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Qualitative analysis of gynecologic oncology patients' experience with treatment holidays

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ARTICLE INFO	A B S T R A C T				
Keywords: Treatment holiday Chemotherapy holiday Qualitative	<i>Objective</i> : Patients with advanced or recurrent gynecologic malignancies occasionally take breaks from systemic treatment colloquially referred to as "treatment holidays" or "chemotherapy holidays." There are no data from the patient perspective that help describe this experience. <i>Methods:</i> Patients with recurrent or advanced primary gynecologic malignancies who had decided to enter a treatment holiday were recruited and interviewed. A treatment holiday was defined as a planned temporary break or delay in treatment for a patient with recurrent or advanced primary gynecologic malignancy for reasons other than pursuit of hospice or best supportive care, research protocol violation or unacceptable toxicity. Interviews were audiotaped, transcribed and then analyzed using an inductive thematic analysis. <i>Results:</i> Of 6 total patients identified for participation, 5 completed interviews with ages ranging from 57 to 80 years. Two participants returned to their previous treatment regimen after their holiday therapy, two switched therapies, and one remained on an extended break from systemic treatment. Treatment holidays were experienced as a break from the physical and psychological routine of being a cancer patient, but also brought about feelings of a lack of structure, uncertainty, and led to a confrontation with mortality issues. Overall, participants had favorable experiences which were initiated by their providers in whom they had a deep sense of trust. <i>Conclusion:</i> Patients experience treatment holidays as a positive and valuable break from the physical and psychosocial routine of stinct emotional needs that clinicians should address to best support patients electing treatment holidays.				

1. Introduction

Recurrent gynecologic cancer generally carries a poor prognosis and is almost universally fatal. Treatment usually consists of systemic therapies (chemotherapy, biologic therapy, immunotherapy or a combination) given with palliative intent to prolong life and improve symptom burden. Patients can expect to be on chemotherapy for most of their remaining life, until they transition to best supportive care. Patients with a partial response or stable disease may continue on chemotherapy with no defined endpoint.

It is an occasional practice for patients on systemic treatment for recurrent or advanced primary gynecologic cancer to take treatment breaks for various reasons on an individualized basis. This is colloquially referred to as a "chemotherapy or treatment holiday" and is not well

described in the gynecologic oncology literature. In contrast to discontinuing treatment due to intolerable side effects or to pursue the next line of therapy, a treatment holiday is a conscious decision between a patient and their provider to pause from systemic cancer treatments for a defined period of time. Little is known about the experience of patients who undergo treatment holidays including the possible rationales, experience of the break in treatment, and psychosocial effects of pausing from treatment.

A number of survey-based patient reported outcome measures are used to quantify quality of life for clinical trials (Greimel et al., 2003; Basen-Engquist et al., 2001; Donovan et al., 2008; King et al., 2014). These evaluations fail to capture detailed accounts of the patient experience, and do not allow for unforeseen important determinants of quality of life in guiding decision-making. In order to more deeply

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understand the decision-making process and implications of patient decisions in these cases, we used a qualitative approach to describe the lived experience of patients taking treatment holidays in order to guide future patients and clinicians in these challenging clinical situations.

2. Methods

Patients with recurrent or advanced primary gynecologic malignancies who were taking a treatment holiday were prospectively identified by clinicians at a weekly division clinical meeting and were subsequently approached about participation in the study from May 2019 through June 2020. A treatment holiday was defined as a planned temporary break or delay in treatment for a patient with recurrent or advanced primary gynecologic malignancy for reasons other than pursuit of hospice or best supportive care, research protocol violation or unacceptable toxicity. Patients were approached by their primary provider by telephone, secure messaging or at a clinic visit and if interested were given information about the study and consented to be contacted by a member of the research team. The research team was composed of a gynecologic oncologist, a gynecologic oncology fellow, and an obstetrics and gynecology educator and a psychologist with experience with qualitative methodology. Patients who agreed to participate were contacted by phone to schedule an in person 30-60 structured interview. Study information was relayed by phone and written informed consent was obtained at the time of the interview. Interviews were scheduled at least 30 days after the decision to take a treatment holiday to allow time for the lived experience to unfold. This study was approved by the Institutional Review Board prior to patient recruitment.

Interviews were conducted by a trained interviewer who used a semi structured interview guide to discuss treatment holiday decision making and the experience of being on a treatment holiday. Interviews were audiotaped with written permission and were transcribed by the interviewer. De- identified interview transcripts were analyzed using inductive thematic analysis with Dedoose software (Dedoose Version 8.0.35, (2018). Los Angeles, CA). Line-by-line coding was first completed independently by two researchers and inter-rater reliability was calculated using a Kappa test. Codes were then grouped and simplified into overarching themes that encompassed the breadth of topics discussed in the interviews. Interviews were then re-coded using the broad thematic codes.

A purposive sample included patients with advanced or recurrent gynecologic malignancies with stable clinical disease whose doctors supported their taking a treatment holiday. While early evidence of saturation of themes was observed after 5 interviews, there were no confirmatory interviews performed as recruiting was stopped after the onset of the COVID-19 pandemic. This decision was made due to concerns among the research team that the presence of the pandemic was altering the decision-making process and reflection on the experience of treatment holidays for patients.

3. Results

A total of 6 patients were initially identified for participation in the study. One patient did not meet criteria for a treatment break based on their clinical history and five patients were contacted for participation. All five patients provided consent and participated in the study. Demographic and clinical characteristics are displayed in Table 1. Participant ages ranged from 57 to 80 (mean 70). All participants had recurrent disease and had previously been on cytotoxic chemotherapy prior to their treatment holiday. Two participants returned to their pretreatment holiday regimen, two participants switched treatment regimens and one participant remained on an extended break from systemic treatment but did receive palliative radiation to a symptomatic bone metastasis two years after initiation of her treatment break. The range of treatment holiday durations was 3-35 months for those who returned to systemic treatment. Inductive coding was separately undertaken by two authors with an inter-rater reliability score of 0.79 (Kappa test) across the five interviews.

Five themes were generated that reflected how patients experienced treatment holidays. Patient experiences were framed by the ingrained sense of identity as a cancer patient with a focus on the implications of ongoing treatment. Their decision making to take a treatment holiday was provider initiated and was met with a deep sense of trust. Treatment holidays were generally not goal oriented but did allow an appreciation of the break from the physical and psychological routine of being a cancer patient. Along with uncertainty around the experience, patients had emotional experiences confronting mortality and coping with the lack of structure during a treatment holiday. Reflecting on their

Table 1

Clinical characteristics of participants and treatment holiday parameters.

ID #	Age	Stage	Disease site	Histology	Line of treatment*	Preceding treatment regimen	Response prior to holiday**	Holiday duration	Disposition
1	57	Recurrent	Ovary	Clear cell	4th line	18 cycles paclitaxel + bevacizumab	Stable, measurable disease	35 months	Extended treatment break, joint decision to enter surveillance, returned to different treatment regimen upon progression of disease
2	74	Recurrent	Fallopian tube	Serous	1st line, followed by radiation for recurrence, initially planned for adjuvant systemic treatment	6 cycles carboplatin + paclitaxel	Stable, measurable disease	48 + months	Remains on extended treatment break, received palliative radiation to a spinal metastasis 2 years after initiation of treatment break
3	62	Recurrent	Endometrium	Serous and clear cell	4th line	8 cycles carboplatin + nivolumab	Progression of disease, delayed next line of treatment	3 months	Progression of disease off treatment, switch treatment regimen
4	77	IVB	Endometrium	Serous	1st line maintenance	16 cycles trastuzumab	Stable, measurable disease	3 months	Resumed preceding treatment
5	80	Recurrent	Primary peritoneal	Serous	2nd line	18 cycles pegylated liposomal doxorubicin + bevacizumab	Stable, measurable disease	6 months	Resumed preceding treatment

ID; identification number.

* Line of treatment: Total number of systemic therapy regimens prior to treatment holiday including upfront adjuvant treatment.

** Response prior to holiday: response and disease status on last CT scan prior to treatment holiday.

treatment holidays, participants had favorable emotions which led to a unanimous recommendation of the experience as a valuable one to a patient for whom it was clinically appropriate.

3.1. Lived experience of being a cancer patient with a focus on ongoing treatment

Interviews began with an open-ended question regarding life on treatment from a physical, emotional and psychosocial perspective to serve as a reference point for the discussion about a treatment holiday. All participants were receiving cytotoxic chemotherapy prior to their treatment holiday, and some participants reported "I didn't have any bad effects" (participant 4, age 77) while others reported feeling like "you'd get knocked down" (participant 2, age 74). There was an acknowledgement that chemotherapy is toxic on several occasions: "It's so amazing to me that the body can actually withstand ... the assault" (participant 1, age 57). Overall, participants reported tolerating treatment well and described typical grade 1 and 2 toxicity as expected with cytotoxic chemotherapy. Despite discussions about toxicity of treatment, no participant discussed these negative aspects of treatment as the basis of the decision for a treatment holiday.

The experience of being a cancer patient extended beyond physical symptoms. Participants commented on the routine and experience of previous treatments to provide insight into the experience of a treatment holiday. In general participants described being motivated and committed to treatment ... "after a while I was looking forward to it" (participant 4, age 77). One participant proudly described taking public transit to make appointments. For the most part, participants described a "rote" aspect to chemotherapy schedules that you "get used to" (participant 1, age 57). The psychosocial burden of being a cancer patient was a central concept that pervaded discussions of treatment and the treatment holiday. One participant stated "I am definitely feeling ... the psychological impact of kind of just being sick, being more obviously sick" (participant 3, age 62). Another participant also brought up beliefs about their cancer etiology such as "I don't even know how I got this" (participant 3, age 62). Participants later referenced the aspects of their lives that related to their lived experience of being a cancer patient to frame the changes they experienced during a treatment holiday.

3.2. Treatment holiday decision making

The participants in this study all identified their providers as the driving factor in the decision to take a treatment holiday. Participants had "never even realized that there was such a thing" (participant 1, age 57) and recalled their providers stating "we're going to give you a break" (participant 3, age 62). Participants reported feeling thankful and at times lucky to have been offered this experience ... "how did I hit bingo?" (participant 4, age 77). One participant remembered their provider using the term "low volume" (participant 5, age 80) disease in their justification of the treatment holiday. Others recalled their providers discussing the need for a rest and discussions of the lack of data about a break from treatment being detrimental. One participant, when discussing the context of their treatment break, said "we sort of killed it, for the meantime" (participant 1, age 57) suggesting an understanding of stable disease while also alluding to the fact that disease would progress in the future. Participant's discussions of their decisions to take treatment holidays were closely tied to expressions of trust, gratitude and warmth towards their clinical team. No one expressed skepticism surrounding the idea of a break from treatment.

3.3. Treatment holiday physical, emotional and psychosocial experience

Participants undergoing treatment holidays discussed the physical and emotional implications of the experience. Participants did not specifically relate their physical state during their treatment holiday to a lack of chemotherapy toxicities, but rather made more broad statements such as "I've been feeling great" and "I can't say I've been feeling sick" (participant 5, age 80). Participants reported reading more, focusing on healthy eating and exercise and reported an increased willingness to leave the house for social events. The characterization of life during a treatment holiday elicited comments on a wider scope of participants' personhood than just their experience with treatment and illness.

When asked if they had specific goals during the treatment holiday, most participants did not report concrete goals. This question did not prompt a discussion of pre-conceived goals that justified or helped shape the decision for a treatment holiday. Participants broadly focused on "enjoy[ing] life" and "tak[ing] it day by day" (participant 4, age 77). Individual participants did provide answers to this question such as an interest in picking up old hobbies or, for one participant, helping care for a friend who was terminally ill.

Faith was mentioned by two of the five participants as a coping mechanism and source of support during a treatment holiday. One participant recalled "God's going to take care of everything, he's your friend" (participant 4, age 77) while another gained valuable insights from a friend who was a practicing Buddhist. Family and friends played a less universally positive role during treatment holidays. Participants reported family members and friends who expressed a lack of understanding or frustration with the concept of a treatment holiday. Some participants were questioned by family and friends about the rationale and the goals of a treatment holiday, and one participant recalled a friend saying "so now you're going to die" (participant 3, age 62). Participants displayed resilience when discussing this topic and did not report that the opinions of their friends and family influenced their overall experience of the treatment holiday. In the context of this topic one participant reported "my closest friends leave me alone" (participant 2, age 74).

3.4. Confronting mortality and uncertainty during a treatment holiday

All participants wove the topic of mortality and uncertainty into their discussions of the emotional and psychosocial experience of being a cancer patient on treatment and the experience of taking a treatment holiday. Cancer treatments were sometimes discussed with a degree of skepticism at their efficacy ... "by the time you get to your third clinical trial you begin to wonder whether we're throwing darts at a board" (participant 3, age 62). For one participant, the experience of a treatment holiday made them confront their mortality in a way that had not been at the front of their mind, while other participants spoke of how the treatment holiday has given them a break from thinking about their illness. Throughout the interviews, participants made references to their limited lifespans usually with sarcasm ... "if I'm going to die tomorrow, I need to know. I need to prepare for that" (participant 3, age 62). Simultaneously expressed alongside the candid topic of mortality was a separate will to live whereby participants looked forward to resuming treatment when the time came and made statements such as "I have no intention of going yet" (participant 2, age 74).

Participants reported being more aware of minor physical symptoms such as aches and pains and symptoms previously attributed to other illnesses such as irritable bowel disease for one participant. Previously innocuous symptoms took on a different significance as the question of whether they "could be cancer" (participant 1, age 57) became present. One participant confidently stated they were "aware of certain things which are changing ... which I which I know are the cancer" (participant 3, age 62). These symptoms and their associated implications were anxiety producing for some participants, and others reported being able to cope with these doubts more easily.

Treatment holidays brought a lack of structure and framework to the course of each participants cancer treatment. One participant described the experience as "amorphous, it's um ... you know there's no goal ... where am I going ... I don't know where I'm going" (participant 3, age 62). Alongside feelings of taking a break from thinking about cancer treatment and its related schedules came a sense of "strange[ness]"

(participant 2, age 74). Participants identified that there was an emotional conflict whereby they were appreciative for the experience to be off treatment and simultaneously questioned whether they could or should be more actively engaged. This dilemma was referred to by one participant as a "mixed blessing" (participant 3, age 62). Participants did generally show an understanding that uncertainty was a part of the treatment holiday experience, and one participant discussed embracing uncertainty as a way to live each day with more presence. Only one participant discussed the hypothetical circumstance of experiencing regret if they experienced progression of disease, and in that case reported they would think "gee should I have been doing something the last few months" (participant 3, age 62).

3.5. Reflections and advice to other patients

When asked if they would recommend a treatment holiday to a patient for whom it was clinically appropriate, all participants responded favorably. Participants reflected that the general experience of being off treatment was a welcome change and expressed differing degrees of enthusiasm, with answers ranging from "why not" (participant 5, age 80) to "I'd say ... you must do this holiday" (participant 1, age 57). There was an acknowledgement that the experience would not be right for every patient at every time, but no participant brought up previously discussed concerns or uncertainties as a justification for recommending caution to a for whom a treatment holiday was clinically appropriate.

4. Discussion

For this sample of patients who elected to take a treatment holiday, the experience was largely favorable, but stirred up complicated emotions and reflections on the patients' identity, relationship to their clinician, and other aspects of their lives and medical care. The present study adds a valuable patient perspective to the discussion of treatment holidays for gynecologic malignancies. Participants in this cohort were introduced to the concept of a treatment holiday by their provider and were open to the idea due to a trusting relationship that is common between patients and their oncologists. In a survey by Kreines et al, a number of patient-initiated reasons for treatment holidays were described such as weddings, vacations and family events (Kreines et al., 2021). The current study suggests that treatment holidays are not necessarily tied to life events. In this cohort of participants, treatment holidays provided time for reflection, a hiatus from the burden of treatment schedules and their associated symptoms and were overall recommended to others by patients.

Issues of mortality and uncertainty were commonly discussed and provide a framework of psychosocial needs that should be addressed by providers during a treatment holiday. The common anxiety of whether or not to attribute symptoms to one's cancer or more innocuous causes is surely not specific to the experience of a treatment holiday but seemed to hold a significant emotional weight in light of the purposeful decision to defer continuous treatment. Addressing the possibility of new symptoms or progression of disease before initiating a treatment holiday could be useful to allow patients to have a framework for these occurrences and not experience disappointment if they happen. The perceived lack of structure during a treatment holiday also provided insight to how patients could be best supported during this time. Unfortunately, we found that a patient's family or social support system may not always play a positive role in supporting these emotions, as their perception of a treatment holiday could lead to a criticism or pressure to resume treatment.

Offering regular visits initially during treatment holidays and discussing a pre-defined end goal or time period for re-evaluation are strategies that could maximize the experience for the patient by providing structure and support. Depending on the individual treatment holiday experience and ongoing symptom burden, some patients might benefit from continued frequent office contact while others might benefit from distance from medical establishments. Telemedicine could provide an opportunity for providers to show support while maintaining distance and convenience for patients. A special role should be taken by the provider during a treatment holiday to assure a patient feels supported and that emotions of uncertainty, guilt or fear be specifically brought to attention and addressed.

Clinical data generally supports the use of treatment holidays or intermittent chemotherapy in breast, colorectal and urologic malignancies (Tonini et al., 2013; Muss et al., 1991; Onishi et al., 2012; Beer et al., 2003). Despite a lack of clinical outcomes data to support or caution against treatment holidays in gynecologic malignancies, they are a common practice. In a physician survey study, 96% of gynecologic oncologists have had a patient take a treatment holiday. Providers were most comfortable with treatment holidays for ovarian and uterine cancer, and less comfortable with treatment holidays for vulvar/vaginal cancer and sarcomas (Kreines et al., 2021). Few (7.2%) providers reported regret after a patient completed a treatment holiday, and 98% agreed that treatment holidays could be valuable.

Frey et al, after conducting a focus group with 22 ovarian cancer survivors, concluded that quality of life and minimization of side effects were among the most important aspects of treatment among women receiving ovarian cancer treatment (Frey et al., 2014). Patients preferred individualized approaches and valued ability to maintain relationships and participation in life events as more important than measuring survival increments. These values affirm that with the right support, the benefits of a treatment break likely outweigh the risks in a well counseled and supported patient.

It is unlikely that prospective studies will be undertaken to evaluate the clinical impact of treatment breaks on the overall disease course in gynecologic malignancies. Intermittent chemotherapy is not standard of care for patients with gynecologic malignancies, and the experience generally exists outside the typical treatment framework as part of the "art of medicine." The current study is limited by its small sample; however, this was a product of the prospective nature of recruitment in which patients were approached as they entered into treatment breaks with their providers. The conclusions drawn from these patients' experiences may not apply to all patients interested in a treatment break. While our participants had varying but also limited circumstances surrounding treatment holidays, thematic saturation was reached with regards to the broad topics discussed. Another limitation is the lack of perspective and reflection from the participants after the treatment holiday ended. Several participants in this study did not return to their intended treatment, and it would have been valuable to obtain their perspective particularly among those who experienced progression of disease.

The decision for a patient to enter a treatment break will likely remain a personalized one that leaves room for a refreshing change of pace, time for reflection and personal growth, and also for uncertainty and anxiety. A patient's identity as a person with cancer who relies on continuous treatment is often firmly established at the time one elects to take a treatment holiday, and this dissonance during a treatment holiday can lead to psychosocial distress. A trusting and strong relationship between a provider and their patient is crucial to the success of a treatment holiday and can allow a patient to overcome the lack of structure to gain the most from their time off treatment. Providers should approach these experiences with a heightened level of sensitivity and responsibility as they may be the sole source of support as a patient navigates a likely beneficial but potentially challenging experience.

CRediT authorship contribution statement

Benjamin Margolis: Conceptualization, Methodology, Investigation, Data curation, Writing – original draft. Megan E. Sutter: Methodology, Investigation, Data curation, Writing – review & editing. Leslie R. Boyd: Writing – review & editing, Supervision. Abigail Ford Winkel: Conceptualization, Methodology, Data curation, Writing – review &

Gynecologic Oncology Reports 39 (2022) 100911

editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics approval and consent to participate

All subjects gave their verbal informed consent for inclusion before they participated in the study and provided written consent in person at the time of their interview. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee at NYU Grossman School of Medicine (study number S19-00208).

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