ISRCTN98158824 https://doi.org/10.1186/ISRCTN98158824

Folic acid supplementation in the management of menopausal symptoms in cancer survivors and healthy postmenopausal women

Submission date 11/03/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 11/03/2015	**Overall study status** Completed	
Last Edited 10/11/2022	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-folic-acid-for-women-having-postmenopausal-symptoms-foam

Contact information

Type(s)
Scientific

Contact name
Ms Claire Gaunt

Contact details
School of Cancer Sciences
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT

Additional identifiers

EudraCT/CTIS number
2013-004246-41

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

18588

Study information

Scientific Title
A phase III randomised study of folic acid supplementation in the management of menopausal symptoms in cancer survivors and healthy postmenopausal women

Acronym
FOAM

Study objectives
FOAM is a phase III, double-blind, placebo-controlled, randomised controlled trial designed to determine whether folic acid supplementation improves the frequency and severity of hot flushes in postmenopausal women, either healthy women or breast and endometrial cancer survivors compared to placebo. The frequency and severity of hot flushes will be recorded on self reporting patient diaries. Effectiveness of folic acid supplementation on other menopausal symptoms, and quality of life will also be investigated. If folic acid is demonstrated to be effective, it would represent a cheap, safe, well tolerated and easily deliverable alternative to the conventional hormone replacement therapy, particularly in cancer survivors who may be experiencing more intense symptoms and certainly cannot take hormone replacement.

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/WM/0093; First MREC approval date 06/05/2014

Study design
Randomised; Interventional; Design type: Screening, Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Cancer; Subtopic: Breast Cancer; Disease: Breast

Interventions

Folic Acid: Folic acid is a member of the B group of vitamins. It participates in cellular division, DNA synthesis and maturation of red blood cells. Patients randomised to the Folic Acid arm will take 5 mg/day; Follow Up Length: 0 month(s); Study Entry : Single Randomisation only

Intervention Type
Supplement

Primary outcome measure
Change in Hot Flush Score; Timepoint(s): Change in Hot Flush Score at 12 weeks from randomisation.

Secondary outcome measures
1. Change in 5-HIAA levels and MHPG metabolites; Timepoint(s): In urine from randomisation at week 12
2. Change in frequency of hot flushes; Timepoint(s): Change from randomisation in frequency of hot flushes (mild,moderate and severe) at weeks 4, 8 and 12
3. Change in longitudinal QoL data; Timepoint(s): As measured by the Utian Quality of Life Scale at weeks 4, 8 and 12
4. Change in other menopausal symptoms; Timepoint(s): Using the Greene Climacteric Scale at weeks 4, 8 and 12
5. Change in whole blood levels of serotonin, plasma nor-adrenaline and serum folic acid; Timepoint(s): From randomisation at week 12
6. Correlation of blood changes with clinical improvement; Timepoint(s): Changes in whole blood levels of serotonin, nor-adrenaline, and serum folic acid at week 12
7. Effects in specific prognostic subgroups; Timepoint(s): Healthy women vs cancer survivors and BMI <30 v >30
8. Interim Change in Hot Flush Score; Timepoint(s): Change from randomisation in Hot Flush Score at weeks 4, 8 and 12
9. Percentage of responders; Timepoint(s): The percentage of responders at weeks 4, 8 and 12; defined as a reduction in Hot Flush Score of =50%

Overall study start date
08/02/2015

Completion date
31/10/2017

Eligibility

Key inclusion criteria
1. Experiencing =50 hot flushes per week, as quantified from daily patient Sloan Diary recordings for 7 days after consent and prior to randomisation
2. Being =40 and =70 years of age
3. Willing to participate in the trial and given informed consent; Target Gender: Female

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
Planned Sample Size: 236; UK Sample Size: 236

Total final enrolment
164

Key exclusion criteria
As of 25/08/2016:
1. Baseline red cell serum folic acid level above the normal laboratory range (3.1 to 20.0µg/L)
2. Smoking >5 cigarettes per day
3. Intestinal malabsorption e.g. coeliac, tropical sprue or Crohn's disease
4. Known chronic renal impairment or failure
5. Known established chronic conditions mimicking climacteric presentation e.g. poorly controlled hypertension, hyperglycaemia or thyroid instability
6. Pernicious anaemia due to vitamin B12 deficiency
7. Alcohol consumption more than 14 units per week
8. Women with phaeochromocytoma or other medullary tumours or carcinoid syndrome
9. Known allergic reactions and/or hypersensitivity to folic acid
10. Women who are, in the opinion of the treating physician, unlikely to be able to give informed consent or successfully complete the trial intervention and procedure
11.Participation in another clinical trial within the last 4 weeks prior to enrolment
12. Administration of the following drugs during study and for the specified number of weeks prior to study entry:
12.1. 24 weeks prior to randomisation:
12.1.1 Bevacizumab (Avastin)
12.1.2. Trastuzumab (Herceptin)
12.2. 8 weeks prior to randomisation:
12.2.1. HRT (women on oestrogen implants are excluded from trial entry)
12.2.2. Herbal remedies
12.2.3. Heparin
12.3. 6 weeks prior to randomisation:
12.3.1. Tamoxifen
12.3.2. Fluoxetine
12.3.3. Venlafaxine
12.4. 4 weeks prior to randomisation:
12.4.1. Phenytoin
12.4.2. Phenobarbitol
12.4.3. Primidone
12.5. 2 weeks prior to randomisation:
12.5.1. Warfarin
12.5.2. Sertraline
12.5.3. Mianserin
12.5.4. Mirtazapine
12.6. 1 week prior to randomisation:
12.6.1. Raloxifen
12.6.2. Chronic use of NSAIDs (including high dose Aspirin* and Cox-2 inhibitors)
12.6.3. Methotrexate
12.6.4. Fluorouracil

12.6.5. Trimethoprim
12.6.6. Co-trimoxazole
12.6.7. Chloramphenicol
12.6.8. Sulfasalazine
12.6.9. Paroxetine
12.6.10. Duloxetine
12.6.11. Clonidine
*low dose Aspirin (75mg daily) is not prohibited
12.7. Stop prior to study entry:
12.8. Cholestyramine
12.9. Antacids (containing aluminium or magnesium)
12.10. Vitamin containing zinc or folic acid

Initial
1. Hormonal or non hormonal treatment (including raloxifen) for menopausal symptoms within 8 weeks of enrolment
2. Baseline serum folic acid level which is above the normal laboratory range (3.1 to 20.0µg/L)
3. Smoking >5 cigarettes per day
4. Intestinal malabsorption e.g. celiac, tropical sprue or Crohn's disease
5. Known chronic renal impairment or failure
6. Pernicious anaemia due to vitamin B12 deficiency
7. Taking the following drugs:
7.1. Nonsteroidal antiinflammatory drugs (NSAIDs) can interfere with folate metabolism
7.2. Cholestrollowering agents such as cholestryamine may decrease folic acid absorption
7.3. Chemotherapeutic agents such as fluorouracil and methotrexate can interfere with conversion of folate into tetrahydrofolate
7.4. Antibiotics such as chloramphenicol, trimethoprim and cotrimoxazole
may inhibit dihydrofolic reductase
7.5. Sulfasalazine may decrease folic acid absorption
7.6. Anticonvulsants such as phenytoin, phenobarbital and primidone can interfere with absorption of anticonvulsants
7.7. Serotonin reuptake inhibitors such as fluoxetine, venlafaxine, sertraline and paroxetine may ameliorate hot flushes
7.8. Serotonin disinhibitants such as mianserin and mirtazapine may ameliorate hot flushes
7.9. a2adrenergic agonist such as yohimbine may aggravate hot flushes
7.10. a2adrenergic antagonist such as clonidine may ameliorate hot flushes
7.11. Antacids containing aluminium or magnesium can interfere with folate metabolism
7.12. Preparations containing zinc such as vitamins or food supplements that may contain folic acid
7.13. Anticoagulant or thrombolytic therapy can interfere with folate assays
8. Therapies containing human antimouse antibodies (e.g. Trastuzumab and Bevacizumab) can interfere with folate assays
9. Alcohol consumption more than 14 units per week
10. Women with phaeochromocytoma or other medullary tumours or carcinoid syndrome
11. Known allergic reactions and/or hypersensitivity to folic acid
12. Women who are, in the opinion of the treating physician, unlikely to be able to give informed consent or successfully complete the trial intervention and procedures
13. Participation in another clinical trial within the last 4 weeks prior to enrolment

Date of first enrolment
15/04/2015

Date of final enrolment
30/04/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Birmingham
School of Cancer Sciences
Edgbaston
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham

Sponsor details
Edgbaston
Birmingham
England
United Kingdom
B15 2TT

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name

National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/11/2021	18/11/2021	Yes	No
Plain English results			10/11/2022	No	Yes
HRA research summary			28/06/2023	No	No