Palliative In-Patient Cancer Treatment in an Anthroposophic Hospital: II. Quality of Life during and after Stationary Treatment, and Subjective Treatment Benefits*

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Summary
Background: There is an increasing demand for comprehensive forms of palliative cancer care, meeting physical as well as emotional, cognitive, spiritual and social needs. Therapy programs of anthroposophic hospitals are aimed at improving health and quality of life (QoL) at these levels. However, data on the influence of these programs on QoL of patients with advanced cancer are scarce. Patients and Methods: 144 in-patients with advanced epithelial cancers were treated at the anthroposophic Lukas Klinik, Arlesheim, Switzerland. QoL was assessed upon admission, discharge and after 4 months, using 20 functional scales from the questionnaires EORTC QLQ-C30, HADS and SELT-M. Statistical testing was performed with the Wilcoxon signed rank test. At month 4, subjectively perceived benefits from anthroposophic medicine (AM) and conventional cancer therapy (CCT) were assessed by telephone. Objective: The aim was to provide an account of global, physical, emotional, cognitive-spiritual and social QoL developments in advanced cancer patients, during and after in-patient AM treatment, and to investigate subjective benefits from AM and CCT. Results: QoL improvements were observed in all 20 dimensions (12 significant). Compared to related studies, improvements were fairly high. At month 4, QoL scores had decreased but were still above baseline in all 20 dimensions. Both AM and CCT were perceived as beneficial. Conclusion: Our data provide evidence that in-patient therapy at an anthroposophic hospital can lead to significant QoL improvements, especially in emotional, but also global, physical, cognitive-spiritual and social aspects. Benefits of AM were experienced on the physical, emotional, cognitive-spiritual and social level. Benefits of CCT were tumor-focused.

Key Words
Cancer treatment, palliative · Anthroposophic medicine · CAM · Quality of life

Schlüsselwörter
Krebstherapie, palliative · Anthroposophische Medizin · CAM · Lebensqualität

Zusammenfassung

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Introduction

Stagnation or only slow, gradual progress still characterizes palliative tumor treatment, and, despite considerable improvements in the control of side effects and relief of tumor-related symptoms, toxicity still poses a major, often therapy-limiting problem of conventional tumor treatment [1]. In this situation, public interest has increasingly turned towards complementary or alternative medicine (CAM), despite the general lack of clear evidence of effectiveness in this area [2–4]. In the last few years, a growing number of investigations into the reasons for this interest have revealed a number of patient needs not met by conventional cancer therapy (CCT) that are not only related to problems of treatment failure and toxicity, but also to basic concepts of our present medical culture. These needs include a less technical or reductionist but instead more holistic and humanistic approach to medical care [5, 6], attention to mind-body issues and spirituality [7, 8], a more emotionally satisfying, communicative doctor-patient relationship [9], the opportunity to be actively involved in the fight against the disease [10, 11], an enhancement of the body’s own defenses and immune processes [11–13], and psychological well-being and quality of life (QoL) [14, 15] – in other words, a treatment strategy encompassing the human being as a whole, with its diversified aspects of body, soul and spirit [16].

Anthroposophic medicine (AM) has created a holistic medical culture along these lines from the beginning and has developed an array of diversified interventions for these purposes [17, 18]. In Switzerland and Central Europe, AM belongs to the most popular methods providing CAM cancer treatment. This relates not only to mistletoe preparations and their immunologic effects [19, 20], but also to anthroposophic hospitals with their holistic spectrum of therapies [21, 22]. The Lukas Klinik (LK) in Arlesheim, Switzerland, is a well known anthroposophic hospital specializing in oncology, that attracts patients from all areas of Switzerland and neighboring countries [22]. Concurrent with the basic concept of AM, the LK provides an integrative approach to AM and CCT [17, 18]. In palliative cancer treatment, it puts a major emphasis on QoL improvement in global, physical, psychological and cognitive-spiritual QoL domains [22, 23]. Yet, so far, the effectiveness of its holistic therapeutic strategy has not been studied systematically. Therefore, the LK was included in a composite research project of the Swiss National Science Foundation Program NFP 34, which we reported about earlier [14, 22–27]. The aim was a first and thorough investigation of QoL development in patients with advanced cancer during and after holistic in-patient treatment at LK. In view of traditional controversies about the role of AM in cancer therapy [28–30] and the lack of reliable data on the subject, a randomized comparative trial would have been desirable. However, because of logistic constraints and patient preferences for AM, randomization to the LK or within a referral system at LK was not possible [23, 27].

Similarly, in another randomized part of our NFP 34 project at the University Hospital in Bern – a 3-arm study which was to test additional AM or supportive-expressive group therapy against no such addition to palliative CCT – not enough patients could be recruited [26]. Hence, for the investigation of QoL at LK, we performed a prospective 1-arm pre/post-observational study, assessing QoL data at admission, discharge and follow-up. In the preceding paper we described the medical characteristics of 144 in-patients at LK, their therapy patterns of CCT, AM and CAM in the 3 phases 4 months before, during and 4 months after hospitalization at LK, and their compliance with AM after discharge [22].

The present paper describes QoL development of the same patients during and after hospitalization. Our main question was whether patients experienced a significant improvement of global, physical, emotional, cognitive-spiritual and social QoL between admission and discharge. We also analyzed the course of QoL in subgroups, formed according to tumor types, performance status and recent CCT prior to admission. Similarly, our secondary questions concerned the further course of QoL after discharge for the whole cohort. Due to patient loss, this could only be analyzed descriptively. Our hypotheses included i) a significant increase of QoL in all major domains during the intensive multimodal in-patient treatment at LK, followed by ii) a moderate decrease until month 4, but possibly not below score levels at baseline (BL). Additionally, a description of benefits from AM at LK and CCT subjectively perceived by patients is given, assessed in retrospective by interview at month 4.

Patients and Methods

Patients, Institution, Treatment Concept and Applied Therapies

A description of LK and its therapeutic concept is given in [22]. In this paper, we investigate QoL development of the same 144 patients with advanced epithelial cancers, whose medical characteristics, CCT, AM and other CAM therapies are described in [22]. At hospital discharge (HD), questionnaires were obtainable from 115 patients and at month 4 from 77 of the original 144 patients. The reasons for non-availability at discharge were: logistics (14), physical status, refusal and death (5 each), and at month 4: death (41), physical status (12), refusal (8), logistics (3), unknown (2), study closure (1). Due to inconsistent completion of some questionnaires at entry and follow-up, the number of questionnaires shrank to ≤110 at discharge and ≤74 at month 4, depending on QoL dimension (table 1).

Assessment and Evaluation of QoL

Patients were asked to fill out the QoL questionnaires on the first or second day of hospitalization for BL, and on the day of hospital discharge. At month 4 after BL, the questionnaires were sent to the patients by mail. The procedure of filling out the set of questionnaires took 30–40 min. To assess QoL for the present study, 3 instruments were used: EORTC QLQ-C30, HADS and SELT-M. The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire QLQ-C30 is a well-validated, widely used multidimensional instrument [31]. We used the official, extensively validated German version [32] which had been previously used in cancer patients with heterogeneous
### Table 1. Improvement of 20 QoL dimensions in a cohort of patients during their hospitalization at LK. A. Score difference hospital discharge minus baseline, B. 4 months minus baseline

<table>
<thead>
<tr>
<th>Domains of life</th>
<th>Instruments</th>
<th>Dimensions</th>
<th>A. HD minus BL</th>
<th>B. 4 months minus BL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>patients, mean median 0.975 CI bounds p-value</td>
<td>patients, mean median 0.95 CI bounds p-value</td>
</tr>
<tr>
<td><strong>Global</strong></td>
<td>EORTC global health/QoL</td>
<td></td>
<td>109 14.30 16.67 8.33 25 0.0001</td>
<td>74 10.47 8.33 6.03 20.83 0.0001</td>
</tr>
<tr>
<td><strong>Physical</strong></td>
<td>EORTC physical functioning</td>
<td></td>
<td>107 5.23 0 0 30 0.0266</td>
<td>71 1.69 0 –10 20 0.7929</td>
</tr>
<tr>
<td></td>
<td>EORTC role functioning</td>
<td></td>
<td>105 9.52 0 0 50 0.0046</td>
<td>71 4.92 0 0 50 0.258</td>
</tr>
<tr>
<td></td>
<td>SELT-M physical well-being</td>
<td></td>
<td>103 7.93 8.33 0 16.67 0.0002</td>
<td>68 9.44 8.33 4.17 16.67 0.0129</td>
</tr>
<tr>
<td></td>
<td>EORTC fatigue</td>
<td></td>
<td>105 –13.65a –11.11 –27.78 –5.55 0.0001</td>
<td>70 –8.89a –11.11 –22.22 –5.55 0.0046</td>
</tr>
<tr>
<td></td>
<td>EORTC pain</td>
<td></td>
<td>110 –10.45a 0 –25 0 0.0002</td>
<td>73 –9.13a 0 –25 0 0.0127</td>
</tr>
<tr>
<td></td>
<td>EORTC nausea/vomiting</td>
<td></td>
<td>108 –4.78a 0 –41.67 16.76 0.056</td>
<td>72 –2.78a 0 –16.67 8.33 0.7972</td>
</tr>
<tr>
<td></td>
<td>EORTC appetite loss</td>
<td></td>
<td>110 –11.52a 0 –50 0 0.0018</td>
<td>73 –12.78a 0 –50 0 0.0155</td>
</tr>
<tr>
<td></td>
<td>EORTC constipation</td>
<td></td>
<td>107 –8.72a 0 –50 0 0.0852</td>
<td>72 –8.33a 0 –50 0 0.116</td>
</tr>
<tr>
<td></td>
<td>EORTC diarrhea</td>
<td></td>
<td>107 –9.35a 0 –66.67 0 0.0111</td>
<td>72 –8.33a 0 –50 0 0.0536</td>
</tr>
<tr>
<td></td>
<td>EORTC dyspnea</td>
<td></td>
<td>109 –2.14a 0 –33.33 0 0.4716</td>
<td>72 –2.78a 0 –33.33 0 0.4331</td>
</tr>
<tr>
<td></td>
<td>EORTC sleep disturbances</td>
<td></td>
<td>109 –3.67a 0 –33.33 0 0.2736</td>
<td>73 –12.78a 0 –33.33 0 0.039</td>
</tr>
<tr>
<td><strong>Emotional</strong></td>
<td>EORTC emotional functioning</td>
<td></td>
<td>107 23.52 16.67 20.83 37.50 0.0001</td>
<td>72 11.69 16.67 8.33 20.83 0.0001</td>
</tr>
<tr>
<td></td>
<td>SELT-M basic mood</td>
<td></td>
<td>107 13.98 12.50 10.42 20.83 0.0001</td>
<td>70 11.37 8.33 6.25 18.75 0.0001</td>
</tr>
<tr>
<td></td>
<td>HADS anxiety</td>
<td></td>
<td>96 –8.73a –4.76 –16.67 –4.76 0.0001</td>
<td>68 –4.98a –4.76 –9.52 0 0.0278</td>
</tr>
<tr>
<td></td>
<td>HADS depression</td>
<td></td>
<td>100 –6.81a –4.76 –14.28 –2.38 0.0001</td>
<td>67 –2.27a 0 –7.14 2.38 0.3774</td>
</tr>
<tr>
<td><strong>Cognitive-</strong></td>
<td>EORTC cognitive functioning</td>
<td></td>
<td>106 8.33 0 0 25 0.0003</td>
<td>71 5.16 0 0 25 0.1589</td>
</tr>
<tr>
<td><strong>spiritual</strong></td>
<td>SELT-M cognitive-spiritual QoL</td>
<td></td>
<td>93 6.38 4.54 1.14 11.36 0.0002</td>
<td>67 3.59 2.27 0 7.95 0.0618</td>
</tr>
<tr>
<td><strong>Social</strong></td>
<td>EORTC social functioning</td>
<td></td>
<td>107 8.88 0 0 25 0.0005</td>
<td>71 10.33 0 0 25 0.0219</td>
</tr>
<tr>
<td></td>
<td>SELT-M social support</td>
<td></td>
<td>107 6.15 8.33 0 12.50 0.0052</td>
<td>73 4.68 0 0 12.5 0.131</td>
</tr>
</tbody>
</table>

*In these dimensions a negative difference signifies improvement of QoL (decrease of symptoms). QoL = Quality of life; HD = hospital discharge; BL = baseline; CI = confidence interval.

### Table 2. Retrospective patients judgment of subjective benefit of various aspects of CCT and AM

<table>
<thead>
<tr>
<th>Domains of patients' experiences</th>
<th>Judgments CCT</th>
<th>Judgments AM at LK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>positive</td>
<td>negative</td>
</tr>
<tr>
<td>Effect on tumor and body</td>
<td>35 (21 neutral)</td>
<td>23</td>
</tr>
<tr>
<td>Emotional effect</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Cognitive-spiritual effect</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Long-term effect</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>1 (1 neutral)</td>
<td>0</td>
</tr>
<tr>
<td>Quality of human relations</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Quality of therapies, equipment, organization</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Overall judgment</td>
<td>10 (2 neutral)</td>
<td>1</td>
</tr>
</tbody>
</table>

CCT = Conventional cancer therapy; AM = anthroposophic medicine; LK = Lukas Klinik.
tumors in advanced disease stages similar to ours [33]. Evaluation was carried out according to the author’s standards [34]. The answers to the 30 questions were grouped into 14 functional scales representing the following QoL dimensions and symptoms: ‘physical functioning’, ‘role functioning’, ‘emotional functioning’, ‘cognitive functioning’, ‘social functioning’, ‘global health status/QoL’, ‘fatigue’, ‘pain’, ‘nausea and vomiting’, ‘appetite loss’, ‘constipation’, ‘diarrhoea’, ‘dyspepsia’ and ‘sleep disturbances’. The Hospital Anxiety and Depression Scale (HADS) is also a validated and widely used instrument used in cancer therapy [35]. For our study, a few minor changes were made in the wording of the German translation in order to adapt it to the linguistic habits of our population. Grammar and meaning remained unaltered. These changes were checked and approved by the publishers [36], but an extra validation was not performed. The scores from the 14 questions were grouped into the dimensions ‘anxiety’ and ‘depression’ and calculated according to standard. The SELT-M is a modified version of the German ‘Skalen zur Erfassung von Lebensqualität bei Tumorphatienten’ (SELT), a validated multidimensional instrument with subscales on the subjectively perceived physical, psychological and social well-being and on the inner orientation of life [37, 38]. With permission of the authors, we modified this instrument by leaving out questions about the physical QoL aspects covered by the EORTC QLQ-C30, and by adding to the remaining 15 points 8 questions about spiritual aspects of QoL that are traditionally relevant in AM. This concerns questions of meaning or possible positive aspects and experiences related to the disease, coping with issues of life and death, finding new inner goals, interests and hope beyond the physical perspective of life, having more courage to be oneself, and the ability to distinguish the essential from the non-essential. The resulting SELT-M contains 5 functional scales: ‘physical well-being’ (3 items), ‘basic mood’ (6 items), ‘social support’ (3 items), ‘inner life orientation’ (3 items) and the newly added ‘spiritual QoL’ (8 items), which had shown good construct and discriminant validity [24]. As the item contents of ‘inner life orientation’ and ‘spiritual QoL’ are very closely related, and as both dimensions with their cognitive and spiritual elements pertain to the spiritual aspects of human being in the perspective of AM, we combined them for evaluation for the present publication to form the dimension ‘cognitive-spiritual QoL’ (13 items). So, taken as a whole, the EORTC QLQ-C30, HADS and SELT-M yielded 20 functional and symptom-based scales, allowing for a differentiated description of QoL, and covering aspects of body, soul, spirit and the social domain, thus equally satisfying demands from conventional medicine and AM with regard to content and methodology.

Retrospective Assessment of Subjectively Perceived Benefits from CCT and AM at LK

In order to obtain from patients a retrospective judgment on the subjectively perceived benefits derived from palliative treatment at LK on the one hand and from conventional medicine on the other, at month 4 patients were asked 2 standardized questions by telephone: ‘What benefit did you draw from conventional treatment, what does it mean to you?’ and ‘What benefit did you draw from your stay at LK, what does it mean to you?’ The answers were taken down by the interviewer as cues and short sentences. For evaluation, these notes were exactly transcribed into a file. In a first step of analysis, 8 categories were formulated, according to the domains of experience mentioned by the patients. The second step was carried out independently by 2 persons who had not been involved in the interview: the contents of the transcribed words and sentences were split up and classified according to the previously defined categories, each category divided into positive, neutral and negative judgments. In a third step, the 2 reviewers met to reach consensus with regard to divergent classifications. The result is summarized in a simple frequency table (table 2).

Statistics

The Wilcoxon signed rank test was used to find significant differences in QoL score medians between BL and HD and between BL and month 4. Two-sided p-values were computed by Monte Carlo approximation. 0-differences were not used. Exact Hodges-Lehmann confidence intervals (CI) for median differences were added. To avoid confusion, it should be mentioned that a Hodges-Lehmann CI may contain the value 0 even if the corresponding Wilcoxon p-value is significant. Because of multiple testing, Bonferroni correction was applied to answer the primary question concerning differences between HD and BL values. Thus, for the 20 score differences of the overall patient cohort, the null hypothesis was rejected with \( p < 0.0025 \), and a CI of 99.75% was determined. In the graphics, mean values were used as they depict average score changes of discrete scales more realistically than medians. For the explorative analysis of the score differences between month 4 and BL, the level of significance was set at \( p = 0.05 \), and 95% CIs were computed. For the explorative subgroup analysis, the entire cohort was subdivided into 3 different subgroups: i) performance status 1-2 vs. 3-4, ii) the latest possible CCT with a possibly weakening effect on QoL (surgery, chemo/radiotherapy) within less vs. more than 4 weeks prior to admission, and iii) tumor location: breast vs. gastrointestinal (GI) tract (upper GI tract, pancreas, colon, rectum, liver, bile duct or bladder) vs. lung vs. genital tract (uterus, ovary). Statistical analysis of score differences between BL and HD was performed as described above, except that Bonferroni correction was omitted. The significance level was set at 0.05, and a 95% CI was determined.

In order to analyze whether score differences between BL and HD differed significantly between subgroups, the following tests were performed. The Wilcoxon rank sum test was used to find significant differences between 2 unpaired samples. Two-sided p-values were computed by Monte Carlo approximation. Exact Hodges-Lehmann CIs for the median differences were added. The Kruskal-Wallis rank sum test was applied to find significant differences between at least 2 out of m > 2 unpaired samples. Asymptotic p-values were computed only. The significance level was set at 0.05 and 95% CIs were added. All calculations were carried out with S-Plus 6.2 Professional Edition (Insightful Corporation, Reinach, Switzerland).

Results

QoL Development during Hospitalization

Figures 1 and 2 illustrate the global course of 20 QoL dimensions in the entire cohort of patients during their hospitalization at LK, which lasted 22 days on average (median 22.0, mean 22.7, 1st quartile 18, 3rd quartile 25, range 7–85). Visually, all QoL dimensions show an improvement. As figure 1 shows, this applies especially to those with a marked increase in ‘emotional functioning’ and ‘basic mood’ and a decrease in ‘anxiety’ and ‘depression’ scores. Also ‘global health status/QoL’, which subsumes all QoL aspects, is notably increased. Lesser increases are seen in the social, spiritual and somatic domains, with ‘physical functioning’ undergoing the smallest increase of all. Figure 2 shows that physical symptoms common in cancer patients and partly related to CCT regress to various extents: regression is most notable with ‘fatigue’, moderate with ‘pain’ and the various GI symptoms, and minor with ‘sleep disturbance’ and ‘dyspnea’. Column A of table 1 shows that during hospitalization an improvement of QoL score means and medians was reached in all 20 dimensions, 12 of which were significant for medians with Bonferroni correction. This concerns ‘global health status/QoL’, 4 of 11 physical, all of 4 emotional, both of 2 cognitive/spiritual and 1 of 2 social dimensions.
The explorative analysis of the subgroups revealed that patients who had undergone a potentially weakening CCT within 4 weeks prior to admission (n = 41–48) showed an improvement until discharge with a p < 0.05 in all QoL dimensions. Patients whose latest toxic CCT had been administered more than 4 weeks prior to admission (n = 52–59), experienced improvement in all emotional and cognitive-spiritual dimensions and in ‘global health status/QoL’, but only in 2 of 11 physical dimensions (‘physical well-being’ and ‘fatigue’, results not shown). Accordingly, the differences between BL and HD were more pronounced (p < 0.05) in the group ‘<4 weeks’ than in the group ‘>4 weeks’ in the following dimensions: ‘global health status/QoL’, ‘physical functioning’, ‘appetite loss’, ‘nausea/vomiting’ and ‘constipation’. Patients with a bad performance status (WHO 2+3, n = 32–43) showed improvements (p < 0.05) in as many (albeit partly different) aspects of global and physical QoL as patients with a good performance status (WHO 0+1, n = 59–67). Regarding the following dimensions, the differences between BL and HD were greater (p < 0.05) in the group with worse performance: ‘nausea/vomiting’, ‘diar-
Palliative Treatment in an Anthroposophic Hospital: Quality of Life and Subjective Treatment Benefits

**Treatment Benefits**

Palliative treatment in an anthroposophic context includes recovery and general improvement (in part after stabilization of the disease), whereas most related answers focused almost exclusively on tumor-related aspects, such as slowing down, stagnation, reduction (of tumor size), remission (of metastases or tumor markers) or freedom from or alleviation of pain. The negative tumor and body-related judgments of CCT pointed mainly to side effects or lacking, insufficient or overly severe effects. As for AM, most negative judgments were related to inadequate effects. The 21 neutral answers on CCT stated that no CCT was administered, 7 of which including refusal of CCT.

**QoL at Month 4 after Hospitalization**

Column B of table 1 shows the result of the exploratory analysis for the remaining 74–67 patients after HD: at month 4, again in all 20 dimensions, the average QoL levels remained above BL values, although in 15 dimensions they were moderately lower than those of the entire cohort at HD. Nevertheless, in 10 dimensions, the QoL improvements at month 4 had a p < 0.05. This concerns global health status/QoL, 5 of 11 physical, 3 of 4 emotional and 1 of 2 social dimensions.

**Retrospective Assessment of Subjectively Perceived Benefit from CCT and AM at LK**

Answers to the questions on the subjectively perceived benefits from both treatment modalities were available at month 4 from 88 of 95 interviewed patients. 2 of these patients had given no answers relating to CCT. The answers could be fully assigned to the 8 domains in table 2, which correspond to the domains of experience mentioned by the patients. Table 2 shows that LK received clearly more positive judgments than CCT in the domains emotional effect, overall judgment, quality of human relations, cognitive-spiritual effect (in this order) and moderately more positive answers in the domains quality of therapies, equipment, organization and long-term effects. With regard to effect on tumor and body, CCT received more positive judgments than LK but also more negative answers. On the other hand, CCT received slightly less negative judgments than LK in regard to long-term effect, quality of therapies, equipment, organization, overall judgment, others and cognitive-spiritual effect. All together, the positive opinions exceeded the negative ones in 7 of 8 domains with LK and in 4 of 8 domains with CCT.

The domain effect on tumor/body deserves a special comment. In this category, all statements relating to tumor and body were taken together since the 2 areas were closely connected in many answers. However, positive judgments on CCT and LK show a differing pattern when analyzing the answers more closely by an additional categorization of their content. Regarding LK, few patients gave an explicitly tumor-related answer (stabilization of the disease), whereas most other statements related to the general physical status, including recovery and general improvement (in part after chemotherapy or surgery), reinforcement of life forces, return of fitness for work and bodily strength or simply well-being. The positive judgments of CCT focused almost exclusively on tumor-related aspects, such as slowing down, stagnation, reduction (of tumor size), remission (of metastases or tumor markers) or freedom from or alleviation of pain.

The negative tumor and body-related judgments of CCT pointed mainly to side effects or lacking, insufficient or overly severe effects. As for AM, most negative judgments were related to inadequate effects. The 21 neutral answers on CCT stated that no CCT was administered, 7 of which including refusal of CCT.

Positive judgments of LK with regard to emotional aspects were mostly related to emotional well-being and recovery, new courage or hope, emotional balance/inner peace or psychological stability. Positive judgment of CCT concerned confidence/hope of tumor response and symptom/pain alleviation and satisfaction with result in terms of performance and QoL/longer life. Cognitive-spiritual aspects appraised positively at LK were return to essentials/to oneself/inner peace, reinforcement of self-confidence, ability to decide/to accomplish by oneself, better coping with disease, destiny, life crises, reorientation/clarification/spirituality, loss of fear of death. Positive long-term effects of AM at LK concerned a continuation of overall positive benefits, altered lifestyle factors (literature, art therapy, no TV). Negative long-term effects included reduction of emotional well-being, tumor progression, remaining or increasing pain. As for CCT, stable disease was mentioned as a positive, progression and lasting side effects as negative long-term effects.

With regard to human relations at LK, positive descriptions were very good care, felt taken serious/supported/like at home, personnel friendly, attentive, caring, conveying security, support, treatment of the whole being, meaningful counseling, to be among equals. Positive judgments on human relations in CCT concerned very good experiences with physicians, improved collaboration with AM and good care. Negative in both settings were various forms of disappointment, primarily related to the course of the disease. Concerning quality of therapies, equipment and organization, the LK received positive judgments for medical care, the holistic or rhythmic therapy concept, a good environment and community with equals and meals. Negative opinions concerned aspects of care, meals or strictness of organization. As for CCT, positive aspects related to treatments, life-saving interventions and control examinations. Negative views mainly concerned aspects of care.

As for overall positive judgments related to LK, more general summaries were made, such as has achieved much or positive memories (of the stay). Whereas for CCT, overall positive judgments referred more explicitly to treatment results. Negative aspects concerned side effects of CCT and overall disappointments at LK.
Table 3. Mean QoL score differences from studies in patients with advanced cancer, obtained with EORTC QLQ-C30 at baseline (BL) and after treatment or at hospital discharge (HD)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Malignancy</th>
<th>Patients, n</th>
<th>Treatment</th>
<th>Timing of QoL assessment</th>
<th>Global QoL</th>
<th>Physical function</th>
<th>Role function</th>
<th>Emotional function</th>
<th>Cognitive function</th>
<th>Social function</th>
<th>Fatigue</th>
<th>Pain</th>
<th>Nausea / vomiting</th>
<th>Appetite loss</th>
<th>Constipation</th>
<th>Diarrhea</th>
<th>Dyspnea</th>
<th>Sleep disturbances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>BR, LU, CR, GI (GA, BI, PA), FG (OV, CE)</td>
<td>110</td>
<td>AM</td>
<td>BL</td>
<td>48.93</td>
<td>66.73</td>
<td>55.24</td>
<td>47.43</td>
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aMatched pairs.
bAssigned in a cluster randomized design.
cRandomized assignment.
dSubsample with ‘quite a bit’ or ‘very much’ pain (n = 86) or dyspnea (n = 56).
QoL = Quality of life; BI = biliary; BR = breast; CE = cervix; CR = colorectal; FG = female genital tract; GA = gastric; GI = gastrointestinal; Ki = kidney; LU = lung; LY = lymphomas; MG = male genital tract; MY = myeloma; OV = ovary; PA = pancreatic; PR = prostate; SK = skin; AM = anthroposophic medicine; BSC = best supportive care; CTh = chemotherapy; CCT = conventional cancer therapy; RTh = radiotherapy; diff. = difference; BL = baseline; HD = hospital discharge.
Discussion

This prospective study shows an improvement of global, physical, emotional, cognitive-spiritual and social QoL in a cohort of 110 patients with advanced epithelial cancer (breast, GI, genital and lung) during an average 3-week palliative treatment at an anthroposophic hospital. In 12 of the 20 tested functional scales from the multi-item questionnaires EORTC QLQ-C30, HADS and SELT-M, improvements were significant (p < 0.0025). In the remaining 8 scales, scores also changed for the better. Quantitatively, the most pronounced improvement occurred in the dimensions 'emotional functioning', 'global health status/QoL', 'basic mood', 'fatigue', 'inappetence' and 'pain'. The considerable rise in the emotional scores corresponds to these patients' prior expectancy of emotional wellbeing — a major reason for choosing the LK for palliative treatment [14]. Various factors of the multimodal therapy, such as art therapy, may have contributed to this improvement [39]. The rise in 'global health status/QoL' is important, as it reflects the sum of various treatment-related factors of the holistic therapy at LK [40]. The improvement in 'fatigue' is also important, in that fatigue is a highly frequent but often neglected cancer-associated problem [41–43]. It has multiple disease- and treatment-related causes, some of which can be met by specific therapies (e.g. infections, hypoxia etc). However, there are no generally accepted treatments available for the fatigue syndrome as a whole. For this reason, Berger [44] proposes a combination of different approaches, including pharmacological support, individually tailored exercise, regular short sleeps, psychotherapy and cognitive therapies, support groups, adequate nutrition etc. This resembles closely the treatment strategy at LK: supportive medication, therapeutic eurythmy, short sleeps after meals, counseling (including psychotherapeutic, cognitive and spiritual issues), art therapy in groups, diet and others [22]. 'Appetite loss' may have improved for similar reasons, apart from specific therapies for GI problems and the almost complete absence of chemotherapy at LK [22]. Pain is the main determinant of QoL, as seen from the patients' viewpoint in the terminal phase of cancer, and adequate pain control is of the utmost importance [45]. However, this often entails more than adequate handling of analgesics. Similar to fatigue, cancer-related pain requires a comprehensive approach which pays 'attention to imbalances in the mind, body and spirit' [44], which again is a major feature of AM at LK [22]. It is noteworthy that the significant score improvement in relation to 'pain' was achieved despite the reduction in conventional analgesics reported in [22]. The combination of conventional and AM analgesics [22], music therapy [46], massage [47] and other ways of emotional and spiritual stress reduction may have contributed to effective pain control [22, 48].

However, in order to interpret the QoL improvements in a larger clinical context, a controlled comparison with other treatment options would have been desirable. This was, however, not possible [22]. For this reason, we searched PubMed for similar studies investigating QoL in palliative cancer treatment. We found 9 studies with relatively similar conditions and a QoL assessment using the EORTC QLQ-C30, including a recent Swedish study comparing AM and CCT in a matched pair design [21, 49–56]. A general orientation in this context shows that the QoL improvements reached at LK are comparatively high (table 3), especially with regard to 'global health status/QoL', 'emotional' and 'cognitive functioning', 'fatigue' and 'diarrhea', where the improvements substantially exceed those encountered in other studies [65]. Keeping in mind that conclusions drawn from historic comparisons remain speculative, one can hypothesize that AM therapy may provide something else than best supportive care (BSC) or comprehensive, holistic treatment in the conventional setting. This is made probable by the contrast between the improvements at LK and the QoL changes in randomized trials, where BSC alone was inferior to chemotherapy [50, 51, 56] or where a holistic interdisciplinary approach, including spiritual needs of patients, did not yield better QoL improvements than the conventional approach [49]. Also, in the Swedish study, patients with AM had a clearly higher QoL gain after 4 weeks than patients with CCT, which included 'global health status/QoL', 'pain', 'emotional', 'cognitive', 'social' and 'role functioning'. Patients had received a 2-week in-patient treatment at the anthroposophic Vidar Klinik, Järna, Sweden, receiving Iscador® (Weleda AG, Arlesheim, Switzerland) and a holistic AM treatment program comparable to that at LK [21].

In a previous paper, we showed that palliative cancer therapy at LK integrates a balanced AM treatment aimed at physical, emotional, cognitive-spiritual and social factors with usual elements of CCT, some of which were clearly reduced (chemo/radiotherapy: sleeping pills, psychoactive and pain medication WHO I/II) [22]. It seems likely that it is this combination that produces the observed multimodal QoL improvements, although, in this frame, it is not possible to discern the contributions of singular elements. However, it is interesting to note that in physical QoL dimensions, the subgroups submitted to potentially toxic CCT within 1 month prior to admission, experienced more and partially better improvements than the group with a larger time interval since CCT. As this concerns QoL aspects which can be impaired (e.g. through side effects [52, 57]) but also improved (e.g. through their effect on tumor containment [49, 50]) by CCT, the improvements at LK may in part be interpreted as value added to positive CCT effects by AM or as alleviation of CCT side effects by AM. Mistletoe treatment for example, apart from its known immunological properties [58, 59] has been reported to ameliorate the tolerability of CCT [60–64]. In this sense, AM may complement CCT. On the other hand, the 2 groups receiving CCT either within 4 weeks prior to admission or further back were similarly responsive in the domains of emotional and cognitive/spiritual QoL. This suggests that these aspects of QoL depend on other disease- and treatment-related factors than the aforementioned physical aspects.
Similarly, patients with a better or worse performance status as well as patients with different types of primary tumors showed similar benefits in physical QoL domains, while patients with a better performance status experienced more improvements in emotional and cognitive/spiritual QoL areas than those with worse performance. As some therapies aiming at emotional or cognitive-spiritual QoL require the ability of patients to actively participate (e.g. art therapy, counseling), the outcome is dependent on the performance status. As regards emotional and cognitive-spiritual QoL improvements observed with HADS and SELT-M, they are clearly in line with those achieved with EORTC QLQ-C30. HADS, although being a valid and frequently used screening tool for affective disorders in the palliative setting [66, 67], is seldom used to study treatment effects [68, 69], and SELT-M has so far only been used in an adjuvant, out-patient setting [70]. Altogether, specific therapy elements but also the relatively high sociodemographic status of this cohort [25] and the expectations of these patients in AM [14] may have facilitated the effects on emotional and cognitive-spiritual QoL.

Among social QoL dimensions, the scores for ‘social functioning’ but not for ‘social support’ improved significantly. A possible reason for this is hospitalization: patients came from all regions of Switzerland, and one third of them from other countries [22]. Thus, social support from family and friends was greatly reduced during the hospital stay. On the other hand, ‘social functioning’ might have improved because at LK social contacts between patients are deliberately fostered by common meals, group eurythmy or group music and cultural events [22].

An important question of our study was whether and how the QoL improvements achieved during the intensive multimodal stationary treatment could be maintained after discharge, when the special setting of LK was no longer available and eventual tumor progression could be expected. Due to patient loss, the answer is only descriptive but basically confirms our assumptions: at month 4, most QoL score averages were lower than those observed at discharge, but all remain above BL values, in 10 of 20 scales with p < 0.05. With the exception of ‘sleep disturbances’, this only concerns QoL dimensions in which significant improvements had already been observed from BL to HD: ‘global health status/QoL’, ‘fatigue’, ‘pain’, ‘nausea/vomiting’, ‘inappetence’, ‘emotional’ and ‘social functioning’, ‘basic mood’ and ‘anxiety’. This QoL pattern, together with the previously described high compliance with AM during the same time period, makes it likely that AM also contributed to QoL after HD. Or phrased contrariwise, the improvement could be stopped because of its toxicity should be offered additional QoL-enhancing treatment options, in particular when these focus not only on the tumor but also on supportive salutogenic physical as well as emotional, cognitive, spiritual and social effects. In this study, such effects could be shown in a cohort of anthroposophically treated patients of whom only a quarter made use of chemotherapy. In other words, there may still be a majority of patients with advanced cancer in whom chemotherapy is not applicable or has to be paused but who may experience clear QoL benefits from holistic treatments such as AM.

The result is very interesting, because here patients describe their true experience or what Gerd Nagel [71] calls ‘mode of thought’ (‘Denkstil’) or ‘expressed need’ of cancer patients, namely the difference between the holistic, ‘salutogenic’ approach of CAM and the ‘pathogenic’ approach of CCT: The pathogenetic approach confines itself to the direct effect on the tumor itself, whereas the salutogenic approach supports the patient’s own health resources at the levels of body, soul and spirit and the social dimension [71]. Our data and the international literature indicate that both approaches are useful and should complement instead of oppose each other. Several studies show that palliative chemotherapy, despite its side effects, may be able to improve QoL in the long term better than (conventional) BSC, especially when it is used for pain management [72, 73]. Nevertheless, the favorable clinical responses to chemotherapy are often sparse, with only a limited number of patients benefiting from a QoL improvement. Furthermore, QoL-reducing overtreatment is a common occurrence [73–75]. Thus, patients under CCT and especially those who are not or no longer helped by CCT or in whom it must be stopped because of its toxicity should be offered additional QoL-enhancing treatment options, in particular when these focus not only on the tumor but also on supportive salutogenic physical as well as emotional, cognitive, spiritual and social effects. In this study, such effects could be shown in a cohort of anthroposophically treated patients of whom only a quarter made use of chemotherapy. In other words, there may even be a majority of patients with advanced cancer in whom chemotherapy is not applicable or has to be paused but who still may experience clear QoL benefits from holistic treatments such as AM.

There are several limiting factors to this study: The results are purely observational, a randomized controlled trial was not possible. Statements derived from historic comparisons must remain speculative. Results for the follow-up after discharge are biased for the patients remaining in the study. Data un-
available due to worsening performance and subsequent death of the patient might have revealed a QoL impairment. The answers to the interview questions concerning therapy benefits were to be given spontaneously and did not have to comply with a standardized format. For this reason, they expressed varying personal topics and emphasis and cannot be readily compared with one another. On the other hand, the very spontaneity of the answers can be viewed as an expression of the patients’ main concerns and thus have a certain authenticity. Also, it is rather unlikely that these answers were given to oblige, since not only were the questions on AM at LK and on CCT asked in pre-formulated identical terms and in parallel, but the interviews were conducted by the coordinators of a non-anthroposophic neutral study coordinators in Bern.

The strengths of the study include i) the cooperative research culture uniting conventional and anthroposophic researchers, ii) the unusually wide QoL assessment with validated instruments giving a meaningful comprehensive overview over global, physical, emotional, cognitive-spiritual and social QoL domains, iii) its relevance for both the anthroposophic and the conventional perspective, and iv) seen together with the previous paper [22], the thorough documentation of CCT, CAM and AM treatments over time and the account of parallel data from therapies, therapy compliance, QoL and subjectively perceived benefits. On the whole, this study provides good descriptive evidence that palliative in-patient cancer treatment in an anthroposophic hospital can result in significant and partially longer lasting improvements in all clinically relevant QoL domains. In this sense, the unique integrative stationary treatment facilities of an AM hospital can meet the demands of not only patients [5–9] but increasingly also of conventional health professionals for a holistic palliative care culture that comprehensively ‘focuses on the physical, emotional, spiritual and social needs of the patients’ [76].

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