Research Grant Application 2024

Diabetes Care Trust and ABCD (Diabetes Ca

Section 1: Project overview

1. Project title

A feasibility study of flash glucose monitoring in patients receiving aleplisib for breast cancer

2. Lead applicant

Dr Elaine Tomlins

3. Host organisation name

The Royal Marsden NHS FT

4. Total project cost £ 49622

5. Type of study Research

6. Proposed start date

August 2024

7. Duration of project in months (max 2 years)

2 years

8. Summary of proposed project (250 words)

Alpelisib in an exciting new treatment for certain patients with metastatic breast cancer. It inhibits PI(3) Kinase, hence inhibiting cancer growth. However it also reduces insulin signalling resulting in an expected rate of significant hyperglycaemia, in up to 70% of those treated, sometimes resulting in Diabetic Ketoacidosis requiring admission. This can occur even in those without pre-existing diabetes. Currently capillary glucose monitoring is recommended, but this poses an additional burden on those starting treatment and can leave those with hyperglycaemia having to access urgent care to seek support. We propose a feasibility study of flash glucose monitoring with remote surveillance, combined with support delivered through a novel patient portal, the My Marsden app, to improve detection and management of hyperglycaemia in this cohort and provide better support to affected individuals.

9. Potential benefits for people with diabetes (150 words)

People with pre-existing diabetes are at particularly high risk of hyperglycaemia with alpelesib, and indeed those without very well controlled diabetes were excluded from clinical trials. Therefore they need especially close monitoring if they are to be treated with this drug. Also, as breast cancer is more common in those with diabetes it is important to be able to use the widest range of therapeutic options. Flash Glucose Monitoring may have particular benefits in those with existing diabetes. However even those without diabetes prior to starting treatment can still develop significant hyperglycaemia. The burden of initiating glucose monitoring and lack of support when high glucose levels are identified at home may be even more problematic in this group who will not have received diabetes education. Flash glucose monitoring will reduce the burden of frequent monitoring, whilst the remote monitoring of results and ability to access support remotely will help to reduce treatment related anxiety.

10. Summary of research in plain English (150 words)

Alpelisib is a new treatment for advanced breast cancer. It blocks the way insulin works inside cells and results in high glucose levels in at least two thirds of patients taking it. This can occur even in those without diabetes, sometimes needing emergency admission. Those starting treatment with this drug need to check glucose levels and current advice is to use finger prick testing. People with other types of diabetes are now routinely using flash glucose monitoring, where a sensor is worn on the arm, and a mobile phone used to scan and see the glucose level. This allows testing multiple times a day without finger picks, and enables readings to be automatically shared with a health care team via the mobile phone/cloud account. The breast cancer team can therefore see when a person is developing high glucose levels and intervene with advice, start treatment promptly, and arrange same day assessment when needed to reduce emergency attendances.

Section 2. Research proposal (1500 words)

Please structure your proposal using the following headlines, with the majority focusing on the project plan:

1. What is the background to this project and why is it important?
2. What are the aims and objectives?
3. Review of existing evidence
4. Project plan
5. How will the study results be analysed?
6. What are the milestones? (Please attach a Gantt chart to the application)
7. Please attach any supporting references as an additional attachment (not part of word count)

Alpelisib is emerging as a promising treatment for hormone positive HER2 negative breast cancer, and is now approved by NICE for this indication.

It inhibits PI3K to block growth signals. However as the same pathway is also important for insulin signalling, hyperglycaemia is a common toxicity, occurring in over two thirds of patients. This can result in emergent pre detail with DKA.

There is little consensus on how best to monitor glucose levels and treat hyperglycaemia. Although the manufacturer is offering support with initiation on set blood glucose monitoring by providing access to capillary glucose monitors it is not know if this will reduce the risk of significant hyperglycaemia.

In particular, in the absence of clear guidelines, people on alpelesib who develop hyperglycaemia need prompt access to specialist advice to initiate appropriate glucose lowering therapy and ensure rapid assessment of those at risk of DKA.

As there is currently a very limited evidence base to support development of guidelines it remains unclear what the optimum frequency and timing of glucose monitoring should be. Nor has the acceptability of multiple daily glucose tests, mostly in patients without pre-existing diabetes been determined. In particular the impact of detecting significant hyeprglycaemia without ready access to specialist support has not been assessed, given most people taking alpelisib will not have pre-existing diabetes and will not have had diabetes education prior to starting therapy.

Research proposal ... continued

2.Aims

-Determine if it is feasible to use Flash Glucose Monitoring at initiation of Alpelisib therapy in metastatic breast cancer

-Determine the incidence and peak time of hyperglycaemia following initiation of alpelisib for metastatic breast cancer.

-Test the feasibility of remote glucose monitoring and messaging to manage a cohort of patients with alpelisib associated hyperglycaemia.

3. Review of evidence

Current guidance for the management of hyperglycemia in patients receiving alpelisib is primarily based on trial experience, which is not necessarily reflective of the experience in real-world patients (Ruga et al 2020). Detailed guidance was lacking on certain aspects of AE management, such as which anti-hyperglycemic agent should be used in the first and subsequent lines for blood glucose elevations. Hence, management remains a challenge. In the absence of definitive evidence, expert consensus recommendations has been provided for clinically useful guidance for AE management (Gallagher et al 2024). This guidance is helpful regarding pre treatment endocrinonology review and appropriate anti hyperglyceamic medicines and reccommends regular glucose monitoring particularly in the early phase of treatment. It does not offer a view on continuous monitoring

In trying to address the hyperglyceamia mangagement Lyengar at Memeorial Sloan Kettering is studying whether a very low carbohydrate diet (ketogenic diet), a low carbohydrate diet, or the study drug canagliflozin can prevent high blood sugar and may improve the effectiveness of cancer therapy in people who are receiving standard treatment with alpelisib as treatment for breast cancer. We can find no other study looking at the issue of hyperglyceamia including using continuous monitoring to identify early concerns .

4. Project Plan

The Royal Marsden anticipates starting 1-2 patients per month on Alpelisib, in line with NICE guidance for treatment of breast cancer.

Current practice is to initiate capillary glucose monitoring and request patients to call the Royal Marsden Hotline if they have elevated glucose levels.

We will recruit 20 participants to initiate Flash Glucose Monitoring with the Freestlyle Libre system, using a compatible smartphone and Libreview account to share their readings with the clinical team.

Particpants will also be provided with a capillary glucose monitor as back up with strips for testing both glucose and ketones.

Full training will be provided.

Clinical Nurse Specialists and Pharmacists from the Breast unit will access Libreview daily Monday to Friday to detect those with hyperglycaemia.

All those with glucose levels >15 mmol/L will be requested to check for plasma ketones, and urgent review either via the Oncology unit or closet ED will be arranged when elevated.

Those with hyperglycaemia without ketosis will be managed as per recent European consensus guidelines (Tankova et al Cancers 2022) with a stepped approach of initiation of oral glucose lowering medication. Those with Grade 3-4 hyperglycamia will have alpelisib treatment suspended until hyperglycaemia has been managed.

Because hyperglycaemia is usually an early toxicity of alpelisib treatment (median onset of grade 3 toxicity was 15 days, (Rugo et al Annals of Oncology 2020) monitoring will be stopped after 1 month in those with no recorded hypoglycaemia.

Structured interviews will be used to assess patient experience of using the flash glucose monitors and remote monitoring.

Research proposal ... continued

5.Analysis

Glucose data will be retrieved from the Libreview platform.

For each participant we will assess, at each of the first 4 weeks:

-Number of days sensor worn

-Mean number of times sensor scanned per day

-Peak fasting glucose in each week (1-4)

-Peak glucose in each week

-Time of peak glucose

-Any readings <4 mmol/L

-Need for glucose lowering therapy

-If glucose lowering therapy initiated did it result in a reduction of Grade of Hyperglycaemia (as per CCTAE Oncological Toxicity reporting criteria)

-Number of ketone tests performed

-Need for emergency assessment

-Need for hospital admission

-Need to suspend alpelisib treatment

At the end of the study thematic analysis will be used to analyse the structured interviews.

6.Milestones

Months 1-3 Ethics and set up, registration of RMH with Libre view and data / IG clearance

Months 3-18 Patient recruitment (estimated 1-2 per month)

Months 3-19 Structured Interviews at end of 1 month of monitoring

Months 20-24 Analysis, final report

How are people with diabetes involved in this study? (150 words)

Commencing Alpelisib in people with existing diabetes may cause some disruption to their diabetes control and those with newly diagnosed diabetics will have greater support and education needs. To explore patient experience of starting Alpelisib, remote monitoring (using the flash glucose monitors) and management in patients with existing diabetes or newly diagnosed diabetes from Alpelisib we will conduct structured interviews. These will be online during an evening and one in-person during the working day, with 10 participants in each group (20 participants in total). Findings from the interviews will be used to determine the acceptability of using Flash Glucose Monitoring at initiation of Alpelisib therapy and co-design with people with diabetes patient education and a novel pathway to monitor and manage Alpelisib associated hyperglycaemia. This will ensure that people with cancer and diabetes have access to the correct information on managing high blood glucose and antidiabetic medication changes during cancer treatment.

Section 3. Applicants

Principal investigator

ELAINE TOMLINS

Title

DR

First name

ELAINE

Surname

TOMLINS

Current post

CONSULTANT NURSE FOR SACT /LEAD CANCER NURSE/HONORARY RESEARCH FELLOW

Department

CANCER SERVICES

Hospital or University address

THE ROYAL MARSDEN NHS FT

Email address

elaine.tomlins@rmh.nhs.uk

Previous posts held (up to three)

CONSULTANT NURSE/ ACADEMIC FELLOW UNIVERSITY HOSPITAL SOUTHAMPTON /UNIVERSITY OF SOUTHAMPTON

SENIOR CLINICAL NURSE SOUTHAMPTON UNIVERSITY HOSPITAL

Research experience

Tomlins E , Foreman E (2024) Efficacy and safety evaluation of oral Akynzeo® in patients receiving MEC at high risk of developing CINV based on a prediction tool. A multinational and multicentre study. Chief Investigator

Droney J Tomlins E (2023) Implementation of integrated palliative care services for patients undergoing CAR-T therapy Co investigator

Wessex cancer alliance Fellowship (2015) Is it safe to use the ipsilateral arm for venepuncture and cannulation prior to chemotherapy for breast cancer? fellow

Finnegan-John, J, Foster, R, Lennan, E, Oakley, C, Richardson, A, Verity, R and Ream, E (2013) A longitudinal qualitative interview study to understand need for support in family members of people having chemotherapy. Psycho-Oncology, 22, supplement 1, 1. (doi:10.1111/j.1099-1611.2013.03239.x). Co investigator

Gurusamy KS, Best LMJ, Tanguay C, Lennan E, Korva M, Bussières JF.
Closed-system drug-transfer devices in addition to safe handling of hazardous drugs versus safe handling alone for reducing healthcare staff
exposure to infusional hazardous drugs.
Cochrane Database of Systematic Reviews 2018, Issue 11. Art. No.: CD012860

Publications (up to 10)

Tomlins E Challinor J (2023) Guest editor Climate change and oncology nursing - ecancer November Climate change and oncology nursing - ecancer
Boltong A, Koczwara B Tomlins E et al (2022) Share your views' —international consultation informs a patient engagement strategy for the Multinational Association of Supportive Care in Cancer Supportive care in cancer October 22nd ' Share your views' —international consultation informs a patient engagement strategy for the Multinational Association of Supportive Care in Cancer | SpringerLink
Tomlins E, (2022) Maintenance niraparib therapy for patients with relapsed platinum sensitive ovarian cancer: experience at a south coast network Journal of prescribing practice 2 March 2022 DOI:

Current research grants

Droney J Tomlins E (2023) Implementation of integrated palliative care services for patients undergoing CAR-T therapy Co investigator
Tomlins E , Foreman E (2024) Efficacy and safety evaluation of oral Akynzeo® in patients receiving MEC at high risk of developing CINV based on a prediction tool. A multinational and multicentre study. Chief Investigator .

Pan London fellowship pending

Previous research grants

Wessex cancer alliance Fellowship 2015
Gilead look and you will see us 2023

Details of co-applicants* (name, position, institution)

Dola Awoyani Specialist pharmacist medicines information and palliative care RMH NHS FT

Martine Milton Lead Breast Clinical Nurse Specialist RMHNHSFT

Dr Daniel Morganstein Consultant Endocrinologist and Hon Clinical Senior Lecturer RMH NHS FT and Chelsea and Westminer NHS FT

**Please also attach a letter of support from all co-applicants and any significant collaborators with your online application submission.*

How would grant award support your career?

This grant aligns to my research goals to be at the forefront of novel new therapies and their clinical implications. It will

Please provide a description of research infrastructure

(eg, where will research be conducted, staff available for research,collaborations, access to laboratory equipment etc)

Research will be conducted wholly with RMH . The full Clinical research network infrastructure will be available to aid

Section 4. Finances requested

Staff

0.4 Band 8b salary	£38 603.6 project lead
0.1 Band 8a salary	£8,218 .4 lead Clinical Nurse Specialist input

Consumables

20 packs of Libre sensors (to give a months monitoring for each patient) ~ £90 each =£1800

Equipment

Training of staff, room hire, adaptation of training resources £1000

Other (please clearly state)

What contingency / margin is planned for any delays / extra costs that may arise?

None are expected,however the research infrastructure at RMH can absorb any unplanned need

Total grant requested £ 49622

Have you applied for funding through another source? If so, please explain and include when will you hear the outcome?

No

Have you made contact with the NIHR Clinical Research Network to explore support for this study? (https://www.nihr.ac.uk/documents/study-support-service-contacts/11921) If so, what was the outcome of the discussion? We strongly encourage you to contact the NIHR to discuss your study because it may be eligible for CRN additional support.

Where appropriate, please provide details of any excess treatment and support costs that can be provided by the NIHR Clinical Research Network. Please attach a completed SoECAT form with your online application submission that has been signed off by an NIHR Accord Specialist.

The CRN are very supportive and enaged in the project.

We are unable to provide SoECAT at time of submission but we have expertise within the organisation in this process and is a requirement for ethics submission

Sent

Is there any support from another grant awarding body or industry for this project?

no

Please provide two referees who could be appointed as experts in the field from whom reports could be requested on the overall value and scientific appropriateness of this research.

1. Dr Safwan Adam, Consultant Endocrinologist, Christie Hospital safwaan.adam1@nhs.net
2. Dr Ellen Copson Consultant Medical Oncologist University Hospital Southampton ellen.copson@uhs.nhs.uk

Section 5. Resubmissions

If this is a resubmission, please outline the changes that have been made

no

Section 6. Declaration and signature

Name of principal applicant

ELAINE TOMLINS

Position

CONSULTANT NURSE for SACT / LEAD CANCER NURSE/HONORARY RESEARCHER

Contact details

07766919754

☑ I confirm full acknowledgment to DCT and ABCD will be given for funding and any other support provided in any publication (electronic or print).

Date

3.6.24

Signature

Application submission and supporting documents

Please upload the following attachments along with this form to:
https://abcd.care/abcd-research-grant-application

1. Supporting letter from host organisation (mandatory)
2. Letter(s) of support from all co-applicants and significant collaborators (mandatory)
3. Support reference(s) (optional)
4. Gantt chart (optional)
5. SoECAT form, letter from CRN or finance department (mandatory)