

ACCEPT[®]: A Complementary Anthroposophical Program for the Palliative Treatment of Lung Cancer – Rationale and a Randomized Feasibility Study

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Keywords

Nonpharmacological interventions · Lung cancer · Health-related quality of life · Complementary medicine · ACCEPT[®]

Abstract

Background: Lung cancer is the oncological disease with the highest mortality worldwide. Health-related quality of life is severely compromised in the majority of patients. While the efficacy of early palliative psychosocial therapy has been demonstrated in several recent studies, appropriate therapy modules could so far not be integrated into daily practice of care. Therefore, an additive multimodal treatment concept for oncological centers was drafted: the Additive anthroposophic integrative medicine Cancer Concept of Early supportive or Palliative lung cancer Treatment (ACCEPT[®]). **Patients and Methods:** The first module consisted of a 3-month health education program, the second module was a concept of psychosocial interventions, and the third module was a supervised home training program. Between 2017 and 2018, 20 lung cancer patients (UICC IIIB/IV) were included and randomly assigned to treatment ($n = 10$) or a waiting control group ($n = 10$). The treatment group started ACCEPT[®] for 3 months immediately after diagnosis and received also standard oncological care (SOC) while the waiting control group received SOC only for 3 months, followed by ACCEPT[®] after this period. Health-related quality of life, disease management, disease-specific symptoms, and feasibility of the ACCEPT[®] were monitored at 4 time points. **Results:** 7 out of 10 patients in the treatment group

(3 dropped out) and 6 out of 10 in the waiting control group (4 died during the intervention) completed treatment. **Discussion/Conclusion:** Lung cancer patients with high symptom load may benefit from ACCEPT[®]. The feasibility of this adjunctive therapy was demonstrated. The combination of SOC and ACCEPT[®] is feasible and applicable to a heterogeneous patient group and should be further evaluated with respect to efficacy and dosing.

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ACCEPT[®]: Ein komplementäres anthroposophisches Programm für die palliative Behandlung von Lungenkrebs – Rationale und randomisierte Machbarkeitsstudie

Schlüsselwörter

Nichtpharmakologische Interventionen · Lungenkrebs · Gesundheitsbezogene Lebensqualität · Komplementärmedizin · ACCEPT[®]

Zusammenfassung

Hintergrund: Lungenkrebs ist die onkologische Erkrankung mit der weltweit höchsten Mortalität. Die gesundheitsbezogene Lebensqualität ist bei der Mehrzahl der Patienten stark beeinträchtigt. Obwohl die Wirksamkeit der frühpalliativen psychosozialen Therapie in mehreren neueren Studien nachgewiesen wurde, konnten entsprechende Therapiemodule bisher nicht in die tägliche Ver-

sorgungspraxis integriert werden. Daher wurde ein additives multimodales Behandlungskonzept für onkologische Zentren entworfen: additives anthroposophisch-integrativ medizinisches Krebskonzept der frühen unterstützenden oder palliativen Lungenkrebsbehandlung (ACCEPT®). **Patienten und Methoden:** Das erste Modul bestand aus einer dreimonatigen onkologischen Gesundheitsschulung, das zweite Modul war ein Konzept für psychosoziale Interventionen, und das dritte Modul war primär ein Training im häuslichen Umfeld. Zwischen 2017 und 2018 wurden 20 Lungenkrebs-Patienten (UICC IIIB/IV) eingeschlossen und nach dem Zufallsprinzip der Behandlung ($n = 10$) oder einer wartenden Kontrollgruppe ($n = 10$) zugeteilt. Die Behandlungsgruppe begann unmittelbar nach der Diagnose für 3 Monate mit ACCEPT® und erhielt auch die onkologische Standardbehandlung, während die wartende Kontrollgruppe für 3 Monate nur onkologische Standardbehandlung erhielt, gefolgt von ACCEPT® nach dieser Zeit. Die Lebensqualität, das Krankheitsmanagement, die krankheitsspezifischen Symptome und die Durchführbarkeit von ACCEPT® wurden zu 4 Zeitpunkten beobachtet. **Ergebnisse:** 7 von 10 Patienten in der Behandlungsgruppe (3 schieden aus) und 6 von 10 Patienten in der wartenden Kontrollgruppe (4 starben während der Intervention) beendeten die Behandlung. **Diskussion/Schlussfolgerung:** Lungenkrebs-Patienten mit hoher Symptombelastung können von ACCEPT® profitieren. Die Durchführbarkeit dieser Begleittherapie wurde nachgewiesen. Die Kombination von onkologischer Standardbehandlung und ACCEPT® ist durchführbar und auf eine heterogene Patientengruppe anwendbar und sollte im Hinblick auf Wirksamkeit und Dosierung weiter evaluiert werden.

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Introduction

Lung cancer (LC) counts among the most frequent malignant oncological diseases and has the highest mortality rate worldwide [1, 2]. Depending on localization of the primary tumor and on metastases, physical symptoms and complaints vary considerably. A predominant symptom, however, is an unspecific fatigue syndrome which can severely compromise the patient's health-related quality of life (QoL). At first diagnosis of LC, already 90% of patients have complaints, and 75% present with metastasis [3].

The understanding of interactions between tumor tissue and organism has changed and has been differentiated fundamentally during the last century – from a cellular-pathological concept towards an interaction between immune system and tumor [4–8].

During recent decades, the relationship between cancer and the psyche received increasing attention [9]. It

became evident that besides somatic symptoms also the psychological state of patients is relevant for prognosis [10].

According to current data, 58% of LC patients suffer from depression, 48% from anxiety disorders, and 58% from a distress syndrome [11]. Consequently, appropriate requirements for treatment standards are integrated into the German national cancer plan [12] and into quality standards for LC centers, as well as into recommendations of international professional societies [13].

However, these standards have not yet been implemented in standard patient care. Moreover, the specific modalities as well as the intensity of supplementary measures to the pharmacological/surgical standard oncological care (SOC) in LC are unclear. A milestone in answering these questions was reached in a randomized, controlled trial conducted by Jennifer Temel, who could show that a psycho-oncological treatment in addition to SOC significantly improved disease-related QoL and increased survival time [14]. An early intervention seems to be particularly important for improvement of QoL in LC patients [15].

Further studies confirmed and expanded the findings of Temel [16–20]. While the evidence supporting the benefits of early palliative psychosocial care on QoL and survival time of cancer patients seems to be conclusive, an active wish to participate in psycho-oncological treatment seems frequently not to exist in LC patients. Possible reasons may be the high symptom burden, high distress level, stigmatization as a result of nicotine abuse and associated feeling of shame, and a high degree of repression and avoidance behavior [21]. In opposition to this, the customary concepts of psycho-oncological therapy and health training presuppose an active wish for change [9, 22].

Current psycho-oncological treatment focusses on coping assistance and underrates disease-related resistance against and refusal of psychosocial support as encountered in LC patients. Therefore, the LC center Havelhöhe looked for a concept representing, on the one hand, an offer for coping assistance acceptable for LC patients, taking into account, on the other hand, the considerable difference between the proactive wish for treatment and a not yet clearly perceived – one could say inactive – need for psycho-oncological support. Also, the integration of psychological and somatic aspects was intended. This approach is supported by findings of psychoneuroimmunological research, which have demonstrated that immunological mechanisms of tumor defense are measurably activated by psycho-oncological intervention [23–29].

The specific concept of anthroposophic medicine tries to do justice to this by offering a holistic approach that diagnostically differentiates and therapeutically integrates different levels of human activity [30]. At the upmost level, which is highly susceptible to perturbation

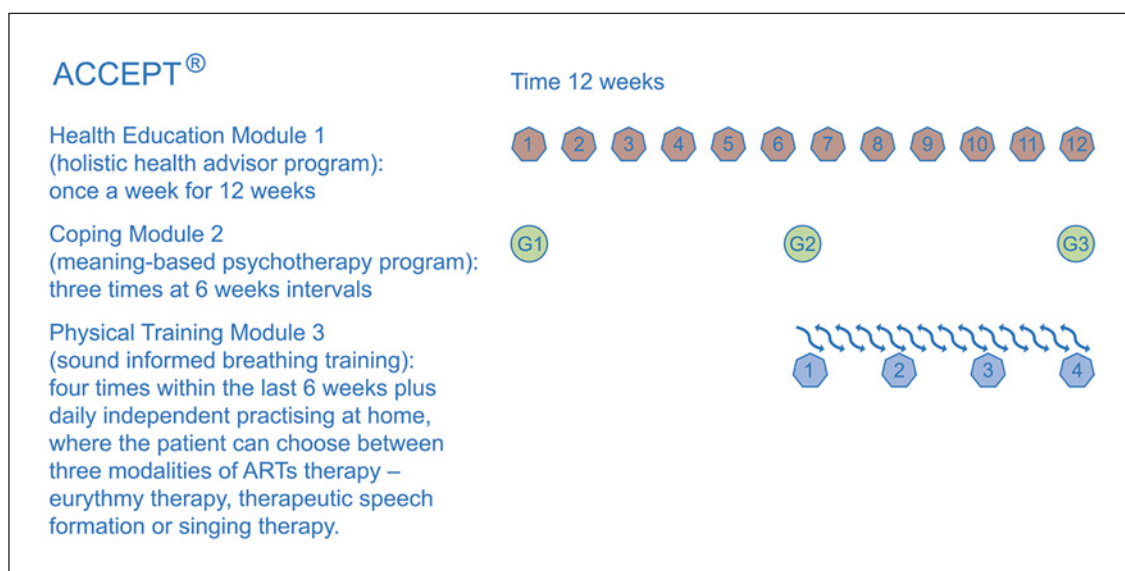


Fig. 1. ACCEPT® modules of treatment.

and is influenced by all psychical, social and biological levels, patients are understood as self-developing beings. This conception has been used in medicine since roughly 100 years [31]. Similar concepts include that of patient-centered psychotherapy by Carl Rogers, which is based on a situative and individual willingness to change [32] and that of Aaron Antonovski, who developed the concept of salutogenesis [33]. Viktor Frankl [34] conceptualized an approach to integrate individual connotation, where biopsychospiritual dimensions are merged into one construct [35].

Research on hygiogenesis [36, 37] forms another basis for our treatment concept. From the starting point of the somatic disease, which is usually understandable by every patient, health-related QoL and disease-related immune reaction are supposed to be influenced by physical and creative activity. Similar to stress-reduction programs, the hypothesis is, firstly, that disease management can be induced by psycho-oncology and, secondly, immunological mechanisms can be triggered to influence the course of disease.

On the basis of this psychosomatic perspective, trainings were iteratively developed and assessed. ACCEPT® is a supplementary program for SOC, including all medical communication tasks. With consideration of proactive and inactive wishes for psycho-oncological support [38], ACCEPT® was divided into three therapy modules, designed to integrate and cater for the spectrum of levels of motivation, symptom loads and practical manageability by the patient, including the individual personal environment (Fig. 1). Details are described in the online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000516820).

Analyzing the implementation of the different modules, the format of an educative and protective group dynamic was identified as a central element for the health education module: with respect to this, studies have confirmed the important role of nursing competence in oncological care [39], including group facilitation. Evidence suggests that the combination of media, social and communicative skills as well as the application competence is pronounced in the nursing profession [40].

Patient orientation is enabled through communication [41], is based on the physical and emotional state of the patient and considers personal values, needs and preferences. If successful and leading to a consensus on the current situation and possible therapies [42], it promotes the patient's self-competence and ability to act. Therefore, the health education module (holistic health advisor program) was realized by nursing staff. Contents were structured in a curricular fashion and enriched by expert lecturers, and feasibility in the home environment was always considered. Furthermore, the benefit of regular daily structure and rhythm during the treatment period is conveyed.

The coping module (meaning-based psychotherapy program) intended besides supporting the competencies for coping with the disease to also strengthen the capability for active self-management. In anthroposophic medicine, the interview has a special function: in the therapeutic encounter the individual biographical and social situation should be recorded, and an overall therapeutic concept should be generated that addresses the patient's resources [43]. This differentiates the anthroposophic approach from standard psycho-oncological interventions. Seven theme complexes were designed as building blocks

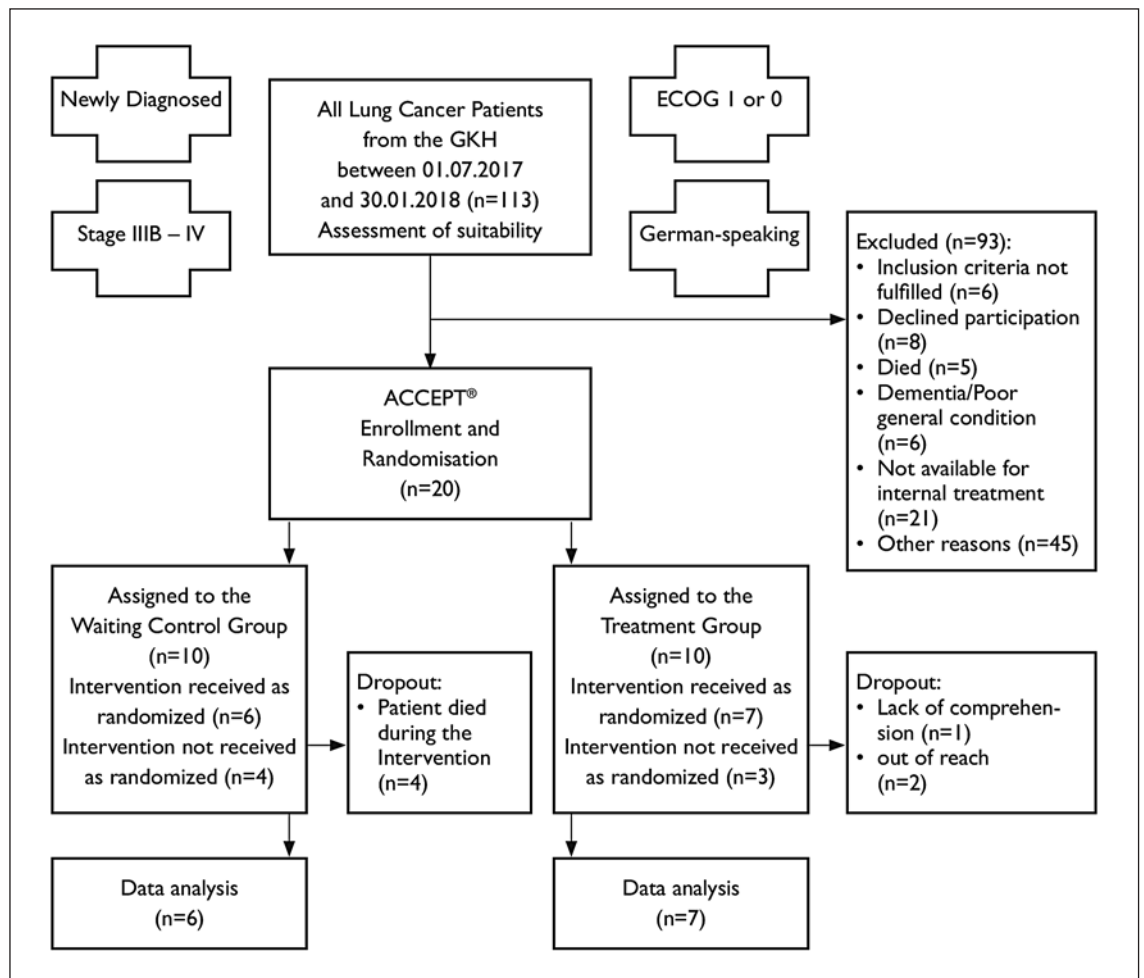


Fig. 2. A flowchart of randomization of patients. GKH, Gemeinschaftskrankenhaus Havelhöhe.

and applied in three consecutive interviews based on an open, qualitative guideline.

The home training module (sound-informed breathing training) is principally based on the assumption of an interaction of biopsychosociospiritual elements. This represents the theoretical basis for three ART therapy trainings, which are instructed by specialized health care personnel and executed in the home environment as a third module. Methodologically, the empirically selected exercise modalities are based on eurythmy therapy [44–46], therapeutic speech formation [47, 48], and singing therapy [49, 50].

In summary, it can be said that the three modules have different emphases, all aiming to strengthen the individual competencies of the patient in coping with the disease.

ACCEPT® was developed between 2012 and 2017 and has since been stepwise implemented in clinical everyday practice, followed by a systematic evaluation, the results of which have first been presented in 2018 [35]. A prior interim evaluation of ACCEPT® included a subgroup ($n = 10$) of the patients participating in the present study [51]. Here, the feasibility of ACCEPT® was tested.

Materials and Methods

The randomized, controlled study was conducted from 2017 to 2018 at the DKG-certified LC center at the Gemeinschaftskrankenhaus Havelhöhe. Newly diagnosed LC patients were asked to participate. Twenty patients (11 female, 9 male) not presenting with limitations to participate in a 3-month supplementary program were enrolled and randomly assigned (blinded lottery procedure: a secretary not working in the study selected a sealed envelope from a basket and handed it over to the patient) to a treatment group or a waiting control group (Fig. 2) after signing the informed consent form for data collection and further processing.

ACCEPT® consisted of 3 modules applied in addition to SOC: a health education module, a coping module, and a home training module (modules 1–3; see online suppl. material).

The treatment group received the supplementary therapy for 3 months, starting immediately after the diagnosis of LC, while the control group received SOC according to guidelines for 3 months, followed by ACCEPT®.

The feasibility of ACCEPT® was to be inferred by the majority of patients finishing the program. Attendance was quantified by counting the completion of items per module by the patients.

Various parameters relating to QoL are recorded. Effects of the multimodal therapy were assessed at 4 time points (T0–T3) where the participants were asked to fill out the following question-

Designation	Research content
FACT-L (Functional Assessment of Cancer Therapy for Lung Cancer)	Investigates physical, social, emotional and functional well-being and additionally symptoms and functions of smoking.
CFS-D (Cancer Fatigue Scale)	Examines the fatigue caused by the cancer.
PSQI (Pittsburgh Sleep Quality Index)	Examines sleep disturbing events, the assessment of sleep quality, the usual sleeping times, the latency and duration of sleep, the intake of sleep medication, and daytime sleepiness.
HADS (Hospital Anxiety and Depression Scale)	Examines anxiety and depression in patients with physical illnesses or (possibly psychogenic) physical complaints.
IPQR (Illness Perception Questionnaire - Revised)	Examines the patients' perception of disease.
F-Sozu (Social Support Questionnaire)	Examines the subjectively perceived, anticipated support from the social environment.
FEAV (Fear Avoidance Questionnaire)	Examines the everyday handling of the patients' symptoms.
PAF (Progressive Anxiety Fear Questionnaire)	Examines the fear of disease progression.
Self regulation according to Großarth-Maticek	Examines the self-regulation of patients.

Fig. 3. Measuring instruments.

naires: as the main variable FACT-L (Functional Assessment of Cancer Therapy for Lung Cancer [52]) was used; as secondary variables served CFS-D (Cancer Fatigue Scale [53]), PSQI (Pittsburgh Sleep Quality Index [54]), HADS (Hospital Anxiety and Depression Scale [55]), a shortened, nonvalidated version of the IPQR (Illness Perception Questionnaire-Revised [56]), a shortened, nonvalidated version of the F-SozU (Social Support Questionnaire [57]), PAF (Progression Anxiety Questionnaire [58]), a nonvalidated instrument FEAV (Fear Avoidance Questionnaire [59]), and self-regulation according to Großarth-Maticek [60] (Fig. 3). IPQR and F-SozU were considered as potential moderators or mediators. Means and standard deviations of the different parameters were calculated.

Support in filling out the questionnaires was offered to the patients.

Results

With respect to demographic data the two groups are balanced (Table 1).

The participants received first-line SOC: 61.5% ($n = 8$) received chemotherapy alone, 7.7% ($n = 1$) received monotherapy, 38.5% ($n = 5$) received targeted therapy with a tyrosine kinase inhibitor (tablets), 15.4% ($n = 2$) received combination therapy with chemotherapy and surgery, and 53.8% ($n = 7$) received combination therapy with chemotherapy and radiation. The study participants were in UICC stage IVa or IVb (UICC 8th generation).

At first assessment (T1) 5 patients of the treatment group ($n = 7$) presented with an ECOG status of 0 and 2 with ECOG status 1. In the waiting control group ($n = 6$)

Table 1. Sociodemographic data (n , %)

	Treatment group ($n = 7$) (mean age 67.00, SD 8.55)	Waiting group ($n = 6$) (mean age 69.00, SD 8.71)
Men	2 (28.6)	3 (50)
Women	5 (71.4)	3 (50)
German	7 (100.0)	5 (83.3)
Other nationalities	0	1 (16.7)
Married	5 (83.8)	4 (66.7)
Partnership	0	1 (16.7)
Divorced	0	1 (16.7)
Widowed	1 (16.7)	0
Currently smoking	1 (16.7)	0
Formerly smoking	3 (50.0)	4 (66.7)
Never smoking	2 (33.3)	2 (33.3)
Primary school certificate	1 (25.0)	1 (16.7)
Secondary school certificate	1 (25.0)	4 (66.7)
High school graduation	2 (50.0)	1 (16.7)

at the time of the start of ACCEPT[®], 3 months after enrollment (T1), the ECOG status was 0 in 4 patients and 1 in 2 patients. With respect to QoL (FACT-L [52]) and physical state as well as social environment, the groups were comparable.

Three of the 10 patients assigned to the treatment group dropped out due to being out of reach, lack of comprehension and articulation problems. The remaining 7 patients concluded the treatment program. In the

Table 2. Mean values and standard deviations (in parentheses) for dependent variables

	Treatment group (<i>n</i> = 7)		Control group (<i>n</i> = 6)	
	T1 ^a	T3 ^b	T0 ^a	T1 ^b
FACT ^c	<i>n</i> = 7 99.21 (11.13)	<i>n</i> = 7 98.3 (23.41)	<i>n</i> = 8 ^f 92.71 (16.21)	<i>n</i> = 8 ^f 94.15 (7.7)
CSF-D ^d	<i>n</i> = 7 29.71 (8.9)	<i>n</i> = 7 27.29 (9.2)	<i>n</i> = 7 ^f 26.57 (5.32)	<i>n</i> = 7 ^f 28.57 (1.13)
PSQI ^c	<i>n</i> = 7 8.29 (4.79)	<i>n</i> = 7 4.14 (2.54)	<i>n</i> = 8 ^f 8 (4.21)	<i>n</i> = 8 ^f 6.25 (4.37)
HADS ^d	<i>n</i> = 7 5.14 (2.54)	<i>n</i> = 7 9 (9.13)	<i>n</i> = 8 ^f 14.62 (6.37)	<i>n</i> = 8 ^f 13.75 (6.07)
F-SozU ^e	<i>n</i> = 6 ^f 4.69 (0.32)	<i>n</i> = 6 ^f 4.84 (0.24)	<i>n</i> = 8 ^f 4.39 (0.43)	<i>n</i> = 8 ^f 4.58 (0.31)
FEAV ^d	<i>n</i> = 7 1.4 (1.17)	<i>n</i> = 7 9.71 (15.61)	<i>n</i> = 7 ^f 1.19 (1.1)	<i>n</i> = 7 ^f 14.14 (11.14)
PAF ^d	<i>n</i> = 5 ^f 8.22 (2.33)	<i>n</i> = 5 ^f 6.33 (0.98)	<i>n</i> = 8 ^f 8.73 (1.86)	<i>n</i> = 8 ^f 8.61 (1.68)

^a Collected at time 1 (T1; treatment group) or time 0 (T0; control group) (before treatment). ^b Collected at time 1 (T1; control group) or time 3 (T3; treatment group) (after treatment). ^c Increases in mean values signify an increase in QoL. ^d Increases in mean values signify a decrease in QoL. ^e Increase/decrease in mean values cannot directly be interpreted with respect to QoL. ^f Due to missing data, the number of evaluable study participants differs. As far as possible, all patients who could be evaluated at a certain time point are included.

waiting control group (*n* = 10) 4 patients died during the study period, but not during the waiting period, so that altogether data from 13 patients were available for evaluation.

In the health education module in the treatment group 68% of the items and in the waiting control group 83% of the items were completed. In the coping module all patients (100%) in both groups attended all interviews. In the physical training module in the treatment group 19% and in the waiting control group 50% of the items were completed. Since the preformatted diaries for listing of the home training activities were only introduced during the course of the study, no data of compliance with home trainings are available. Means and standard deviations of the psychometric parameters are presented in Table 2.

Due to unsystematically incomplete questionnaires, the self-regulation according to the Großarth-Maticsek [60] questionnaire could not be evaluated. The IPQ-R cannot be interpreted as a mean value due to the item construction.

Besides the questionnaires, the participants could return free text feedback: 1 patient from the treatment group considered health education as particularly helpful; 1 negative feedback was received. All patients in the treatment group were able to conduct the module 2 interviews according to the qualitative guideline. The module 3 home training was conducted as described above.

In summary, the majority of the patients in the treatment group completed ACCEPT[®]. With respect to compliance and satisfaction with treatment, but also organizationally as a supplement to SOC in LC, ACCEPT[®] was shown to be feasible.

Discussion/Conclusion

National guidelines and international professional societies recommend supportive psychosocial therapy for LC (see online suppl. material [61, 62]). However, so far, no program adapted to LC patients and consisting of clearly defined modules has been described. ACCEPT[®] meets these requirements and was tested here in an environment of everyday oncological clinical practice.

Actual Discussion

The health education module which was applied by trained nursing staff met with high appreciation by patients and regular participation of more than overall 75% of the items completed by the patients. The coping module of psycho-oncological interventions was completely attended by all patients. The physical training module met with an unsatisfactory attendance of overall 34.5% of the items completed by the patients. However, compliance with the program seemed to improve near the end

of the study after the patients had been asked to take notes of their home activities. Moreover, only eurythmy therapy could be offered in this study, so that the intended choice between the different modalities (physical therapy/eurythmy, speech therapy, singing therapy) was not available.

Integration of ACCEPT[®] into the daily patient care was unproblematic except for considerable additional effort for coordination of visits.

The high number of dropouts (Fig. 2) was unexpected: factors like remote domiciles of the patients leading to high costs of transport, foreseeable medical procedures in other clinics etc. should be reflected in the inclusion criteria.

Limitations

The high number of questionnaires (9) which had to be filled out by the patients at three time points exceeded the energy and willingness of some patients, leading to unsystematically missing data. Appropriate support and active encouragement to report difficulties should be implemented. Also, online instruments (questionnaires, parts of modules 1 and 3) might support the patient's compliance and satisfaction.

Due to the small patient number no conclusive results with respect to an effect of ACCEPT[®] on QoL or to a superiority versus SOC only could be demonstrated.

Conclusion

The multimodal ACCEPT[®] was implemented in the environment of an anthroposophic clinic, where all resources needed for the three treatment modules are available and might therefore not be directly transferable to other cancer centers. However, trained staff for health education, psycho-oncological interventions and physical training exists at most cancer clinics, which should enable similar multimodal programs.

In conclusion, the supplementary multimodal ACCEPT[®] can be integrated into everyday practice of an oncological care unit. ACCEPT[®] with its three modules and with its biopsychosociospiritual concept of anthroposophic integrative medicine met with a satisfactory

compliance in a heterogeneous group of advanced-stage LC patients despite the burden of SOC including surgery, radiotherapy, and pharmacotherapy.

Having confirmed feasibility, efficacy and dosing of ACCEPT[®] will be evaluated in a larger clinical trial, taking into account the limitations of the present study as described above.

Statement of Ethics

We herewith confirm that the trial protocol has been approved by the EC 1 of Campus Charité Mitte, Charitéplatz 1, 10117 Berlin, approval No.: EA1/231/16, in accordance with the World Medical Association Declaration of Helsinki. All patients have given their written informed consent.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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Author Contributions

Silke Schibel, Marie Steinert: study conduct, data evaluation, analysis and interpretation of the data, preparation of the manuscript. Harald Matthes: critical revision of important contents and final approval. Christian Grah: conception of the work, critical revision of important contents and final approval. The authors agree to take responsibility for all aspects of the work and to ensure that all questions regarding the accuracy and completeness of all parts of the manuscript are properly investigated and clarified.

Data Availability Statement

The study plan and the data that support the findings of this study are available from the corresponding author C.G. upon request.

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