“One more chance to survive” The experiences of patients with advanced melanoma and their partners with Tumor-infiltrating Lymphocyte Therapy: a qualitative study and recommendations for future care

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Abstract

Purpose Patients with advanced melanoma refractory to first-line treatment have a need for effective second-line treatment options. A recent phase 3 trial showed promising results for adoptive cell therapy with tumor-infiltrating lymphocytes (TILs) as second-line therapy in patients with advanced melanoma. However, it remains unknown how patients and their partners experience TIL therapy, which is key to evaluate and improve the quality of care.

Methods Semi-structured interviews about the experience of TIL therapy were conducted with patients with advanced melanoma and their partners 2-4 weeks post-treatment (short-term) and >6 months after treatment (long-term).

Results In total, 25 interviews were conducted with advanced melanoma patients treated with TIL (n=13) and their partners (n=12), with the majority being short-term interviews (n=17). Overall, patients and partners experienced TIL therapy as intense (uncertainty of successful TIL culture, multiple treatment-related toxicities, and extensive hospitalization). Patients and partners with young children or other caregiving responsibilities encountered the most challenges during TIL therapy. All patients, however, reported a recovery of all treatment-related toxicities within 2-4 weeks (except fatigue).

Conclusion Clinical data justify the role of TIL therapy in the treatment of advanced melanoma. With the distinct nature of TIL therapy compared to the current standard of care, we have provided patient-centered recommendations that will further enhance the quality of TIL therapy. Implications for Cancer Survivors As more patients with advanced melanoma are expected to receive TIL therapy in the future, our findings could be incorporated into survivorship care plans for this novel group of advanced melanoma survivors treated with TIL.

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Introduction

The introduction of immune checkpoint inhibitors (ICIs), such as ipilimumab (anti-CTLA-4) and nivolumab or pembrolizumab (anti-PD-1) has substantially improved survival outcomes in patients with advanced melanoma (unresectable stage IIIC-IV) [1, 2]. However, approximately 50% of patients have no durable benefit from ICIs, and effective second-line treatment options are still scarce [3-6]. Adoptive cell therapy with tumor-infiltrating lymphocytes (TILs) can serve as an effective second-line treatment modality for this patient group, as its efficacy has been demonstrated in multiple clinical trials [7-11].

TIL therapy is an intensive treatment comprising of the surgical removal of the patients' metastasis for the isolation and outgrowth of tumor-resident T cells, a hospital admission to receive lymphodepleting, non-myeloablative chemotherapy, followed by the adoptive transfer of TILs and
subsequent intravenous high-dose interleukin-2 (IL-2) [9, 11]. Previous studies evaluating the experiences and perspectives of patients treated with adoptive cell therapy (CAR-T cell therapy) have shown that patients frequently experience uncertainty regarding the consequences of treatment, decreased physical and social functioning, and heightened emotional distress due to treatment-related toxicities [12, 13]. In addition, Wong et al. and Fox and colleagues showed that advanced melanoma patients treated with novel therapies experience difficulties balancing hope with a realistic expectation of treatment outcomes [14, 15]. Furthermore, the experience of the patients’ partner is commonly omitted in patient experience research, although they provide substantial emotional and day-to-day support that significantly influences the patient’s overall experience of treatment [16-21]. This level of provided support harms the partners’ mental health, as they experience comparable levels of distress, anxiety, and depression as the cancer patients themselves [16, 17, 22, 23]. Several studies even suggest that the impact of cancer and its treatment is larger on partners than on cancer patients [22, 24-26]. While it is possible that patients with advanced melanoma and their partners will face similar challenges during TIL therapy, data on this subject are currently non-existent [8, 27].

A recently completed phase 3 trial comparing TIL to ipilimumab in patients with advanced melanoma (most of whom were refractory to first-line anti-PD-1 therapy) showed a high objective response rate (49%) in patients who received TILs [10]. These results support the use of TIL therapy as a second-line treatment option for these patients, and more patients are expected to receive TIL therapy in the near future [10, 28]. Therefore, it is increasingly important to evaluate the patients and their partners’ experience with TIL therapy to identify specific issues, needs, and preferences during treatment, which in turn can enhance the quality of care [29-31]. Therefore, this study aimed to qualitatively evaluate patients’ and partners’ experiences of TIL therapy and to provide recommendations through an evidence-based patient-oriented framework that can guide improvements in the quality of care given during the different stages of TIL therapy.

Methods

Study design

A qualitative study was conducted to evaluate the experiences of the patients and their partners during TIL therapy. We conducted semi-structured interviews and used an inductive approach to capture the full experiences of patients and partners. To incorporate both short- and long-term impressions of TIL therapy, we interviewed patients and partners immediately after treatment (within 2-4 weeks) and >6 months after treatment. We performed a reflective thematic analysis by Braun and Clarke to analyze the interviews and detect themes that were reflective of the data [32, 33]. Themes were connected to the hemes were connected to the Warwick Patient Experiences Framework (WaPEF), a construct from the National Institute for Health and Clinical Excellence (NICE), with seven evidence-based dimensions to evaluate the quality of care based on patient experiences [34]. We linked the themes identified in this study to WaPEF dimensions to provide evidence-based recommendations that can guide patient-oriented improvements to clinical care [32, 34].
The Standards for Reporting Qualitative Research (SRQR) were followed in this study to ensure the data quality and transparency of the methods and results [35].

**Participants**

Eligible patients received TIL treatment at the Netherlands Cancer Institute (NKI) in a randomized phase 3 trial that evaluated the effectiveness of TIL therapy [10]. Included patients were diagnosed with unresectable or metastatic melanoma (stage III-C-IV according to the American Joint Committee on Cancer (AJCC) 7th edition), received (a maximum of) one line of prior systemic therapy (except ipilimumab) for this disease stage, and were in an intimate relationship during treatment [1, 2, 10]. Patients and partners had to be between 18-75 years of age with sufficient understanding of the Dutch language. Patients were identified by their treating healthcare professional (HCP) and were invited along with their partners to participate in this study. The Central Committee for Human Research and the Institutional Review Board of the Netherlands Cancer Institute approved this study (NL47475.000.14). The study was conducted in accordance with the guidelines of the Declaration of Helsinki. Written informed consent was obtained from all the patients and their partners.

**Data collection**

Three researchers conducted semi-structured interviews with the patients and their partners separately between August 2021 and May 2022. The interviews were conducted in person, via teleconference, or by telephone, using an interview guide with open-ended questions or probes (see Supplementary Materials for the full interview guide). The interview guide was drafted based on scientific literature [12, 14, 15, 36-40] and was refined based on feedback from clinicians involved in TIL treatment. The interviews were divided into three sections: pretreatment, treatment, and post-treatment. After analyzing the first 10 interviews, the guide was amended by removing one question and adding three more questions.

**Data analysis**

Interviews were analyzed thematically by EB and ME, who double-coded all transcripts to provide different perspectives on the data [41]. No specialized software was used [42], and discrepancies were resolved by a senior researcher (AB). Two codebooks were created after analyzing five interviews, which were adjusted when new codes were identified. Inclusion stopped at theme saturation, defined as the point where no new codes were found in the data from the last interview [43]. EB and ME iteratively named and defined themes with the assistance of AB.

**Results**

**Study population**

Of the 26 patients identified for inclusion (14 patients and 12 partners), one did not want to participate in the study. Data saturation was reached after completing 17 short-term and eight long-term interviews.
The median age of both patients (62% male) and partners (67% female) was 64 years, with ranges of 31 – 73 years and 29 – 73 years, respectively. The majority of patients (62%) and partners (75%) had lower general secondary education or vocational training, while the remaining patients (38%) and partners (25%) had either high vocational training or (pre) university education. Approximately half of the interviews (52%) were conducted via teleconferencing or phone because of COVID-19 restrictions at the time of this study. The interviews lasted 38 minutes (range, 24–60 minutes) on average. For a complete overview of the interviewees’ characteristics, see Table 1.

Themes

Three broad themes were formed based on the interview results: expectations and experiences of treatment, self-care, and emotional care. All identified (sub)themes were present in both patient and partner interviews, except for the subtheme ‘juggling between needs’, which was present only in interviews with partners. Supporting quotes for these themes are presented in Tables 2, 3, and 4. The three broad themes and their corresponding subthemes are described below.

1. Theme 1: Expectations and experiences of treatment
   Patients and partners approached TIL therapy with various expectations, which upon reflection during the interviews, were not always compatible with their experiences. Five subthemes were identified within this theme (see Table 2).

   1.1 Information and communication
   Participants found the information and communication related to TIL therapy satisfactory, and a number of patients and partners accessed a specially designed website providing more details about the treatment. The website’s animation explaining TIL therapy was frequently mentioned as educational and helpful (see Table 2).

   1.2 Shared decision making
   All patients were actively involved in shared decision-making regarding their treatment and felt that TIL therapy was the "best option" for prolonging their life expectancy. Other topics highlighted by patients and partners related to shared decision making were the potential risks and benefits of TIL therapy and the decision to continue treatment when experiencing severe toxicities. Partners were not always aligned with patients when evaluating whether to terminate treatment prematurely, as partners were more likely to favor continuing treatment. However, both the patients and partners mentioned an understanding of others’ viewpoints.

   1.3 Treatment burden
   Patients and partners found TIL therapy to be an intense but short treatment, with the most challenging aspect being the toxicities related to IL-2 (e.g. cold chills, fever, physical weakness) for most patients. Notably, some patients reported the chemotherapy-related toxicities to be the most debilitating toxicities,
as they would more often persist after finalizing treatment. A number of patients and partners experienced mental challenges related to social isolation and loneliness during treatment. The COVID-19 pandemic potentially exacerbated the feeling of social isolation because patients had to stay in an isolated hospital room during treatment, while their partners were self-isolating. For partners, the perception of their loved one's (physical) suffering during treatment was reported as the most stress-inducing challenge of TIL therapy (see Table 2).

1.4 Uncertainty
TIL therapy is a highly personalized treatment that makes it difficult for patients and partners to anticipate what to expect. For example, earlier phase 1/2 studies have shown that manufacturing TILs after surgery fails in 10% of cases [7, 11], and tolerability to high-dose IL-2 cannot be accurately predicted even though it frequently causes severe toxicities that may lead to premature treatment termination [44]. Patients and partners often reported that these unexpected events substantially affected their mental health.

1.5 Novelty of treatment
Nearly all patients found the novelty of TIL therapy special and were particularly impressed by the receipt of "their own cells", which they frequently described as a "special" and "moving" experience. The high level of attention received from clinicians throughout the treatment trajectory was also seen as a positive experience by most patients, but a few patients expressed discomfort due to this high level of received attention.

2. Theme 2: Self-care
All the interviewed patients and partners expressed the importance of physical and mental fitting during treatment. The following subthemes were identified within this theme (see Table 3).

2.1 Coping
Most patients entered treatment with a flexible mindset ("we will see what happens") and expressed little distress before hospitalization because of their trust in the medical team. The remaining patients expressed the need to gather additional information in order to feel more prepared for treatment. Nearly all patients and partners reported to use coping strategies to deal with uncertainties before starting TIL therapy, such as humor, artistic expression, and retaining a daily routine during hospitalization. Dyadic coping strategies (joint problem-solving, shared gathering of information, and bidirectional expression of empathy) were also used by a number of patients and partners.

2.2 Recovery and rehabilitation
All patients and their partners reported a fast recovery from nearly all treatment-related toxicities after TIL therapy, allowing them to perform domestic activities within 2-4 weeks post-treatment. However, persistent fatigue seemed to remain in most patients after treatment, limiting their engagement in
hobbies, work, or sports. Furthermore, while most patients and partners expressed no need for additional supportive care during or after treatment, both strongly preferred receiving such care near their homes. Lastly, all patients from the long-term interviews expressed that they had still not fully recovered from treatment (mainly due to fatigue-related symptoms), but accepted their current state of health and were grateful for the opportunity to receive TIL therapy (see Table 3).

2.3 Waiting time
Patients and partners reported mixed experiences with the waiting times between screening for TIL eligibility and surgical resection of the tumor material and during the TIL manufacturing process. While most patients and partners appreciated these time intervals and used them for leisure activities or to work on their physical and mental fitness, others found them stressful ("a ticking time bomb"), especially when patients had to wait for their metastasis to be of sufficient size for the surgical resection of the tumor material (see Table 3).

2.4 Juggling between needs
Nearly all partners found managing their daily responsibilities (work, family, and caregiving for their sick spouse/partner) as one of the most significant challenges during TIL therapy. This was especially true for partners with young children, for those who continued to work or for those who had caregiving responsibilities for other family members. However, these additional responsibilities (next to caregiving) were also described as a coping method and helped to maintain their own lives during the treatment course. Finally, some partners appreciated the stricter visitor regulations installed during the COVID-19 pandemic, as it clarified who and when people could visit during hospitalization (see Table 3).

3. Theme 3: Emotional support
Patients and partners described this theme as the emotional support they received when talking to family, friends, and the healthcare team (nurses, nurse specialists, physicians, psychologists, physical therapists, and catering staff during hospitalization). The following two subthemes were identified within this theme (see Table 4).

3.1 Support from social circle
All patients and most partners described support from family and friends as being important for their emotional well-being during TIL therapy. Furthermore, nearly half of the patients and partners expressed the will to get (or were already) in contact with fellow patients who received TIL therapy and their partners. The other half reported not wanting this contact as it could negatively affect their expectations and experiences with TIL therapy (see Table 4).

3.2 Support from healthcare system
Most patients and partners expressed their appreciation for the emotional support they received from the healthcare team, such as informal talks and active listening during stressful situations. These moments fostered a sense of connection and safety during treatment. Partners were especially surprised to receive
such supportive actions as they reported that it was uncommon for them to receive this type of support from the healthcare team (see Table 4).

4. Warwick’s patients’ experience framework

We have provided a list of practical recommendations matching identified themes with the seven domains of the WaPEF (e.g. the subtheme “decision making” was matched with the WaPEF domain “patient as an active participant”) that have the potential to improve the quality of care provided during the different phases of TIL therapy for future patients and their partners (Table 5).

4.1 Pre-treatment phase

Clinicians involved in TIL therapy should be aware that patients and partners often have high expectations for the efficacy of TIL therapy and use the internet to gather information to assess the treatment’s risks and benefits. Providing visual aids and repeating salient information about TIL therapy could help to set a more realistic expectation.

4.2 Treatment phase

Clinicians should emphasize and repeat providing information about the challenging components and unlikely modifications that can occur during TIL therapy, such as the possibility of a second surgery after unsuccessful TIL outgrowth and the occurrence of multiple severe toxicities due to IL-2. Patients and partners often do not expect these events to happen, and reported that the ‘unexpected’ element of these events exacerbated the negative impact they had on them mentally. Furthermore, Clinicians should offer additional supportive care for patients and partners with young children or with caregiving responsibilities for other family members as they experience more challenges during TIL therapy. Finally, healthcare teams may consider implementing a restricted visitation policy during hospitalization to provide a structure for partners regarding who can visit and when to visit.

4.3 Post-treatment phase

When offering additional supportive care (e.g., physiotherapy and psychotherapy), clinicians should consider that patients and partners strongly prefer to receive this help near their homes. Furthermore, centers providing TIL therapy should consider a platform that allows patients and partners to communicate with other patients and partners who have received TIL therapy.

Discussion

Clinical data support the use of TIL therapy for the treatment of advanced melanoma, and it is expected that more patients will benefit from this treatment in the near future. This qualitative study is the first to describe the experiences of patients with advanced melanoma and their partners with TIL therapy, and the results suggest that their challenges, needs, and preferences differ from those during ICI treatment.
Patients and partners’ experiences with TIL therapy were divided. While patients and partners frequently described the treatment period as intense, they also expressed gratitude for having received TIL therapy and reported a fast recovery time (2-4 weeks) for nearly all treatment-related toxicities. Fatigue was the only persisting toxicity reported in our cohort, which is likely chemotherapy-related [10]. While the ongoing quality of life analysis can better assess the long-term toxicities of patients after TIL therapy, the variety of long-term toxicities may be smaller than that after ICI treatment [45-47].

Patients with advanced melanoma and their partners have identified several opportunities to improve the quality of care they receive during treatment. Transparent communication about the expectations of treatment, visual aids explaining the treatment’s mechanism of action, and clear information about potential setbacks that can occur during treatment were reported to enhance satisfaction with treatment. Furthermore, clinicians should encourage partners of patients to set boundaries to external demands during the hospitalization period, as their stress levels are substantially elevated during that time. Lastly, hospitals that (plan to) implement TIL therapy should provide patients and partners with a platform that facilitates contact with patients who previously received TIL and their partners. Multiple patients reported that such interactions improved their understanding of the treatment process and reduced their stress level.

A limitation of this study was that all interviewed patients participated in a clinical phase 3 trial [10]. As clinical trial patients are generally subjected to rigorous selection, the average ‘trial’ patient does not fully represent the average ‘real-world’ patient [48]. Therefore, future research should investigate the degree to which our findings are compatible with those of real-world settings. Furthermore, nearly all the interviewed patients did not know if they had a positive clinical response (9/13) or knew they had a positive clinical response (3/13). The hope for a positive clinical response (or having one) may have created an expectation or positivity bias while reporting their experiences with TIL therapy [49, 50]. The strengths of this study include interviewing patients and partners at different time points after treatment, interviewing patients and partners separately to enhance the free expression of opinions, and a high response rate.

In conclusion, the main findings of this study reflect that patients with advanced melanoma and their partners experience TIL therapy as an intense treatment but with a fast recovery. With TIL therapy becoming a viable treatment option for patients with advanced melanoma, the results of this study provide an evidence-based, patient-centered set of practical recommendations that can enhance the quality of care for hospitals that (are considering to) provide TIL therapy.

Declarations

ACKNOWLEDGMENTS
We thank the patients and partners for participating in this study and Inge Eekhout for assisting in transcribing the interviews.

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DISCLOSURE OF CONFLICTS OF INTERESTS


References

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33. V. Braun and V. Clarke, "Conceptual and design thinking for thematic analysis," *Qualitative Psychology*, vol. 9, no. 1, p. 3, 2022.


Tables

Table 1. Characteristics of the interviewees
<table>
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<tr>
<th>Interview ID</th>
<th>Age</th>
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Table 2. Expectations and experiences of treatment
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<th>Quotes</th>
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<tbody>
<tr>
<td>1. 1.1 The provision and quality of the received information about TIL therapy</td>
<td>Information and communication</td>
<td>&quot;I watched the video [about TIL therapy] on the hospital's website and thought it was very clear and open. It really was for me like 'wow', that they did not think of that before because it makes so much sense.&quot; Patient 08, F, 66 years, short-term interview</td>
</tr>
<tr>
<td>1. 1.2 The various decisions regarding their treatment</td>
<td>Decision-making</td>
<td>&quot;The patient information booklet was very clear. We read it slowly and had very few questions, I must say. Well, after that, I think a week later, we were back at the doctor and discussed it, and it was clear what awaited us.&quot; Partner 01, 29 years, short-term interview</td>
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<tr>
<td>1. 1.3 The impact of treatment-related toxicities on functioning and well-being</td>
<td>Treatment burden</td>
<td>1. &quot;During this [receiving IL-2], I thought, you couldn't do this to people of 70 plus. This is torture.&quot; Patient 04, F, 49 years, long-term interview</td>
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<tr>
<td>1. 1.4 The emotional impact of uncertainties and unexpected occurrences during TIL therapy</td>
<td>Uncertainties</td>
<td>&quot;Then the doctor came, and they said we are not going to do it [continue IL-2 treatment], or you will be in intensive care. I got myself all pumped up, and I was really annoyed [not to continue treatment].&quot; Patient 08, F, 66 years, short-term interview</td>
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<td>1. 1.4 The emotional impact of uncertainties and unexpected occurrences during TIL therapy</td>
<td>Uncertainties</td>
<td>&quot;It would be helpful for people to know that at first, uh, that yes, there is a possibility that several operations may be needed to culture the cells. That, we actually missed that [information] a bit. We never expected that [it would fail]. Yes, that gave uh, then that also gives us&quot;</td>
</tr>
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</table>
uh, again, a particular feeling of disappointment."
Partner 04, M, 57 years, short-term interview

<table>
<thead>
<tr>
<th>1.1.5 The impact of TIL therapy as a new treatment option</th>
<th>Novelty of treatment</th>
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</table>
| "You can see it happening [the return of the TIL cells]. It is something very special to receive your own cells. It is an emotional moment."
Patient 06, M, 65 years, short-term interview |
| "I thought it was very interesting to see how it became, a bit official. I took a picture of that bag that contained those [TIL] cells."
Partner 01, F, 29 years, short-term interview |

IL-2 = interleukin-2, TIL = tumor-infiltrating lymphocytes

Table 3. Self-care
<table>
<thead>
<tr>
<th>Description of the subtheme's content</th>
<th>Subtheme</th>
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</table>
| 1. Strategies that patients and partners used to diminish negative emotions during TIL therapy | Coping | "I made a daily plan for myself. (..). It just felt really good. (..). Because when you take care of yourself, the mental aspect gets better, even if you feel physically worse. I also planned to go on the home trainer at specific times. This helps you to go [to move]. I did not want to just stupidly stare straight ahead, waiting, and let things happen." Patient 03, M, 61 years, Short-term interview  
"And I did have those expectations or [formed by] people you know that you already know who had chemo. It makes you think: oh, will it be a bit like this? Or just completely like: well, we'll see. (..) does he or doesn't he get sick? And if he is not in pain, then he is not in pain. And yes, just assume that he will be sick of it. Then it can only be better than expected." Partner 05, F, 55 years, short term interview |
| 2.2 Perceptions of recovery and rehabilitation after TIL therapy | Recovery and rehabilitation | "I have already accepted that I cannot make big steps [in improving my condition]. I just should not do that [to expect a faster improvement in condition] because I will reencounter myself. [I take] tiny steps, and then you notice, well, there is some improvement. (..) What you could normally build up much easier takes ten times more effort now." Patient 01, M, 66 long-term interview  
"She needed a few weeks to recover physically and work on her fitness, but she’s already doing some things outside the house. She will never be at her old level [of fitness], but we are pretty happy with this." Partner 04, M, 50 years, long-term interview |
| 2.3 Experiences of time spent waiting during the course of TIL therapy | Waiting time | "It’s just because you have cancer in your body and you want it to be removed as soon as possible. This [waiting] takes too long for everybody. Just one day of waiting is too much." Patient 02, F, 66 years, short-term interview  
"I made a list [of activities] of what I still wanted to do. Not that he would be gone, but you know, his energy goes away, and when can you do it again? We did all that properly. He didn’t think it was necessary, but I did. (..) They were small things, but I really enjoyed doing that. I
could also completely let it go [the stress regarding the waiting time], like, we have to wait now, and we can do nothing about it."
Partner 01, F, 29 years, short-term interview

1. *The experience of partners balancing the demands of their caregiver responsibilities and other societal demands*  

<table>
<thead>
<tr>
<th>Juggling between needs</th>
<th>&quot;I also worked for 32 hours, so time passed fast, which helped me cope. (..) Getting time off work to be a part of everything was also difficult.&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Partner 02, F, 70 years, long-term interview</td>
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<tr>
<td></td>
<td>&quot;I consciously thought about it [staying and sleeping in the hospital’s guesthouse], but then I could not have a break. Then I stay in the atmosphere of that disease [cancer]. There is nothing wrong with that, but I also need a moment for myself from time to time.&quot;</td>
</tr>
<tr>
<td></td>
<td>Partner 08, M, 68 years, short-term interview</td>
</tr>
</tbody>
</table>

*TIL = tumor-infiltrating lymphocytes*

**Table 4. Emotional support**
<table>
<thead>
<tr>
<th>Subtheme</th>
<th>Quotes</th>
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</thead>
</table>
| **1. Received support from social circle during TIL therapy** | Support from social circle | "Every so often, I would go home to do the laundry or other things. Then I would see the neighbors again or my children. Then I could face it again."
Partner 08, M, 68 years, short-term interview
| | Support from the healthcare system | "Such a person [a patient that previously received TIL therapy] knows what will happen. He knows what you’re going through. Even though everyone goes through it [treatment] differently. (...) When you have questions, you can also ask them more easily."
Patient 05, M, 58 years, short-term interview
| | Support from healthcare system | "I really found it to be a very nice [treatment] team. In that team, I was the wheel that had to turn, and the people around my bed were dancing and doing things for me. We were all parts of the chain that kept me moving. I think, seeing it that way was very rewarding and enabled me to keep a positive attitude."
Patient 03, M, 61 years, short-term interview
| | Support from healthcare system | "It [going to the NCI*] feels just like coming home. You meet the people who cared for you, and they are acquaintances. You interact with people so much that it is almost like family. That's how it felt. It's nice to have been treated there, and we felt we were in excellent hands."
Partner 08, M, 68 years, short-term interview

*NCI = Netherlands Cancer Institute, TIL = tumor-infiltrating lymphocytes*

Table 5. Recommendations for future care in...
<table>
<thead>
<tr>
<th>WaPEF</th>
<th>Evaluation based on Theme Analysis</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-treatment period</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Information &amp; communication</td>
<td>Information and communication</td>
<td>Visual material (videos) and repetition of important information about treatment are highly appreciated by patients and partners, and could help improve their understanding of the implications of treatment.</td>
</tr>
<tr>
<td><strong>Decision making</strong></td>
<td>Patients as active participant</td>
<td>Patients and partners see TIL treatment as their primary option to prolong survival and nearly all expect TIL therapy to work.</td>
</tr>
<tr>
<td>Lived experience/information</td>
<td>Novelty of treatment</td>
<td>The novelty of TIL therapy influences the perceptions of patients and partners about the risks and benefits of TIL therapy.</td>
</tr>
<tr>
<td>Responsiveness of services— an individualized approach</td>
<td>Waiting time</td>
<td>Patients and partners either appreciate the waiting time during their treatment or experience it as stressful.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients and partners frequently expressed using the waiting time to plan social activities or to mentally and physically prepare for treatment.</td>
</tr>
<tr>
<td><strong>Treatment period</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lived experience</td>
<td>Treatment burden</td>
<td>Patients and partners often underestimated the severity of IL-2 and chemotherapy-related toxicities.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients and partners often reported</td>
</tr>
</tbody>
</table>

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experiencing mental challenges in relation to isolation measures set in place during the hospitalization period, which were exacerbated due to the COVID-19 pandemic.

### Support

<table>
<thead>
<tr>
<th><strong>Support from healthcare system</strong></th>
<th>Nearly all patients and partners reported that instances in which they received personalized attention from their healthcare professionals aided them in coping with TIL therapy.</th>
<th>Appointing a permanent contact healthcare professional during the course of treatment may aid in promoting feelings of familiarity and personalized attention.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Juggling between needs</strong></td>
<td>Partners commonly reported experiencing stress while managing the demands of their family, home, and their own lives during their loved one’s hospitalization.</td>
<td>Encourage partners to set boundaries for external demands during hospitalization. In addition, setting a restricted visitation policy can help partners decide who and when to visit during hospitalization.</td>
</tr>
<tr>
<td><strong>Coping</strong></td>
<td>Nearly all patients and partners mentioned that their trust in the medical team improved their ability to cope with the therapy.</td>
<td>Provide honest and transparent communication about treatment prospects and a fixed medical contact person during the treatment trajectory to enhance the coping capabilities of patients during TIL therapy.</td>
</tr>
<tr>
<td><strong>Uncertainty in the treatment trajectory</strong></td>
<td>A group of patients and partners who experienced unexpected treatment-related events during TIL therapy (TIL production failure and early termination of IL-2 administration) did not expect this to occur during treatment.</td>
<td>Frequent repetition to patients and partners regarding uncertain aspects of TIL therapy can diminish the adverse effects of these events on patients and partners.</td>
</tr>
<tr>
<td><strong>Recovery and</strong></td>
<td>Patients and partners with...</td>
<td>Emphasize providing...</td>
</tr>
</tbody>
</table>

**Support from healthcare system**

Nearly all patients and partners reported that instances in which they received personalized attention from their healthcare professionals aided them in coping with TIL therapy.

**Juggling between needs**

Partners commonly reported experiencing stress while managing the demands of their family, home, and their own lives during their loved one's hospitalization.

**Coping**

Nearly all patients and partners mentioned that their trust in the medical team improved their ability to cope with the therapy.

**Uncertainty in the treatment trajectory**

A group of patients and partners who experienced unexpected treatment-related events during TIL therapy (TIL production failure and early termination of IL-2 administration) did not expect this to occur during treatment.

**Recovery and**

Patients and partners with...
relationships rehabilitation young children or additional caregiving responsibilities reported experiencing more psychosocial challenges than those with adult children or no other caregiving responsibilities did.

patients and partners with young children or caregiving responsibilities with additional supportive care options.

<table>
<thead>
<tr>
<th>Post-treatment period</th>
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<tr>
<td>Continuity of care and relationships</td>
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</table>

Support

| Support from social circle | A group of patients and partners reported positive psychological benefits due to the social support they received from previous patients and partners who had received TIL therapy. | Provide a platform where patients and partners can contact patients previously treated with TIL and their partners. |

IL-2 = interleukin-2, TIL = tumor infiltrating lymphocytes, WaPEF = Warwick’s patient experience framework

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- interviewscriptpatientsupplementarymaterial.docx