



## Original Article

## Attitudes, expectations, and lived experiences of cancer patients receiving dendritic cell vaccine therapy in Japan

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## ABSTRACT

**Objective:** Immunotherapeutic approaches to cancer, such as dendritic cell vaccine therapy, promise to improve survival rate but may present unique challenges to patients. However, there is no research on the lived experiences of cancer patients receiving dendritic cell vaccine therapy. The aim of this study was to explore the attitudes, expectations, and experiences of cancer patients receiving dendritic cell vaccine therapy in Japan.

**Methods:** This was an exploratory qualitative study. A descriptive phenomenological approach was used to investigate the experiences of eight advanced-stage cancer patients (median age: 59.5 years). Data were collected between July 2018 and March 2020 using in-depth semi-structured interviews. Data were analyzed according to Colaizzi's seven-step phenomenological strategy, and EQUATOR's Consolidated Criteria for Reporting Qualitative Research (COREQ) guidelines for qualitative studies were followed.

**Results:** Four themes emerged from the data analysis: strong concerns about chemotherapy, faith in dendritic cell vaccine therapy, motivation to succeed, and physical and mental changes. The first two themes related to pre-treatment attitudes and expectations. The latter two themes expressed participants' experiences during and after therapy.

**Conclusions:** Dendritic cell vaccine therapy patients expressed fears about the effects of standard treatment, and hope and uncertainty regarding immunotherapy treatment decisions and efficacy. The findings suggest that such patients require nursing care that includes prevention and reduction of chemotherapy side effects, careful observation of patients' well-being, management of patients' expectations and uncertainty, formation of patient–health care practitioner partnerships, and team medicine.

## Introduction

The number of cancer patients worldwide continues to increase annually.<sup>1,2</sup> In Japan, cancer has been the leading cause of death since 1975, and its incidence continues to increase. There were an estimated 900,000 new cases in 2015 and 970,000 in 2017.<sup>3</sup> To address the substantial effects of cancer on people's health and daily lives, in 2007, the Japanese government enacted the Cancer Control Act, which stipulates the comprehensive and systematic promotion of cancer prevention, early diagnosis, and equalization of cancer treatment. Since then, cancer research and treatment have progressed. The Third Cancer Control Act in 2017 clearly identified immunotherapy as the fourth most important treatment method following surgery, chemotherapy, and radiotherapy.

New therapies that combine conventional chemotherapy and immunotherapy are at the forefront of cancer treatment and seem to offer

greater anti-cancer effects and improved patient survival rates.<sup>4–9</sup> One type of cancer immunotherapy is active immunotherapy. This involves the administration of immunostimulating drugs or cells, such as immune checkpoint inhibitors, which release immunosuppressants.<sup>10</sup> Following promising clinical results in recent years, these drugs are now part of standard care in cancer treatment.

A new type of immunotherapy involves the application of dendritic cells, antigen-presenting cells that boost the immune response and are central to immunosurveillance.<sup>11–13</sup> These cells have been used to develop vaccines against cancer.<sup>14</sup> Targeted cancer antigens are incorporated into dendritic cells to produce vaccines. Because they are generated from the patient's own monocytes, they have fewer physical effects than other therapies or drugs.<sup>13,15</sup> A recent meta-analysis found that dendritic cell vaccines showed promising effectiveness and safety in cancer patients,<sup>16</sup> and their efficacy has been investigated in clinical

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trials within the public health care system in Japan. These trials commonly use dendritic cells activated by Wilms' tumor oncogene protein-derived peptides.<sup>17–21</sup> Studies have demonstrated the safety and efficacy of vaccine therapies using Wilms' tumor oncogene protein peptides.<sup>22,23</sup>

In Japan, the manufacturing and provision of dendritic cell vaccines follow regenerative medicine regulations.<sup>24</sup> Patients are checked for major organ damage, infections, and blood abnormalities. Immature dendritic cells are then collected and cultured at a cell-processing facility to produce mature dendritic cells. After a quality check, the cells are provided as a vaccine in a course of seven intradermal injections.

Unlike countries such as the United States, which have health care systems based on private medical insurance (and large numbers of uninsured citizens),<sup>25</sup> Japan has a universal medical insurance system that provides equal access to necessary medical services. However, this system covers only evidence-based standard treatments. In Japan, dendritic cell vaccine therapy is categorized as a complementary and alternative medicine, not as a standard treatment; therefore, treatment costs must be borne by patients and these are considerable (approximately 3 million yen [USD 23,000]).

Many patients who opt for dendritic cell vaccine therapy have cancer that is considered incurable using standard therapy. Although it is uncommon for patients in Japan to choose dendritic cell vaccine therapy following standard care, those that do hope that the treatment will provide a complete cure. Such patients are not yet ready to enter palliative care and are actively seeking a cure. However, few medical institutions in Japan provide dendritic cell vaccine therapy and have systems in place to review its effectiveness and safety. Therefore, patients receiving this therapy must spend time traveling to (sometimes distant) treatment facilities for regular appointments and must pay the full cost of treatment. Some of the decision-making challenges faced by immunotherapy patients likely overlap with those of advanced cancer patients receiving standard treatment. However, the novelty of some immunotherapies may pose unique challenges and experiences.

A few survey studies have examined attitudes to human papillomavirus vaccination as part of cancer prevention programs<sup>26–28</sup> and have identified generally low awareness and knowledge of this type of vaccination. However, there are no studies on the attitudes of patients to dendritic cell vaccine therapy.

An increasing number of studies have used the qualitative methods to investigate the experiences and attitudes of cancer patients receiving different types of immunotherapy. Themes frequently expressed by patients in these studies are experiences of living with both hope and uncertainty. For example, cancer patients receiving immune checkpoint inhibitor therapy experience uncertainty about the novel therapy and about their disease trajectory,<sup>29</sup> as well as feelings of hope and faith in the treatment.<sup>30</sup> Langmuir et al<sup>31</sup> conducted a systematic review and thematic synthesis of experiences of uncertainty in advanced cancer patients receiving immunotherapy. They identified different emotional, financial, and social sources of uncertainty and pointed out the importance of strategies to manage uncertainty in immunotherapy patients.

As with patients undergoing other types of cancer therapy, immunotherapy patients must sometimes manage expectations and experiences of therapy side effects. For example, the immune checkpoint inhibitor therapy patients interviewed by Cappelli et al<sup>32</sup> expressed fear and uncertainty about the treatment and the impact of side effects on their quality of life. Dombeck et al<sup>33</sup> found that, when making treatment decisions, patients with multiple myeloma tried to balance treatment efficacy with quality of life. Ihrig et al<sup>34</sup> pointed out that German patients' expectations of immunotherapy may sometimes be unrealistic. Despite patients' initial lack of understanding about the treatment, positive presentations of immunotherapy (compared with chemotherapy) in the media, and favorable perceptions of the immune system as the body's own defense system, raise expectations of the treatment's success.<sup>34,35</sup> These findings highlight the need for health care practitioners to manage both side effects and expectations.

Even some of the positive effects of immunotherapy may be challenging for patients. Zwanenburg et al<sup>36</sup> found that immunotherapy patients struggled to cope with living in a state of uncertainty and having to adapt to a new identity. Similarly, Kamminga et al<sup>37</sup> found that patients who had received immune checkpoint inhibitor therapy identified difficulties adapting to life after treatment.

Messina et al<sup>38</sup> used interviews and a survey to explore the prior expectations and experiences of patients undergoing chimeric antigen receptor T-cell therapy. Although patients reported heterogeneous experiences, a common issue was their concern about the effects of therapy on their quality of life.

There are no studies on the experiences of patients receiving dendritic cell vaccine therapy. Cancer treatment is entering a new phase, in which therapy is shifting from standardized treatment to personalized medicine. The number of patients receiving self-funded personalized treatment such as dendritic cell vaccine therapy will likely increase. Therefore, oncology nurses need to understand the expectations and experiences of patients receiving self-funded, non-standard treatments. We suggest that the experiences of such patients may differ compared with that receiving standard cancer care. The results of this study may have important implications for patients receiving other advanced cancer treatments. In this study, we aimed to explore the attitudes, expectations, and experiences of cancer patients receiving dendritic cell vaccine therapy in Japan from the perspective of nursing science.

## Methods

### Study design

This was an exploratory qualitative study that used a descriptive phenomenological approach.<sup>39</sup> This approach is suitable when the phenomenon of interest (ie, life experiences) has not been fully conceptualized.<sup>40</sup> Descriptive phenomenology focuses on describing and uncovering the meaning behind people's lived experiences.<sup>41–43</sup>

This method was chosen to investigate the meaning of the experiences of patients who chose to receive dendritic cell vaccine therapy in addition to standard care (surgery, chemotherapy, or radiation) following cancer diagnosis. We used interviews to examine patient attitudes, expectations, and experiences from the decision to undergo dendritic cell therapy to the end of treatment. Our aim was to understand the entire process of treatment from the perspective of the patients involved. The Consolidated Criteria for Reporting Qualitative Research (COREQ) were followed.<sup>44</sup>

### Participants and recruitment methods

Participants were cancer patients who had a short life expectancy following diagnosis, had received dendritic cell vaccine therapy, were aged  $\geq 20$  years, understood the purpose of the study, and had given their consent for participation and recording of the interviews. The rationale for the age threshold was that, at the time of the study, the age of adulthood in Japan was  $\geq 20$  years.<sup>45</sup> Both male and female patients were included (gender was self-reported). We obtained referrals from attending physicians at the university hospital that provided the immunotherapy; all patients receiving dendritic cell vaccine therapy met the inclusion criteria and all were referred to us. The study purpose, methods, and ethical considerations were verbally explained to the patients face-to-face as well as in writing, and their written consent was obtained. None of the patients refused to participate; therefore, eight patients were included in the study after providing consent. However, one patient withdrew from the study owing to the mental burden of discussing their cancer experience. To support this participant, we informed them that counseling was available at the university hospital where they were receiving treatment. Based on the number of dendritic cell vaccine therapy patients at this hospital in the previous year, the initial enrollment target was 30 patients, and data for seven patients were included in the analysis.

### Data collection

Face-to-face interviews were conducted in Japanese with each participant in a private room in the university hospital. The partners of participants A, B, F, and G were present during the interviews. The other participants were interviewed alone. The interviewer, who is female, is the first author. She has a doctorate on the experiences of cancer patients and is a qualified registered nurse and researcher in the nursing department of the university affiliated with the hospital where participants were being treated. She has substantial experience in oncology nursing and qualitative research, has conducted several similar studies in the past, and is familiar with the relevant methods and procedures. The interviewer was interested in exploring the attitudes, expectations, and experiences of patients undergoing dendritic cell vaccine therapy following standard cancer treatments in Japan (surgery, chemotherapy, and radiotherapy). This was explained to participants before the interviews. The interviewer had no previous relationships with any of the participants. The interviewer underwent relevant training in qualitative methods and conducted fieldwork before the study. She also attended a professional university program in grief care (including listening skills). Because dendritic cell vaccine therapy is not covered by insurance in Japan, participation in the study may have been biased toward patients with higher income levels. Additionally, standard cancer treatment rarely provides a complete cure for advanced-stage cancer patients. Therefore, patients may have had unrealistic expectations about dendritic cell vaccine therapy, which may have affected the results. However, the interviewer assumed that the study findings would inform mental health support and nursing care for dendritic cell vaccine therapy patients. A semi-structured interview guide was developed to explore patients' experiences of dendritic cell vaccine therapy. The research focus was explained to participants before the interview. The interviewer asked participants the following: "Please tell me about your treatment experiences since your cancer diagnosis, and how your life story has progressed since your cancer diagnosis. If possible, please begin by describing when you received your cancer diagnosis. Then, tell me about your decision for dendritic cell vaccine therapy and how you got to where you are today."

In the interviews conducted after participants had completed their treatment, the interviewer asked participants the following: "Please tell us how things have progressed since the treatment. We are interested in anything that is important to you, so please feel free to take your time." Before data collection commenced, one pilot interview was conducted with each of the three nurses in charge of cancer care. During the interviews, the interviewer attempted to facilitate an in-depth dialog to derive the meaning of participants' experiences and to build a relationship of trust with participants. To this aim, the interviewer listened to participants' narratives carefully and regularly checked with participants to confirm their meaning.

Data were collected between July 2018 and March 2020. The data collection period was relatively long because we recruited participants from only one institution and because there was a gap of 5–6 months between the first and second interviews. Two interviews were conducted per participant. The first interview occurred prior to dendritic cell vaccination; the second interview occurred after the first course of vaccination. Each interview lasted approximately 30–50 min. The interviews were conducted between consultations and recorded using an IC recorder (ICD-UX533FA, Sony, Japan) and transcribed verbatim.

### Data analysis

Data analysis followed the seven-step strategy proposed by Colaizzi.<sup>46</sup> Step one: each transcript was read several times to ensure that the content was understood and that participants' thoughts and feelings had been identified. Step two: significant statements and phrases related to the lived experience of dendritic cell therapy were extracted from each

transcript. These statements were written on separate sheets and coded according to their transcript, page, and line numbers. Step three: meanings were extracted and formulated from the significant statements. Each underlying meaning was coded under one category, and the categories were discussed with research team members. Efforts were made to elaborate on the meaning of each significant statement. Step four: all formulated meanings were grouped according to the similarity of the ideas they expressed to produce clusters of themes, and the theme clusters were compared with significant statements for validation. Groups of theme clusters that reflected a particular perspective or issue were then incorporated to form a distinctive theme construct. Step five: all results thus obtained were integrated to provide an exhaustive description of participants' lived experience and to create an overall structure of the phenomenon. Step six: the findings were examined to clarify the identified fundamental structure and reduce repetition. Step seven: the results were validated among the coresearchers. The data were analyzed twice: first to analyze pretreatment attitudes and expectations and second to analyze treatment experience. Feedback was provided informally to participants during the second interview (while data collection was still occurring) to establish the credibility of the results and to check their responses. We informed participants that we would provide feedback on all the findings after completion of the analysis; however, none of the participants requested feedback. Because of their medical condition and physical status, we did not ask for any feedback from the participants. All authors reviewed the interview content and were involved in data coding, and records were kept of all analytical steps. The study was conducted at a single institution, so the number of participants was limited, which meant that data saturation could not be reached. We were unable to extend the data collection further because changes to dendritic cell vaccine therapy provision in Japan mean that researchers can no longer meet patients in person. However, although the sample was small, each participant was interviewed twice and the interviews were in-depth. Therefore, we determined that the data were sufficient to address our research aims.

### Study rigor

Qualitative rigor was guided by Lincoln and Guba's criteria (credibility, dependability, confirmability, and transferability).<sup>47</sup> Credibility was ensured through the comprehensiveness of data collection and analysis. The interviewer reviewed the interview content and underwent several training sessions. The interviewer was also screened to ensure her personal perspectives and tendencies did not unduly influence the interview process. Member checking provided informal feedback during the second interview. Dependability involved maintaining consensus among study members throughout the analysis process. Confirmability was ensured by keeping verbatim transcripts of interviews and records of all data and analysis processes. Transferability was achieved by using direct quotes to illustrate the results.

### Ethical considerations

Approval was obtained from the Medical Ethics Review Committee of the first author's institution (approval date: 27 August, 2018; approval No. I309). The study was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects developed by the World Medical Association and stated in the Declaration of Helsinki.<sup>48</sup> The study purpose was explained to participants orally and in writing, and they were informed that they would experience no treatment disadvantage if they declined to participate or withdrew from the study. Participants provided informed consent, and we obtained their permission in advance to record the interviews and take notes as appropriate. Considering the physical and psychological burden placed on participants, we checked with them throughout the study whether they wished to continue. Patient anonymity was strictly maintained to protect personal information. We assured

participants that all personal information obtained would be destroyed after being converted into data.

**Results**

**Table 1** summarizes participant background. There were six men and two women; the median age was 59.5 years. All participants had advanced cancer or cancer with poor prognosis. The time of the first interview ranged from 1 month to 4 years after the initial diagnosis. All participants received surgery, radiotherapy, or chemotherapy (some had refused the chemotherapy recommended by their physicians). All participants cited a concern with the strong side effects of chemotherapy as a motivator for choosing dendritic cell therapy.

We extracted 138 significant statements from participants' narratives. A total of 11 theme clusters were derived from the meanings of the statements. Analysis of the intrinsic meaning of the clusters produced four themes. Themes 1 and 2 described participants' attitudes and expectations about receiving dendritic cell therapy (**Table 2**). Themes 3 and 4 described participants' experiences of seeking and receiving dendritic cell therapy (**Table 3**).

*Theme 1: Strong concerns about chemotherapy*

This theme expressed participants' reactions to the recommendations they received from health care providers about their medical condition and associated standard care and comprised three theme clusters. The theme clusters expressed participants' substantial distrust and worries about the effects and safety of chemotherapy, which led them to consider other treatment options on their own.

*Fear of side effects*

This cluster was common to all participants. Those who did not receive chemotherapy felt a deep-seated fear of its side effects. Participants attributed this fear to the information provided by their physicians and the experiences of other chemotherapy patients.

"Human beings are born with a fixed lifespan. But I do not want to die. In fact, I want to be treated. However, when I was receiving chemotherapy, I experienced intense pain several times. I believed that I was dying." (Patient B)

"I think the doctors are offering anti-cancer drugs to cure my condition. This decision is normal because it is the standard treatment. My doctor explained to me the side effects in detail. He said that I might have mouth ulcers, my hands could get numb, and I would be unable to eat a

**Table 1**  
Participant background information.

Patient ID	Age (years)	Gender	Cancer type and stage	Period from initial diagnosis to first interview	Treatment history
A	58	Male	Gastric cancer (IV), peritoneal dissemination	1 month	XELOX
B	68	Male	Gastric cancer (at time of diagnosis IIa), cancerous peritonitis	4 years	CDDP + S-1 HER + XP Total gastrectomy + lymph node dissection WT1 peptide vaccine therapy
C	60	Male	Gastric cancer, liver metastasis	4 months	Total gastrectomy + cholecystectomy
D	57	Male	Parotid gland cancer (IVa)	3 months	Subtotal parotid gland removal + neck dissection CDDP
E	74	Female	Sigmoid colon cancer (II) Liver metastasis	3 years	FOLFIRI + Cet 11 courses mFOLFOX 11 courses Trifluridine-tipiracil hydrochloride Gene therapy etc.
F	61	Male	Multiple colorectal cancer	2 months	Enlarged right hemicolectomy + sigmoid colectomy
G	52	Male	Rectal cancer, liver metastasis	2 years	Surgery
H	59	Female	Cervical adenocarcinoma (Ia)	1 year	Radiation therapy 50 Gy CBDCA + PTX 6 course Radical hysterectomy

All patients except C, F, and G received chemotherapy. Patient E withdrew during the study period so data for this patient were not included in the analysis. CBDCA, combination therapy with carboplatin; CDDP, cisplatin; S-1, tegafur/gimeracil/oteracil; Cet 11, carboplatin, 4-epiadriamycin, and teniposide; FOLFIRI, folinic acid, fluorouracil, and irinotecan; HER, human epidermal growth factor receptor protein; mFOLFOX 11, 5-fluorouracil and oxaliplatin; PTX 6, paclitaxel; WT1, Wilms' tumor oncogene protein; XELOX, oxaliplatin and capecitabine; XP, capecitabine and cisplatin.

**Table 2**  
Attitudes and expectations about dendritic cell vaccine therapy.

Theme	Cluster
Strong concerns about chemotherapy	Fear of side effects
	Doubts about treatment efficacy
	Tensions after telling physicians and families about treatment decision
Faith in dendritic cell vaccine therapy	Conviction about the effects of immunotherapy on cancer
	Immunotherapy as a ray of hope amidst uncertainty and confusion
	Desire to care for body and mind damaged by standard treatment
	Strong hopes for therapeutic effects

**Table 3**  
Experiences of seeking and receiving dendritic cell therapy.

Theme	Cluster
Motivation to succeed	No expense spared
	Striving to boost one's immunity
	Completing the treatment
Physical and mental changes	Physical changes
	Feeling unsettled

range of foods. Moreover, other effects could occur. Of all the effects that I experienced, the rash on my face was unbearable. The doctor said that I was not in a state to serve customers or work and that I could no longer perform activities of daily living. I felt I could not bear the treatment." (Patient G)

"I have seen my fellow cancer patients who were treated with anti-cancer drugs. I realized that I am not afraid of dying. Rather, I do not want to live with long-term pain associated with cancer treatment. The anti-cancer drugs that I took as a prophylaxis have undesirable side effects. I do not think I can stand the thought of this going on forever." (Patient H)

*Doubts about treatment efficacy*

The participants who expressed this theme cluster had received surgery. However, they had refused pre- and post-operative chemotherapy because they had found information about the efficacy of chemotherapy drugs on the Internet, instead of relying solely on information provided by their doctors. They were not convinced of the value of chemotherapy and insisted they did not want it.

"I will take anti-cancer drugs if they can cure me. This is not a joke. My doctor said that the good cells will regenerate. When I told him that the bad cells will also recur, he kept quiet." (Patient C)

"I did my own research on the Internet regarding cancer treatments used worldwide. Anti-cancer drugs can decrease body temperature. Moreover, cancer cells are most active when the body temperature is about 35 °C. I do not understand why they are providing intravenous treatment, which causes pain and creates an extremely favorable environment for the development of cancer cells. I have no choice but to accept the fact that I have cancer. However, I cannot accept treatment with anti-cancer drugs." (Patient F)

"I did a lot of research on the Internet about my disease and its treatment. Moreover, I ordered some papers. I was convinced to undergo surgery. Cancer cells cannot be identified until they are resected, and the tissue is assessed with the naked eye. I do not understand why the drugs are needed when the PET scan clearly shows where the cancer is. Cancer drugs kill normal cells and can affect the immune system. I do not believe that these drugs can make me healthy." (Patient G)

#### *Tensions after telling physicians and families about treatment decision*

All participants expressed their desire to receive dendritic cell vaccine therapy to their physicians and families. This cluster described the experiences of patients and their families who refused chemotherapy and made the decision to seek non-standard treatment. Patients made their decision despite tensions in their relationships with their physicians and families. This tension often manifested as worries experienced by patients and/or their families and was sometimes expressed as conflict with physicians or families.

"I told my doctor that I would not take TS-1 or any other cancer drugs. It took a lot of courage for me to tell my doctor that I wanted to have dendritic cell vaccination. Thus, I did not receive the treatment recommended by my doctor. I heard that some doctors tell patients they must change hospitals if their instructions are not followed. My young doctor said, 'I can't make a decision on my own; I will consult my superior.' I think this is what they call the doctor-patient relationship." (Patient C)

"My wife wants me to receive anti-cancer treatment. I take strong drugs for the management of cancer, but these only reduce the tumor marker levels. However, when I look at myself, I see a mummy. So, I do not feel alive. Even so, my family is focused on prolonging my life, and they want me to live no matter what. My wife and I have talked about this several times. I told her that I was sorry because I could not do it. I am open about surgical treatment. Thus, we chose this treatment [dendritic cell vaccine therapy]." (Patient G)

"The economic aspect is also an issue. However, this is not really a problem for us. They [my family] are against alternative treatments because they believe they are folk remedies. My sons insisted that I should be treated in a university hospital." (Patient H)

#### *Theme 2: Faith in dendritic cell vaccine therapy*

This theme described the attitudes and expectations of patients who chose dendritic cell vaccine therapy as a suitable treatment and comprised three theme clusters.

##### *Conviction about the effects of immunotherapy on cancer*

This theme cluster described participants' interest in immunotherapy, and their expectation that dendritic cells are effective when used as cancer antigens. Participants believed this therapy was appropriate for their illness.

"My doctor said that only anti-cancer drugs are effective. So I received treatment for a year and a half. During the treatment course, the drug was switched to HER2, and my ascites improved. Therefore, I decided to try an advanced medical treatment." (Patient B)

"Monocytes, the descendants of macrophages, are collected from my own blood. Then they are cultured and placed back into the body. So they eat cancer cells, pass on the information, and treat cancer. In other words,

I decided to receive this treatment because it is in line with the laws of nature." (Patient F)

##### *Immunotherapy as a ray of hope amidst uncertainty and confusion*

This cluster was common across all participants: those who had received standard treatment, those who had just been diagnosed, and those who had relapsed. Participants were anxious, confused, and lost for words when their physicians informed them about the bad news regarding their condition. They felt that dendritic cell vaccine therapy was a ray of hope at this time.

"At the start, my doctor informed me that I had advanced-stage cancer and that I did not have long to live. I consulted my doctor about advanced medical treatment. However, he informed me that it was not effective. My family and I searched for hospitals that offered advanced medical treatment and immunotherapy. We visited institutions in Tokyo, Nagoya, and Kyushu. We also tried to get help from private hospitals. Then, Dr. XX told us that he could provide the vaccine, that we were going to be fine, and that we should do our best. So, I was extremely happy." (Patient B)

"I have relapsed once. I am always worried that I will relapse. I worry about when I will be notified. Some of my friends have relapsed and are in a difficult situation. I'm scared because I've seen it happen. I have been praying for a long time to receive the ideal treatment, the dendritic cell vaccine." (Patient H)

##### *Desire to care for body and mind damaged by standard treatment*

This cluster described the attitudes of one participant who experienced physical and mental trauma caused by standard cancer treatment. The patient presented with impaired physical functions, which interfered with activities of daily living and caused negative body image. This prompted them to seek a treatment that would restore their well-being.

"The tumor was small (approximately 7 mm). However, it was an adenocarcinoma, and the prognosis was relatively poor. My doctor said that the size was a blessing in disguise. Hence, surgical resection was recommended. The lymphatic system was extensively resected. After 8 months, the cancer had recurred. This time the tumor was still small (about 5 mm). I was shocked by the recurrence. I immediately underwent radiation therapy. I kept it a secret from my colleagues because I knew that if I took a leave of absence from work, I would not be able to return. Work is where I belong. When the radiation treatment was over, my doctor recommended surgery again. I managed to avoid having an artificial bladder and anus. However, I had to wear diapers. Anti-cancer drugs were also provided. I lost my long, straight black hair, eyebrows, and eyelashes, which I was proud of. Now I wear a wig. I could not sleep or go out anymore. My doctor advised me to go to a psychosomatic doctor. I knew I needed treatment, but I was really scared that, although it might save my life, I would lose some things and never get them back. My desire to receive immunotherapy started from the fact that I did not want my children to worry anymore, and I wanted to be healthy for myself. I wondered if there was any way that I could get my life back." (Patient H)

##### *Strong hopes for therapeutic effects*

This cluster described participants' hopes that dendritic cell vaccine therapy would prove to be an effective cure. Underlying their hopes was the realization of the severity of their condition.

"It has been one year since I was diagnosed with cancer. At first, I was told I would be cured if I underwent surgery. However, that didn't work. So, I am a little freaked out [silent for about 5 seconds]. It would be great if the dendritic cell vaccine really worked. I hope researchers can develop a new treatment soon." (Patient C)

#### *Theme 3: Motivation to succeed*

This theme comprised four clusters and described aspects of decision-making, dendritic cell vaccine therapy treatment experience, and treatment efficacy.

*No expense spared*

All participants reported that they were prepared to cover the substantial costs of dendritic cell vaccine therapy.

“Even once I had decided to have the treatment, I was unable to travel to the hospital without money, and the treatment I wanted was expensive. Looking back now, I spent a lot of money. At the same time, all my friends with cancer who were in the same hospital room passed away, one after another. Thus, I will do everything I can to survive, in memory of my friends who had cancer.” (Patient B)

*Striving to boost one's immunity*

This theme cluster focused on the constant efforts made by all participants to maximize their immunity and improve vaccine efficacy.

“When I was healthy, I frequently ate out every day because of my work. I drank and ate foods, such as steak, grilled meat, and sushi, whenever I wanted. Now, I only eat what my wife cooks. I eat hot vegetables for all three meals. I try not to eat sweet foods. I sleep at night and try to live a regular life and increase my basal metabolism.” (Patient F)

“Cancer is originally made up of your own cells, right? So, I generate a positive image of my immune cells working hard to kill the cancer cells.” (Patient H)

*Completing the treatment*

All participants reported that they made efforts to complete their scheduled treatment without missing a single session, even if it required substantial travel time to the treatment facility.

“I am going to take the Shinkansen [bullet train] for 5 hours each way. It is hard on the body. However, it is not too difficult if you think of it as a chance to rest your body.” (Patient A)

“Since the treatment is not covered by insurance and is still in the research stage, I have high hopes. However, I believe that it will be worth it if it can repair my body.” (Patient D)

*Theme 4: Physical and mental changes*

This theme comprised three theme clusters that expressed the physical, mental, and emotional changes experienced by patients after completing the planned dendritic cell vaccine therapy.

*Physical changes*

This cluster described participants' experiences of physical changes associated with the effects of dendritic cell vaccine therapy.

“I do not know for sure. However, I feel as if this immunotherapy has been effective. My appetite is great, my physical strength is not a problem at all, and I feel more positive. It is not that I am pushing myself. However, I feel like I can live a normal life, and I think I can survive.” (Patient A)

*Feeling unsettled*

Participants described their experiences of feeling uncomfortable when they had completed dendritic cell vaccine therapy because their post-treatment situation was not proceeding as expected.

“I had lymph node metastasis, so I had immunotherapy. But now I'm wondering what I'm being treated for. I have had to follow a gluten-free, restricted diet and no alcohol until the PET scan. I am hoping to find satisfaction in my work, but my employees are telling me not to push myself. I have been working hard for the sake of others and for the sake of my employees, but things are no longer going the way I want. I'm starting to think about my life. I'm going to have a PET scan next week, and even if the cancer comes back, I'm going to stop the treatment and not have any more treatment with nivolumab [an immunotherapeutic drug]. I think I should just end my life, slow down, don't think about anything, don't think about sales, and do a good job. I want to do a job that will produce effects that remain even after I die. If I don't have a goal and work toward it, something will go wrong. I can finally sleep each day with that goal in mind.” (Patient D)

“I told myself that I would be fine this time because I received anti-cancer drugs and immunotherapy. However, there are various types of immunotherapy, including natural killer cells. I don't know if the dendritic cell vaccine is right for me. I want to hear about the experiences of people who have had the same therapy. I want more data, such as how long it takes for the disease not to recur. Moreover, I want to meet other people who have had the therapy in person and tell them that if they are okay, then I feel I am okay too. I am scared because I am alone.” (Patient H)

**Discussion**

This investigation of cancer patients' lived experiences of dendritic cell vaccine therapy identified several themes that provide an insight into participants' attitudes and expectations. In discussing the reasons for choosing this new type of therapy, participants cited fears about the side effects of standard therapy, hopes that immunotherapy would provide a complete cure, and feelings of uncertainty throughout the decision-making and treatment/post-treatment process. Participants' feelings and experiences in this transitional stage, which is characterized by both hope and fear for the future, were similar to those reported by cancer patients in previous qualitative studies.<sup>31,36</sup>

In addition to negative emotional responses to prognosis and possible treatments, participants reported difficulties and concerns about the financial and social challenges involved in seeking immunotherapy treatment. For example, similar to the immunotherapy patients in the studies reported by Levy et al<sup>29</sup> and Langmuir et al<sup>31</sup> several of our participants experienced problems with family relationships in negotiating their treatment decisions. These ranged from disagreement about the effectiveness of non-standard treatments to a focus by family members on prolonging life rather than on quality of life, an issue also reported by immunotherapy patients in a qualitative study by Cappelli et al.<sup>32</sup>

A range of factors affect the expectations and experiences of patients with cancer, including personality differences, social and economic status, and cancer type and stage.<sup>49</sup> However, negative emotional states such as fear and distress, as well as feelings of uncertainty, are common experiences in oncology patients generally.<sup>50</sup> Although our participants reported such feelings, they also experienced challenges that may be more unique to immunotherapy patients, such as distrust and doubts about standard therapy, coping with the financial and social challenges inherent in choosing a self-funded treatment, and a combination of faith and uncertainty in the novel treatment. Such experiences have been reported in previous studies of patients with advanced cancer undergoing immunotherapy.<sup>29–32,36</sup>

*Managing patients' treatment concerns*

Previous research showed that the experiences of cancer patients undergoing chemotherapy are diverse, according to cancer type, disease stage, and effect of specific treatments.<sup>51</sup> Side effects often cause negative experiences,<sup>52</sup> which can interrupt or delay cancer treatment,<sup>53</sup> reduce adherence to treatment, negatively affect survival,<sup>54</sup> and reduce patients' well-being.<sup>55–57</sup>

For our participants, substantial concerns about chemotherapy were the main factor that prompted the search for alternative treatments to standard therapy. Chemotherapy nursing has always emphasized the importance of countermeasures for side effects to ensure patient safety and treatment efficacy. Within the framework of evidence-based medicine, the findings of clinical trials have supported standard cancer treatments, such as chemotherapy as the most effective modality, and are generally recommended for patients. Usually, the attending physician follows and implements treatment guidelines. However, the participants in this study did not want to experience chemotherapy-associated side effects, despite chemotherapy being the standard of care, and emphasized the importance of being able to control and maintain their own

well-being. They were not prepared to accept the negative impact of side effects on their well-being, even if standard treatment could prolong their life. This preference may reflect previous findings that older patients with cancer are more likely to prioritize quality of life over survival.<sup>58</sup>

These findings indicate that nurses should strive to prevent and reduce chemotherapy side effects in the early stage of treatment and closely monitor patients' well-being. Nursing care that prevents or does not aggravate symptoms is essential. A recent overview of systematic reviews of nursing interventions for cancer patients identified a wide range of different intervention types (including patient education, counseling, and exercise), which had varying effects on patients' well-being and symptoms.<sup>59</sup> Educational interventions in particular had positive effects on symptom severity, and interventions that involved psychological/psychosocial approaches or supported patients' coping skills reduced fatigue.<sup>59</sup> Messina et al<sup>38</sup> have highlighted the need for greater one-to-one discussion with care team members to manage cancer patients' concerns about the effects of treatment on their quality of life.

#### *Formation of partnership with patients and promotion of team medicine*

One reason that our participants chose dendritic cell vaccine therapy was their desire to both experience a cure and to maintain their well-being. Because of their substantial concerns about chemotherapy, participants searched throughout Japan for doctors and hospitals that offered dendritic cell vaccine therapy and they expressed faith in the treatment and strong motivation to succeed. Cancer treatment is constantly evolving and is entering a new phase characterized by a shift from standard treatment to personalized medicine. It is becoming increasingly difficult to fully ensure the well-being of patients with current standard treatment alone. In addition, patients worldwide can now easily obtain information on cancer treatment from the Internet, as did our participants, who not only found online information on dendritic cell vaccine therapy but also used the Internet to search for doctors and hospitals in Japan that offered immunotherapy. However, sole reliance on the Internet for information may sometimes have negative consequences for patients' health. Therefore, patients need support during decision-making about appropriate treatments.

Patient–nurse partnerships are invaluable to ensure this support is provided. Nurses need to help patients obtain accurate information from reliable sources. The rationale underlying the information must be understood to determine its accuracy. Nurses also need to check whether the information is up-to-date and validate the date of the update. They must understand the safety, efficacy, and cost of specific treatments and make objective decisions about their suitability for individual patients. The promotion of team medicine and collaboration with other professionals are also important to support patients in making appropriate treatment decisions.

Recently, the importance of advance care planning for cancer patients has been emphasized. In advance care planning, patients and their families, together with health care providers and other professionals, discuss not only the present but also future personal and health care values toward the end of the patient's life.<sup>60,61</sup> To achieve patient-centered health care delivery, health care providers should communicate appropriately with patients and build trust. This would help patients to make informed choices about cancer treatment and how to live their lives, including palliative and end-of-life care.<sup>62,63</sup>

All participants in this study had advanced-stage cancer or a poor prognosis. However, the time between diagnosis and interviews varied. Therefore, there were differences in participants' experiences of side effects and in their feelings and mental states. For example, Patient B was interviewed 4 years after diagnosis, whereas Patient A was interviewed 1 month after diagnosis, and was experiencing emotional distress and the side effects of prompt chemotherapy. However, both patients reported experiences associated with all four extracted themes. Therefore, we believe that any differences resulting from variation in time since diagnosis were less important than the similarities in patients' experiences of

living with cancer and coping with standard treatments (eg, chemotherapy). The findings showed that participants were experiencing not only physical pain but also feelings of deep grief, intense concern, fear, worry, effort, tension, and emotional instability. Despite this, they actively sought an institution that could provide dendritic cell vaccine therapy and strove to maximize the effects of the treatment. They attempted to take control of their own well-being and exercise their independence, despite experiencing deep grief.

An important issue within oncology nursing is ensuring the provision of grief care that maintains patients' dignity.<sup>64</sup> Recent studies have demonstrated that interventions using dignity therapy, which attempts to reduce distress and promote dignity and hope in terminally ill patients, can improve negative experiences such as anxiety and depression, although findings regarding the effect of dignity therapy on quality of life are conflicting.<sup>65,66</sup> Outstanding nursing practice skills are required to effectively manage patients' experiences of grief. Nurses must be able to coordinate relationships, even for patients who receive alternative treatments to the standard of care at different medical institutions. During the post-treatment phase, patients need tailored support to manage this difficult stage of their treatment journey.<sup>37</sup>

Nurses should communicate closely with both patients and attending physicians to maintain patient–health care provider relationships. Attending physicians can provide a prognosis from a comprehensive perspective and advice on the necessary treatment, including palliative care. Tetsuro Shimizu, a Japanese philosophical researcher, has emphasized that the patient–physician relationship in Japan is paternalistic; the physician is a specialist, and the patient submits to their superior knowledge.<sup>67</sup> Within this context, it is difficult for patients to express their opinions and thoughts to their attending physicians. In contrast, a more equal patient–physician relationship is characterized by a process of shared decision-making and sincere communication. Nurses need to intervene to ensure that this process is beneficial to patients. For patients with advanced cancer, this process must be conducted with speed owing to short life span.

#### **Conclusions**

In this study, we aimed to explore and validate the experiences of cancer patients seeking and receiving dendritic cell vaccine therapy in Japan. The findings demonstrated participants' concerns about chemotherapy and their wish to seek alternative treatments that could both prolong their lives and provide better quality of life. Participants discussed the challenges of finding institutions that offered this new therapy, their hopes and fears about therapy, their difficulties voicing their own treatment wishes to their physicians and families, their determination to maximize the positive effects of immunotherapy, and the physical and mental changes they encountered. The experiences expressed in patients' narratives may help to inform strategies for the existential support of cancer patients receiving dendritic cell vaccine therapy and develop measures to adapt cancer nursing to the future provision of personalized medicine.

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#### **CRedit author statement**

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Formal analysis. Yoshiko Kitamura: Writing – Original Draft. Yoshiko Kitamura, Chizuko Konya: Writing – Review & Editing. Yoshiko Kitamura: Funding. All authors were granted complete access to all the data in the study, with the corresponding author bearing the final responsibility for the decision to submit for publication. The corresponding author affirms that all listed authors fulfill the authorship criteria and that no others meeting the criteria have been omitted.

### Declaration of competing interest

All authors have none to declare.

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### Ethics statement

Approval was obtained from the Medical Ethics Review Committee of the first author's institution (approval date: 27 August, 2018; approval No. I309). All participants provided written informed consent.

### Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

### Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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