Impact of cutaneous adverse events on the quality of life in patients receiving anticancer agents: Results from an observational, cross-sectional study

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Abstract

Background: despite the growing interest in cutaneous adverse events (CAEs) and their management in oncology patients, they are often under-reported and there are no extensive data on their impact on quality of life. Health care professionals should pay attention to this issue in order to minimize its negative impact on quality of life (QoL) and improve patient outcome. The aim of this study was to evaluate the impact of CAEs on QoL in patients receiving anticancer drugs and to determine differences in QoL between conventional chemotherapy versus targeted therapies. Methods: 114 cancer patients with CAEs were included in this observational, cross-sectional study. Patient-reported outcomes instruments (FACT-G, DLQI and SKINDEX-16) were used. Results: Mean (SD) score in FACT-G was 65.3 (13.4), while in DLQI it was 8.4 (5) and in SKINDEX-16 it was 30.8 (16.9), showing a moderate impact on QoL. No significant differences in QOL indices according to the type of treatment (conventional chemotherapy vs targeted therapy) were observed Conclusions: CAEs had a moderate impact on QoL in cancer patients, evaluated with three different PRO instruments, but having more severe or two or more CAEs had a significant negative impact on QoL. No differences between conventional chemotherapy and targeted therapy were observed.

Introduction

In recent years, significant progress has been made in the development of more effective anticancer agents. Many studies have demonstrated that new agents, including targeted therapies, offer better disease control and survival rates compared to classical cytotoxic chemotherapies. [1–6]. Concurrently, new drugs usually mean new adverse event profiles, including cutaneous adverse events (CAEs) [10–15].

Multiple systems have been developed for rating the adverse effects of cancer treatment. The National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) is a standardized tool commonly used in both research and clinical settings to recognize and grade side effects of therapies [7]. However, it is not uncommon to find discrepancies in the severity grading between patients and clinicians. Hence, the use of patient self-reporting of symptoms can improve recognition and timely management of adverse effects of anticancer therapies [8–12]. Patient-reported outcomes (PRO) instruments are increasingly used in cancer patients to evaluate the impact of dermatologic adverse events on QoL and they can be helpful as a supplement to CTCAE in the assessing of overall effect of dermatologic adverse events on physical, emotional and psychosocial wellbeing. In general, patients with cancer are inclined to accept repeated PRO evaluations making its implementation feasible. In addition, the use of these instruments encourage patient to talk with their doctors about the impact of cutaneous adverse events on overall wellbeing [16–25].

To our knowledge, the impact of cutaneous adverse events on the QoL in patients receiving anticancer in agents has not been extensively studied. In this study, we aimed to assess this impact through three different PRO questionnaires, an approach that to our knowledge is original.

Material And Methods

-Objectives

The main objective of the study was to evaluate the impact of CAEs on QoL of patients receiving anticancer drugs. Secondary objective was to evaluate differences in the overall QoL and cutaneous QoL according to anticancer treatment (chemotherapy versus targeted therapies).

-Study design

Observational, cross-sectional, single-center study with duration of 9 months, between April 2018 and December 2018, involving the collection of clinical data and subjective patient data in relation to their quality of life.

-Study population and recruitment

A total consecutive sampling of patients meeting eligibility criteria (age equal to or greater than 18 years old, active antineoplastic treatment and presence of cutaneous adverse event) was performed at the Medical Oncology Service of the University Hospital Center (CHU) Pontevedra, Spain. Patients receiving radiotherapy at the time of initial evaluation and those not able to answer PRO questionnaires were excluded.

Physicians and nursing staff at the Day Hospital of the Medical Oncology Service, and at the hospital dispensing office of cancer drugs carried out recruitment.

-Study procedures and variables

Informed consent was obtained from study participants before performing any study procedure.

A medical oncologist and a dermatologist evaluated patients that met the eligibility criteria. Detailed history and examination were performed to confirm the CAE and classify it according to usual clinical practice.

The main study variable was the impact of cutaneous adverse effects of anticancer drugs on (QoL). Different QoL questionnaires were selected according to previous clinical experience [16–28].

To assess patient overall QoL, Functional Assessment of Cancer Therapy - General questionnaire was used (FACT-G: scale range 0-108, higher score reflects better QoL). QoL related to cutaneous adverse events was assessed using patient reported outcomes (PRO) measures such as Dermatology Life Quality Index (DLQI: scale range 0–30, higher score reflects worse QoL), Skindex-16 (scale range: 0–96, higher score reflects worse QoL), and the Functional Assessment of Cancer Therapy - Epidermal Growth Factor Receptor Inhibitor 18 (FACT-EGFRI-18: scale range 0–72, higher score reflects better QoL) questionnaires. FACT-G, DLQI and Skindex-16 were delivered to all patients. In addition, FACT-EGFRI-18 was administered

to patients who had CAEs related to epidermal growth factor receptor inhibitors (EGFRI). The necessary licenses for the use of the different QoL questionnaires were obtained.

Data on demographic and clinical characteristics were collected. This was done through an interview with the participants, as well as with the review of their medical history at IANUS, an informatic program designed by the Department of Health to digitize clinical files [26].

CTCAE (version 4.03) was used to determine the severity of the CAE [7].

Targeted therapies were considered all those that act against specific molecular targets (e.g., EGFR, HER-2, RAS, BRAF, MEK, KIT, RET, mTOR, VEGFR). Tyrosine kinase inhibitors, monoclonal antibodies, immuno-oncological treatments and immunotherapies, such as anti-CTLA-4 or anti-PD-1/PD-L1 antibodies, were also included in the group of targeted therapies.

All classic antineoplastic drugs (e.g., alkylating agents, antimetabolites, vinca alkaloids, antimicrotubule agents and others) were considered non-targeted therapies.

-Sample size and statistical analysis

-Sample size

To assess differences in impact on QoL between conventional chemotherapy and targeted therapy, a sample size of 84 people was determined with a 95% confidence level. Considering a possible non-response rate of 15%, a sample size of 98 people was calculated.

-Statistical analysis

Stata V12.0 statistical software (Stata Corporation, College Station, TX, USA) was used for statistical analysis.

-Descriptive analysis

The clinical and sociodemographic characteristics of the sample were described using measures of central tendency (mean or median) and dispersion (standard deviation or interquartile range) in the case of quantitative variables, as well as frequency tables and distribution of percentages in the case of qualitative variables.

The frequency and description of the cutaneous adverse events was accompanied by a classification of their severity according to CTCAE, version 4.03.

-Quality of life

Patients with different levels of QoL were compared using statistical hypothesis testing (Student t-test, Mann-Whitney U test). The existence of differences in QoL based on the type of antineoplastic treatment

received was especially explored. For all tests the level of significance was set to p = 0.05 (level adjusted according to Bonferroni procedure when necessary).

In addition, the effects of possible confounding factors (type of tumor, preventive treatment, type of antineoplastic treatment, general condition, age and sex) were controlled.

Results

-Characteristics of the study population

A total of 131 patients were eligible for the study, and 17 declined to participate. Thus, 114 patients were included in the study. Demographic and clinical characteristics of study population are summarized in Table 1.

Table 1

Demographic and clinical characteristics

Variable	Total (n = 114)
Gender, n (%) - Male - Female	49 (43.0) 65 (57.0)
Age at diagnosis, years - Mean (SD) - Median (IQR)	59.9 (11.7) 62.5 (50.3–68.5)
Tumor type, n (%) - Gastrointestinal - Breast - Lung - Urological/renal - Gynecologic - Other	42 (36.8) 33 (28.9) 19 (16.7) 11 (9.6) 4 (3.5) 5 (4.4)
Tumor stage, n (%) - Stage 2 - Stage 3 - Stage 4	11 (9.6) 16 (14.0) 87 (76.3)
Treatment type, n (%) - Conventional chemotherapy - Targeted therapy - Combined therapy (targeted + chemotherapy)	46 (40.3) 44 (38.6) 24 (21.0)
Type of dichotomous treatment, n (%) - Conventional chemotherapy - Targeted therapy + Combined therapy (targeted + chemotherapy)	46 (40.3) 68 (59.6)
Previous lines of treatment, n - Mean (SD) - Median (IQR)	1.46 (0.96) 1 (1–2)
Treatment duration, months - Mean (SD) - Median (IQR)	6.7 (6.5) 4 (2–9)
Previous dermatological disease * - No - Yes	110 (96.5) 4 (3.5)*
ECOG Performance Status - 0 (Asymptomatic) - 1 (Symptomatic, but completely ambulatory) - 2 (Symptomatic, < 50% of time in bed) - 3 (Symptomatic, > 50% of time in bed)	2 (1.7) 89 (78.1) 21 (18.4) 2 (1.7)
* Four patients presented previous dermatological disease including psoriasis (2 patients), paraneoplastic dermatomyositis and simple chronic lichen (1 patient each)	

-Type of treatment

Regarding classic chemotherapy medicines, the most frequently drugs were part of schemes that included 5-FU or derivatives in combination with oxaliplatin or irinotecan (41.9%), followed by taxanes in monotherapy (20.9%), regimes with anthracyclines and alkylating agents (14.8%), schemes with platinum salts and taxanes, vinca alkaloids or others (12.3%), and others (9.8%).

Of targeted therapies, immunotherapy (27%) was the most frequently used, followed by EGFR inhibitors (21%), VEGF inhibitors (17%), multi-kinase inhibitors (14%), HER2 inhibitors (13%), and others (8%).

-Identified Cutaneous Adverse Events

Among the 114 patients included, the total number of CAEs was 177. The most frequent CAEs were pruritus, xerosis, palmar-plantar erythrodysesthesia (PPE), alopecia and papulopustular eruption (Table 2). Regarding the number of CAEs, a majority of patients reported one CAE (56.1%), while 37 (32.5%) and 13 (11.4%) subjects had two or three CAEs, respectively.

Table 2
Cutaneous Adverse Events (CAEs)

Variable	**Total (177 CAEs)**
Type of CAE, n (%) - Pruritus - Xerosis - Palmar-plantar erythrodysesthesia (PPE) - Alopecia - Papulopustular eruption - Ungual apparatus lesions - Pigmentary changes - Rash - Hand foot skin reaction (HFSR) - Photosensitivity - Other*	29 (16.3) 24 (13.5) 24 (13.5) 21 (11.8) 17 (9.6) 13 (7.3) 13 (7.3) 9 (5.0) 6 (3.3) 6 (3.3) 15 (8.4)
Number of CAE, n (%) - Patients with only one CAE - Patients with two CAEs - Patients with three CAEs	64 (56.1) 37 (32.5) 13 (11.4)
Severity of CAE, n (%) - Grade 1 - Grade 2 - Grade 3 - Grade 4	112 (63.2) 53 (29.9) 12 (6.7) -
*Other: bullous pemphigoid, eyelid edema, telangiectasis, purpura, hypertrichosis, trichomegaly, folliculitis, balanitis	

According to severity of CAEs, most patients experienced CAEs grade 1 (54.3%), while 35.1% and 10.5% experienced CAEs grade 2 and 3, respectively. No grade 4 CAE were observed.

-Quality of life indices

Mean (SD) score of total study population in FACT-G was 65.3 (13.4). We did additional sub-analysis according to the specific domains of FACT-G. Scores according to Physical Well-Being (PWB), Social/Family Well-Being (SWB), Emotional Well-Being (EWB), and Functional Well-Being (FWB) domains are presented in Table 3.

Table 3
Quality of life indices

Indices	Total (114)
FACT-G - Mean (SD) - Median (IQR)	65.3 (13.4) 66 (57–74)
Subscale Physical Well-Being (PWB) - Mean (SD) - Median (IQR)	17.2 (5.0) 17 (14–21)
Subscale Social/Family Well-Being (SWB) - Mean (SD) - Median (IQR)	19.3 (4.3) 20 (17–21)
Subscale Emotional Well-Being (EWB) - Mean (SD) - Median (IQR)	14.3 (4.0) 14 (11–18)
Subscale Functional Well-Being (FWB) - Mean (SD) - Median (IQR)	14.5 (4.8) 14.5 (11–18)
DLQI - Mean (SD) - Median (IQR)	8.4 (5) 8 (5–12)
SKINDEX-16 - Mean (SD) - Median (IQR)	30.8 (16.9) 29 (19–44)
Symptoms domain - Mean (SD) - Median (IQR)	10.6 (6.1) 11 (6–15)
Emotions domain - Mean (SD) - Median (IQR)	15.0 (8.8) 13 (9–21)
Functioning domain - Mean (SD) - Median (IQR)	5.2 (5.7) 3 (0–8)

Mean (SD) score of total study population in DLQI was 8.4 (5) while mean (SD) score of SKINDEX-16 was 30.8 (16.9). Additional sub-analyses were carried out according to the specific domains of SKINDEX-16. Scores of Symptoms, Emotions and Functioning domains can be seen in Table 3.

A total of 17 patients with anti-EGFR toxicities completed the FACT-EGFRI-18 questionnaire. The mean (SD) score of this subgroup was 47,2 (SD 13,2). In this group, mean (SD) values of FACT-G, DLQI and SKINDEX-16 were 64.1 (18.7), 8.4 (4.5) and 33.5 (19.7), respectively.

Quality of life (QoL) indices and differences between conventional chemotherapy vs. targeted therapy.

In our study, no significant differences in QoL indices (FACT-G, DLQI, SKINDEX-16) were observed according to the type of treatment (conventional chemotherapy vs Targeted therapy plus combined therapy). Mean (SD) and median (IQR) scores for Skindex-16 Symptoms, Emotions and Functioning domains are presented in Table 4.

Table 4

Quality of life (QoL) indices and differences between conventional chemotherapy vs targeted therapy.

	Total (n = 114)	**Conventional chemotherapy (n = 46)**	**Targeted therapy + Combined therapy (n = 68)**	**p**
FACT-G - Mean (SD) - Median (IQR)	65.3 (13.4) 66 (57–74)	66.5 (13.2) 69 (58–73)	64.1 (13.4) 61 (54–75)	0.573
DLQI - Mean (SD) - Median (IQR)	8.4 (5.0) 8 (5–12)	7.7 (5.3) 7 (4–11)	8.9 (4.8) 8 (5–12)	0.160
SKINDEX-16 - Mean (SD) - Median (IQR)	30.8 (16.9) 29 (19–44)	29.2 (17.1) 28.5 (18–42)	31.9 (16.8) 29.5 (19–44)	0.477
Skindex symptoms - Mean (SD) - Median (IQR)	10.6 (6.1) 11 (6–15)	10.6 (6.8) 11 (5–16)	10.5 (5.6) 11 (6–14)	0.864
Skindex emotions - Mean (SD) - Median (IQR)	15.0 (8.8) 13 (9–21)	13.7 (8.8) 11 (8–18)	15.9 (8.7) 15 (9–21)	0.148
Skindex functioning - Mean (SD) - Median (IQR)	5.2 (5.7) 3 (0–8)	4.9 (5.4) 3 (0–8)	5.5 (6.0) 3 (0–8)	0.799

-Cutaneous toxicities and quality of life

Cutaneous toxicities related to QoL indices (FACT-G, DLQI and Skindex-16) are presented in Table 5.

Table 5
Cutaneous toxicities and quality of life

CAE	FACT-G Mean (SD)	DLQI Mean (SD)	SKINDEX 16 Mean (SD)
- PPE	61.0 (12.6)	8.9 (3.6)	31.1 (13.9)
- Pruritus	61.4 (14.1)	7.5 (3.9)	23.9 (14.8)
- Papulopustular rash	64.1 (18.7)	8.4 (4.5)	33.5 (19.7)
- Alopecia	62.6 (10.4)	5.8 (4.4)	24.6 (13.9)
- Xerosis	68.0 (7.9)	5.3 (3.6)	24.3 (23.7)
- Ungual apparatus	62.2 (14.9)	6.2 (5.5)	23.4 (15.1)
- Rash	63.1 (15.4)	10.1 (7.4)	40.3 (16.4)
- HFSR	60.7 (3.4)	14.5 (4.4)	45.6 (7.3)
- Pigmentary changes	73.1 (18.8)	3.1 (6.0)	10.0 (18.1)

The CAEs that had the greatest impact on quality of life were HFSR, rash and PPE. Mean (SD) for HFSR was 14.5 (4.4) in DLQI and 45.6 (7.3) in Skindex-16, while mean (SD) for rash was 10.1 (7.4) in DLQI and 40.3 (16.4) in Skindex-16. Mean (SD) values for PPE were 8.9 (3.6) and 31.1 (13.9) in in DLQI and Skindex-16, respectively.

The CAEs that had the least impact were pigmentary changes, alopecia and xerosis. Pigmentary changes had mean (SD) scores of 3.1 (6.0) in DLQI and 10.0 (18.1) in Skindex-16, while alopecia had mean (SD) scores of 5.8 (4.4) in DLQI and 24.6 (13.9) in Skindex-16. Mean (SD) values for xerosis were 5.3 (3.6) and 24.3 (23.7) in in DLQI and Skindex-16, respectively.

-Other results

-Treatment interruption CAE related

Treatment interruption due to CAE was observed in 17/114 (14.91%) patients. Of those, 13/17 (76.47%) had DLQI $\geq$ 10 and 10/17 (58.82%) had 2 or more CAE.

Of those 17 treatment interruptions, 7 were associated to PPE and 4 to papulopustular lesions, while 2 interruptions were observed in patients with HFSR, 2 with rash, and 2 in subjects with ungual apparatus lesions. Regarding severity of CAE related to treatment interruption, 3/17 patients had a CAE grade 1, 9/17, and 5/17 had a CAE grade 2 and grade 3, respectively.

-Total number of CAEs per patient between treatment groups

No differences were found regarding the total number of CAE per patient between conventional chemotherapy vs targeted therapy (number of patients with 1 CAE: targeted therapy + combined therapya 38 vs conventional chemotherapy 26; number of patients with 2 or more CAEs: targeted therapy + combined therapy 30 vs conventional chemotherapy 20; p = 0.94).

-Patients with DLQI ≥ 10 and number of CAEs

Patients with 2 or more CAEs and patients with moderate to severe CAEs had significantly more impact on QoL as measured by DLQI vs patients with one or mild CAEs (Table 6).

Table 6
Patients with DLQI ≥ 10 and number of CAEs

Number of CAEs	Total (n = 114)	DLQI ≥ 10 (n = 43)	DLQI < 10 (n = 71)	P value
- 1 CAE - 2 or more CAE	64 50	16 27	48 23	0.002
- Mild (grade 1) - Moderate-severe (grade 2–3)	62 52	15 28	47 24	0.002

Discussion

The objective of our study was to evaluate the impact of CAEs on QoL in patients receiving anticancer drugs. In our study, using multiple QoL indices, we have observed that CAEs have a moderate impact on the QoL. A secondary objective was to determine if there are differences in the overall QoL and cutaneous QoL according to the treatment of cancer patients with conventional chemotherapy versus targeted therapies. Our study did not found differences in QoL measured by PRO questionnaires between classical chemotherapy and targeted therapy. Additionally, no differences were found in the total number of CAEs between conventional chemotherapy and targeted therapy but having more severe CAEs or two or more CAEs had a significant impact on QoL.

Despite the growing interest and attention on skin toxicities induced during cancer treatment, their impact on QoL sometimes is not much considered. The underrated impact of skin toxicities may stem from the nature of the underlying problem, a potentially fatal disease, and also from the popularly known side effects of anticancer therapies, such as hair loss, mucosal, gastrointestinal or hematological toxicities. [1–10, 12–17, 30–32].

In the past, alopecia and mucositis were the most common CAEs associated with conventional chemotherapy. With the development of target-specific therapies, other CAEs have become more common, including PPE, papulopustular rash, HFSR, xerosis, fissures, pruritus, pigmentary or ungual apparatus changes (paronychia, onycholysis). In our study, pruritus, xerosis and PPE were the most frequent CAE, followed by alopecia and papulopustular rash. Ungual apparatus changes, rash, HFSR, and

pigmentary changes were also common [1–7, 35]. In a clinical trial using EGFRI, Joshi et al reported that the most common skin toxicities were rash, xerosis, paronychia, and pruritus [30].

According to Lacouture et al, cutaneous toxicities are very common and varied in patients treated with targeted therapies. These toxicities diminish patients' QoL, which impacts their adherence to the treatment, jeopardizing its success and patients' survival [31]. High-grade CAEs may have a significantly impact on QoL and may lead to treatment interruption or dose modification. In our study, treatment interruption due to CAE was observed in 14.91% of patients (17 cases). Of 17 treatment interruptions, 7 were associated to PPE and 4 to papulopustular rash, while 2 interruptions were observed in patients with HFSR, 2 with rash, and 2 in subjects with ungual apparatus changes. Tischer et al affirm that although CAEs are associated with lower QoL, correlation studies demonstrated that the occurrence and severity of CAEs are associated with higher response rates and a survival benefit [3].

Some CAEs are of special interest. Although alopecia is a well-known side effect that impacts negatively the QoL in cancer patients, our study suggested that hair loss induced by anticancer therapy did not cause additional distress in dermatology-specific QoL. Perhaps the disfiguration itself has little effect on the QoL in patients treated with anticancer therapy since it is not associated with discomfort, such as itching or pain. In addition, because hair loss is one of the best-known adverse reactions, usually patients expected hair loss during anticancer therapy and took it for granted, whereas they did not expect other skin toxicities to be induced by anticancer therapy. [1–2, 13–15, 30–32]. Therefore, pretreatment patient counseling and preventive interventions are crucial to minimize the negative impact on QoL and improve adherence to treatment.

The severity of the patient's skin condition is not easily assessed and communicated. The visible degree of the disease often does not correlate with patient distress and impact on QoL. Therefore, the severity of CAEs must be related both to its type and clinical extent and its effects on a patient's QoL. In our study we found that CAEs had a moderate impact on the QoL. There is no gold standard instrument for assessing QoL in dermatological patients. In our study, we assessed patient overall QoL using FACT-G questionnaire, as it is an effective scale that has been validated for use with cancer patients and it is one of the most widely used measures of cancer-specific health-related QoL. Patient perceiving of QoL was assessed using PRO measures related to cutaneous adverse events, such as DLQI, Skindex-16, and FACT-EGFRI-18 [16–29].

Self-report of symptoms can help to improve CAE reporting and treatment in both research and clinical settings [1–4, 7, 10–12]. Discordance can be observed many times between objective and subjective measures of CAEs in the management of many types of cancer, which indicates that there may be a need to incorporate PRO instruments to regularly assess CAEs from the patient's perspective. According to Chan et al, close monitoring, early recognition, and early intervention of CAEs may relieve symptoms and reduce their duration, ultimately leading to improvements in patients' QoL [1]. Therefore, PRO instruments that evaluate HRQoL of cancer patients with CAEs are increasingly relevant in the evaluation of novel therapies. [16–25]. In a clinical trial using EGFRI, Joshi et al reported that skin toxicities, including rash,

xerosis, paronychia, and pruritus, adversely affected QoL, and rash was associated with a QoL greater decrease [30].

Skin is one of the organs that is most frequently affected by molecularly targeted drugs [3–6, 10–15]. Our study did not found differences in QoL between classical chemotherapy and molecularly targeted therapy. On the contrary, Rosen et al. addressed this issue and found that patients on targeted therapies experienced a significantly greater number of CAEs and worse QoL with regards to total Skindex-16 and emotion subdomain compared with patients on non-targeted therapies [32]. Lee et al also found that patients on targeted therapy experienced worse QoL by means of DLQI [33]. Additionally, Unger et al did not find differences in QoL between targeted therapy only and both targeted and chemotherapy [34]. These discrepancies may be due to differences in study designs and PRO instruments used to evaluate QoL and highlight the interest of addressing this topic.

A limitation of our study is that it had an observational design and was limited to patients from one institution. Statistical testing for adequacy of sample size suggested it was large enough for the objectives of the study. Other limitations are related to PRO instruments. DLQI is a validated instrument and with widespread use for assessing quality of life in individuals with skin conditions, although it was not created specifically for the purpose of our study. Skindex-16 does not specifically address hair, nails, or mucous membranes, which are additional significant targets for EGFR inhibitors-induced toxicity. To offset this limitation, in our study we additionally used the specific PRO FACT-EGFRI-18. Although only patients can subjectively assess some symptoms of skin toxicities, such as pruritus and pain, the most commonly used endpoints traditionally have been clinician-reported outcomes. PRO measures provide useful and reliable information, but only a thorough clinical examination and a personal discussion of skin toxicities allows for an evaluation of its full impact on QoL. [1–3, 16, 27]. In our study, both interventions were performed. Every included patient completed all of the three PRO questionnaires (FACT-G, DLQI, SKINDEX-16) and was evaluated by an oncologist and a dermatologist to confirm the adverse event and determine its severity. To our knowledge this is an original approach.

Conclusion

In our study we observed that CAEs had a moderate impact on QoL, measured with three different PRO instruments, but having more severe or two or more CAEs had a significant negative impact on QoL.

The CAEs that had the greatest impact on quality of life in our study were HFSR, rash and PPE, and those with the least impact were pigmentary changes, alopecia and xerosis. Most of the patients had mild to moderate CAEs but among those who had severe CAEs, the majority presented a significant impact on QoL. No significant differences in QoL indices were observed according to the type of anticancer therapy.

Declarations

-Ethics approval and consent to participate:

This study was conducted in accordance with the ICH Harmonised Tripartite Guideline, as well as current national regulations and the ethical principles for medical research of the Declaration of Helsinki.

The confidentiality of the data of the subjects participating in the study is guaranteed, ensuring compliance with Spanish Organic Law 15/1999, of December 13, on the Protection of Personal Data.

The present study was remitted to the Clinical Research Ethics Committee (Research Ethics Committee of Pontevedra-Vigo-Ourense) for evaluation and subsequent approval before its publication.

Written informed consent was obtained from study participants before performing any study procedure. The researchers informed the subjects about all the relevant aspects of the study so that they can decided whether or not to participate in it. They had enough time to read the information sheet, as well as the opportunity to ask any questions about the study.

-Consent for publication: Not Applicable

-Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

-Competing interests: The authors declare no competing interests.

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