

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

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**Background:** Cancer is an important health problem in Thailand and all over the world. Cancer patients usually receive standard treatments, which causes adverse events. The advanced-stage cancer patients may not be responsive to treatments; therefore, supportive or palliative care is usually required. Canacea is a traditional medicine consisting of herbs with antioxidant and antimutagenic activities.

**Objective:** To determine the efficacy, quality of life (QoL), and safety of Canacea in advanced-stage cancer patients.

**Materials and Methods:** The present study was conducted at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Thailand between January 2020 and March 2022. All 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), the Palliative Performance Status (PPS), the pain score, and the World Health Organization Quality of Life Brief - Thai (WHOQOL-BREF-THAI), respectively.

**Results:** Seventeen patients were enrolled in the present study. The average age was 64.29±9.14 years, with eleven males and six females. At 24 weeks, the average pain score was 0.33±0.47 (range of 0 to 1) which was mild pain. The average ECOG and PPS were 1.7±0.75 (range of 1 to 3) and 70±18.26% (range of 40 to 90), respectively, which reflected a stable health status. The total QoL score from WHOQOL-BREF-THAI was 94.5±8.44 (range of 78 to 105), which reflected a moderate-to-high QoL. The safety outcome was monitored throughout the study using Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Eleven patients developed adverse events, with four patients who had to withdraw from Canacea (23.53%).

**Conclusion:** The treatment of Canacea with other supportive care showed a 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

Received 8 June 2023 | Revised 17 April 2024 | Accepted 22 April 2024

**J Med Assoc Thai 2024; 107(6):445-51**

**Website:** <http://www.jmatonline.com>

Cancer has become a major health issue and a primary cause of death in Thailand and globally. Cancer ranks as the second highest cause of death globally, accounting for an estimated 9.6 million deaths in 2018<sup>(1)</sup>. Primary treatment methods for cancer patients in clinical operations 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 curable in every patient or every stage of the disease. Some patients might not survive cancer. In addition, a number of patients suffer from the spread of the disease, and some are found to be incurable from the first time of cancer diagnosis.

Thai traditional medicine is an art of treatment and relief of symptoms originates from Thai folk wisdom. Knowledge is passed from older generations to the present generation. Evidence has shown the presence of Thai traditional medicine existed before the Sukhothai era. At present, the World Health Organization has promoted Thai traditional medicine as a general practice for basic disease treatment and relief for Thai people, especially for those who cannot access modern medicine. Thai traditional medicine has been studied to explore scientific evidence that could validate the efficacy, safety, and medical properties that could make it become globally accepted<sup>(2)</sup>.

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## How to cite this article:

Phenphinan S, Phunmanee A, Lertsinudom S. Efficacy, Quality of Life, and Safety of Canacea in Palliative Cancer Patients. *J Med Assoc Thai* 2024; 107:445-51.

DOI: 10.35755/jmedassocthai.2024.6.13998

Canacea, drug registration number G907/45, is a Thai traditional drug recipe 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 seven out of nine types of plants that are ingredients of Canacea can counteract cancer cells<sup>(3-17)</sup>.

From the aforementioned information, it can be seen that Canacea could be a useful drug for cancer patients. Treatment using Canacea on cancer patients is 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 the efficacy and safety of Canacea with advanced-stage cancer patients receiving palliative care. There is also no previous research on quality of life of patients receiving treatment with Canacea. The present research aimed to study the efficacy, quality of life, and safety of Canacea 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 between January 1, 2020 and March 31, 2022. Every patient received the treatment by capsulated Canacea with the dosage of three capsules per meal, two meals per day, before breakfast and dinner.

The patients underwent physical examination, chest X-ray (CXR) 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 complete blood count (CBC), alanine transaminase (ALT), and serum creatinine (SCr) on the first day of the study as baseline information and follow up checks at 4, 8, and 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 before the study as a baseline and were followed up every four weeks, for 24 weeks, or until the patient passed away. In case the patient could not show up, follow up would be done at their house and if the patient were not living in North-Eastern region, a phone call follow up was adopted.

### Populations

The participants were advanced-stage cancer patients 18 years and older who 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 signed a consent to participate in the research.

### Evaluation

Information analysis and study results were followed up by volunteers for intention-to-treat analysis.

Pain score adopted a visual analog scale with a range from 0 to 10 for the pain. The evaluation was carried out before the study as baseline and then followed up every four weeks, for 24 weeks, or until the patient passed away. In case the patient could not show up, follow up would be done at their house and if the patient were not living in North-Eastern region, a phone call follow up was adopted.

Performance status utilized the evaluation from Eastern Co-operative Oncology Group (ECOG) with a score range of 0 to 5 and Palliative Performance Status (PPS) with a score range of 0% to 100%. The evaluation was carried out the same fashion as the pain score.

Quality of life utilized the evaluation from the World Health Organization Quality of Life Brief - Thai (WHOQOL-BREF-THAI). This classified quality of life into five components, physical domain, psychological domain, social relationships, environment, and overall quality of life. The total score of the quality of life ranged from 26 to 130. The evaluation was also carried out at the same time as above.

Regarding safety, there were regular follow ups on undesirable symptoms exhibited by patients throughout the 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 that occurred during the follow up period of the volunteers participating in the present research.

Evaluation on performance status, pain control, and quality of life were taking ECOG, PPS, pain score, and total WHOQOL-BREF-THAI into consideration. The first evaluation was before receiving Canacea and

then followed up every four weeks, for 24 weeks. The evaluation utilized descriptive analysis.

The information was presented in mean ± standard deviation (SD), range, and percentage. The present study was analyzed using Microsoft Excel for descriptive analysis.

### Ethical approval

All subjects provided informed consent prior to study participation and the study protocol was approved by the Ethic Committee in Human Research, Khon Kaen University, Thailand, reference No. HE621299.

### Results

The prospective research had the data collected between January 1, 2020 and March 31, 2022. There were 17 patients participating in the study. The average age was 64.29±9.14 years. Eleven were male and six were female. The majority of the patients, 94.12%, 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 painkillers, antitussives, inhaled bronchodilators, and vitamins. There were comorbidities which were the patients' underlying diseases. Details are illustrated in Table 1.

All patients participating in the present 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 two and six patients who had to stop taking Canacea prematurely because of cancer disease progression and side effects from Canacea, respectively. There were three patients lost to follow up. One patient could not provide the data and one patient died, which was a death from any cause. The six patients receiving Canacea who underwent 24 weeks follow up, had 100% drug adherence.

### Pain control results

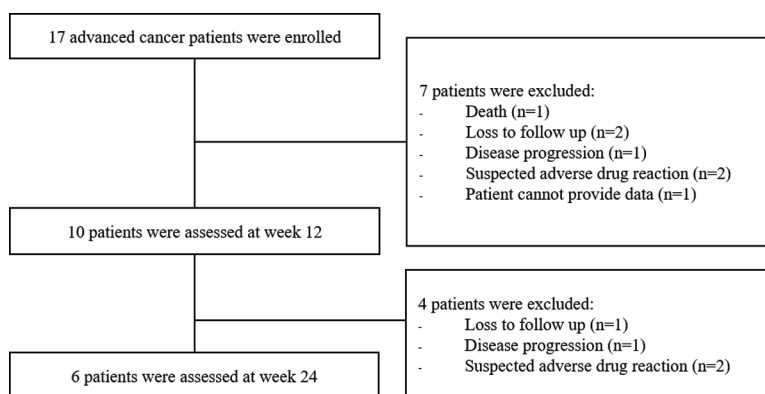
Pain score evaluation by visual analog scale was a self-scoring evaluation by the patients. The average pain score was 0.9±1.14 (range of 0 to 3) and 0.33±0.47 (range of 0 to 1) at the twelfth week and twenty-fourth week, respectively (Table 2). These were categorized as mild pain. Upon examining six patients who had the follow up on pain control throughout 24 weeks, it could be seen that one patient had reduced pain, two patients had increased pain, and three patients maintained the same level of pain

**Table 1.** Baseline characteristic (n=17)

Basic information of patients	
Age (years); mean±SD	64.29±9.14
Sex; n (%)	
Male	11 (64.71)
Female	6 (35.29)
Weight (kg); mean±SD	52.86±10.49
BMI (kg/m <sup>2</sup> ); mean±SD	20.31±3.45
Type of cancer; n (%)	
Lung cancer	16 (94.12)
Bile duct cancer	1 (5.88)
Prior treatments; n (%)	
Chemotherapy	17 (68.00)
Radiation therapy	7 (28.00)
Targeted therapy	-
Immunotherapy	1 (4.00)
Other congenital diseases; n (%)	
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 drugs; n (%)	
Codeine	13 (21.67)
Tramadol	9 (15.00)
Folic acid	6 (10.00)
Vitamin B complex	5 (8.33)
Ferrous fumarate	4 (6.67)
Cyproheptadine	4 (6.67)
Ipratropium/fenoterol inhaler	3 (5.00)
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)

BMI=body mass index; SD=standard deviation

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



**Figure 1.** A chart describing the enrollment of patients.

**Table 2.** Canacea treatment results followed up

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

ECOG=Eastern Co-operative Oncology Group; PPS=Palliative Performance Status; WHOQOL-BREF-THAI: The World Health Organization Quality of Life Brief - Thai

# Visual analog scale (score 0 to 10), \* ECOG (grade 0-5), \*\* PPS v.2 (score 0% to 100%); † WHOQOL-BREF-THAI (score 26 to 130)

as progression of cancer and usage of opioid-type painkillers.

### Performance status results

Performance status evaluation on the patients utilized two types of evaluation, which were ECOG and PPS. These were self-scoring evaluations, and it was found that the average score of ECOG were 1.6±0.66 (range of 1 to 3) and 1.7±0.75 (range of 1 to 3) for the twelfth and twenty-fourth week, respectively (Table 2). The average value of ECOG between 0 and 2 indicated that the patients had moderate condition of physical health. PPS score had an average percentage of 79±10.44 (range of 60 to 90) and 70±18.26 (range of 40 to 90) for the twelfth and twenty-fourth week, respectively (Table 2). The average percentage of PPS between 70 and 100 indicated that the patients were in stable stage. Upon

examining six patients who fully had the follow up on performance status throughout 24 weeks, one patient had improved performance status, one patient had the same, and four patients had declined performance status compared to baseline at pre-treatment as shown in Table 3. However, the declined performance status could have progression of cancer as an influencing factor.

### Quality of life results

Quality of life evaluation used WHOQOL-BREF-THAI evaluation form, which was self-evaluated by the patients. Quality of life could be classified into five components which were physical domain, psychological domain, social relationships, environment, and overall quality of life. At the twenty-fourth week, average scores of quality of life classified by components were quality of life

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

Outcomes	n (%)
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	-

by physical domain at  $22.83 \pm 3.24$  (range of 20 to 29), quality of life by psychological domain at  $19.5 \pm 2.69$  (range of 16 to 24), quality of life by social relationships at  $13.67 \pm 1.49$  (range of 11 to 15), quality of life by environment at  $31 \pm 3.70$  (range of 25 to 36), and overall quality of life at  $7.5 \pm 1.38$  (range of 6 to 10). The average accumulated quality of life at the twenty-fourth week was  $94.5 \pm 8.44$  (range of 78 to 105) which was in the range between moderate quality of life with a score of 61 to 95 and good quality of life with a score of 96 to 130. This indicated that the patients tend to have improved quality of life (Table 2). Upon examining the six patients who had the follow up on performance status throughout 24 weeks, five patients had improved quality of life and one patient had a lower 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 standard treatment.

### Safety results

Of the 17 participants, eleven had 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 two patients having dosage reduction to four tablets per day. There were four patients that had to stop taking Canacea due to undesirable symptoms. This accounted for 23.53% of total research participants. Moreover, there were patients experiencing undesirable symptoms

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

Undesirable symptoms	Severity* (grade)	n (%)	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

\* Common Terminology Criteria for Adverse Events v5.0

due to the progression of cancer and two of them had to be dismissed from the study and one patient passed away.

### Discussion

Canacea is a traditional drug used for health improvement. The herbs forming part of the Canacea drug formula have antioxidant and anti-mutation properties. In-vitro studies showed that Canacea could also suppress cancer cells. However, there has never been any clinical research on utilizing Canacea for advanced-stage cancer patients with metastasis. Therefore, the present study is the first that evaluate the results of Canacea on cancer treatment in terms of safety as well as the quality of life of advanced-stage cancer patients who do not receive chemotherapy, radiation therapy, targeted therapy, and immunotherapy. Patients received Canacea in conjunction with other symptom relieving treatments such as painkillers, antitussives, bronchodilators, and vitamins. The results were evaluated through surveys that were evaluated and self-scored by the patients. To reduce discrepancies in communication, the same researcher was used in the interviews.

The research yielded quite good results for 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 the twelfth and twenty-fourth 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 six of them had completed 24 weeks of follow up. The results should be interpreted with



caution due to the limited number of subjects included in the study. This study was conducted on advanced cancer patients with palliative aims, requiring a follow-up period of 24 weeks, and was affected by the COVID-19 situation during the study period. Most of the patients had lung cancer, or 94.12%, 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 had to stop taking the drug and were dismissed from the study due to the 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 of the patients throughout the 24 weeks 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 traditional Thai herbal drug that has previously been reported to have antioxidant, anti-mutation, and activities against cancer cells. Canacea treatment with other symptomatic treatment may be beneficial for advanced-stage cancer patients.

### What does this study add?

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 to or could not tolerate the previous standard treatment such as chemotherapy, targeted therapy, or immunotherapy.

### Acknowledgement

The present work was supported by HERB THAI ZHONG COMPANY LIMITED in the form of the study drug (Canacea) and laboratory examinations. The funder did not have any additional role in the study design, data collection and analysis, decision to publish, or the preparation of the article.

### Conflicts of interest

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

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