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GuARD - GR1014 cutaneous gel Against Radiation Dermatitis

Submission date	Recruitment status	[_] Prospectively registered
20/01/2024	Recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
01/08/2024	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
25/09/2025	Skin and Connective Tissue Diseases	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The aim of this study is to assess the ability of GR1014 Cutaneous Gel (GR1014-CG) to prevent or reduce radiodermatitis occurring with adjuvant radiotherapy (RT) for localised breast cancer after lumpectomy.

Who can participate?
Female patients aged 18 years and over with primary, localised breast cancer without metastases who have undergone breast-conserving surgery and require adjuvant RT.

What does the study involve?
Participants will be randomly allocated to one of three treatments: vehicle, 4.7% GR1014-CG, and 2.4% GR1014-CG. PK assessments, serum calcium level measurements and vital signs (heart rate and blood pressure) will be collected.

What are the possible benefits and risks of participating?
Adjuvant radiotherapy decreases the chances of local cancer reappearance and improves survival rates. However, radiotherapy is often associated with side effects, including radiation-induced dermatitis (radiodermatitis). Symptoms of radiation-induced dermatitis include skin redness (erythema), swelling (oedema), dry or moist peeling of the skin (desquamation), and varying degrees of pain. GR1014-CG is a gel that contains an active substance, GR1014, that belongs to a group of agents with well-established radioprotective effects. The protective properties of GR1014-CG are potentially beneficial in preventing radiodermatitis, particularly in patients with breast cancer treated with adjuvant RT.
The use of GR1014-CG does not necessitate any modifications to the planned course of RT. At the tested doses, there is no observed risk of compromising the antitumour effectiveness of radiotherapy.
GR1014-CG may induce local inflammatory reactions, but they are temporary and resolve on their own. There is a potential risk of skin damage resulting from GR1014-CG, which could exacerbate radiation-induced skin damage. Additionally, there is a risk of immune mediated adverse cutaneous reactions. However, at the exposure levels studied, the likelihood of experiencing hypotension, hypocalcaemia, nausea, and vomiting appears to be extremely low. The doses under evaluation are deliberately kept at levels that will not lead to substantial local

adverse effects. The intention is to limit the extent of irritation to mild or moderate manifestations, including erythema, oedema, pruritus, pain, and mild hyperpigmentation. By employing such low exposures, the likelihood of any systemic adverse effects is effectively mitigated, ensuring the treatment remains safe and well-tolerated. Measures are in place to detect potential adverse reactions, for example, vital signs are taken pre- and post-dosing.

Where is the study run from?
Excelya (France)

When is the study starting and how long is it expected to run for?
January 2024 to December 2026

Who is funding the study?
Graegis Pharmaceuticals Ltd (UK)

Who is the main contact?
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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2023-508728-36-00

Integrated Research Application System (IRAS)
1009515

ClinicalTrials.gov (NCT)
NCT07192588

Protocol serial number
GRA.05.SPR.0001, CPMS 60245

Study information

Scientific Title
A randomised, double-blind, vehicle-controlled, multi-centre, parallel-group study to investigate the safety, tolerability, and efficacy of GR1014 cutaneous gel as a topical radioprotector in the prevention of the radiodermatitis occurring with adjuvant radiotherapy for localised breast cancer after lumpectomy

Acronym
GuARD

Study objectives
Primary objectives:
To investigate the safety, tolerability, and efficacy of GR1014-CG (4.7%; 2.4%) as a treatment to prevent radiodermatitis occurring with adjuvant ultra hypofractionated RT for localised, non-metastatic breast cancer after lumpectomy, versus vehicle gel.

Secondary objectives:
1. To assess the efficacy of GR1014-CG (4.7%; 2.4%):
1.1. In reducing radiodermatitis severity versus vehicle gel
1.2. In reducing peak radiodermatitis severity versus vehicle gel

1.3. In reducing radiodermatitis emergence versus vehicle gel
1.4. In delaying the onset of radiodermatitis versus vehicle gel
1.5. In reducing the duration of radiodermatitis versus vehicle gel
1.6. In reducing severe radiodermatitis versus vehicle gel
1.7. In reducing the side effects of RT other than dermatitis versus vehicle gel
1.8. In reducing patient-reported pain intensity in the irradiated skin region induced by RT versus vehicle gel
1.9. In reducing patient-reported pruritus intensity in the irradiated skin region induced by RT versus vehicle gel
1.10. On participants' assessment of their quality of life during and after RT versus vehicle gel
2. To characterise the plasma Cmax of amifostine thiol after application of GR1014-CG

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 17/04/2024, London - Chelsea Research Ethics Committee (Research Ethics Committee (REC) London Centre, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048181; chelsea.rec@hra.nhs.uk), ref: 24/LO/0121

2. approved 21/05/2024, CPP SUD EST III (59 Boulevard Pinel, BRON, 69 500, France; +33 (0) 427856245; cpp.sud-est-3@chu-lyon.fr), ref: 2023-508728-36-00-SM-2

Study design
Double-blind randomized placebo-controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Radiodermatitis occurring with adjuvant radiotherapy for localised breast cancer after lumpectomy

Interventions
Participants will be randomised in a 1:1:1: ratio into each of the three arms: vehicle gel, GR1014-CG 4.7%, and GR1014-CG 2.4% (block randomisation, online tool). GR1014-CG or vehicle gels will be applied topically on the skin surface to be irradiated (0.5 ml per 100 cm2) each day of the radiotherapy, 15-30 min before irradiation. Participants will be followed up weekly for up to 8 weeks after the last session of radiotherapy.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
GR1014 Cutaneous Gel

Primary outcome(s)
Percentage of participants with no radiation dermatitis (Common Terminology Criteria for Adverse Events latest version [CTCAE LV] grade of 0) measured at each study visit between the first radiotherapy session and 4 weeks after the last one.

Key secondary outcome(s))
1. Percentage of participants with a radiodermatitis grade ≥2 (CTCAE LV) occurring at any time between the first RT session and 4 weeks after the last one.
2. Percentage of participants with no radiation dermatitis (CTCAE LV, grade of 0), 4 weeks after the last RT session (at Visit 10).
3. Maximum grade of radiodermatitis (CTCAE LV) reached in each participant between the first RT session and 4 weeks after the last one.
4. Assessments of radiodermatitis grade (CTCAE LV) between the first RT session and the last visit.
5. Time to onset of radiodermatitis grade ≥2 (CTCAE LV).
6. Duration of radiodermatitis grade ≥2 (CTCAE LV).
7. Percentage of participants with severe radiodermatitis (grade ≥3; CTCAE LV) occurring at any time between the first RT session and 4 weeks after the last one.
8. Number of cases of side effects of RT other than radiodermatitis occurring at any time between the first RT session and the last visit (oedema; hyperpigmentation; skin infection; need for topical and systemic antibiotics; need for topical steroids; need for analgesics; need for silicone-based dressings).
9. Absolute change from baseline in weekly averaged worst skin pain score in the irradiated area. Worst pain intensity (during the last 24 hours) will be scored daily on a 0-10 Numeric Rating Scale (NRS) from first to last visit.
10. Absolute change from baseline in weekly averaged peak pruritus score in the irradiated area. Peak pruritus intensity (during the last 24 hours) will be scored daily on a 0-10 NRS from first to last visit.
11. Total score and sub-scores of Dermatology Life Quality Index (DLQI) addressed from the first RT session to the last visit.

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 08/04/2025:

1. Dated, signed informed consent obtained from individuals who agree to participate in the study
2. Female patients with age ≥18 years. Those of childbearing potential1 must be using highly effective contraception methods during the study and for 30 days after the last administration of the study treatment and have a negative pregnancy test at screening and no more than 10 days prior to the administration of the first dose of study treatment
3. Patients with primary, localised breast cancer without metastases pTis, T1-3, pN0-N1mi, M0, who have undergone breast-conserving surgical excision and require adjuvant RT. The patients should be randomised after having recovered from the last surgery and, if delivered, the adjuvant chemotherapy. The patients can be included no matter the status of oestrogen and progesterone receptors, malignancy grade, or HER2 status.

4. Eastern Cooperative Oncology Group (ECOG) performance status 0-2
5. Patients to be treated with ultra hypofractionated RT, 26 Gy in 5 fractions (5.2 Gy) on whole breast (EQD2 > 42.6 Gy for α/β of 3)
6. Patients with no signs of dermatitis in the breast area to be irradiated, i.e., assessed Grade 0 as per CTCAE LV radiation dermatitis grading
7. Patients whom the investigator has deemed able to comply with the RT and investigational treatment done under the supervision of the medical personnel throughout the study period
8. Patients affiliated with the Social Security System (France)
9. Patients who have completed the appropriate washout period for any prior interventions or treatments

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Previous inclusion criteria:

1. Dated, signed informed consent obtained from individuals who agree to participate in the study
2. Female patients with age ≥18 years. Those of childbearing potential1 must be using highly effective contraception methods during the study and for 30 days after the last administration of the study treatment and have a negative pregnancy test at screening and no more than 10 days prior to the administration of the first dose of study treatment
3. Patients with primary, localised breast cancer without metastases pT1--3, pN0--N1mi, M0, who have undergone breast-conserving surgical excision and require adjuvant RT. If adjuvant chemotherapy is delivered, the patient must be randomised within 4 weeks after the last series of adjuvant chemotherapy. If no adjuvant chemotherapy is delivered, the patient must be randomised within 8 weeks from the last surgery. The patient can be included no matter the status of oestrogen and progesterone receptors, malignancy grade, or HER2 status.
4. Eastern Cooperative Oncology Group (ECOG) performance status 0-2
5. Patients to be treated with ultra hypofractionated RT, 26 Gy in 5 fractions (5.2 Gy) on whole breast (EQD2 > 42.6 Gy for α/β of 3)
6. Patients with no signs of dermatitis in the breast area to be irradiated, i.e., assessed Grade 0 as per CTCAE LV radiation dermatitis grading
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9. Patients who have completed the appropriate washout period for any prior interventions or treatments

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex

Female

Key exclusion criteria
1. Pregnant and breastfeeding women
2. Patients under any treatment concomitant to RT tested in another clinical study
3. Allergies to any of the ingredients in GR1014-CG
4. Patients protected by law (legal guardianship or protection)
5. Patients unable to adhere to the requirements of the study
6. History of thoracic RT
7. Participants with the presence of skin rash, ulceration, unhealed surgical wounds, biopsy sites, or open wound in the breast or chest area at visit 2
8. Patients suffering from scleroderma, auto-immune disease, micro-vascular diseases, collagen tissue diseases, lupus, pre-existing loss of skin integrity, active eczema in the region to be treated or with a history of any of the following: drug-induced severe cutaneous adverse reaction (SCAR; including, but not limited to Stevens-Johnson syndrome/toxic epidermal necrolysis [SJS/TEN], or drug reaction with eosinophilia and systemic symptoms)

Date of first enrolment
26/07/2024

Date of final enrolment
30/09/2026

Locations

Countries of recruitment
United Kingdom

England

France

Study participating centre
The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research
Downs Road
Sutton
United Kingdom
SM2 5PT

Study participating centre
Institut Gustave Roussy
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Study participating centre
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Sponsor information

Organisation
Graegis Pharmaceuticals Ltd

Funder(s)

Funder type
Industry

Funder Name
Graegis Pharmaceuticals Ltd

Results and Publications

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

IPD sharing plan summary
Data sharing statement to be made available at a later date