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Feasibility, reliability, usability, and satisfaction of a digital medical device (ZEMY) for symptom management in patients treated for breast cancer: a single-arm interventional study

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Abstract

Background and methods E-health solutions are a promising tool to assist patients in self-managing symptoms for various diseases. This study aimed to assess the feasibility, reliability, usability, and satisfaction of a digital medical device (ZEMY) for patients' self-monitoring of symptoms commonly experienced during breast cancer treatment and to enhance interaction with healthcare professionals. In this open-label, interventional, multicentre, single-arm clinical trial (NCT03558490), patients at all stages of breast cancer initiating oral and/or parenteral treatment were recruited at initiation of therapy and followed for 3 months. During treatment, the patients reported 9 symptoms (diarrhoea, nausea/vomiting, fever/febrile neutropenia, fatigue, pain, cutaneous and mucosal toxicities, hypertension, anxiety/depression) through the ZEMY application, which provided self-management recommendations and sent message alerts to healthcare professionals. To reach the primary feasibility endpoint, more than 50% of patients with one-sided 95% confidence interval (exact CI computed using Clopper-Pearson method) had to complete at least 3 symptoms entries, of which more than 60% complete until receiving a recommendation.

Results Out of the 56 screened patients, 54 were included in the analysis between June 12th 2018 and January 11th 2019, and 52 completed the study. Over half of patients (31/54 [57.4%]) were feasibility responders, but this percentage was not significantly higher than the predefined minimum feasibility cut-off of 50%, as the lower limit of the one-sided 95% exact CI was 45.3%. Nonetheless, 87.0% of patients reported at least 3 symptoms with ZEMY and 66.0% had an entry completion rate ≥ 60%. Six of the 9 symptoms were reported at least once by more than 30% of the patients. The recommendations were considered relevant at least once for more than 80% of cases for each symptom. Patients were more satisfied (mean 10-point visual analogue scale score: 6.3 ± 2.9) with ZEMY than healthcare professionals (4.4 ± 1.5). The global patients' quality of life remained stable during the study.

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Conclusions ZEMY provided satisfactory recommendations for the self-management of selected symptoms occurring during anti-cancer treatment and demonstrated good usability, but its feasibility was indemonstrable.

Trail registration The trial was registered on June 14th 2018 at ClinicalTrails.gov (Trial Registration Number: NCT03558490).

Keywords Breast cancer, Medical device, Feasibility, Symptom management, Treatment management, Patient Reported Outcome

Background

In 2018, approximately 58,500 new cases of breast cancer (BC) were diagnosed in France, making it the most common solid cancer among women and the leading cause of cancer-related deaths, with around 12,000 deaths annually. Advances in the diagnosis and treatment of BC cancer led to a 1.6% decrease in the annual mortality rate between 2010 and 2018 [1]. The improving survival rate and long-term survival prospects call for increased attention to the patients' quality of life (QoL), and to the social and economic impact of BC. Chemotherapy is a key component of the therapeutic approach for advanced or metastatic BC. Its use as (neo)adjuvant therapy reduces the risk of recurrence and improves overall survival in patients with early-stage BC [2]. However, chemotherapy and targeted therapy often cause side effects that typically appear after treatment cycles, when patients are at home. Reduced contact with healthcare professionals often leads to poorly assessed and managed toxicity symptoms [3]. This situation results in dose delays and dose reductions as the primary means of managing these toxicities to preserve patients' QoL, albeit at the expense of the treatment's effectiveness [3–5]. Tele- and e-health solutions are cost-effective [6, 7] tools that improve communication between patients and physicians, enhance patients' QoL [8], and aid in the management of chemotherapy-related toxicities [9] in several chronic diseases, including cancer [10–13].

ZEMY is an e-health solution (software medical device) developed to improve the management of selected symptoms frequently experienced during cancer treatment in patients with BC, and to promote better interactions between patients and healthcare professionals. ZEMY comprises an iPhone operating system (iOS) application that collects toxicity data and provides recommendations for symptom self-management, along with a web platform that assists healthcare professionals in remotely monitoring their patients.

The aim of this study was to assess the feasibility, defined as the potential for successful adoption of a new treatment or innovation within a specific context [14], as well as the reliability, usability, and satisfaction of ZEMY for remotely managing symptoms commonly experienced during cancer treatment at home. The primary objective was to reject the null hypothesis defined by a minimum response rate for ZEMY $\leq$ 50% in terms of feasibility. Additionally, the study analysed the device's use, its impact on the QoL, and healthcare resource consumption.

Methods

This study is reported in line with the CONSORT statement guidelines for feasibility trials. The relevant checklist is provided in Supplementary file 1.

Study design and participants

ZEMY (registered on June 14th 2018 at ClinicalTrails.gov, Trial Registration Number: NCT03558490) was a 3-month open-label, multicentre, interventional, single-arm clinical trial conducted at 5 French sites. Patients were recruited in university hospitals (Saint-Louis Hospital, Paris Cité University), private hospitals (Private Hospital de Provence, Private Hospital Jean Mermoz), and a cancer centre (Centre François Baclesse). Adult women initiating a treatment for either early or advanced BC, including oral and/or parenteral anticancer drugs (chemotherapy and/or targeted therapy, combined hormonal therapy) were eligible. Key inclusion criteria included inter-cycle duration between hospital visits $\geq$ 14 days, ability to use a smartphone equipped with ZEMY, and having signed a written informed consent before any study-specific screening procedures. Were excluded: pregnant women, patients with another concomitant malignancy, patients with Eastern Cooperative Oncology Group performance status > 2, patients treated with single hormonotherapy, single surgery, or single radiotherapy, or with immunotherapy, patients not trained to use ZEMY or to measure their own blood pressure.

Nurses and medical doctors were trained in the use of ZEMY solution. Patients received an Apple iPhone 6 s smartphone with the pre-installed ZEMY application and were trained to its use just before or after their enrolment in the study. Patients started anti-cancer treatment on Day 1 and were followed for 3 months. During the study period, the patients independently used ZEMY daily. Patients' data were collected at screening, inclusion, week (W)1 and every 3 weeks (at W3, W6, W9, and W12).

Follow-up visits were scheduled at the same intervals. Regular phone calls with patients were conducted during follow-up according to predefined parameters set by the healthcare professional team, with at least one call occurring in the week following the start of BC treatment.

Ethics

The study received ethical approval from the Independent Ethics Committee (comité de protection des personnes) Sud-Ouest and Outre-Mer IV, Limoges, France and from the French health authorities (Agence nationale de sécurité du médicament et des produits de santé). The methods of the study were designed and conducted in accordance with Good Clinical Practice and the Declaration of Helsinki.

ZEMY medical device

This investigational medical device, manufactured by Voluntis France, was ZEMY version 1.0. It is made up of two main components: a user interface and a web platform. The user interface is an application which can be installed on iOS, and it is used by patients to report 9 predefined symptoms: diarrhoea, nausea/vomiting, fever/febrile neutropenia, fatigue, pain, cutaneous and mucosal toxicities, hypertension, anxiety/depression, and clinical parameters (weight, temperature, blood pressure). The web platform processes and stores the data received from the user interface and can be accessed by healthcare professionals to remotely monitor the evolution of the patient's symptoms and to alert them if medical support is needed. The functionalities of ZEMY are to:

a. Provide real-time patient-specific recommendations to initiate and continue symptomatic treatments (e.g., anti-diarrheal and antiemetics) in response to symptoms or clinical parameters provided by the patient, as part of a treatment plan defined by the medical team;
b. Help healthcare professionals to remotely monitor their patients' symptoms, as well as their progress. Messages are automatically and securely sent in real time to the care team's centre: alerts regarding low patient usage, low/mid-level messages when patients encounter no or mild to moderate self-manageable symptoms, and high-level messages when patients need medical support;
c. Provide health and diet recommendations adapted to the patient's medical condition.

This device was intended to complement care procedures carried out by a healthcare professional, including prescriptions, and was not intended to be used as an emergency medical system. Patients were required to authenticate themselves to access the application. The healthcare professionals were required to authenticate themselves using a two-factor authentication system (password and through Google Authenticator) to access the ZEMY web platform. Once in the platform, they could create a patient file, enter the patient's personal, clinical, and treatment data, the contact of the patient's treating physicians, as well as activate ad-hoc reminders to be sent to the patient via the ZEMY user interface (e.g., blood pressure follow-up reminder, prevention recommendations, treatment reminders). The healthcare professional could review via the platform all the symptom reported connections (SRCs) made by the patient, the recommendations sent by the application to the patient, as well as the eventual actions to be undertaken by the healthcare professionals (e.g., follow-up call to the patient).

Outcomes

The objective of the primary analysis was to reject the null hypothesis defined by a minimum response rate for ZEMY $\leq 50\%$ in terms of feasibility in the intent to treat population. The response rate was defined by the number and proportion of feasibility responders, with its one-sided 95% confidence interval (CI) (exact CI computed using Clopper-Pearson method). If the lower confidence limit of the feasibility rate for ZEMY was $> 50\%$, then the minimum rate was reached (null hypothesis was rejected). A patient was considered a feasibility responder if, by the end of follow-up, they entered at least 3 completed SRCs via ZEMY and if the rate of completed SRCs was $\geq 60\%$. A SRC was considered as complete if the patient documented a symptom or a clinical parameter until the end of the questionnaire and obtained a recommendation through the device. Hence, a patient was considered a feasibility responder if they reported a symptom or a clinical parameter via ZEMY at least 3 times and if more than 60% of these entries were completed until the point of receiving a recommendation.

Secondary objectives for this study included: the assessment of symptoms' management and appropriateness of generated messages and recommendations, as evaluated by the investigator during the study visits; the usability, assessed with a system usability scale that included a set of 10 questions, to be scored from 1 (strongly disagree) to 5 (strongly agree); satisfaction of patients and healthcare professionals by means of a 10-point visual analogue scale (VAS) from 0 (unsatisfied) to 10 (completely satisfied); the evaluation of the use of ZEMY, measured by the entry rate of solicited symptoms, number of automatic messages, and recommendations generated per patient and per symptom; the extent of exposure to ZEMY; device deficiencies and safety, assessed by number and

type of adverse device events and serious adverse device events collected at each follow-up visit. The evolution of patients' QoL was assessed in the QoL populations, using 3 questionnaires, completed by patients at each follow-up visit. The EuroQol-5 Dimension, 5-level questionnaire (EQ-5D-5L) is a self-assessed, health related QoL questionnaire that consists of 2 parts: the EQ-5D descriptive part that assesses 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) at 5 levels each (no problem to extreme problem) and a VAS for self-rated health [15]. The European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 includes 5 functional scales, 3 symptom scales, a global health status/QoL scale, and 6 single items [16]. The BC module of the EORTC QLQ, QLQ-BR23, incorporates 5 multi-item scales to assess systemic therapy side effects, arm symptoms, breast symptoms, body image and sexual functioning. In addition, single items assess sexual enjoyment, hair loss and future perspective [17]. Additional exploratory objectives included the evaluation of the healthcare resources consumption, assessed as number of emergency room admissions, unscheduled hospitalizations and visits, calls to and from the patient, and time spent by healthcare professionals on patients' training and follow-up with ZEMY.

Statistical analysis

The primary feasibility analysis was based on a one-stage Fleming design for phase II studies [18]. Assuming a risk of $\alpha = 0.05$ (one-sided) and $\beta = 0.10$ (type II error), 53 patients had to be included in the primary feasibility analysis according to A'Hern's sample size tables [19]. Secondary endpoints were analysed using summary statistics. In addition, continuous and categorical endpoints were described using the two-sided 95% CI for the mean using respectively Student's t distribution and Clopper-Pearson method. Recommendations and automatic messages were summarized using median and interquartile range (IQR). The α risk was fixed to 5% in one-sided situation for the primary analysis and to 5% in two-sided situation for the other analyses. Analyses were performed using SAS® software version 9.4.

Results

Patient's disposition

Among the 56 screened patients who signed the informed consent form, 54 eligible patients (96.4%, intent to treat population) were included in the study between June 12th 2018 and January 11th 2019. Of these 54 patients, 52 (96.3%) were followed for 3 months and hence completed the study. Patient disposition is illustrated in Fig. 1. Patients were on average 51.9 ± 11.3 years old. Over half of patients had early-stage BC (30/54 [55.6%]), whereas 8 (14.8%) had locally advanced BC and 16 (29.6%) had metastatic BC. Most of the BCs were negative for the human epidermal growth factor receptor 2 (HER2-; 50/54 [92.6%] patients) and positive for hormone receptors (HR+; 42/54 [77.8%] patients). Almost all patients (49/54 [90.7%]) commonly used smartphones.

Primary feasibility of ZEMY

To assess ZEMY's feasibility, the total number and rate of completed SRCs by patients at the end of follow-up were analysed. A completed SRC was defined as one that documented a symptom thoroughly and resulted in a recommendation being received. Even though most patients (31/54 [57.4%]) were assessed as feasibility responders (entered at least 3 completed SRCs with a completion rate ≥ 60%; Fig. 2), this percentage was not significantly higher than the predefined minimum feasibility cut-off of 50%, as the lower limit of the one-sided 95% exact CI was 45.3%. A high response rate was recorded for the endpoint's single components: 47/54 (87.0%, 95% CI: 75.1%-94.6%) patients completed at least 3 SRCs, and 33/50 (66.0%, 95% CI: 51.2%-78.8%) patients had a SRC completion rate ≥ 60%. Four patients reported no connections: they were not included in the completed rate analysis and were thus considered as non-responders.

Management of symptoms and relevance of ZEMY recommendations

Fifty patients (92.6%) out of the 54 of the intent to treat population initiated at least one SRC during the study period. A total of 3815 SRCs were initiated (between 1 and 519 SRCs per patient), of which 2979 (78.1%) were completed (between 1 and 454 per patient) and led to a device recommendation. Among the 2979 device recommendations sent to patients, 615 (20.6%) triggered a message sent to healthcare professionals. Device recommendations related to fatigue, pain, anxiety/depression, and vomiting were the most frequently sent to patients while messages for pain or vomiting were more frequently provided to healthcare professionals (Fig. 3a).

The number and percentage of patients having experienced, at least once, the 9 selected symptoms were described at each follow-up visit (W3, W6, W9, W12), and overall. Over the study period, 6 symptoms were reported at least once by more than one third of the patients: fatigue (45/54 [83.3%]), nausea (40/54 [74.1%]), pain (39/54 [72.2%]), diarrhoea (25/54 [46.3%]), cutaneous and mucosal toxicities (24/54 [44.4%]), and anxiety/depression (22/54 [40.7%]) (Fig. 3b and c). The device recommendations provided by ZEMY to patients reporting symptoms, as well as the messages sent to healthcare professionals, were considered relevant at least once for more than 80% of cases for each symptom (Fig. 3b and

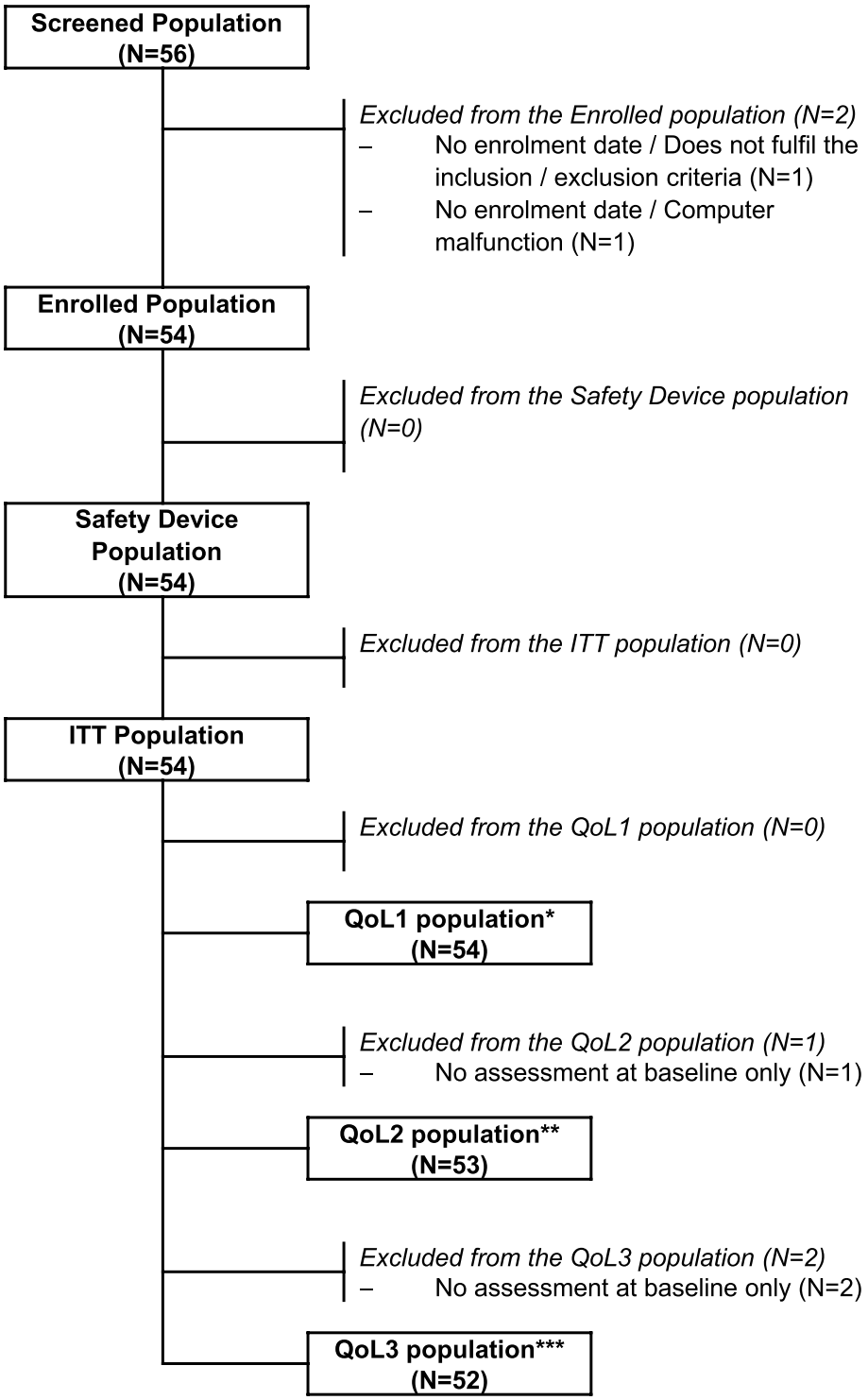

Fig. 1 Population flowchart. Overview of the number of patients according to study populations. The populations were defined as: all patients having signed an informed consent form (Screened population), all screened patients having an enrolment date (Enrolled population), all enrolled patients having an account activation date (from ZEMY use data) and/or a ZEMY training date (Safety Device population), all patients from the Safety Device population having received at least one dose of anti-cancer treatment (start date of treatment available; Intent to Treat [ITT] population). Quality of life (QoL) populations were defined as all patients from the ITT population having at least one baseline (week 1) and at least one post-baseline QoL assessment. *QoL1 population was based on the EuroQol-5 Dimension, 5-level questionnaire (EQ-5D-5L). ** QoL2 population was based on the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire. *** QoL3 population was based on the breast cancer module of the EORTC QLQ, QLQ-BR23

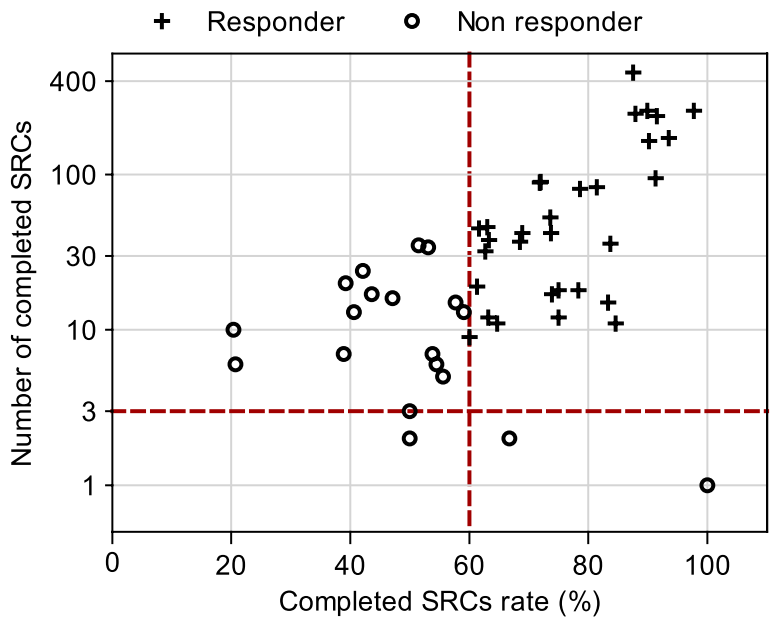

Fig. 2 Primary feasibility: composite endpoint per patient. Graphical representation of feasibility responders and non-responders according to the 2 criteria taken into consideration in the response definition: number of completed SRCs (y-axis) and rate of completed SRCs (x-axis) *(N* = 54). The 4 non-responder patients with no connections are not included in the graph. *SRC: symptom reported connection*

c). However, for pain, the device recommendations and messages to healthcare professionals were deemed not relevant at least once in over half of the cases (23/54 [59.0%] and 25/54 [64.1%] respectively). When messages to healthcare professionals were considered not relevant, this was mainly attributed to an insufficient level of intervention for fatigue and to an excessive level of intervention for other symptoms.

Usability and satisfaction of patients and healthcare professionals

The usability of ZEMY was assessed by patients and investigators at W12 based on the rating of 5 negative and 5 positive statements, using a scale from 1 (strongly disagree) to 5 (strongly agree). Most patients had a positive opinion. More than half of them either agreed or strongly agreed with positive statements (between 60.8% and 85.5%, depending on the statement), or strongly disagreed or disagreed with negative sentences (between 68.8% and 89.6%, depending on the statement). Only the positive statement "I think that I would like to use this system frequently" received a low favourable opinion (15/45 [33.3%] patients agreed or strongly agreed). Healthcare professionals completed one usability and satisfaction evaluation for each patient, resulting in an equal number of evaluations and patients, and they conveyed a less favourable opinion. For instance, for the statement "I thought the system was easy to use", only half of the healthcare professionals' evaluations agreed or strongly agreed (26/52 [50.0%]) with this statement, compared to most patients (41/48 [85.4%] patients; Fig. 4a). Similarly, the satisfaction with ZEMY, evaluated at W12 using a VAS, was higher and more heterogeneous among patients (mean: 6.3 ± 2.9, ranging from 0 to 10) than among healthcare professionals (4.4 ± 1.5, ranging from 2 to 8). Furthermore, the median VAS satisfaction score for patients was 7.0 (IQR: 5.0, 9.0), indicating that at least 75% of the patients provided a score ≥ 5, whereas for the healthcare professionals' evaluations the median VAS satisfaction score was 4.0 (IQR: 4.0, 5.0), indicating that only a quarter of them scored ≥ 5 (Fig. 4b).

Quality of life of patients using ZEMY

Three questionnaires were used to assess patients' QoL. Based on the EQ-5D-5L questionnaire, the global health state of patients remained steady throughout the study (*N* = 54; mean score at baseline: 68.4 ± 22.8, W3: 72.5 ± 20.9, W6: 73.4 ± 18.0, W9: 71.1 ± 19.0, W12: 72.6 ± 19.9; Fig. 5a). Based on the EORTC QLQ-C30 questionnaire for cancer patients (*N* = 53), the changes in global health status were categorized into 3 classes (worsening, no change, improvement) and visualized at each visit. The biggest improvement was observed at W3, with 20/52 (38.5%) patients reporting little, moderate, or very much improvement, while the smallest improvement was observed at W9 with 14/50 (28.0%) patients. The biggest worsening in global health status was observed at W6, with 23/49 (46.9%) patients reporting little, moderate,

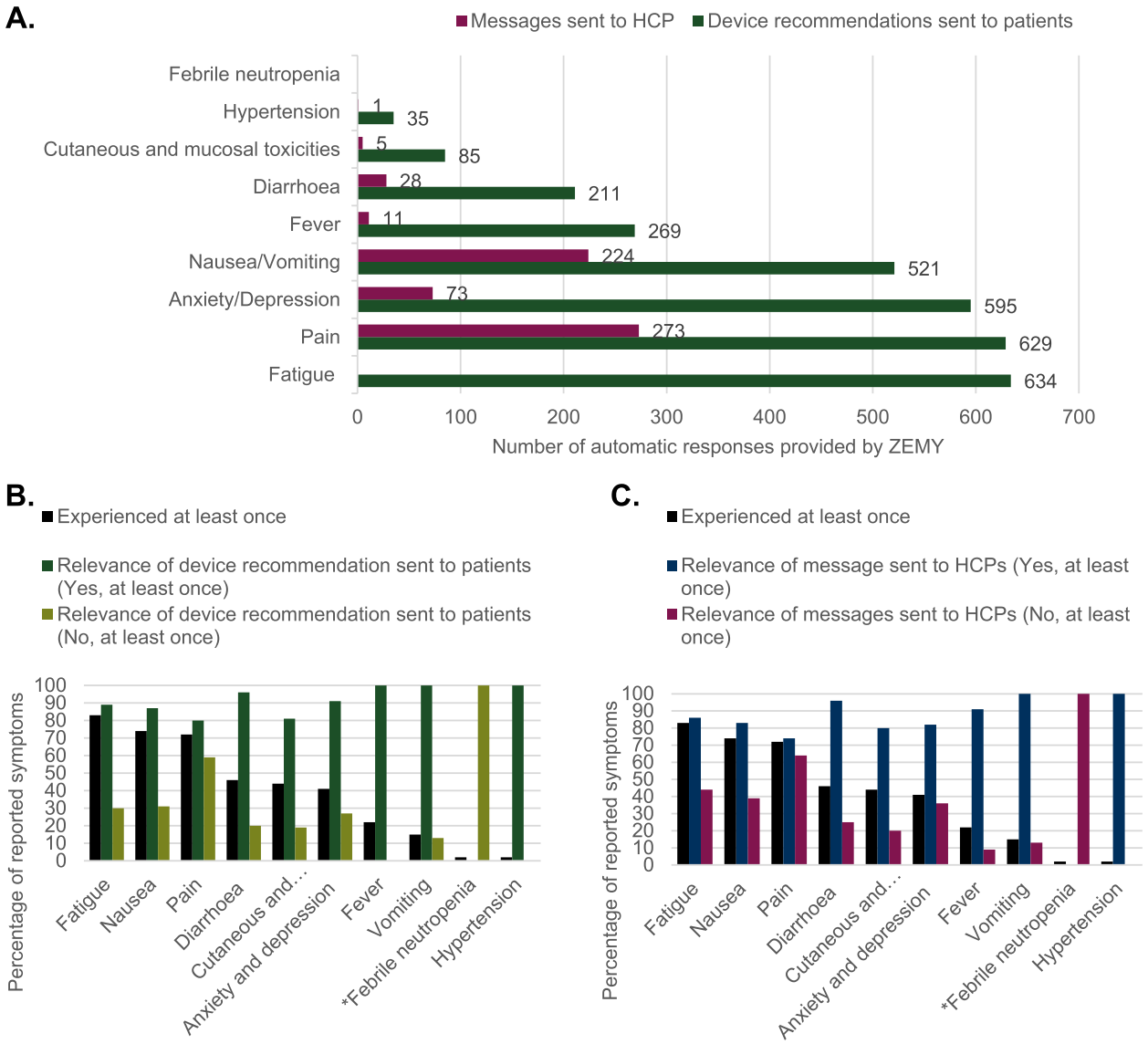

Fig. 3 Use of ZEMY and symptoms management. **a** Total number of automatic responses by ZEMY, divided into device recommendations sent to patients and messages sent to healthcare professionals ($N=54$). Percentage of patients who reported each symptom at least once and relevance of device recommendations (**b**) and messages sent to healthcare professionals (**c**) as evaluated by investigators, described overall for each symptom. Of note, vomiting was reported together with nausea in the ZEMY application but evaluated separately by healthcare professionals. *Febrile neutropenia was reported by healthcare professionals for one patient, but it was not reported in the ZEMY device

or very much worsening, while the smallest worsening was observed at W3, with 17/52 (32.7%) (Fig. 5b). The mean score given by patients to the items of the functional scales of the EORTC QLQ-BR23 questionnaire for patients with BC remained stable during follow-up compared to baseline, apart from the future perspective score which increased (i.e. improved) between baseline and W12 (from 43.8 ± 34.5 to 65.3 ± 29.1) (Fig. 5c). For the items of the EORTC QLQ-BR23 symptom scale, the mean value of the systemic therapy side effects score increased (i.e. worsened) between baseline and W12 (from 10.7 ± 11.9 to 30.2 ± 17.5), while the others remained mostly stable (Fig. 5d).

ZEMY safety and device deficiencies

Patients used ZEMY for a median duration, defined as the time between the start of treatment visit (Day 1) and W12, of 85 days (IQR: 85; 89). Overall, 95 device deficiencies were reported in 37/54 (68.5%) patients of the safety device population (Table 1). Device deficiencies were

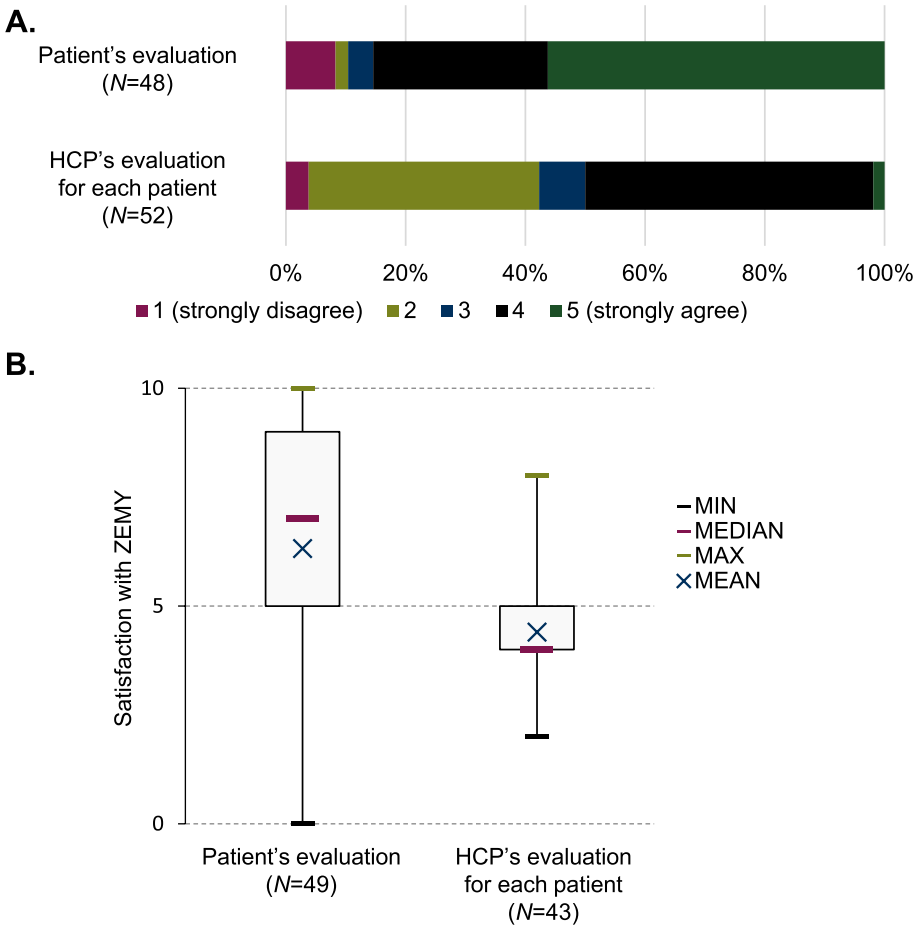

Fig. 4 Usability and satisfaction with ZEMY. **a** Rating for the positive statement "I thought the system was easy to use" as part of the general usability assessment by patients and healthcare professionals. **b** Satisfaction with ZEMY according to patients and healthcare professionals as assessed using a VAS with a score from 0 (unsatisfied) to 10 (completely satisfied). Mean, median, minimum (min) and maximum (max) (whiskers), quartile 1 (Q1) and 3 (Q3) (box) are represented in the graph

defined as an inadequacy of an investigational medical device related to its identity, quality, durability, reliability, safety, or performance, including malfunctions, use error, or inadequacy in the information supplied by the manufacturer. Of those 95, 14 deficiencies reported in 11/54 (20.4%) patients led to an action taken with the device. No device deficiencies were associated with an adverse device event, defined as an adverse event (AE) related to the use of an investigational medical device, and none were judged as potentially leading to an AE. The device deficiencies were related to inappropriate communications sent to patients (such as extreme recommendations for limited symptoms; $N=51$), device malfunctions (such as time lags between data entry by patients and data visualization by healthcare professionals, discrepancies between captured and stored dates, and difficulties for patients in capturing data; $N=36$), and limited response options for certain patients and symptoms ($N=8$). No adverse device event was reported related to the use of ZEMY.

Patients' healthcare consumption

For the assessment of healthcare consumption, the numbers of emergency room admissions, unscheduled visits and hospitalizations, calls to and from the patient, and inappropriate calls from the patient during the study period were considered. The most frequent use of healthcare services during the study were phone calls, with 34/54 (63.0%) patients receiving at least one phone call and 19/54 (35.2%) of patients making a phone call at least once (Fig. 6). Of the latter, 14 patients called their medical team at least 4 times. 13/54 (24.1%) and 5/54 (9.3%) patients went through unscheduled visits and hospitalizations respectively. To evaluate the healthcare consumption related to ZEMY, the initial patients' training time was also taken into consideration. A mean of 43.9 ± 15.2 min were invested in training the patients.

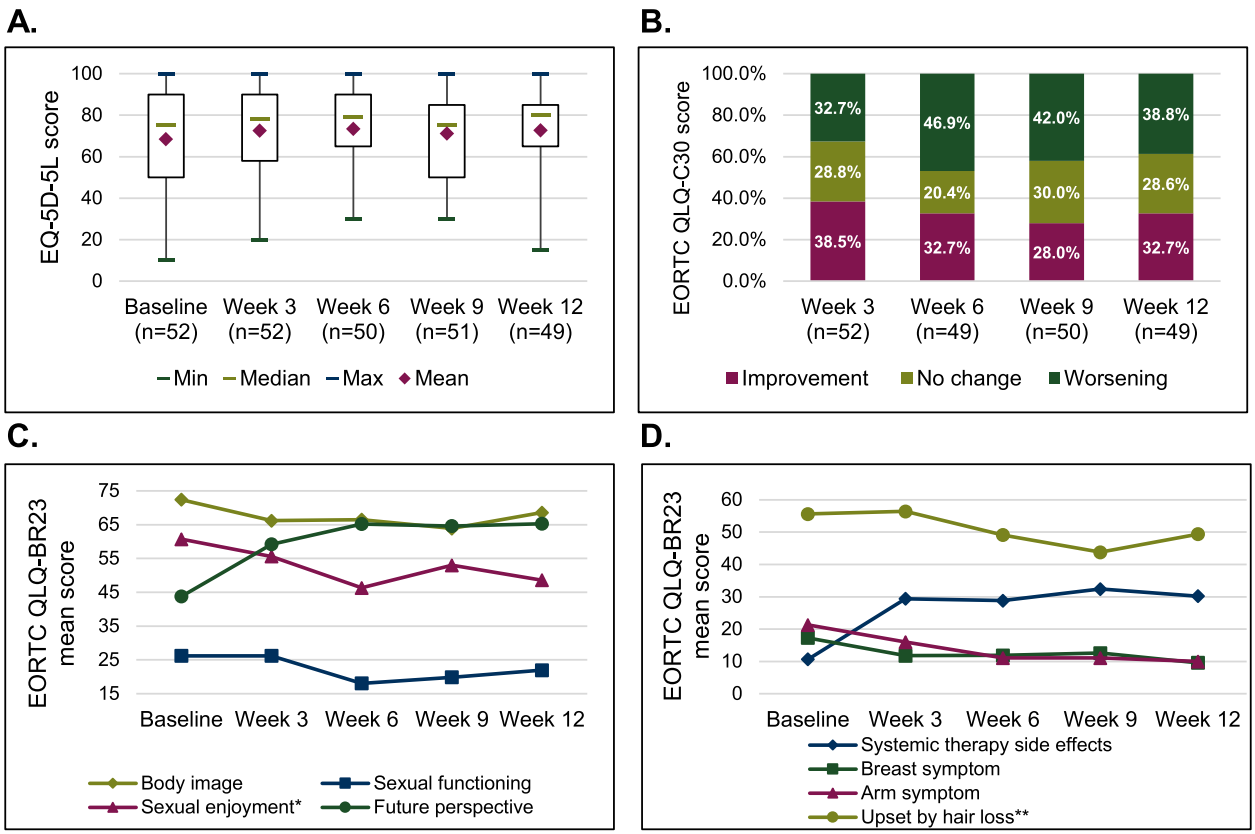

Fig. 5 Patient's quality of life. **a** Health state score of patients during follow-up assessed with the EQ-5D-5L questionnaire (*N* = 54). Mean, median, minimum, and maximum (whiskers), Q1 and Q3 (box) are represented in the graph. **b** Changes in global health status during follow-up assessed with the EORTC QLQ-C30 questionnaire at each follow-up visit (*N* = 53). **c** Evolution of the EORTC QLQ-BR23 functional score during follow-up (mean values) (*N* = 52). *The number of patients having answered to the items related to sexual enjoyment was limited as these conditional questions depended on answers relative sexual functioning. **d** Evolution of the EORTC QLQ-BR23 symptom score during follow-up (mean values) (*N* = 52). ** The number of patients having answered to the items related to upset by hair loss was limited as these conditional questions depended on answers relative sexual functioning

Table 1 Device deficiencies (*N* = 54)

	Number of events	Number of patients (%)
All device deficiencies	95	37 (68.5%)
Device deficiency associated to an adverse device effect	0	0 (0.0%)
Device deficiency that could have led to an adverse event	0	0 (0.0%)
Device deficiency that led to an action taken with the device	14	11 (20.4%)

Patients were mostly trained by a nurse (20/54 [37.0%] patients) or someone other than an investigator or nurse (33/54 [61.1%] patients). Furthermore, as per protocol recommendation, patients were contacted by phone one week after enrolment. This contact was conducted by nurses in 50.0% of the cases and revealed that 96.3% of the patients were able to use ZEMY correctly. In addition, during the study, 11/54 patients (20.4%) required retraining (for an average of 15.0 ± 11.8 min) or additional explanation on the ZEMY application at least once.

Discussion

Since the 1990s, a steady decline in BC mortality has been observed in Europe [20]. With the increase in survival rate, greater attention has been given to managing treatment-related toxicities and preserving patients' QoL.

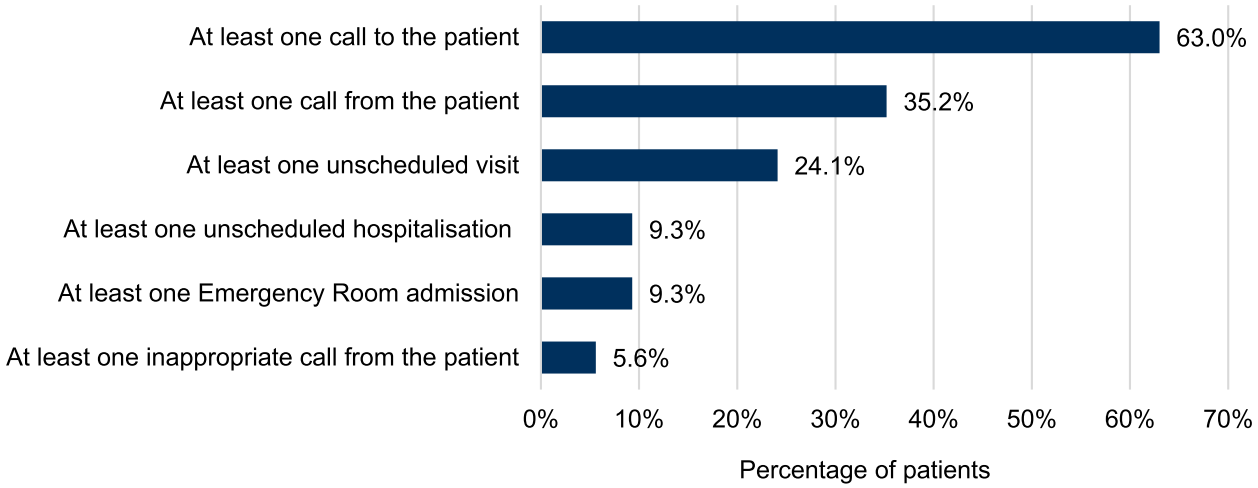

Fig. 6 Healthcare consumption during follow-up. Percentage of patients performing at least once one of the described actions over the study period, considered as healthcare consumption ($N = 54$)

Digital medical devices use technology and telecommunications to complement traditional patient management and facilitate health improvement. ZEMY was developed to provide home support for the self-management of selected symptoms frequently observed during cancer treatment in patients with BC, supporting their monitoring. ZEMY uses integrated algorithms based on international and validated guidelines to generate real-time recommendations offering a rapid response without involving the healthcare professionals. In addition, the system automatically alerts the healthcare professionals if medical support is desirable. As a result, the use of ZEMY aims to improve interactions between patients and healthcare professionals, as well as among healthcare team members (nurses, oncologists, general practitioners).

This clinical trial is one of very few studies aiming to assess a medical device with an interventional and multicentre design for the symptoms management of patients with cancer. This study failed to reach its primary feasibility endpoint, which was partially ascribable to the difficulty to foresee the feasibility of a medical device in a formal statistical test. However, the high response rate achieved in terms of number and completion rate of SRCs demonstrated that the use of ZEMY was well received. The management of toxicity symptoms by ZEMY was generally evaluated as appropriate by the investigators for most symptoms. As expected, most patients communicated fatigue, nausea, and pain at least once during the study period. Consequently, automatic recommendations were sent to patients mainly for fatigue and pain, but also for anxiety/depression, and vomiting. Pain and vomiting SRCs often led to an automatic message sent to healthcare professionals. In most cases the usability and the satisfaction of ZEMY were rated positively by the patients and by the healthcare professionals. Telemonitoring and smartphone systems have previously shown efficacy in enhancing patients' QoL [9]. Indeed, the global health status of patients was stable across the study period, despite the expected increased impact of systemic therapy side effects on QoL. However, these results should be interpreted carefully as the limited follow-up time does not allow an observation of proper QoL evolution, especially in patients with early BC.

This study contributes to the growing body of evidence that digital medical devices can serve as a valuable tool to improve the management of treatment-related side effects among patients affected by several pathologies. Other studies have demonstrated improved outcomes with the integration of electronic patient-reported outcome measures to monitor patients undergoing routine cancer treatment with systemic therapies. These improvements include enhanced physical function, better symptom management, improved health-related QoL, reduced hospitalizations, increased overall survival, higher patient satisfaction, and enhanced cost-effectiveness [21–29]. Based on these results, digital symptom monitoring with patient-reported outcome measures is now recommended by the European Society of Medical Oncology in routine clinical care during systemic cancer treatment [30]. To implement a medical device like ZEMY in clinical practice, efforts should be made to obtain a high satisfaction from the healthcare professionals. An American survey conducted among groups of patients, the US Food and Drug Administration, investigators, and nurses reported a strong consensus (93.0%)

on the fact that the use and implementation of patient-reported outcomes for adverse event reporting improves the understanding of what patients experience during treatment, and would improve the completeness, accuracy, and efficiency of symptom data collection [31].

This study presents several limitations. The limited sample size as well as the heterogeneity of the study population affected the results strength and the interpretation of the results. In contrast to randomized controlled trials that directly compared the standard of care with an e-health system for the management of cancer treatment-related toxicities and reported numerous clinical advantages of the e-health system [21, 32], our single-arm study did not allow for such a comparison. Moreso, comparison across studies is difficult due to the wide range of assessment tools. There is a need to develop standardised guidelines for assessing and reporting engagement with digital systems [33]. Another factor that affected the success of this study was the complexity of the 2-factor authentication needed to access ZEMY. The investigators pointed out that this was a deterrent to using the system, even though it was not recorded as a device deficiency. Lastly, patients were not systematically contacted by the healthcare professionals in the first week following the study initiation. Hence, if patients experienced technical difficulties with the use of the device, they did not receive any support, which could have affected their participation.

Conclusions

The present study, despite not confirming the feasibility of ZEMY, supports the idea that digital medical devices represent a valid support to standard management of chemotherapy toxicities and could represent a return on investments.

Abbreviations

AE	Adverse Event
BC	Breast Cancer
CI	Confidence Interval
EORTC	European Organisation for Research and Treatment of Cancer
EQ-5D-5L	EuroQol-5 Dimension, 5-level questionnaire
HER2	Human Epidermal growth factor Receptor 2
HR	Hormone Receptor
iOS	IPhone Operating System
IQR	Interquartile Range
Q1-3	Quartile 1–3
QoL	Quality of life
SRC	Symptom Reported Connection
VAS	Visual Analogue Scale
W	Week

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s44247-024-00110-y.

Supplementary Material 1.

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Authors' contributions

LT, CL, DC, RG, JD, NE, OD participated in the study design and the interpretation of the study results. JD performed the statistical analysis. LT, CL, DC, RG, JD, NE, OD participated in the writing of the manuscript.

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Availability of data and materials

All data needed to evaluate the conclusions are presented in the paper. Additional data generated and/or analysed during the study are available from the corresponding author upon reasonable request. Data sharing requests for study data underlying this publication requires a detailed research protocol developed by the requestor. Direct such requests to data_sharing.france@roche.com for consideration.

Declarations

Ethics approval and consent to participate

The study received ethical approval from the Independent Ethics Committee (comité de protection des personnes) Sud-Ouest and Outre-Mer IV, Limoges, France and from the French health authorities (Agence nationale de sécurité du médicament et des produits de santé). The study was designed and conducted in accordance with the study protocol, the ethical principles of the "Declaration of Helsinki", the International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines, and applicable laws and regulations. In addition, the study was performed in accordance with current regulations relative to medical devices (ISO 14155: 2011). All patients signed a written informed consent before any procedure related to the study was performed.

Consent for publication

Not applicable.

Competing interests

The authors declare the following competing interests: LT is an Advisory Board member of AZD, Daiichi, Eisai, Gilead, Invectys, Lilly, MSD, Novartis, Pfizer, Roche, Seagen. CL is an Advisory Board member of AstraZeneca, Daiichi, Lilly, MSD, Novartis, Pfizer, Roche, Seagen. DC is an Advisory Board member of Roche, Pfizer, AstraZeneca, Astellas, GSK. RM, NE, JD are Roche employees. OD is an Advisory Board member of Roche, Pfizer, AstraZeneca, Novartis, GSK, Seagen.

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