Efficacy, Quality of Life, and Safety of Canacea in Palliative Cancer Patients

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Efficacy, Quality of Life, and Safety of Canacea in Palliative Cancer Patients

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Background
Cancer is the important health problem in Thailand and all over the world. Cancer patients usually receive the standard treatment which would be causing the adverse events. The advanced-stage cancer patients may not be response to treatments, the supportive or palliative care is usually required. Canacea is a traditional medicine consist of many herbs with the antioxidant and antimutagenic activities.
Objective
The purpose of this study was to determine the efficacy, quality of life (QoL), and safety of Canacea in advanced-stage cancer patients.
Materials and Methods
The study was conducted at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Thailand during January 2020 – March 2022. All the patients received Canacea with supportive care medications. The performance status, pain control, and QoL were measured 24 weeks after Canacea treatment by using The Eastern Co-operative Oncology Group (ECOG) and the Palliative Performance Status (PPS), pain score, and The World Health Organization Quality Of Life Brief – Thai (WHOQOL-BREF-THAI), respectively.
Results
A total of 17 patients were enrolled in the study. The average age was 64.29±9.14 years, with 11 males and 6 females. At 24 weeks, the average pain score was 0.33±0.47 (range 0-1) which was mild pain. The average ECOG and PPS were 1.7±0.75 (range 1-3) and 70±18.26% (range 40-90%), respectively, which were stable health status. The total QoL score from WHOQOL-BREF-THAI was 94.5±8.44 (range 78-105), which was moderate-to-high QoL. The safety outcome was monitored throughout the study using Common Terminology Criteria for Adverse Events (CTCAE) v5.0. There were 11 patients developed adverse events, with 4 patients who had to withdraw Canacea (23.53%).
Conclusion
The treatment of Canacea with other supportive care showed the moderate-to-high score of pain control, health status, and QoL. Particularly, the total QoL showed an improvement after 24 weeks of treatment and the patients tended to have a better QoL.

Keywords: Canacea, advanced-stage cancer, palliative care, supportive care, quality of life

ประสิทธิผล คุณภาพชีวิต และความปลอดภัยของยาคานาเซีย ในการรักษาผู้ป่วยโรคมะเร็งระยะประคับประคอง

ศิริน เพ็ญภินันท์, อนัฆพงษ์ พันธุ์มณี, สุณี เลิศสินอุดม

ที่มาและความสำคัญ

โรคมะเร็งเป็นปัญหาด้านสุขภาพที่สำคัญในประเทศไทยรวมถึงทั่วโลก ผู้ป่วยโรคมะเร็งได้รับการรักษามาตรฐานที่มักจะก่อให้เกิดผลข้างเคียงต่าง ๆ ผู้ป่วยโรคมะเร็งระยะสุดท้ายอาจไม่ตอบสนองต่อการรักษา จำเป็นต้องได้รับการรักษาตามอาการหรือการรักษาแบบประคับประคอง ยาคานาเซีย (Canacea) เป็นตำรับยาแผนโบราณที่มีส่วนผสมของสมุนไพรหลายชนิดซึ่งมีฤทธิ์ต้านอนุมูลอิสระและต้านการก่อกลายพันธุ์

วัตถุประสงค์

การศึกษานี้จึงได้จัดทำขึ้นเพื่อศึกษาประสิทธิผล คุณภาพชีวิต และความปลอดภัยของยาคานาเซีย ในการรักษาผู้ป่วยโรคมะเร็งระยะสุดท้าย

วิธีดำเนินการวิจัย

การศึกษานี้จัดทำขึ้น ณ โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ระหว่างเดือน มกราคม 2563 – มีนาคม 2565 ผู้ป่วยทุกรายได้รับยาคานาเซียร่วมกับยารักษาตามอาการ มีการประเมินสภาวะร่างกาย ระดับความปวด และคุณภาพชีวิตของผู้ป่วยในสัปดาห์ที่ 24 โดยใช้ Eastern Co-operative Oncology Group (ECOG) และ Palliative Performance Status (PPS) pain score และ The World Health Organization Quality Of Life Brief – Thai (WHOQOL-BREF-THAI) ตามลำดับ

ผลการวิจัย

จากการศึกษามีผู้ป่วยที่เข้าร่วมการศึกษาทั้งหมด 17 ราย อายุเฉลี่ย 64.29±9.14 ปี เป็นเพศชาย 11 ราย และเพศหญิง 6 ราย เมื่อครบระยะเวลาศึกษาที่ 24 สัปดาห์ พบว่าผู้ป่วย 6 รายมีค่าคะแนนความปวดเฉลี่ย 0.33±0.47 (ค่าพิสัย 0-1) ซึ่งเป็นความปวดในระดับเล็กน้อย ผลสภาวะร่างกายมีค่า ECOG และ PPS เฉลี่ย 1.7±0.75 (ค่าพิสัย 1-3) และร้อยละ 70±18.26 (ค่าพิสัย 40-90) ตามลำดับ ซึ่งแสดงให้เห็นว่าผู้ป่วยมีสภาพร่างกายที่คงที่ ผลรวมของคุณภาพชีวิตเฉลี่ยเท่ากับ 94.5±8.44 (ค่าพิสัย 78-105) ซึ่งอยู่ในช่วงของคุณภาพชีวิตระดับกลางถึงคุณภาพชีวิตที่ดี สำหรับผลด้านความปลอดภัย ได้มีการติดตามอาการไม่พึงประสงค์ของผู้ป่วยตลอดระยะเวลาที่ทำการศึกษา โดยใช้ Common Terminology Criteria for Adverse Events (CTCAE) v5.0 ในการประเมิน พบว่าผู้ป่วยที่เข้าร่วมการศึกษา เกิดอาการไม่พึงประสงค์ทั้งหมด 11 ราย โดยเป็นผู้ป่วยที่ต้องหยุดยาคานาเซีย จำนวน 4 ราย คิดเป็นร้อยละ 23.53 ของจำนวนผู้ป่วยทั้งหมดที่เข้าร่วมการศึกษา

สรุปผลการวิจัย

การรักษาผู้ป่วยโรคมะเร็งระยะสุดท้ายด้วยยาคานาเซีย โดยเมื่อใช้ร่วมกับยาบรรเทาอาการของผู้ป่วยตามมาตรฐานการรักษาแล้ว ผลการความคุมความปวด การประเมินสภาวะร่างกาย และคุณภาพชีวิตของผู้ป่วยในการศึกษาให้ผลในระดับกลางถึงดี โดยเฉพาะอย่างยิ่งคุณภาพชีวิตที่ดีกว่าก่อนเริ่มการศึกษา แสดงให้เห็นว่าผู้ป่วยมีแนวโน้มคุณภาพชีวิตที่ดีขึ้น

Introduction and Background

Nowadays, cancer has become a major health issue and primary cause of death in Thailand and in global level. Cancer ranks the second of the cause of death globally with approximate figure of 9.6 death in 2018[(1)]. In clinical operation, primary treatment methods for cancer patient are surgery, radiation therapy, and chemotherapy. Some patients also receive targeted therapy or immunotherapy. However, radiation therapy and chemotherapy often result in side effects, which include nausea, vomiting, and bone marrow abnormality. Furthermore, cancer might not be totally curable in every patient or every stage of the disease. Some patients might not survive cancer. Besides a number of patients suffer the spread of the disease and the cancer is found uncurable from the first time of cancer diagnosis.

Thai traditional medicine is an art of treatment and relief on disease which originates from Thai folk wisdom and the knowledge is passes from older generations through present generation. Evidence shows the presence of Thai traditional medicine since before Sukhothai era. At present, World Health Organization has promoted Thai traditional medicine as general practice for basic disease treatment and relief of Thai people, especially for the ones who do not have access to modern medicine. Thai traditional medicine has been medically utilized in clinical research to explore scientific evidence that could validate efficacy, safety, and medical properties of Thai traditional medicine in a way that could make it become globally accepted[(2)].

Canacea, drug registration number G907/45, is a traditional drug recipe that consists of various herbs including Zedoary, Gloriosa Lily, Chaulmoogra, White crane flower, Smilax corbularia kunth, Sea Holly, Piper polycarpum Ridl, Long pepper, and Pepper. The research indicates that 7 out of 9 types of plants that are ingredients of Canacea have the ability to counteract cancer cells[(3-17)].

From the aforementioned information, it can be seen that Canacea could be a useful drug for cancer patients. Treatment using Canacea on cancer patients are critical in terms of efficacy, safety and quality of life and this requires further study to maximize the benefits of the treatment. However, there is no previous research on efficacy and safety of Canacea on advanced-stage cancer patients that receive palliative care. There is also no previous research on quality of life of patients adopting treatment with Canacea. This research aims to study the efficacy, quality of life, and safety of Canacea for using in cancer patients with palliative care.

Materials and Methods

Methods

- Quasi experimental study that collected prospective research data and studied the usage of Canacea in advanced-stage cancer patients from 1 January 2020 – 31 March 2022. Every patient received the treatment by capsulated Canacea with the dosage of 3 capsules per meal, 2 meals per day: before breakfast and dinner.

- The patients underwent physical examination, CXR examination (for lung cancer or other types of cancer that spread to the lung) and blood test to evaluate functionality of corpuscle, liver, and kidney. This was done by measuring CBC ALT and SCr on the first day of the study as baseline information and followed up checks 4, 8, 12 weeks after receiving the drug. The doctor evaluated efficacy of the treatment from general symptoms of the patients.

- The patients were educated about Canacea treatment by the pharmacist and underwent evaluation on performance status, pain control, and quality of life firstly before the study

(baseline) and every followed up on the study which was every 4 weeks, for the total length of 24 weeks or until passed away. In case the patient could not show up, follow up would be done at the house and if the patient was not living in North-Eastern region, phone call follow up shall be adopted.

Populations

Advanced-stage cancer patients 18 years old and older that received treatment in Srinagarind Hospital, Faculty of Medicine, Khon Kaen University. The patients received palliative care as per standard treatment. During the usage of Canacea, they did not take any other method of cancer treatment. Every patient had signed the consent to participate in the research.

Evaluation

- Information analysis and study results had the follow up on the volunteers by intention-to-treat analysis.

- Pain score adopted visual analog scale with the range from 0 – 10 for the pain. The evaluation was carried out firstly before the study (baseline) and then followed up every 4 weeks, for the total length of 24 weeks or until passed away. In case the patient could not show up, follow up would be done at the house and if the patient was not living in North-Eastern region, phone call follow up shall be adopted.

- Performance status utilized the evaluation from Eastern Co-operative Oncology Group (ECOG) with the score range of 0 – 5 and Palliative Performance Status (PPS) with the score range of 0 – 100 percent. The evaluation was carried out firstly before the study (baseline) and then followed up every 4 weeks, for the total length of 24 weeks or until passed away. In case the patient could not show up, follow up would be done at the house and if the patient was not living in North-Eastern region, phone call follow up shall be adopted.

- Quality of life utilized the evaluation from WHOQOL-BREF-THAI. This classified quality of life into 5 components, which were physical domain, psychological domain, social relationships, environment, and overall quality of life. Total score of the quality of life ranged from 26 – 130. The evaluation was carried out firstly before the study (baseline) and then followed up every 4 weeks, for the total length of 24 weeks or until passed away. In case the patient could not show up, follow up would be done at the house and if the patient was not living in North-Eastern region, phone call follow up shall be adopted.

- Regarding safety, there were regular follow up on undesirable symptoms on patients throughout that study. This utilized Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

Statistics implemented for the analysis

- Descriptive analysis was used to present general information, treatment history, and undesirable symptoms occurred during the follow up period of the volunteers participated in the research.

- Evaluation on performance status, pain control, and quality of life were take ECOG, PPS, pain score, and total WHOQOL-BREF-THAI into consideration. The first time was

before receiving Canacea and then followed up study results every 4 weeks, total length of 24 weeks. The evaluation utilized descriptive analysis.

- The information was presented in mean ± SD, range, and percentage.

Results

The prospective research had the data collected between 1 January 2020 – 31 January 2022. There were 17 patients participating in the study with the average age of 64.29±9.14 year. Eleven were male and 6 were female. The majority of the patients, 94.12 percent, had lung cancer. All the participating patients no longer received chemotherapy, radiation therapy, targeted therapy, or immunotherapy but still received other supportive care drugs such as painkiller, antitussives, inhaled bronchodilator, and vitamins. There were comorbidities which were the patients underlying diseases. Details were illustrated in *Table 1*.

All patients participating in the study received Canacea. The number of patients who underwent the follow up for 12 weeks and 24 weeks were 10 and 6, respectively, as shown in *Figure 1*. There were 2 and 6 patients who had to stop taking Canacea prematurely because of cancer disease progression and side effects from Canacea, respectively. There were 3 patients that were lost to follow up. One patient could not provide the data and 1 patient was dead (death from any causes). All the 6 patients receiving Canacea underwent all the follow ups throughout 24 weeks and had 100 percent drug adherence.

Table 1 Baseline characteristic (n=17).

Basic information of patients	
Age; year (mean ± standard deviation)	64.29±9.14
Gender; number of patients (percentage)	
Male	11 (64.71)
Female	6 (35.29)
Weight; kilogram (mean ± standard deviation)	52.86±10.49
BMI; kilogram/metre^2 (mean ± standard deviation)	20.31±3.45
Type of cancer; number of patients (percentage)	
Lung cancer	16 (94.12)
Bile duct cancer	1 (5.88)
Prior treatment; number of patients (percentage)	
Chemotherapy	17 (68)
Radiation therapy	7 (28)
Targeted therapy	-
Immunotherapy	1 (4)
Other congenital disease; number of patients (percentage)	
Diabetes	2 (12.50)
Hypertension	2 (12.50)
Tuberculosis	2 (12.50)
Cerebrovascular disease	1 (6.25)
Benign prostate hyperplasia	2 (12.50)
Hypothyroidism	1 (6.25)
Gout	1 (6.25)
Chronic kidney disease	1 (6.25)
Asthma and chronic obstructive pulmonary disease	3 (18.75)
Allergy	1 (6.25)
Received drug; number of patients (percentage)	
Codeine	13 (21.67)

Tramadol	9 (15)
Folic acid	6 (10)
Vitamin B complex	5 (8.33)
Ferrous fumarate	4 (6.67)
Cyproheptadine	4 (6.67)
Ipratropium/Fenoterol inhaler	3 (5)
Morphine	2 (3.33)
Lorazepam	2 (3.33)
Sennosides	2 (3.33)
Omeprazole	2 (3.33)
Metoclopramide	2 (3.33)
Acetylcysteine	1 (1.67)
Paracetamol	1 (1.67)
Dexamethasone	1 (1.67)
Simethicone	1 (1.67)
Fluticasone/Salmeterol inhaler	1 (1.67)
Multivitamin	1 (1.67)

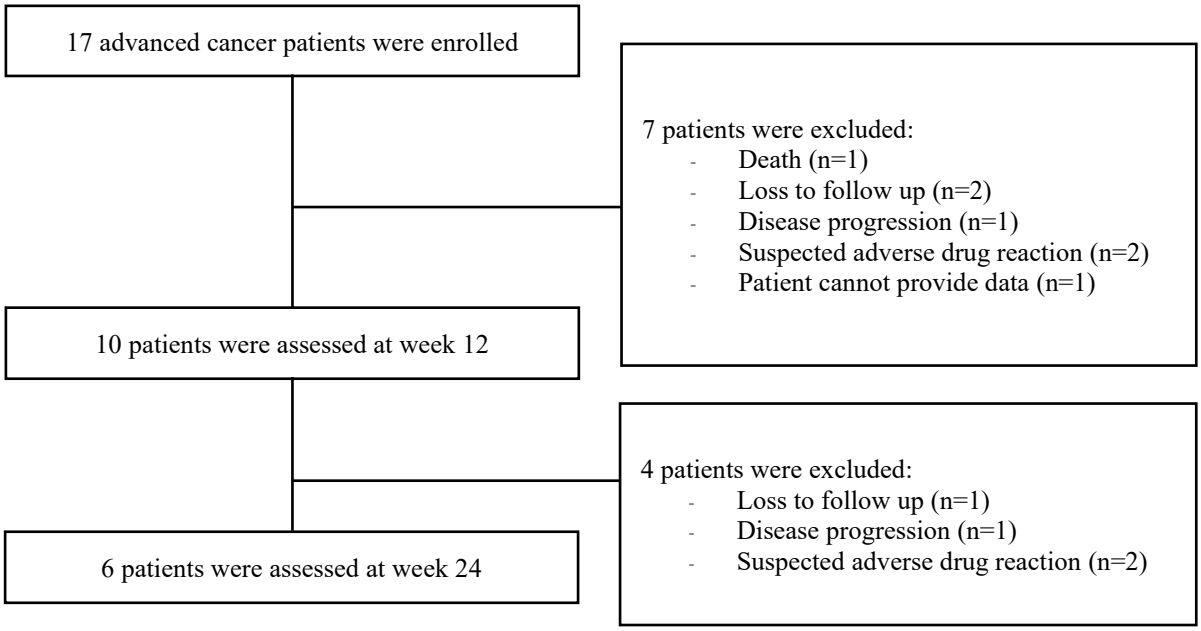

Figure 1 A chart presented the enrollment of patients.

Pain control results

Pain score evaluation on patients by visual analog scale was a self-scoring evaluation by the patients. The average pain score was 0.9±1.14 (range of 0-3) and 0.33±0.47 (range of 0-1) at 12th week and 24th week, respectively (*Table 2*). These were categorized as mild pain. Upon examining 6 patients who fully had the follow up on pain control throughout 24 weeks, it could be seen that 1 patient had reduced pain, 2 patients had increased pain, and 3 patients maintained the same level of pain compared to baseline at pre-treatment as shown in *Table 3*. However, pain control of the patients might need to take other factors into consideration such as disease progression of cancer, usage of opioids type painkiller.

Performance status results

Performance status evaluation on the patients utilized two types of evaluation which were Eastern Co-operative Oncology Group (ECOG) and Palliative Performance Status (PPS). These were self-scoring evaluation and it was found that the average score of ECOG were 1.6±0.66 (range of 1-3) and 1.7±0.75 (range of 1-3) for 12th week and 24th week, respectively (*Table 2*). The average value of ECOG between 0-2 indicated that the patients had moderate condition of physical health. PPS score had average percentage of 79±10.44 (range of 60-90) and 70±18.26 (range of 40-90) for 12th week and 24th week, respectively (*Table 2*). The average percentage of PPS between 70-100 indicated that the patients were in stable stage. Upon examining 6 patients who fully had the follow up on performance status throughout 24 weeks, it could be seen that 1 patient had improved performance status, 1 patient had same performance status, and 4 patients had declined performance status compared to baseline at pre-treatment as shown in *Table 3*. However, the declined performance status could have the disease progression of cancer as an influencing factor.

Table 2 Canacea treatment results followed up.

Outcomes	Pre-treatment (n=17) Mean±SD (range)	12th week (n=10) Mean±SD (range)	24th week (n=6) Mean±SD (range)
Pain control			
- Pain score[#]	2±2.74 (0-8)	0.9±1.14 (0-3)	0.33±0.47 (0-1)
Performance status			
- ECOG*	2±0.73 (1-3)	1.6±0.66 (1-3)	1.7±0.75 (1-3)
- PPS**	75±9.77 (50-90)	79±10.44 (60-90)	70±18.26 (40-90)
Quality of life (WHOQOL-BREF-THAI) [†]			
- Physical domain	21±3.89 (15-29)	22±2.79 (15-25)	22.83±3.24 (20-29)
- Psychological domain	19±4.19 (10-24)	20.4±2.76 (16-24)	19.5±2.69 (16-24)
- Social relationships	12±2.16 (7-15)	12.5±1.80 (9-15)	13.67±1.49 (11-15)
- Environment	29±4.46 (19-36)	29.6±4.32 (23-37)	31±3.70 (25-36)
- Overall quality of life	5±1.50 (2-8)	6.6±1.62 (4-9)	7.5±1.38 (6-10)
- Total score for quality of life	86±12.20 (56-106)	91.1±9.44 (71-105)	94.5±8.44 (78-105)

[#]Pain score: visual analog scale (score 0-10)

*ECOG: Eastern Co-operative Oncology Group (grade 0-5)

**PPS: Palliative Performance Status v.2 (score 0-100%)

[†]WHOQOL-BREF-THAI: The World Health Organization Quality of Life Brief – Thai (score 26-130)

Quality of life results

Quality of life evaluation using The World Health Organization Quality of Life Brief – Thai (WHOQOL-BREF-THAI) evaluation form which was self-evaluated by the patients. Quality of life could be classified into 5 components which were physical domain, psychological domain, social relationships, environment, and overall quality of life. At 24th week, average scores of quality of life classified by components were as follow: quality of life by physical domain 22.83±3.24 (range of 20-29), quality of life by psychological domain 19.5±2.69 (range of 16-24), quality of life by social relationships 13.67±1.49 (range of 11-15), quality of life by environment 31±3.70 (range of 25-36), and overall quality of life 7.5±1.38 (range of 6-10). The average accumulated quality of life at 24th week was 94.5±8.44 (range of 78-105) which was in the range between moderate quality of life (score 61-95) and good quality

of life (score 96-130). This indicated that the patients tend to have improved quality of life (*Table 2*). Upon examining 6 patients who fully had the follow up on performance status throughout 24 weeks, it could be seen that 5 patients had improved quality of life and 1 patient had worsen quality of life compared to baseline at pre-treatment as shown in *Table 3*. However, quality of life might need to take other factors into consideration such as drugs given for symptomatic treatment according to treatment standard.

Safety results

From the 17 participants, there were 11 persons having undesirable symptoms as shown in *Table 4*. Eight of which were patients having undesirable symptoms from Canacea usage. In case of minor undesirable symptoms from Canacea (grade 1), the patients could withstand and after continuously taking the drug, the symptoms would reduce gradually. There were 2 patients that had dosage reduction to 4 tablets per day. There were 4 patients that had to stop taking Canacea due to undesirable symptoms. This accounted for 23.53 percent of total research participants. Moreover, there were patients experiencing undesirable symptoms due to worsen disease progression of cancer and 2 of them had to be dismissed from the study and there was 1 patient that passed away.

Table 3 Clinical outcomes in patients given Canacea and undergo full 24 weeks of follow up (n = 6).

Outcomes	Number of patients (percentage)
Pain control	
Improved pain control	1 (16.67)
Worsen pain control	2 (33.33)
Stable pain control	3 (50.00)
Performance status	
Improved performance status	1 (16.67)
Worsen performance status	4 (66.67)
Stable performance status	1 (16.67)
Quality of life	
Improved quality of life	5 (83.33)
Worsen quality of life	1 (16.67)
Stable quality of life	-

Table 4 Adverse events and management (n=11).

Undesirable symptoms	Severity* (grade)	Number of patients (percentage)	Management
Diarrhea	1	2 (18.18)	Reduce dosage and monitor
Nausea	3	1 (9.09)	Discontinue the drug
Thirsty	3	1 (9.09)	Discontinue the drug
Transaminitis	1	1 (9.09)	Monitor
Transaminitis	2	1 (9.09)	Monitor
Transaminitis	3	1 (9.09)	Discontinue the drug
Increased serum creatinine	2	1 (9.09)	Discontinue the drug
Disease progression	4	2 (18.18)	Dismiss from the study
Death from any cause	5	1 (9.09)	Dismiss from the study

*CTCAE: Common Terminology Criteria for Adverse Events v5.0

Discussion

Canacea is a traditional drug using for health nourishing. Moreover, it is found that the herbs forming part of Canacea drug formular have antioxidant properties and anti-mutation properties. In-vitro studies showed that they could also suppress cancer cells. However, there has never been any clinical research on utilizing Canacea for advanced-stage cancer patients with metastasis. Therefore, this study is the first study that evaluate the results of Canacea on cancer treatment in terms of safety as well as quality of life of the advanced-stage cancer patients who do not receive chemotherapy, radiation therapy, targeted therapy, and Immunotherapy. The patients receive Canacea in conjunction with other symptom relieving treatment such as painkiller, antitussives, bronchodilator, and vitamins. The results were evaluated through surveys that were evaluated and self-scored by the patients. To reduce the discrepancy from communication, the same researcher was used in the interviews.

The research yielded quite good results on pain control, performance status, and quality of life of the patients. Especially the quality of life, which was the main target of treatment for this group of patients. It could be seen that accumulated quality of life results from WHOQOL-BREF-THAI evaluation on the research participants at 12^{th} week and 24^{th} week were higher than before the study and ranged in moderate to good level.

However, the research population was only 17 participants which were patients receiving Canacea and only 6 of them had completed 24 weeks of follow up. Most of the patients had lung cancer (94.12 percent) therefore the research results might not be applied for patients with other types of cancer. The effect from other symptom relieving drugs might also need to be considered. Furthermore, there were patients who were required to stop taking the drug and dismissed from the study due to disease progression of cancer, which also were influencing factors.

Conclusion

Treatment for advanced-stage cancer patients using Canacea with standard symptomatic treatment seems to enhance quality of life for the patients throughout the 24 weeks of the treatment. Therefore, Canacea could become an alternative to enhance quality of life for advanced-stage cancer patients who do not respond to or do not receive chemotherapy, radiation, targeted therapy, and Immunotherapy.

What is already known on this topic?

Canacea is a Thai traditional herbal drug which has previously been reported to have antioxidant, anti-mutation, and anti-cancer activities against cancer cells. Canacea treatment with other symptomatic treatment may be beneficial for advanced-stage cancer patients

What this study adds?

The use of Canacea in combination with supportive treatment could control pain, health status, and quality of life in advanced-stage cancer who did not response or could not tolerate to the previous standard treatment such as chemotherapy, targeted therapy, or immunotherapy.

Ethical statement

All subjects given informed consent prior to study participation and the study protocol was approved by the ethic committee in human research, Khon Kaen University, Thailand. The reference No. HE621299.

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Declaration of competing interest

The authors declare no conflict of interest with respect to the research, authorship, and publication of this article.

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