupilumab. Despite familiarity with MTX still need more data/ few trials.
- Consequence/impact of study? MTX prescribed as 1st line treatment anyway. What effects on change in practice would it have?

All agreed this is a much needed study and further development work will continue with full support of the UK DCTN.

Outline proposal – Can we manage keratoacanthoma better? Can we defer surgery to improve outcomes?

D Koch presented this proposal on behalf of the study team. This study is investigating tackling the unnecessary surgery often undertaken for large and rapid growing keratoacanthomas (KA), which are benign and disappear with time, but often treated as SCC. Despite the low-risk nature of most KA lesions and potential for spontaneous resolution, many clinicians decline to distinguish KA from SCC and excise all KA-like lesions as for SCC. It is also suggested that some pathologists also decline to distinguish KA from SCC.

This idea was submitted previously to the UK DCTN (as part of the 2014 Themed Call on Dermatological Surgery) and has since been further developed (including a survey to dermatologists and pathologists and some patient involvement work) and was recently considered by the NCRI non-melanoma skin cancer studies group.

In summary, the proposal is for a prospective cohort study of 100 patients in three groups where surgery is deferred for 4/5 weeks for clinical assessment/ observation. Full details of the study can be found in the embedded presentation.

The following questions were addressed within the presentation:
1. Is such a trial clinically safe / 'ethical'? Yes
Clinical risk is mitigated by:
- Excision of all lesions which continue to grow at 4-5 weeks
- Histology will pick up any clear-cut SCC, all excised
- Treatment ensured within NHS cancer 31/62 targets
- Clinical follow-up

2. Is the study design/intervention acceptable to patients? Yes
At Dorchester they are already confirming acceptability in routine clinical practice.

3. Would patients need additional surgical procedures or clinic visits? No
The study mirrors real-life clinical practice at DCH & does not introduce additional visits.

The main discussion points raised about the study were:

- Is 4/ 5 weeks long enough period to assess the KA?
- Patient view – many patients would prefer to avoid surgery so recruitment might be easier than first thought. Engaging with elderly – good. Some patients would want it cut out when cancer risk is mentioned but consent to collect data would be valuable.
- Concern that KA could turn out to be SCC (putting patients at risk?) Concern about waiting 2 months before any treatment. Just one bad outcomes could scupper the study
- Many hospitals will remove SCCs at four weeks, or sooner, sometimes excising them on the same day. Need to look at current practice and variations between regions.
- Study has potential to reduce surgical procedures.
- Audit needed to convince dermatologists to take part in the study. Cleary demonstrate no harm/ risk to patients – keep within four weeks.
- Important to include/ consult with plastic surgeons.
- Need to consider logistics of surgery – speed of appointments, waiting lists etc.
- Time from history, not referral date is important.
- Need to engage with pathologists.
- Clear criteria for KA so less risk of misdiagnosing a SCC?

H Williams summarised this as good proposal – where there is a disagreement in practise, points to the need for more research. He also suggested that the team could go a long way to answering the natural history of KA lesions by taking advantage of the natural experiment that occurs across the UK with a range of waiting times for surgery. Plotting time waited and whether resolution had occurred by the time surgery was scheduled would provide the basis of an informative Kaplan-Meier survival curve. If a randomised element us needed, the team need to find hospitals to be willing to be a recruiting centre (demonstrate interest in the dermatology community). Team encouraged to continue with the proposal and maintain contact with the UK DCTN for advice and support and progress to full vignette stage.

5. Trial Generation & Prioritisation Panel Update

R Matin as new chair of the panel provided an update to the group as outlined below. J Ingram (previous chair) was thanked for this work and commitment.

- 2018 UK DCTN Themed Call is 'Supporting Recently Completed Priority Setting Partnerships. Disease areas covered are cellulitis and lichen sclerosus. Deadline for applications is 20th August 2018 and further details are available at http://www.ukdctn.org/ukdctn-funding-awards/ukdctn-funding-awards.aspx .

- 2018 UK DCTN Trainee Groups. The theme for the 2018 cohort across all groups is Dermatological Surgery. The trainees (23) and mentors (12) have been allocated into four research groups with each working on a specific research idea. These will be presented at a training day in September 2018.

- Opportunities to get further involved in the TGPP will be highlighted later in the year

6. Ongoing trials and trials in development

Due to time constraints updates here were limited to the Eczema Education Study. Updates on all other studies in development and on-going trials can be found in the embedded AGM presentation.

Trials in Development - Eczema Education Study

K Jackson presented this study which looks at the effectiveness of a nurse-led education programme for patients and parents/carers with eczema. The study has been in development for a number of years and has not been successful in obtaining funding to date. First presented to the UK DCTN in Nov 2015, the study team (including C Flohr and S Ersser) were seeking continued advice and support from the UK DCTN on next moves for this trial.

Details of the update can be found in the embedded presentation; it was recommended that the study team contact Prof T Sachs (Norwich) for support and advice with regards to the health economics aspect of the study and return to the October Steering Committee to allow a more thorough discussion to take place.

Date of next UK DCTN Steering Committee meeting

1.30pm 16th October 2018
BAD House, London


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