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Clinical study to evaluate the effectiveness of hyaluronic acid 0.2% cream for the prevention of skin toxicity in breast cancer patients treated with post-operative radiotherapy

Submission date
09/11/2018

Recruitment status
No longer recruiting

Registration date
03/12/2018

Overall study status
Completed

Last Edited
28/05/2024

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Breast irradiation (radiotherapy) after breast surgery is a standard of care for about half of the patients with breast cancer. Localized radiotherapy is delivered daily during a few weeks to the breast area. During this period, the irradiated skin can be damaged. Mild redness is the first sign to appear generally within few hours of radiation exposure, even if the most common skin reactions occur about 10–14 days after the beginning of the therapy and may include symptoms like skin swelling, dryness, burning, itching, tenderness, change in skin colour and skin lesions. Such symptoms disappear after the radiation therapy has finished. However, sometimes skin reactions are so intense that the patient is obliged to discontinue radiotherapy. The application during radiotherapy of hydrating creams on the irradiated skin area can help reducing the risk of severe skin damage. The product used in this study is a cream containing hylauronic acid, a natural component of the skin with hydrating and cicatrizing properties. This product is already used for the treatment of skin wounds, including chronic wounds like leg ulcers. The aim of this study is to find out whether twice daily application (morning and evening) of the cream with hyaluronic acid before, during and after radiotherapy, is able to reduce the severity of skin damage.

Who can participate?
Women aged 18 years and over who have undergone surgery for breast cancer and are scheduled for radiotherapy

What does the study involve?
Participants are randomly allocated to receive either the test cream or a neutral cream (the same cream without hyaluronic acid). The occurrence and the intensity of skin reactions are assessed both by the responsible physician and by means of an instrument (spectrophotometer) that can measure exactly the intensity of the colour of the irradiated skin and depict any change that occurred during the study as a consequence of the radiotherapy. Moreover, any other discomfort caused by the radiotherapy and its impact on daily life or any side effects of the

applied cream are reported during the study period. Participants attend a maximum of 9 visits at the clinical site where the radiotherapy is delivered. Also, participants have to avoid the application on the irradiated skin area of any other product (including cosmetic products) and have to avoid exposure of the area to sun/sunbed during the whole study period. The patients under chemotherapy or who are under treatment with corticosteroids or other drugs known to or suspected of compromising the immune system (immunosuppressive therapy) are not allowed to participate. Patients who are allergic to the test cream or to one of its components should not participate in the study. If an allergic reaction develops during the study, the treatment with the cream has to be stopped. However, the radiotherapy can be continued, based on the opinion of the responsible physician.

What are the possible benefits and risks of participating?
The prevention or reduction in the intensity of the skin reaction generally experienced during and after radiotherapy are potential benefits for study participants. Possible risks include the occurrence of eczema, allergy, and hypersensitivity reactions to the tested creams. Severe reactions to the test cream have been very rarely reported.

Where is the study run from?
Istituto Oncologico della Svizzera Italiana (IOSI) in Bellinzona (Ticino, Switzerland)

When is the study starting and how long is it expected to run for?
May 2018 to August 2021

Who is funding the study?
IBSA Institut Biochimique S.A (Switzerland)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
18CH-Iccr05

Study information

Scientific Title
Mono-centre, prospective, placebo-controlled, double-blind, in parallel groups randomized clinical trial to evaluate the effectiveness of hyaluronic acid 0.2% cream for the prevention of skin toxicity in breast cancer patients treated with post-operative radiotherapy

Study objectives
To demonstrate the superiority of HA 0.2% cream in reducing the incidence of Grade ≥ 2 radiodermatitis, as compared to a neutral comparator (placebo) cream, when daily applied starting 2 weeks before local radiotherapy (LRT), during the LRT period until 2 weeks after the end of LRT.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Comitato Etico del Cantone Ticino, Bellinzona, Ticino-Switzerland, 22/10/2018

Study design
Monocentric prospective double-blind (Investigator- and patient-blinded) controlled clinical trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Radiodermatitis

Interventions

The tested Investigational Product HA 0.2% cream, or Ialuset® cream, is a CE-marked medical device, classified as Class IIb, available as 100 g tubes. The neutral comparator (placebo) cream is physically and visually indistinguishable from the test.

Adult female subjects having undergone curative surgery for unilateral stage I-III breast cancer and being scheduled for adjuvant LRT with conventional fractionation or hypofractionation at the investigation site, will be enrolled in the trial after having given written informed consent. According to a pre-established randomization sequence, the subjects will be treated daily with either HA 0.2% cream or neutral comparator cream, for 2 weeks before starting LRT up to 2 weeks after the end of a 6-week LRT (10 weeks of cream treatment) or 3-week LRT if hypofractionated schedule [15 fractions] (7 weeks of cream treatment in total). Patients will apply the cream twice daily, every 12 hours, with a dose sufficient to uniformly cover with a thin layer the whole cutaneous irradiated area (breast or chest wall). A wash out period of at least 6 hours has to be observed between the cream application and the irradiation. During the study participants attend a maximum of 9 control visits, always at the clinical site where the radiotherapy is delivered, to follow up treatment performance and tolerability.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Not provided at time of registration

Primary outcome measure
Proportion (%) of patients developing skin reactions (radiodermatitis) of Grade ≥ 2, as assessed by the Investigator according to the RTOG score, at the end of the LRT period

Secondary outcome measures
1. Proportion (%) of patients developing skin reactions (radiodermatitis) of Grade ≥ 2, as assessed by the Investigator according to the RTOG score, during the LRT period and in the 2-week follow-up
2. Skin reaction (erythema/inflammation) severity, as assessed by skin reflectance spectrophotometry (SRS) at the Screening/Enrolment visit (baseline assessment), after irradiation on Day 1 (LRT start), and on each of the subsequent weekly Control Visits during LRT, as well as at the end of the 2-week follow-up period (End-of-Study visit)
3. Time (days) to reach a Grade ≥ 2 skin reaction (radiodermatitis), as assessed by the Investigator according to the RTOG score at each post-baseline control visit
4. Total delivered dose (Gy) to reach a Grade ≥ 2 skin reaction (radiodermatitis), as assessed by the Investigator according to the RTOG score at each post-baseline control visit
5. Proportion (%) of patients developing a Grade ≥ 3 skin toxicity at the irradiated site, as assessed by the Investigator according to the RTOG score, at each control visit
6. Patient's self-perceived Level of Discomfort at the irradiated site as assessed on a 0-100 mm Visual Analog Scale (VAS), anchored to 0 = no discomfort at all and 100 = worst possible discomfort, at each control visit
7. Patient’s Quality of Life (QoL), as assessed by the patient using a self-administered QoL questionnaire (Short Form 36 – SF36) at screening/enrolment visit, start of LRT visit and at the follow-up visit
8. The Overall Treatment Performance, judged by the Investigator using a 5-point scale (4 =

Excellent; 3 = Good; 2 = Fair; 1 = Poor; 0 = None) at the end of the study
9. The safety of use of study medication evaluated by means of AEs and Treatment Emergent AEs (TEAEs) (Common Terminology Criteria for Adverse Events v4.03) (incidence, severity, duration, and causal relationship with the IP will be assessed), occurring at any time during the study
10. Overall Treatment Tolerability, independently judged by the Investigator and Patient using a 5-point scale (4 = excellent; 3 = good; 2 = fair; 1 = poor; 0 = none) at the end of the study

Overall study start date
09/05/2018

Completion date
11/08/2021

Eligibility

Key inclusion criteria
1. Females aged ≥18 years
2. Having undergone curative surgery for unilateral stage I-III breast cancer and scheduled for adjuvant LRT with conventional fractionation or hypofractionation according to the site guidelines; performance status ECOG 0-1
having given written informed consent to participate in the study according to Good Clinical Practice (GCP)
3. Able to comprehend the full nature and the purpose of the study, including possible risks and side effects, and able to cooperate with the Investigator and to comply with the requirements of the entire study (including ability to attend all the planned study visits according to the time limits), based on Investigator's judgement
4. Females of childbearing potential (i.e., not permanently sterilised - post hysterectomy or tubal ligation status – or not postmenopausal) must use an appropriate method of contraception for at least 30 days before inclusion in the study and during the whole study period; for all females of childbearing potential (i.e., not permanently sterilised - post hysterectomy or tubal ligation status – or not postmenopausal) the pregnancy test result must be negative at Screening /Enrolment visit of the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
120 participants (60 in each treatment group)

Total final enrolment

Key exclusion criteria
1. Presence of any dermatologic disease or condition or conditions known to alter skin appearance or physiologic response that might interfere with evaluation of the test site reaction or contraindicate participation
2. Ipsilateral relapsing/second breast tumour or previous LRT on the same volumes
3. Concomitant chemotherapy
4. Patients treated with mastectomy and autologous reconstruction
5. Positioning of “bolus” on chest wall
6. Allergy to the components contained in the IP; history of anaphylaxis or allergic reactions to any other allergens potentially affecting the study outcome
7. Underlying disease (T-lymphocytes impairment) or concomitant treatment with systemic (oral, parenteral) corticosteroids, as well as with any other drugs known to or suspected of compromising the subject's immune system (immunosuppressive therapy)
8. Clinically significant or unstable concurrent disease whose sequelae or treatment might interfere with the study evaluation parameters
9. Major psychiatric disorders that, in the view of the Investigator, could compromise the patient’ s participation in the study
10. Positive or missing pregnancy test at Screening/Enrolment visit, or breastfeeding women
11. Concomitant participation in other clinical trials or participation in the evaluation of any IMDs /IMPs during 3 months before this study or previous participation in the same study
12. Participation in the study is also not permitted to employees of the Investigator or study centre with direct involvement in the trial or in other trials under the direction of that Investigator, as well as family members of the employees or the Investigator

Date of first enrolment
18/04/2019

Date of final enrolment
04/06/2021

Locations

Countries of recruitment
Switzerland

Study participating centre
Istituto Oncologico della Svizzera Italiana (IOSI)
Ente Ospedaliero Cantonale (EOC)
Via Ospedale
Bellinzona
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Sponsor information

Organisation
IBSA, Institut Biochimique S.A

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Industry

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Funder type
Industry

Funder Name
IBSA, Institut Biochimique S.A

Results and Publications

Publication and dissemination plan
The results will be published in one or more separate articles following the completion of the clinical investigation.

Intention to publish date
31/12/2023

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		24/05/2024	28/05/2024	No	No