Impact of dermatological toxicities on quality of life in patients with early breast cancer exposed to adjuvant endocrine therapy: a real-world cross-sectional study

BCARE (Breast Cancer Adjuvant Real-world Evaluation of Dermatological adverse events)

Version 3.0 - Date 23 May 2025

Sponsor	PIERRE FABRE MEDICAMENT
Protocol number	NIS18999
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HISTORY OF CHANGES

Protocol N°	Date	Countries involved	Main changes
Amended protocol 3.0	23 May 2025	All	Modification of the inclusion criterion #3 and addition of an interim analysis in order to communicate preliminary results to congress.
Amended protocol 2.0	04 November 2024	All	Updated as all PROs were finally available in Greek and could be completed by Greek patients.
Initial 1.0	05 July 2024	All	

SUMMARY OF CHANGES

Summary of changes from version 2.0 dated 4 November 2024 to version 3.0 dated 23 May 2025

Section # and Name	Description of Change	Brief Rationale
Sections 1 Synopsis (inclusion and exclusion criteria) and 4.2.1.1 Inclusion criteria as well as any section where the time window "…2 to 3 years…" is mentioned	Modification of the inclusion criterion #3. The sentence: "*Still being treated with adjuvant endocrine monotherapy, initiated 2 to 3 years ago before the inclusion in the study*" is changed by: "*Still being treated with adjuvant endocrine monotherapy, initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before the inclusion in the study*."	The modification of inclusion criterion #3 aims to introduce a more accurate and flexible time window for initiation of adjuvant endocrine therapy, allowing inclusion of patients treated for 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) prior to study inclusion. This will help with the identification of eligible patients in a real-world setting.
Section 4.7.8 Interim analysis	This section has been added due to the addition of an interim analysis on Q2-Q3 2025.	An interim analysis will be performed to communicate preliminary results to congress.
Section 7 Plans for disseminating and communicating study results	The following sentence has been added: "*Of note, no clinical study report will be written for the interim analysis*."	This sentence has been added for clarification due to the addition of an interim analysis.

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LIST OF ABBREVIATIONS

BCARE	Breast Cancer Adjuvant Real-world Evaluation of Dermatological adverse events
BCS	Breast-Conserving Surgery
ChT	Chemotherapy
CI	Confidence Interval
CTCAE	Common Terminology Criteria for Adverse Events
CRO	Contract Research Organization
DLQI	Dermatology Life Quality Index
EADV	European Academy of Dermatology and Venereology - European Task Force
EBC	Early Breast Cancer
eCRF	electronic Case Report Form
ePRO	electronic Patient Reported Outcome
EMA	European Medicine Agency
ER	Estrogen Receptor
ESMO	European Society for Medical Oncology
GCP	Good Clinical Practice
GVP	Good Pharmacovigilance Practice
HER2	Human Epidermal growth factor Receptor 2
ICF	Informed Consent Form
ICH	International Conference of Harmonization
IRB/IEC	Institutional Review Board/Independent Ethics Committee
MRI	Magnetic Resonance Imaging
PgR	Progesterone Receptor
QC	Quality Control
QoL	Quality Of Life
RT	Radiotherapy
SAP	Statistical Analysis Plan
TNBC	Triple-Negative Breast Cancer
TNM	Tumor Node Metastasis
WHO	World Health Organization

1 SYNOPSIS

STUDY TITLE	Impact of dermatological toxicities on quality of life in patients with early breast cancer exposed to adjuvant endocrine therapy: a real-world cross-sectional study. BCARE (Breast Cancer Adjuvant Real-world Evaluation of Dermatological adverse events)
SPONSOR	PIERRE FABRE MEDICAMENT
STUDY RATIONALE	Dermatological toxicities are among the most common adverse events experienced by patients treated with anti-cancer therapies. With improved efficacy of anticancer treatments, cancer patients are living longer and report a better quality of life; however dermatological toxicities, such as skin inflammation, hair/nail changes, facial flushing, erythema or dry skin are still associated with a negative effect on patient's physical, functional, emotional, and social well-being. For these patients, the initiation of a skin care management is crucial to improve quality of life and ensure compliance to treatment. It has been confirmed that adverse events of endocrine therapy are significantly associated with anxiety and depression. Very few studies explored the quality of life related to dermatological toxicities of breast cancer patients exposed to endocrine therapy for a prolonged period. The use of endocrine agents is associated with frequent dermatological toxicities, including skin lesions, oral symptoms, nail changes or alopecia. Besides quality-of-life impairment of cancer patients, these reactions can lead to treatment adjustment or interruption. As patients live longer on cancer therapies, there is a need to identify factors of clinically significant events and to develop improved and widely available preventive strategies, all of which would contribute to the optimal and comprehensive care of cancer patients. Dermatological toxicities induced by adjuvant endocrine therapy can have a negative effect on cancer patients' quality of life (QoL) but has been exceptionally described in literature. To improve the QoL of patients treated with adjuvant endocrine therapy, a comprehensive understanding of the ongoing impact of these dermatological toxicities is lacking. This transversal study aims to describe the dermatological toxicities reported by European patients with early breast cancer treated with adjuvant endocrine therapy. This study will describe specifically the impact on quality of life related to dermatological toxicities of this population. To avoid catching dermatological toxicities related to prior treatments, only early breast cancer in female patients, currently treated with adjuvant

	endocrine monotherapy initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before the present study, will be included.
STUDY OBJECTIVES	**Primary objective** To measure the quality of life related to dermatological toxicities, using Dermatology Life Quality Index (DLQI) questionnaire, in female patients with early breast cancer (defined according to World Health Organization [WHO] classification and the 8th edition of the American Joint Committee on Cancer tumor, node, metastasis [TNM] staging system) being treated with ongoing adjuvant endocrine therapy in monotherapy, initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before inclusion in the study. **Secondary objectives** Secondary objectives aim, in female patients with early breast cancer (EBC), being treated with ongoing adjuvant endocrine monotherapy initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before inclusion in the study, to describe: 1. The dermatological quality, using Skindex-16, Hairdex, and ItchyQoL questionnaires. 2. The real-world dermatological toxicities present at inclusion. 3. The demographics characteristics, and the clinical characteristics. **Exploratory objectives** To describe real-world dermatological toxicities, from the beginning of their endocrine therapy to the time of data collection, of female patients with EBC, being treated with ongoing adjuvant endocrine monotherapy initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before inclusion in the study.
STUDY OUTCOMES	**Primary outcome** Quality of life data collected at the time of inclusion using the validated DLQI questionnaire. The primary endpoint is the rate of patients with a DLQI score ≥ 6. The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired: 0 – 1 corresponds to no effect at all on patient's life; 2 – 5 corresponds to small effect on patient's life; 6 – 10 corresponds to moderate effect on patient's life; 11– 20 corresponds to very large effect on patient's life; 21 – 30 corresponds to extremely large effect on patient's life.

	Secondary outcomes 1. Quality of life data collected at the time of inclusion using the Skindex-16, Hairdex, and ItchyQoL questionnaires. 2. Ongoing dermatological toxicities reported by investigator according to Common Terminology Criteria for Adverse Events (CTCAE) (version 5.0, November 2017): a. Type of toxicity b. Surface area involved (except for nails and oral dryness) c. Start date d. Clinical grading of the toxicity 3. Demographics, and clinical characteristics at the time of inclusion, including the following items: a. Age, gender, weight, height b. Menopausal status c. Date of cancer diagnosis d. Primary tumor location e. T stage f. Prior therapies for breast cancer (type, agent name, start date, stop date) g. Endocrine therapy (agent name, start date) for breast cancer h. Current dermatological care and sun-protective behaviors **Exploratory outcomes** History of dermatological toxicities from the beginning of current treatment to the time of inclusion: a. Type of dermatological toxicity b. Surface area (except for nails and oral dryness) c. Start date and end date d. Grade of the toxicity, if available

	e. Change in hormonal treatment (adaptation, interruption), if applicable.
STUDY DESIGN	European (including France, Greece, Italy, Spain), multicenter (from the EADV European Academy of Dermatology and Venereology - European Task Force "Dermatology for cancer patients"), real world observational, cross-sectional study, to describe the quality of life related to dermatological toxicities, in female patients with EBC, treated with ongoing adjuvant endocrine monotherapy initiated for 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before inclusion in the study. This is a cross-sectional, non-interventional study in which physicians and patients will follow local clinical practice. Patients will be asked to complete 4 questionnaires at the time of their inclusion. Medical history, demographics, clinical characteristics, dermatological toxicities from the beginning of their endocrine therapy to the time of data collection will be collected from their medical charts. As this is a transversal study, there will not be any follow-up, and no safety data will be collected.
STUDY POPULATION	The study population will include approximately up to 156 patients with EBC being treated with adjuvant endocrine monotherapy initiated 2 years (up to 1 year and 9 months) and 3 years (up to 3 years and 6 months) before inclusion in the study. Participating sites will be encouraged to propose the study to all patients meeting the eligibility criteria, in a consecutive manner, when they come for consultation, in order to minimize bias in patient selection.
INCLUSION AND EXCLUSION CRITERIA	**Inclusion criteria** Patients will be eligible for inclusion if they fulfill ALL the following criteria: 1. Females aged ≥ 18 years at inclusion. 2. Histologically confirmed diagnosis of EBC, according to the WHO criteria and the TNM classification, at any time before inclusion. 3. Still being treated with adjuvant endocrine monotherapy, initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) ago before the inclusion in the study. 4. Signed Informed Consent Form (ICF) or non-opposition, according to local regulations. **Exclusion criteria**

<table>
<tr><td></td><td>Patients will <u>not</u> be eligible for inclusion if they fulfill <u>ANY</u> of the following criteria:
1. Patients not able to read, understand and complete Questionnaires in local language.
Exclusion criteria (cont'd)
2. Patients with chronic dermatological conditions (treated or not) before initiating the adjuvant endocrine therapy that could interfere with the quality of life.
• Patients with concomitant targeted therapies with adjuvant endocrine therapy such as CDK4/6 inhibitors or trastuzumab, and patients with ongoing treatment with neratinib.
3. Patients having relevant or severe comorbidities requiring complex therapeutic treatment.
4. Patients having a persistent post-chemotherapy alopecia (at least of grade 1)</td></tr>
<tr><td>SAMPLE SIZE</td><td>Up to 156 patients to reach 140 evaluable patients.</td></tr>
<tr><td>STATISTICS</td><td>Sample size calculation
Within this study, it is planned to recruit 156 patients.
Accrual of 140 evaluable patients permits to estimate a 95% confidence interval of a proportion equals to 40% with an accuracy of +/-8%. The following table presents the accuracy for different proportions:
<table><tr><td></td><td colspan="4">Proportion of DLQI score ≥ 6</td></tr><tr><td></td><td>10%</td><td>20%</td><td>30%</td><td>40%</td></tr><tr><td>Accuracy (%)</td><td>+/-5</td><td>+/-6.5</td><td>+/-7.5</td><td>+/-8</td></tr></table>Assuming a rate of around 10% of non-evaluable patients (missing data), 156 patients will be included to reach 140 evaluable patients.
Statistical analyses
Statistical analyses will be fully described in a written Statistical Analysis Plan (SAP). The study endpoints will be analyzed overall and by predefined subgroup(s) of interest. Analyses will be descriptive in nature, as no hypothesis will be tested. In general, missing data will not be imputed (except for dates) and the data will be analyzed according to the complete case approach.</td></tr>
</table>

	As regard to the descriptive nature of this study, an interim analysis will be performed on the patients included in the study coordinator's site (France) until the 15th of May 2025 in order to communicate preliminary results to congress. The demographic and clinical characteristics will be described using summary statistics. Categorical variables will be summarized by frequencies and percentages. Continuous variables will be summarized by descriptive statistics (mean, and standard deviation, median, 25th and 75th percentiles, minimum and maximum). The number of missing observations for each variable will also be reported.

2 BACKGROUND AND RATIONALE

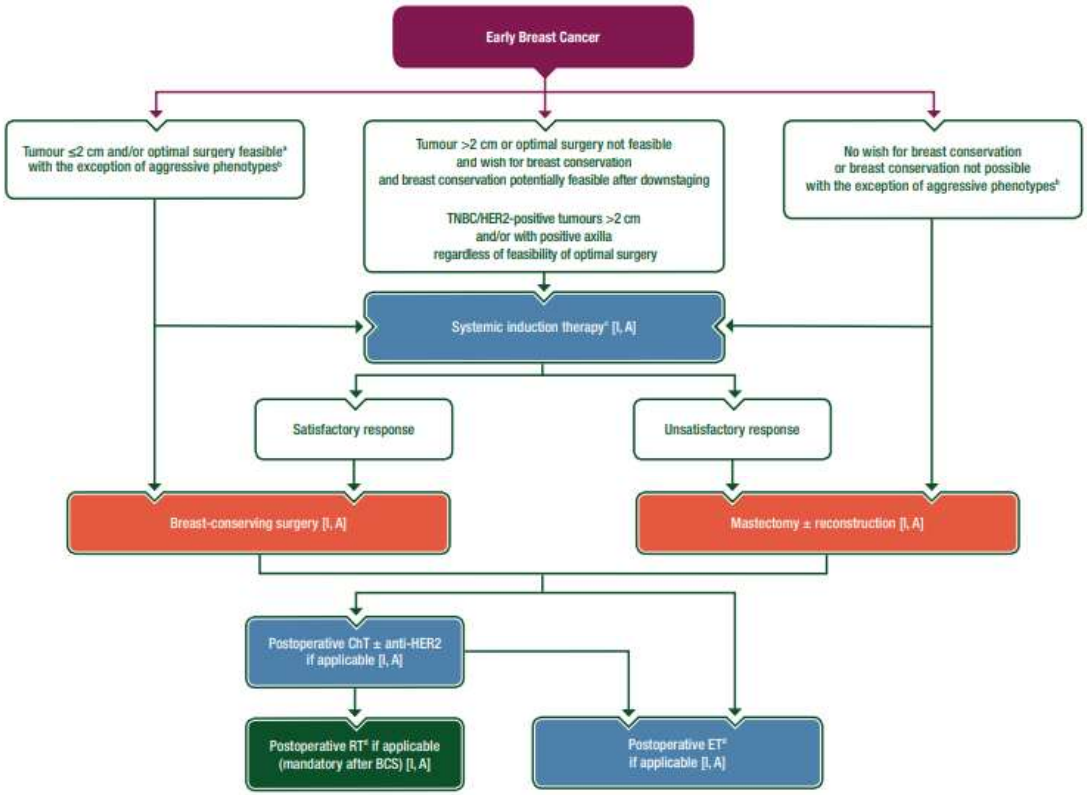
2.1 BACKGROUND

In 2020, about 2.3 million new cases of breast cancer were diagnosed worldwide, accounting for almost one in four cancer cases among women, and nearly 30% died of it according to European Society for Medical Oncology (ESMO) (**Loibl, 2024**). The predicted number of new breast cancers in 28 European Union countries was 404 920, with estimated age-adjusted annual incidence of breast cancer of 144.9/100 000 and mortality of 32.9/100 000 (**Dafani, 2019**). About a quarter of breast cancers occurred before age 50, and less than 5% before age 35 (**Cardoso, 2019**). In 2018, ten-year survival of breast cancer exceeds 70% in most European regions, with 89% survival for local and 62% for regional disease (**Cardoso, 2019; Nardin, 2020**). The annual hazard of recurrence peaks in the second year after diagnosis but remains at 2%–5% in years 5–20 (**Cardoso, 2019**).

Diagnostic of primary tumor of breast cancer is obtained thanks to physical examination, mammography, breast ultrasound, breast Magnetic Resonance Imaging (MRI), and core biopsy with pathology determination of histology grade, estrogen receptor (ER), progesterone receptor (PgR), human epidermal growth factor receptor 2 (HER)2 and a proliferation marker, Ki67 (**Cardoso, 2019**). Final pathological diagnosis should be made according to the World Health Organization (WHO) classification (**Lakhani, 2012; Cardoso, 2019; Tan, 2020**), and the eighth edition of the American Joint Committee on Cancer tumor, node, metastasis (TNM) staging system (**Teichgraeber, 2021**).

Early Breast Cancer (EBC) is defined by the European Society for Medical Oncology (ESMO) (**Loibl, 2024**) as a stage where the tumor is 20 mm or smaller and has not spread to more than 3 lymph nodes. Alternatively, if the tumor is 20 to 50 mm in size and has not spread to any lymph nodes, it is also considered early-stage breast cancer. According to the European guidelines published by ESMO, the following decision tree for early breast cancer should be followed (see **Figure 1** hereafter):

Figure 1 - Early breast cancer treatment algorithm according to ESMO (Cardoso, 2019).



BCS, breast-conserving surgery; ChT, chemotherapy; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; RT, radiotherapy, TNBC, triple-negative breast cancer.
[a]Biology that requires chemotherapy (TNBC, HER2-positive, luminal B-like), to assess response and prognosis and eventually decide on postoperative therapies, should preferentially receive preoperative chemotherapy.
[b]Aggressive phenotypes: TNBC or HER2-positive breast cancer.
[c]If chemotherapy is planned, it should all be given as neoadjuvant.
[d]Concomitant postoperative radiotherapy, postoperative endocrine therapy and anti-HER2 therapy.

Depending on the phenotypes and the retrieved biomarkers, the chemotherapy w/o endocrine therapy (tamoxifen) w/o anti-ER2 agents such as trastuzumab ± pertuzumab are chosen according to ESMO (**Cardoso, 2019**). Adjuvant endocrine therapy is one of the most important treatments of hormone-receptor-positive breast cancer and includes selective estrogen receptor modulators such as tamoxifen, aromatase inhibitors, and luteinizing hormone-releasing hormone analogs (**Madigan, 2020; Rossi, 2021**). Adjuvant systemic treatment should preferably start within 3–6 weeks after surgery and neoadjuvant systemic therapy should start as soon as diagnosis and staging are completed (ideally within 2–4 weeks) (**Cardoso, 2019**).

Endocrine therapy should be used in all luminal-like cancers according to ESMO (**Cardoso, 2019**). For premenopausal women, tamoxifen for 5−10 years is a standard of care (**Cardoso, 2019**).

Breast cancer is associated with adverse events related to depression, anxiety, chronic fatigue, sleep problems, joint symptoms, pain, sexual dysfunction, genitourinary syndrome of menopause and sleep disorders **(Alnaim, 2022; Chan, 2020; Galvano, 2019; Lubián, 2022; Merlino, 2023; Roberts, 2022**). Besides the systemic reactions (dyslipidemia, weight changes and bone mineral density modifications), local reactions such as dermatological toxicities including skin inflammation, hair/nail changes, facial flushing (hot flushes), erythema or dry skin due to cancer treatments are still associated with a negative effect on patient's physical, functional, emotional, and social well-being (**Diana, 2021; Ferreira, 2019; Fessele, 2022; Lacouture, 2008; Lacouture, 2021; Wagner, 2007**).

Hair changes (hair thinning and alopecia) is a common adverse event (overall incidence of 4.4%; and highest incidence of 25% with tamoxifen in a phase II trial) as reported in a larger study of a cohort, 19,430 patients with endocrine-related cancers in 35 clinical trials (**Dell'Acqua, 2020**). Although the alopecia is not severe, alopecia-related quality of life is deeply affected as the Hairdex questionnaire is reported to be 25.6, with a higher negative impact on emotions (**Rossi, 2021**).

Common impact on skin such as rash, erythema or dry skin (23.66%) were also reported in 79 trials comparing 8669 patients receiving trastuzumab *versus* 9556 receiving no trastuzumab (**Jackson, 2022**). Hot flushes are also reported as a common event (**Cavadias, 2020; Peddie, 2021**).
The importance of the quality of life was highlighted as an important factor influencing breast cancer survivors adherence to and persistence with their medication (**Peddie, 2021**).

2.2 RATIONALE

The rationale for conducting this transversal real world observational study is the following:

- There is a lack of data regarding dermatological events impact on quality of life in early breast cancer females receiving adjuvant endocrine therapy: dermatological toxicities induced by adjuvant endocrine therapy can have a marked effect on cancer patients' quality of life but are rarely described in literature). This transversal real word observational study aims to describe the dermatological toxicities reported by patients with breast cancer treated with adjuvant endocrine therapy.

- The justification for the targeted population is the following:

    - Age and sex

Females aged above 18 years old will be considered in this study. Breast cancer mainly concern females as only 1% of males are affected according to ESMO (**Cardoso, 2019**). Considering females about a quarter of breast cancers occurred before age 50, and less than 5% before age 35 (**Cardoso, 2019**). The same range of proportion is therefore expected in the study to be representative of the general population.

    - Early breast cancer status

All early breast cancer stages status according to WHO (**Tan, 2020, Cardoso, 2019; Lakhani, 2012**) and TNM classification (**Teichgraeber, 2021**) will be included in the study in order to have an overall view of the whole population of patients treated with adjuvant endocrine therapy for breast cancer. The cancer status will be reported in the characteristics baseline.

- Justification of the study timepoint

To avoid catching dermatological reactions related to prior treatments, only early breast cancer female patients treated, with ongoing adjuvant endocrine therapy in monotherapy initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) ago will be included.

- Justification of the Quality of Life (QoL) questionnaires

For the primary objective, the Dermatology Life Quality Index (DLQI) questionnaire will be used for evaluating the overall quality of life regarding dermatological concerns.

For the secondary objectives, the QoL questionnaires were selected according to the common adverse events related to dermatological toxicities:

- Skindex-16 questionnaire for dermatological disease on quality of life (**Chren, 2012**),
- Hairdex questionnaire for evaluating of disease-specific quality of life in patients with hair diseases (**Fischer, 2001**),
- ItchyQoL questionnaire for assessing quality of life in patients with chronic pruritus (**Gabes, 2021**).

3 STUDY OBJECTIVES

3.1 PRIMARY OBJECTIVE

To measure the quality of life related to dermatological toxicities, using DLQI questionnaire, in female patients with early breast cancer (defined according to WHO classification and the 8th edition of the TNM staging system), being treated with ongoing adjuvant endocrine therapy in monotherapy, initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before inclusion in the study.

3.2 SECONDARY OBJECTIVES

Secondary objectives aim, in female patients with EBC, being treated with ongoing adjuvant endocrine monotherapy initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before inclusion in the study, to describe:

1. The dermatological quality, using Skindex-16, Hairdex, and ItchyQoL
2. The real-world dermatological toxicities present at inclusion.
3. The demographics characteristics, and the clinical characteristics.

3.3 EXPLORATORY OBJECTIVES

To describe real-world dermatological toxicities, from the beginning of their endocrine therapy to the time of data collection, of female patients with EBC, being treated with ongoing adjuvant endocrine monotherapy initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months), before inclusion in the study.

4 RESEARCH METHODS

4.1 STUDY DESIGN

This is an European (including France, Greece, Italy, Spain), multicenter (from the European Academy of Dermatology and Venereology - European Task Force "dermatology for cancer patients"), real word observational, cross-sectional study, to describe the quality of life related to dermatological toxicities, in female patients with EBC, treated with ongoing adjuvant endocrine monotherapy initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before inclusion in the study.
This is a cross-sectional, non-interventional study in which physicians and patients will follow local clinical practice. The study will not provide or recommend any treatment or procedure.

Participating sites will be encouraged to propose the study to all patients meeting the eligibility criteria, in a consecutive manner, when they come for consultation, in order to minimize bias in patient selection. Around 9 centers are expected to participate in the study.

Eligible patients will be selected among patients treated with ongoing adjuvant endocrine monotherapy initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before inclusion, in one of the study centers. Patients will be asked to complete 4 questionnaires at the time of their inclusion. Medical history, demographics, clinical characteristics, current and dermatological toxicities from the beginning of their endocrine therapy to the time of data collection will be collected from their medical charts.
As this is a transversal study, there will not be any follow-up, and no safety data will be collected. However, the investigator shall report all necessary information about any suspected adverse reaction to a product to the regulatory agency and to the marketing authorisation holder/manufacturer.

The decision to prescribe adjuvant endocrine monotherapy will be taken before the inclusion in the study. The study will not impose any treatments or visits.
European countries, including France, Greece, Italy, and Spain, will enroll patients. Dedicated reference centers (Dermatology For Cancer Patients Task Force) will be able to recruit.
The study will address oncologists, oncodermatologists and/or radiotherapists treating patients with adjuvant endocrine therapy. Physicians will be selected on their clinical research experience, the availability of their resources to conduct the study and their ability to recruit and follow a sufficient number of patients in the study. Only patients who provide written informed consent or non-opposition to data collection, as per local regulations, will be enrolled.

The enrolment period is expected to extend up to 12 months from the study start.

Approximately 156 eligible patients will be selected.

4.2 POPULATIONS

4.2.1 Study population

Approximately 156 patients will be included in the study to get about 140 evaluable patients.

The source population in this study is female patients suffering from EBC and treated with adjuvant endocrine monotherapy for 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months), who spontaneously visit a hospital from the EADV European task force, in European countries (including France, Greece, Italy and Spain). They will be invited to participate in the study, during the inclusion period. The study population is the source population meeting eligibility criteria listed hereafter during the inclusion period.

4.2.1.1 Inclusion criteria

Patients will be eligible for inclusion if they fulfill ALL The following criteria:

1. Female aged ≥ 18 years at inclusion.
2. Histologically confirmed diagnosis of EBC, according to the WHO criteria (**Lakhani, 2012; Cardoso, 2019; Tan, 2020**) and the TNM classification, (**Teichgraeber, 2021**) at any time before inclusion.
3. Still being treated with adjuvant endocrine monotherapy, initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before the inclusion in the study.
4. Signed Informed Consent Form (ICF) or non-opposition, according to local regulations.

4.2.1.2 Exclusion criteria

Patients will not be eligible for inclusion if they fulfill ANY of the following criteria:

1. Patients not able to read, understand and complete Questionnaires in local language.
2. Patients with chronic dermatological conditions (treated or not) before initiating the adjuvant endocrine therapy that could interfere with the quality of life.
3. Patients with concomitant targeted therapies with adjuvant endocrine therapy such as CDK4/6 inhibitors or trastuzumab, and patients with ongoing treatment with neratinib..
4. Patients having relevant or severe comorbidities requiring complex therapeutic treatment.
5. Patient having a persistent post-chemotherapy alopecia (at least of grade 1).

4.2.2 Patient selection

4.2.2.1 Study centers

The target countries for study participation will include European countries such as France, Greece, Italy, and Spain.

4.2.2.2 Patient selection

- Study initiation, patient selection, and data abstraction are planned to start in 2024.
- All female patients ≥ 18 years old with early breast cancer who are treated with any adjuvant endocrine monotherapy for 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before the inclusion date.
- After verification of the eligibility criteria, the investigator or qualified designee will inform the patient about:
  - The study objectives,
  - The possibility of refusing to participate without any prejudice to the relationship with the investigator and the patient's medical care,
  - Processing of personal data that will be collected during this study and the rights of access, opposition, and rectification to this data.

The patient will be provided with a written or electronic information sheet about the study prior to data abstraction from patient records and completion of the questionnaires. If the patient agrees to participate, she will be asked to provide their written informed consent or non-opposition to study participation to the investigator (depending on local regulations), which will be documented in the patient's medical file before data collection.

Data that will be collected upon study inclusion are detailed below:

- Patient demographics,
- History of early breast cancer stage and date of diagnosis,
- History of procedures and treatments before the initiation of the adjuvant endocrine therapy in monotherapy,
- History of the adjuvant endocrine therapy in monotherapy (date of initiation, type of treatment),

- History of dermatological toxicities from the beginning of current treatment to the time of inclusion,
- Ongoing dermatological toxicities,
- Dermatological care and sun protective behaviors,
- Quality of life questionnaires.

4.3 STUDY OUTCOMES

The outcomes of this real word observational study are purely descriptive. They aim to describe mainly the quality of life related to dermatological toxicities of female patients with early breast cancer under adjuvant endocrine therapy in monotherapy, and also the demographics and clinical characteristics at the time of inclusion.

4.3.1 Primary outcome

The primary outcome is the description of the quality-of-life data collected at the time of inclusion using the validated DLQI questionnaire. The DLQI consists of 10 questions concerning patients' perception of the impact of skin diseases on different aspects of their health-related quality of life over the last week, including symptoms, feelings, daily activities, leisure, work, school, personal relationships, and treatment.

The primary endpoint is the rate of patients with a DLQI score ≥ 6. The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired:

- 0 – 1 corresponds to no effect at all on patient's life,
- 2 – 5 corresponds to small effect on patient's life,
- 6 – 10 corresponds to moderate effect on patient's life,
- 11 – 20 corresponds to very large effect on patient's life,
- 21 – 30 corresponds to extremely large effect on patient's life.

4.3.2 Secondary outcomes

1. Quality of life data collected at the time of inclusion using the Skindex-16, Hairdex, and ItchyQoL questionnaires.

   The Skindex-16 includes items distributed across three domains symptoms (items 1 to 4), emotions (items 5 to 11) and functioning (items 12 to 16) and are answered on a seven-point Likert scale (varying from 0-never bothered, to 6-always bothered), which represents the frequency with which the skin problem bothered the respondent during the past week. This is a 0-100 scale, higher the score, the more quality of life is impaired.

   The Hairdex is a valuable tool for evaluating disease-specific QoL in patients with hair disorders. It consists of 48 questions across five sections: symptoms, functioning, emotions, self-confidence, and stigmatization. Each question is self-graded on a scale of 0-4, with a score of 4 indicating the most severe change from a patient's baseline quality of life.

   The ItchyQoL is a questionnaire used to measure the QoL in patients with chronic pruritus. It is composed of 22 items regarding symptoms, functions, emotions and self-perception, and is currently under copyright protection. In addition to the total score, a subscore for "symptoms", "functioning" and "emotions" can also be calculated. Each item is rated on a 5-point scale, ranging from 1 = never to 5 = all the time.

2. Ongoing dermatological toxicities reported by investigator according to Common Terminology Criteria for Adverse Events (CTCAE) (version 5.0, November 2017):
   a. Type of toxicity
   b. Surface area involved (except for nails and oral dryness)
   c. Start date
   d. Clinical grading of the toxicity
3. Demographics, and clinical characteristics at the time of inclusion, including the following items:
   a. Age, gender, weight, height
   b. Menopausal status
   c. Date of cancer diagnosis
   d. Primary tumor location
   e. T stage
   f. Prior therapies for breast cancer (type, agent name, start date, stop date)

g. Endocrine therapy (agent name, start date) for breast cancer
h. Current dermatological care and sun-protective behaviors

4.3.3 Exploratory outcomes

History of dermatological toxicities from the beginning of current treatment to the time of inclusion, including:

a. Type of dermatological toxicity
b. Surface area (except for nails and oral dryness)
c. Start date and end date
d. Grade of the toxicity, if available
e. Change in hormonal treatment (adaptation, interruption), if applicable

4.3.4 Subgroups of interest

The following subgroups described are of interest:

- Age repartition by class (< 35 years old, 35-50, 50-65, > 65 years old)
- Menopause status
- Therapeutical choice before the 2/3 years of adjuvant endocrine therapy (2 years up to 1 year and 9 months, to 3 years up to 3 years and 6 months).
  - Radiotherapy (yes / no)
  - Chemotherapy (yes / no), if yes, the information whether taxane was received or not will be collected
  - Adjuvant (yes/no)
  - Neoadjuvant (yes/no)
  - Target therapy (yes / no)
  - Type of adjuvant endocrine therapy

Analyses of primary, secondary, and exploratory outcomes may be performed for some or all of these subgroups, subject to pertinence and the number of patients in each subgroup.

4.4 DATA SOURCES

Data for each patient will be collected until the date of inclusion. Questionnaires will be filled by patients at the time of their inclusion and data will be collected in their medical records during data abstraction period.
The source of collected data will include all elements that constitute a reliable source of patient-level information and are available at the center.
This includes inpatient medical charts (*e.g.*, consultation notes, discharge summaries, laboratory test results, recorded prescription data and any other documentation of communication with other health care providers). The center investigator will be responsible for ensuring that all the required data is collected and entered into an electronic Case Report Form (eCRF). The pseudonymization of entered data will be guaranteed by the use of a Subject Identifier. This pseudonymization will be maintained in the database used for statistical analysis.

Electronic Patient Reported Outcome (ePRO) will be used to collect questionnaires. Patients will be asked to fill questionnaires on site using tablets specifically dedicated to the present study.

Key data items that will be collected are listed in section Study outcomes.

4.5 STUDY SIZE

Within this study, it is planned to recruit 156 patients.
Accrual of 140 evaluable patients permits to estimate a 95% confidence interval of a proportion equals to 40% with an accuracy of +/-8%. The following table presents the accuracy for different proportions:

	Proportion of DLQI score ≥ 6			
	10%	20%	30%	40%
Accuracy (%)	+/-5	+/-6.5	+/-7.5	+/-8

Assuming a rate of around 10% of non-evaluable patients (missing data), 156 patients will be included to reach 140 evaluable patients.

4.6 DATA MANAGEMENT

A Data Management Plan will be created before the start of data collection and will describe all functions, processes, and specifications for data collection, cleaning and validation to ensure that the data are as clean and accurate as possible when presented for analysis. Data collection and validation procedures will be detailed in the appropriate operational documents.

A study monitoring plan, including for-cause monitoring, that is appropriate for the study design will be developed and implemented. Data quality control (QC) will be performed remotely and at the center level, where permissible according to local regulations, by qualified designated personnel under professional secrecy.

All medical data will be confidential. Pierre Fabre Médicament, as the Sponsor of the study and data controller, is responsible for the processing of personal data in accordance with the provisions of Regulation 2016/679/EU of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and the free movement of such data (GDPR), the data collected being for research purposes in the field of health, the legal basis of the processing being the legitimate interest of the data controller.

Data from patient medical records will be entered by the investigator or delegated data entry specialists in the eCRF. The qualified designee for data entry must ensure that:

- Data entry is performed in a timely manner,
- Data entry is complete and accurate,
- All eCRF data are verifiable in the source documentation,
- Data queries are resolved and documented by authorized study staff,
- All eCRFs are approved with an electronic signature (changes to data previously submitted will require a new electronic signature to acknowledge/approve the changes).

All data collected within the eCRF will be approved and electronically signed and dated by the investigator. This approval will acknowledge the investigator's review and acceptance of the data as being complete and accurate.

At study end and before the final statistical analysis, the eCRF and other study data will be locked to further additions or corrections. Locking the study data represents the acknowledgement that all data have been captured and confirmed as accurate.
Quality assurance department representatives from Pierre Fabre Médicament and/or Contract Research Organization (CRO) may visit a study center to conduct quality assurance audit and ensure the study is conducted in compliance with protocol, Standard Operating Procedures and all applicable legal requirements.

4.7 DATA ANALYSIS

4.7.1 General considerations

Statistical analyses will be fully described in a Statistical Analysis Plan (SAP). Analyses will be conducted with SAS® software, version 9.4 or higher.

Analyses will be descriptive in nature, as no hypothesis will be tested.
Demographic and clinical characteristics will be presented in the overall population using usual statistics. Quantitative data will be summarized as median, min, max and number of missing data. Qualitative variables will be described as number, percentage and number of missing data.

4.7.2 Data-set definition

Analysis population (full analysis set) consists of all patients fulfilling inclusion and exclusion criteria with at least one QoL score not missing.

4.7.3 Analysis of primary outcomes

The primary endpoint is the rate of patients with a DLQI score ≥ 6. It will be described as number and percentage with corresponding 95% interval (binomial exact).

4.7.4 Analysis of secondary outcomes

Quality of Life Scores will be calculated using recommendations provided in the literature and will be described by means, standard deviations, medians, and percentages. The percentage of missing Quality of life scores will be also provided and patients' missing score profiles will be then generated to assess the impact on QoL scores.
Dermatological toxicities ongoing at inclusion will be described. Each of the following will be assessed:

- Dermatological toxicities by type,
- Dermatological toxicities for each type and by grade.

Frequency, percentage with 95% Confidence Interval (CI) will be computed for each event.

4.7.5 Analysis of exploratory outcomes

History of dermatological toxicities will be described. Each of the following will be assessed:

- Dermatological toxicity by type,
- Dermatological toxicity for each type and by grade.

4.7.6 Missing data

In general, missing data will not be imputed (except for dates) and the data will be analyzed according to the complete case approach. Proportion of missing data will be provided for all variables during descriptive analyses.

4.7.7 Interim analysis

As regard to the descriptive nature of the study, an interim analysis will be performed on Q2-Q3 2025 on the patients included in the study coordinator's site (France) until the 15th of May 2025 in order to communicate preliminary results to congress. The interim analysis will describe patients' characteristics and the quality-of-life data collected at the time of inclusion using the validated DLQI questionnaire (*i.e.* primary outcome) and the Skindex-16 (*i.e.* one of the secondary outcomes). Details of the interim analysis will be described in the SAP.

4.8 QUALITY CONTROL

After formal agreement of participation, centers will be trained in the protocol's procedures by a designated Clinical Research Associate. The frequency of subsequent contacts (monitoring on center visits, phone, or e-mail) with the centers will be decided with the Sponsor and will be adapted if specific difficulties are identified during the training. A study monitoring plan, including for-cause monitoring, that is appropriate for the study design will be developed and implemented. Data QC will be performed remotely and at the center level, where permissible according to local regulations, by qualified designated personnel under professional secrecy.
To ensure compliance with relevant regulations, data generated by this study must be available for inspection upon request by representatives of national authorities, and local health authorities as applicable, the Sponsor and representatives, and the Institutional Review Board/Independent Ethics Committee (IRB/IEC) for each study center. The investigator will permit authorized representatives of the Sponsor, the respective national or local health authorities, and auditors to inspect facilities and records relevant to this study.

The Sponsor or representative CRO is responsible for verifying the eCRFs at regular intervals throughout the study to verify adherence to the protocol and the Sponsor or representative CRO applicable SOPs, completeness, accuracy and consistency of the data, and adherence to the Good Pharmacovigilance Practice (GVP): Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (**EMA/873138/2011 Rev 2, 2017**), International Conference of Harmonization (ICH) Good Clinical Practice (GCP) (**ICHE6, 2017**) and local regulations on the conduct of clinical research. Source data to be reviewed during this study will include but will not be restricted to: patient medical files, patient questionnaires and pathology reports. All key data must be recorded in the patient hospital notes.

During and/or after completion of the study, quality assurance auditor(s) named by the Sponsor or the regulatory authorities may wish to perform on-center audits. The investigator will be expected to cooperate with any audit and provide assistance and documentation (including source data) as requested.

The Sponsor representatives are responsible for contacting and visiting the investigator for the purpose of inspecting the facilities and, upon request, inspecting the various records of the clinical study (*e.g.*, eCRFs and other pertinent data) provided that patient confidentiality is respected.

The investigator agrees to cooperate with the monitors to ensure that any problems detected in the course of these monitoring visits, including delays in completing CRFs, are resolved.

4.9 STUDY MANAGEMENT

PIERRE FABRE MEDICAMENT is the Sponsor of the study. The Sponsor will be responsible, among others, for:

- Initiating, managing, and financing the study,
- Selecting the qualified Principal Investigators,
- Providing necessary information to the study centers to allow them to successfully conduct the study,
- Obtaining the investigator agreement from all participating study centers,
- Ensuring that the required regulatory approvals / favorable opinions are received,
- Ensuring that any modifications required by the ethics committee or regulatory authority are implemented,

- Performing and documenting root cause analysis and implementing appropriate corrective and preventive actions if non-compliance significantly affects or has the potential to significantly affect subject protection or reliability of clinical study results,
- Ensuring that study procedures comply with applicable regulation for data protection.

4.10 LIMITATIONS OF THE RESEARCH METHODS

The biggest strength of this study is that it will be able to yield data on the dermatological toxicities in real-life conditions of use and in the current treatment landscape, and in a varied profile of patients.

However, an observational study comes with its limitations which are as follows:

1. Selection bias:

   The target population (the entire set of individuals to which the findings of the study are to be extrapolated) of this study is the population of female patients suffering from EBC, currently treated with adjuvant endocrine monotherapy, initiated 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months) before the inclusion in the study, in real-life setting Sample representativeness may be compromised by selection biases. The sites who will accept in participating in the study could preferentially be those who are more involved in assessing quality of life of their patients. They can preferentially be those who have a more significant number of patients corresponding to the target population in their practice. To prevent patient selection bias, participating investigators will be advised to recruit consecutively eligible patients who meet the inclusion criteria.

   Patients (or their next of kin/legal representative) who refuse to participate may limit the representativeness of the study results. Confounding can occur due to unobservable characteristics of patients. Investigators will be asked to prospectively enrol consecutive patients who meet the eligibility criteria.

2. Design:

   Since some data in the study will be extracted from past medical records, investigators will have no control over how the data was recorded and managed prior to the study.

3. Missing data:

   Depending on physician practices, some data might not be systematically measured or available. COVID-19 pandemic could also contribute to missing data. Missing data can bias the descriptions if it is not completely random. Even in cases where missing data is truly random, a potential impact on the precision of the estimates cannot be overlooked. Remote Monitoring procedures will be implemented, wherein it will be ensured that the eCRFs have been

comprehensively filled. Sensitivity analyses may be carried out, where applicable, to estimate the impact of missing data on the study's outcomes. Furthermore, if a non-negligible proportion of missing data is observed for a certain parameter, groups of patients with and without missing data may be compared.

PROs will be collected with tablets, which minimizes the number of missing data through the use of drop-down lists and mandatory fields.

4. Memory bias:

   As dermatological events will be collected during the last 2 years (up to 1 year and 9 months) to 3 years (up to 3 years and 6 months), they could be underestimated reported number of punctual or mild dermatological toxicities.

5. Heterogeneity between study centers:

   Since this is an observational study of real-life dermatological toxicities, reporting of toxicities can vary widely based on standard practices in each country and/or investigating center. This could lead to an over or under-reporting of certain data. Where deemed appropriate subgroup analyses by country could be performed for certain outcomes or variables of interest.

6. Measurements bias:

   Data regarding primary and secondary outcomes are mainly declarative data collected directly from patient and may thus not completely reflect reality. Data collected through self-questionnaire which are completed by the patient may lead to a reporting bias. However, as this is data related to quality of life and facts experienced by patients, this collection method was the best compromise. To maintain confidentiality and to avoid bias, data gathered at the patient level will not be accessible to investigators and only be processed in the research perspective of this study.

Further details on how biases in the study design are to be addressed will be elaborated in the SAP.

5 PROTECTION OF HUMAN SUBJECTS AND LOCAL REGULATORY ASPECTS

The study will be conducted in accordance with the ethical principles of the declaration of Helsinki and the General Data Protection Regulation (UE 2016/679) and other local regulatory requirements. The need to submit the protocol to an Institutional Review Board/Independent Ethics Committee (IRB/IEC) and the requirement of informed consent will be considered in accordance with local law. Any amendments to the study protocol, as well as the associated Informed Consent Form will be submitted to the appropriate IRB/IEC for approval prior to implementation, according to the requirement of each IRB/IEC.

This observational study does not involve any changes in the local care standards of the patients participating in the study, does not compromise their physical or psychological integrity and does not require any special follow-up visits for these patients.
Each patient will be fully informed before enrollment in the study and start of data abstraction, and their written consent or verbal non-opposition will be taken, as per the local regulations of each target country.
Wherever applicable, an Informed Consent Form waiver will be obtained, depending on approval by Ethics Committees and/or local regulations.

Investigators shall ensure that personal identifiers will be removed from any study files that are accessible to non-study personnel in accordance with applicable laws and regulations. In case of sub-contracting, it is the responsibility of the service provider concerned to ensure that computerized processing is in conformity with the applicable national regulations regarding the protection of personal data and, if necessary, carry out any formality with the supervisory authorities and transmit the declaration date to Sponsor.

The investigator must ensure that patient confidentiality is maintained. It is required that the investigator and institution permit authorized representatives of the Sponsor, of the regulatory agency(s), and the institutional ethics committees' direct access to review the patient's original medical records for verification of study-related procedures and data. Direct access includes examining, analyzing, verifying, and reproducing any records and reports that are important to the evaluation of the study. Access to the patient's medical file is to be granted under the supervision and responsibility of the principal investigator or their center personnel. The investigator is obligated to inform and obtain the consent of the patient to permit named representatives to have access to their study-related records without violating the confidentiality of the patient. The study will be registered on ClinicalTrials.gov and will be in national registries where applicable.

6 MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

As the objective of this study is not to assess the efficacy nor the safety of a Pierre Fabre Médicament product and as no solicited data of safety or Pierre Fabre Médicament product are collected, the investigator shall report all necessary information, about any suspected adverse reaction to a product, to the regulatory agency or to the marketing authorization holder/manufacturer of the concerned product, according to the local regulation.

7 PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Data will be analyzed and presented in a final report which will be submitted to the Sponsor. This final report will help in the preparation of one or more publications.

Of note, no interim clinical study report will be provided.

Any written or oral communication of the research results will receive prior consent of the Sponsor and, if necessary, of any committee formed for the research. All publications will follow the International Committee of Medical Journal Editors guidelines (**International Committee of Medical Journal Editors, 2023**). In addition, communication in appropriate scientific meetings will be considered.

8 OWNERSHIP OF RESULTS

The results of the Study shall be owned exclusively by PIERRE FABRE MEDICAMENT and/or any designee shall have free use of the same in France and worldwide.
Such ownership shall apply to any data, patentable or non-patentable inventions, know-how and any invention resulting from the Study.

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10 APPENDICES

10.1 Signature Pages

AGREEMENT PAGE

Protocol Version 3.0 dated 23 May 2025

Sponsor Medically Qualified Representative Signatory:

[redacted] **– Global Medical Advisor**

[redacted]

27-mai-25 | 00:25:03 PDT

_____ _____

Date

[redacted] **– Real-word Evidence Project Leader**

[redacted]

27-mai-25 | 08:59:37 CEST

_____ _____

Date

Coordinating Investigator Signatory:

[redacted] - Oncodermatologist - Chair of the European Task Force
[redacted]

[redacted]

28-mai-25 | 04:06:26 PDT

Date

Statistician:
[redacted]
Head Biostatistics & Health Data Science Unit / Methodologist Biostatistician [redacted]
[redacted]

[redacted]

27-mai-25 | 14:37:29 CEST

Date

Statistician Real-world Evidence:
[redacted] on behalf of [redacted]

[redacted]

27-mai-25 | 10:34:41 CEST

Date

Other signatures

Principal Investigator signature

BCARE (Breast Cancer Adjuvant Real-world Evaluation of Dermatological adverse events): Impact of dermatological toxicities on quality of life in patients with early breast cancer exposed to adjuvant endocrine therapy: a real-world cross-sectional study

Sponsor	**PIERRE FABRE MEDICAMENT**
Protocol number	**NIS18999**
Protocol Version	**Version 3.0 dated 23 May 2025**

Principal Investigator Statement:

I have read this protocol and agree that it contains all necessary details for carrying out this observational study.
I will conduct the observational study as outlined herein and according to the ICH guideline for Good Clinical Practice and all applicable regulations.
I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Pierre Fabre Médicament and ensure that they are fully informed regarding the conduct of the observational study and the obligations of confidentiality.

_____ _____
Principal Investigator Name (typed or printed): Signature

_____ _____ Country: _____
Date Study Site Number and Country

10.2 Questionnaires

10.2.1 DLQI questionnaire - 2019

DERMATOLOGY LIFE QUALITY INDEX

DLQI

Hospital No: Date:
Name: Score:
Address: Diagnosis:

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick ■ one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	❒ ❒	Not relevant ❒
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	❒ ❒ ❒	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant ❒

Please check you have answered EVERY question. Thank you.

10.2.2 Skindex-16 questionnaire – 2001

DERMATOLOGY SURVEY

This survey concerns the skin condition which has bothered you the most during the past week.

Skindex16 - United States/English
Skindex16_AU2.1_eng-USon.doc

THESE QUESTIONS CONCERN THE SKIN CONDITION WHICH HAS BOTHERED YOU THE MOST DURING THE PAST WEEK

During the past week, how often have you been bothered by:	Never Bothered ↓			•			Always Bothered ↓
1. Your skin condition **itching**	☐0	☐1	☐2	☐3	☐4	☐5	☐6
2. Your skin condition **burning** or **stinging**	☐0	☐1	☐2	☐3	☐4	☐5	☐6
3. Your skin condition **hurting**	☐0	☐1	☐2	☐3	☐4	☐5	☐6
4. Your skin condition **being irritated**	☐0	☐1	☐2	☐3	☐4	☐5	☐6
5. The **persistence / reoccurrence** of your skin condition	☐0	☐1	☐2	☐3	☐4	☐5	☐6
6. **Worry** about your skin condition (For example: that it will spread, get worse, scar, be unpredictable, etc)	☐0	☐1	☐2	☐3	☐4	☐5	☐6
7. The **appearance** of your skin condition	☐0	☐1	☐2	☐3	☐4	☐5	☐6
8. **Frustration** about your skin condition	☐0	☐1	☐2	☐3	☐4	☐5	☐6
9. **Embarrassment** about your skin condition	☐0	☐1	☐2	☐3	☐4	☐5	☐6
10. **Being annoyed** about your skin condition	☐0	☐1	☐2	☐3	☐4	☐5	☐6
11. **Feeling depressed** about your skin condition	☐0	☐1	☐2	☐3	☐4	☐5	☐6
12. The effects of your skin condition on your **interactions with others** (For example: interactions with family, friends, close relationships, etc)	☐0	☐1	☐2	☐3	☐4	☐5	☐6
13. The effects of your skin condition on your **desire to be with people**	☐0	☐1	☐2	☐3	☐4	☐5	☐6
14. Your skin condition making it hard to **show affection**	☐0	☐1	☐2	☐3	☐4	☐5	☐6
15. The effects of your skin condition on your **daily activities**	☐0	☐1	☐2	☐3	☐4	☐5	☐6
16. Your skin condition making it hard to **work or do what you enjoy**	☐0	☐1	☐2	☐3	☐4	☐5	☐6

Have you answered every item? Yes ☐ No ☐

Skindex16 - United States/English
Skindex16_AU2.1_eng-USen.doc

10.2.3 Hairdex questionnaire – version 2010

Hairdex: **Fischer, 2001**

HairDEX © (English-Version, 2010) Code:_____

Date: _____ Name: _____ D.O.B.:_____ Gender: __

Below you will find some problems that can occure in the context of your hairloss. Please mark with a cross to what extent the message of every sentence personally applies to you.

	never	rarely	some-times	often	always
1. My scalp skin hurts	⓪	①	②	③	④
2. The condition of my hair affects how well I sleep	⓪	①	②	③	④
3. I worry that something serious could be with my hair	⓪	①	②	③	④
4. The condition of my hair impairs my well-being in my job or in my leisure activities	⓪	①	②	③	④
5. The condition of my hair impairs my society and social life	⓪	①	②	③	④
6. The condition of my hair makes me depressive	⓪	①	②	③	④
7. My scalp skin burns	⓪	①	②	③	④
8. Due to my hair loss I stay more often at home	⓪	①	②	③	④
9. I worry that the condition of my scalp skin could lead to scaring/disfigurement	⓪	①	②	③	④
10. My scalp skin itches	⓪	①	②	③	④
11. The condition of my hair influences how close I can be with people which are on close terms with me	⓪	①	②	③	④
12. I am ashame of my hair	⓪	①	②	③	④
13. I am afraid that my hair loss could get worse	⓪	①	②	③	④
14. I do things more often alone due to my hair loss	⓪	①	②	③	④

Hairdex: Fischer, Schmidt, Strauss & Elsner, 2001

	never	rarely	some-times	often	always
15. The condition of my hair makes me furious	⓪	①	②	③	④
16. Water (e.g. while washing my hair), impairs the condition of my hair and my scalp skin	⓪	①	②	③	④
17. Due to the condition of my hair it is difficult for me to show affection towards other people	⓪	①	②	③	④
18. My scalp skin is in a bad condition	⓪	①	②	③	④
19. My scalp skin is irritable	⓪	①	②	③	④
20. The condition of my hair has an influence on my relationships with others	⓪	①	②	③	④
21. My hair loss is embarrassing	⓪	①	②	③	④
22. My hair loss is a problem for people which are on close terms with me	⓪	①	②	③	④
23. The condition of my hair frustrates me	⓪	①	②	③	④
24. My hair is very sensitive	⓪	①	②	③	④
25. I interact with people less often because of the condition of my hair	⓪	①	②	③	④
26. I feel humiliated because of the condition of my hair	⓪	①	②	③	④
27. My scalp skin bleeds	⓪	①	②	③	④
28. The condition of my scalp skin/hair makes me angry and irritable	⓪	①	②	③	④
29. My sexual life is impaired due to my hair loss	⓪	①	②	③	④
30. The condition of my hair gets on my nerves	⓪	①	②	③	④
31. I have the condition of my hair under control	⓪	①	②	③	④

Hairdex: Fischer, Schmidt, Strauss & Elsner, 2001

	never	rarely	some-times	often	always
32. It causes me problems to sit in the bus, the cinema or the theatre where other people can see my hair at close	⓪	①	②	③	④
33. Despite the condition of my hair I am contented with myself	⓪	①	②	③	④
34. I feel like an outsider due to the condition of my hair	⓪	①	②	③	④
35. My life is still worth living, despite the condition of my hair	⓪	①	②	③	④
36. I worry that I look old because of my hair	⓪	①	②	③	④
37. The condition of my hair makes it difficult for me to achieve as much as I usually achieved	⓪	①	②	③	④
38. Other people make fun of me because of of my hair	⓪	①	②	③	④
39. Generally, I have self-confidence despite the condition of my hair	⓪	①	②	③	④
40. Other people show understanding for the condition of my hair	⓪	①	②	③	④
41. Despite the condition of my hair/scalp skin, I go as often as usual to the hairdresser	⓪	①	②	③	④
42. People talk behind my back about my hair loss/the appearance of my hair	⓪	①	②	③	④
43. Compared to others, I am lucky that I have this hair	⓪	①	②	③	④
44. The condition of my hair disfigures me	⓪	①	②	③	④
45. I hate my hair when I see it in the sink, on the comb or on the sofa	⓪	①	②	③	④
46. The condition of my hair is what people percept most in me	⓪	①	②	③	④
47. I look in the mirror every morning/evening to check whether my hair got thinner	⓪	①	②	③	④
48. So far, my doctor has not at all taken me serious with my hair problems	⓪	①	②	③	④

Hairdex: Fischer, Schmidt, Strauss & Elsner, 2001

10.2.4 ItchyQoL questionnaire – Version 2012

Site number: _____ Subject initials: _____ Subject number: _____ Visit date (dd/mmm/yyyy): _____

ItchyQoL™

ITCHING QUALITY OF LIFE SURVEY

The following questions concern your feelings about your itchy skin condition. Please check the answer that best describes your experience.	**How often during the past week do these statements apply to you?**				
	NEVER	RARELY	SOMETIMES	OFTEN	ALL THE TIME
1. My itchy skin condition bleeds.	☐1	☐2	☐3	☐4	☐5
2. My skin hurts because of my itchy skin condition.	☐1	☐2	☐3	☐4	☐5
3. My itchy skin condition burns or stings.	☐1	☐2	☐3	☐4	☐5
4. I get scars from my itchy skin condition.	☐1	☐2	☐3	☐4	☐5
5. I need to scratch my itchy skin condition.	☐1	☐2	☐3	☐4	☐5
6. Temperature or seasonal changes aggravate my itchy skin condition.	☐1	☐2	☐3	☐4	☐5
7. I spend a lot of money treating my itchy skin condition.	☐1	☐2	☐3	☐4	☐5
8. My itchy skin condition makes it hard to work or do what I enjoy.	☐1	☐2	☐3	☐4	☐5
9. My itchy skin condition affects my interaction with others. (For example: family, friends, close relationships, etc.)	☐1	☐2	☐3	☐4	☐5

The following questions concern your feelings about your itchy skin condition. Please check the answer that best describes your experience.	**How often during the past week do these statements apply to you?**				
	NEVER	RARELY	SOMETIMES	OFTEN	ALL THE TIME
10. My itchy skin condition affects how well I sleep.	☐1	☐2	☐3	☐4	☐5
11. My itchy skin condition often makes it difficult to concentrate.	☐1	☐2	☐3	☐4	☐5
12. My itchy skin condition limits the types of clothes I can wear.	☐1	☐2	☐3	☐4	☐5
13. My itchy skin condition forces me to buy special soaps, detergents, and lotions.	☐1	☐2	☐3	☐4	☐5
14. I am frustrated by my itchy skin condition.	☐1	☐2	☐3	☐4	☐5
15. I am embarrassed by my itchy skin condition.	☐1	☐2	☐3	☐4	☐5

	How often during the past week do these statements apply to you?				
	NEVER	RARELY	SOMETIMES	OFTEN	ALL THE TIME
16. My itchy skin condition drives me crazy/nuts.	☐1	☐2	☐3	☐4	☐5
17. My itchy skin condition makes me angry or irritable.	☐1	☐2	☐3	☐4	☐5
18. My itchy skin condition makes me feel depressed or sad.	☐1	☐2	☐3	☐4	☐5
19. I worry about what other people think about me because of my itchy skin condition.	☐1	☐2	☐3	☐4	☐5
20. I worry that the itching will last forever.	☐1	☐2	☐3	☐4	☐5
21. I feel self-conscious because of my itchy skin condition.	☐1	☐2	☐3	☐4	☐5
22. My personality has changed because of my itchy skin condition.	☐1	☐2	☐3	☐4	☐5

_____ _____

Subject signature Date