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Experience with solid organ transplantation in patients with previous immunotherapy treatment is still limited but this is changing: The survey-based view of the global transplant society

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Brief communication

Experience with solid organ transplantation in patients with previous immunotherapy treatment is still limited but this is changing: The survey-based view of the global transplant society

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ABSTRACT

Background: The use of immunotherapy for cancer is increasing and is expected to continue growing. The outcomes after solid organ transplantation(SOT) in patients who received immunotherapy before SOT remain unclear. We evaluated the global transplant surgery community's attitude towards and experience with patients who received immunotherapy for malignancy before SOT.

Methods: An online-based survey was sent to North American transplant program directors in December-2020 and members of the International Liver Transplant Society in November-2021 evaluating experiences with and attitudes towards SOT in recipients with previous immunotherapy for cancer.

Results: A total of 119 respondents completed the survey(119/175;completion rate:68%), representing centers from North America, South America, Europe, Asia, and Australia. Seventy-one(62%) respondents would consider SOT in patients with a previous history of immunotherapy for cancer, whereas thirty-nine(34%) were aware of such immunotherapy-treated recipients being transplanted, with an increasing trend over the last few years(2016 [$n = 1$]-2020[$n = 14$]). Institutional clinical management policies in this setting were lacking in most centers($n = 85$[75%]).

Conclusions: The international transplant community is receptive to transplanting transplant candidates previously treated with immunotherapy for cancer, although experience is still limited. In this context, more centers have started to offer SOT to patients with a history of immunotherapy for cancer in recent years. However, support from clear and robust institutional policies in this endeavor is scant. Therefore, there is a high need for consensus guidelines to inform future clinical management, especially as immunotherapy for cancer is likely to continue to increase in the coming years.

1. Introduction

The use of immunotherapy for cancer is increasing and is expected to continue to grow [1,2]. Outcomes after solid organ transplantation (SOT), specifically the risk of post-transplant rejection, remain unclear in patients who have received pre-transplant immunotherapy for cancer indications.

The use of checkpoint inhibitors has been associated with a high allograft rejection rate and mortality in the posttransplant setting [3]. Regarding the pretransplant setting, nivolumab and toripalimab as a

Abbreviations: AST, American Society of Transplantation; CPI, checkpoint inhibitor; ILTS, International Liver Transplant Society; IQR, interquartile range; LT, liver transplantation; SOT, solid organ transplantation; REB, research ethics board; UHN, University Health Network; UNOS, United Network for Organ Sharing; US, United States.

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bridging therapy for hepatocellular carcinoma (HCC) has been associated with fatal hepatic necrosis after liver transplant [4,5]. In contrast, another recent case with pretransplant use of nivolumab had a favorable outcome post-liver transplant without tumor recurrence or graft rejection at a follow-up of one year [2]. In the former case, the last dose of nivolumab was given eight days before transplantation, whereas in the latter case, 15 weeks elapsed before the last dose of nivolumab and the transplant. This suggests that the time between immunotherapy and SOT may be relevant. Nonetheless, no guidelines exist for managing transplant candidates and recipients who have received immunotherapy for cancer indications before listing SOT. Within this context, whether these patients should be offered transplant listing and, if so, what constitutes an optimal duration between immunotherapy and transplant remains to be determined. Moreover, the global transplant community's experience with this clinical scenario is unknown, but is likely limited. Consequently, there is suspected heterogeneity in transplant practice, making understanding what constitutes optimal management of patients who have received previous immunotherapy for cancer and who could subsequently benefit from an SOT challenging.

Therefore, this study aimed to explore the contemporary global transplant surgery community's attitude towards and experience with patients who have received immunotherapy for cancer before SOT.

2. Methods

This study is an international multicenter survey that was distributed to program directors of North American transplant centers through the American Society of Transplantation (AST) Liver and Intestinal Community of Practice (LICOP) Education Subcommittee and members of the International Liver Transplant Society (ILTS). A 31-question survey was developed to query transplant program directors regarding their experience with and attitudes towards SOT in patients with previous cancer immunotherapy (Supplementary material). The information from survey respondents was collected using an online survey distributed through REDCap via email to 113 program directors beginning on 3-December 2020. This was followed by two reminder emails at bimonthly intervals. Additionally, members of the International Liver Transplant Society (ILTS) were contacted in November-2021 in a similar fashion. The study was closed on 20-December 2021. All the respondents' survey responses were identified (Fig. 1).

2.1. Objectives

The primary objective of the survey was to explore the experience of transplant centers globally with respect to SOT following immunotherapy for malignancies. The secondary objectives are as follows:

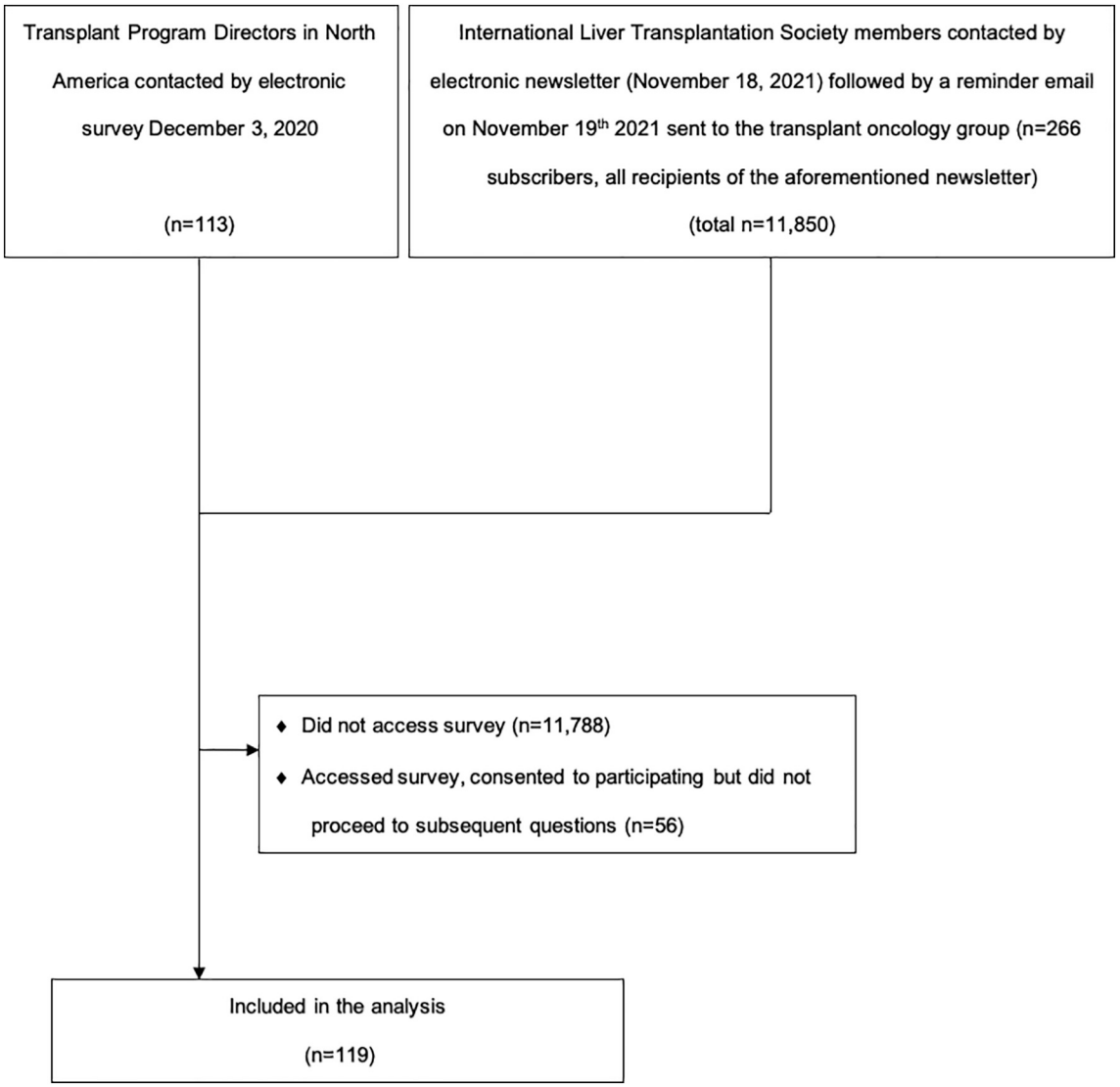

Fig. 1. STROBE-compliant diagram of respondent inclusion and exclusion for the survey.

1. Evaluation of the attitudes of transplant centers globally towards SOT following immunotherapy treatment for malignancies.
2. An assessment of how many individuals may have been denied a transplant because of prior exposure to immunotherapy.
3. A description of the immunotherapy regimens used in patients who underwent transplantation.
4. An estimation of the average post-transplantation outcomes in patients who received prior immunotherapy for malignancy with regard to rejection episodes, graft and patient survival.
5. An evaluation of center interest in performing a subsequent multi-institutional retrospective study to evaluate this clinical situation.

Before distribution, the survey proposal was discussed at the AST LICOP Meeting of 16-March 2020 and approved for distribution to the liver and intestinal directors of programs in the United States. Similarly, the ILTS approved the distribution of the survey on 27-October 2021. Additional approval by the Institutional Research Ethics Board (REB) of the University Health Network (UHN) was obtained (REB#20–5464). All respondents were required to provide informed consent to participate in the survey.

2.1.1. Study population

Qualified physicians hold the role of director of a North American transplant program or member of the ILTS.

2.1.2. Survey

The survey was administered by REDCap, a secure online data capture application supported by the UHN infrastructure. A generic link to the REDCap survey was emailed to the transplant center programme directors and members of the ILTS. The email content explained that the recipients were invited to participate in the study. The exact content language is appended in a document entitled "letter of intent". Consent to participate in the study was obtained prior to proceeding. Consent and survey information are included in the Supplementary Information (Supplementary Material). The survey instrument is provided as supplementary material (Supplementary Material). All the survey respondents were anonymous.

2.2. Statistical analysis

Descriptive data are expressed as the median and interquartile range (IQR). Categorical variables were expressed as numbers and percentages (%). Statistical analyses were performed using R version 4.1.1 (R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org/).

3. Results

3.1.1. Survey responses and program demographics

One hundred and nineteen of the 175 respondents completed the survey for a completion rate of 68% (i.e., 175 respondents accessed the survey and consented to participate, but only 119 responded to subsequent questions) (Fig. 1). Respondents represented centers from North America, South America, Europe, Asia, and Australia. Most represented centers were from the United States ($n = 27$ [30%]), followed by India ($n = 10$ [11%]), and Italy ($n = 7$ [8%]) (Table 1).

3.1.2. Annual transplant volumes

Respondents reported the number of annual transplants performed at their center for various organs as follows: median (IQR), liver 65 (38–111), kidney 75 (30–192), pancreas 2 (0−10), heart 3 (0–24), and lung 0 (0−11) (Table 1).

Table 1
Baseline information.

	Overall (N = 175)
Country	
Afghanistan	1 (1%)
Argentina	3 (3%)
Australia	1 (1%)
Austria	2 (2%)
Azerbaijan	1 (1%)
Belgium	1 (1%)
Brazil	2 (2%)
Chile	1 (1%)
China	1 (1%)
Costa Rica	2 (2%)
Ecuador	1 (1%)
France	1 (1%)
Germany	1 (1%)
India	10 (11%)
Italy	7 (8%)
Japan	2 (2%)
South Korea	1 (1%)
Mexico	2 (2%)
Netherlands	1 (1%)
Norway	1 (1%)
Philippines	1 (1%)
Poland	1 (1%)
Singapore	3 (3%)
Spain	5 (6%)
Switzerland	1 (1%)
Taiwan	1 (1%)
Turkey	4 (4%)
United Kingdom	3 (3%)
United States	27 (30%)
Uruguay	2 (2%)
Annual liver transplant volume	
Median (Q1, Q3)	65 (38, 111)
Annual kidney transplant volume	
Median (Q1, Q3)	75 (30, 192)
Annual pancreas transplant volume	
Median (Q1, Q3)	2 (0,10)
Annual heart transplant volume	
Median (Q1, Q3)	3 (0, 24)
Annual lung transplant volume	
Median (Q1, Q3)	0 (0,11)
1a. Would you consider offering an organ transplant to a patient with a previous history of immunotherapy treatment for cancer?	
N-Missing	61
Maybe/Don't know	29 (25%)
No	14 (12%)
Yes	71 (62%)
2a. Are you aware of any transplant recipients at your institution that were denied listing for transplantation based on prior immunotherapy exposure?	
N-Missing	61
Don't recall	15 (13%)
No	87 (76%)
Yes	12 (11%)
3a. Are you aware of any transplant recipient in your institution that received immunotherapy for cancer before an organ transplant?	
N-Missing	61
Don't recall	9 (8%)
No	66 (58%)
Yes	39 (34%)
4a. Does your transplant program have any policies in place regarding clinical management of these patients?	
N-Missing	62
Don't know	4 (4%)
No	85 (75%)
Yes	24 (21%)
5a. Would you be interested in compiling a case series to study the results of organ transplantation in patients who received immunotherapy before transplantation?	
N-Missing	65
	33 (30%)

(continued on next page)

Table 1 (*continued*)

	Overall (*N* = 175)
Maybe/Don't know/Need to determine feasibility of participation	
No	6 (6%)
Yes	71 (65%)

3.1.3. Attitudes and experience

Fourteen (12%) respondents would not consider offering an organ transplant to a patient with a previous history of immunotherapy treatment for cancer whereas twenty-nine (25%) responded maybe/do not know. Seventy-one (62%) respondents considered offering an organ transplant to such a patient (Table 1), and of these, thirty-nine (55%) considered an acceptable time frame between the treatment and transplant as 4–12 months (Table 2).

Twelve (11%) respondents were aware of transplant recipients at their institution who were denied listing for transplantation based on prior immunotherapy exposure (Table 1). Of these, seven (58%) recalled 1–2 patients, four (33%) recalled 3–5 patients, and one (8%) recalled more than 5 patients denied listing for transplantation (Table 2). Thirty-nine (34%) respondents were aware of transplant recipients in their institution who received immunotherapy for cancer before an SOT, whereas 66 (58%) did not (Table 1). Of the respondents who were aware of transplant recipients, twenty-six (67%) were aware of 1–2 patients, five (13%) of 3–5 patients and eight (21%) of >5 patients. There was a progressively increasing trend in the number of patients respondents were aware of having been transplanted with prior immunotherapy receipt for cancer over time (before 2016, $n = 2$ [5%], 2016 $n = 1$ [3%], 2017 n = 1 [3%], 2018 $n = 9$ [24%], 2019 $n = 10$ [26%], and 2020 $n = 14$ [37%]) (Table 2).

3.1.4. Policies

Twenty-four (21%) respondents reported that their transplant program had policies regarding the clinical management of these patients, whereas eighty-five (75%) did not (Table 1). Of the twenty-four with policies in place, 20 (83%) reported that their institution required a certain time period between the last dose of immunotherapy and SOT. Thirteen (54%) respondents reported required <6 months, two (8%) 6–12 months, three (13%) 12–24 months, and two (8%) required >24 months (Table 2).

3.1.5. Pre-transplant immunotherapy cancer treatment in patients who then underwent SOT

Immune checkpoint inhibitors were the most frequently used immunotherapy ($n = 29$ [76%]). The duration of immunotherapy was <6 months ($n = 11$ [29%]), 6–12 months (n = 11 [29%]), 12–24 months ($n = 4$ [11%]), >24 months (n = 1 [3%]), and do not know/do not recall (n = 11 [29%]) (Table 2). The immunotherapy treatment regimens were single-dose ($n = 3$ [8%]), multiple-dose ($n = 27$ [71%]), full regimen (n = 3 [8%]), and do not know/do not recall ($n = 5$ [13%]). The approximate time periods between the last dose of immunotherapy and transplant were < 6 months ($n = 20$ [53%]), 6–12 months ($n = 13$ [34%]), 12–24 months (n = 1 [3%]), >24 months (n = 3 [8%]), and do not know/do not recall (n = 1 [3%]) (Table 2).

3.1.6. Post-transplant

3.1.6.1. Rejection. Of the respondents who were aware of transplant recipients with previous immunotherapy receipt for cancer at their institution, ten (26%) reported these recipients experiencing any episodes of acute rejection (Table 2). Twenty-four (63%) responded no, four (11%) did not recall, and there was one missing response. In patients who experienced rejection, the approximate period of rejection was <1 month ($n = 7$ [70%]), 1–3 months (n = 1 [10%]), >3 months (n

Table 2
Immunotherapy for cancer before transplantation.

Time-frame between treatment and transplant – If "yes" to 1a. Would you consider offering an organ transplant to a patient with a previous history of immunotherapy treatment for cancer?	Overall (*N* = 71)
1b. What would you consider an acceptable time-frame between the treatment and transplant?	
<4 months	17 (24%)
4–12 months	39 (55%)
12–24 months	7 (10%)
>24 months	8 (11%)
Number of denied listings - If "yes" to 2a. Are you aware of any transplant recipients at your institution that were denied listing for transplantation based on prior immunotherapy exposure?	Overall (*N* = 12)
2b. How many such patients are you aware of at your institution?	
1–2	7 (58%)
3–5	4 (33%)
>5	1 (8%)
Transplant recipients with prior immunotherapy – If "yes" to 3a. Are you aware of any transplant recipient in your institution that received immunotherapy for cancer before an organ transplant?	Overall (*N* = 39)
3b. How many patients are you aware of at your institution received immunotherapy for cancer before an organ transplant?	
1–2	26 (67%)
3–5	5 (13%)
>5	8 (21%)
3c. Approximately when did you transplant your first patient who had received prior immunotherapy for cancer?	
Missing	1
Earlier	2 (5%)
2016	1 (3%)
2017	1 (3%)
2018	9 (24%)
2019	10 (26%)
2020	14 (37%)
3d. In the patients that received an organ transplant after immunotherapy receipt for cancer - what was the immunotherapy treatment for?	
Missing	1
Don't recall	1 (3%)
Liver cancer	30 (79%)
Hematological	3 (8%)
Melanoma	1 (3%)
Other	3 (8%)
3e. What type of immunotherapy was used	
Missing	1
Don't recall	2 (5%)
Immune checkpoint inhibitor	29 (76%)
Immune system modulator	2 (5%)
Monoclonal antibody	4 (11%)
T-cell transfer therapy	1 (3%)
3f. For how many months was the immunotherapy used?	
Missing	1
Don't know	11 (29%)
<6 months	11 (29%)
6–12 months	11 (29%)
12–24 months	4 (11%)
>24 months	1 (3%)
3g. Were these treatments a single dose, multiple doses, or full regimen?	
Missing	1
Don't know	5 (13%)
Full regimen	3 (8%)
Single	3 (8%)
Multiple	27 (71%)
3h. What was the approximate time period between the last dose of immunotherapy and transplant?	
Missing	1
Don't know	1 (3%)
<6 months	20 (53%)
6–12 months	13 (34%)
12–24 months	1 (3%)
>24 months	3 (8%)
3i. Did any of these patients experience any episodes of acute rejection after transplant?	
Missing	1
Don't recall	4 (11%)

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Table 2 (*continued*)

Time-frame between treatment and transplant – If "yes" to 1a. Would you consider offering an organ transplant to a patient with a previous history of immunotherapy treatment for cancer?	Overall (*N* = 71)
No	24 (63%)
Yes	10 (26%)
3j. Did any of the transplanted patients die (for any reason)?	
Missing	1
Don't recall/Don't know	4 (11%)
No	27 (71%)
Yes	7 (18%)
3k. Graft survival: In your opinion and experience, how do the outcomes of these patients compare to the average transplant patient?	
Missing	1
Have not followed them for enough time to make this determination	14 (37%)
Better	1 (3%)
Same	21 (55%)
Worse	2 (5%)
3l. Patient survival: In your opinion and experience, how do the outcomes of these patients compare to the average transplant patient?	
Missing	1
Have not followed them for enough time to make this determination	16 (42%)
Better	1 (3%)
Same	18 (47%)
Worse	3 (8%)
Time-period between immunotherapy and transplant - If "yes" to 4a. Does your transplant program have any policies in place regarding clinical management of these patients	Overall (*N* = 24)
4b. Do you require a certain time period between last dose of immunotherapy and transplant?	
No	4 (17%)
Yes, <6 months	13 (54%)
Yes, 6–12 months	2 (8%)
Yes, 12–24 months	3 (13%)
Yes, >24 months	2 (8%)
Acute rejection after transplant - If "yes" to 3i. Did any of these patients experience any episodes of acute rejection after transplant?	Overall (N = 10)
3i.S1 What was the approximate period of rejection if there was a rejection?	
Don't know/Don't recall	1 (10%)
<1 month	7 (70%)
1–3 months	1 (10%)
>3 months	1 (10%)
3i.S2 Estimate how many of these patients lost their grafts/died because of severe rejection?	
Don't know/Don't recall	3 (30%)
1–3	6 (60%)
3–5	1 (10%)
Contributing cause of death - If "yes" to 3j. Did any of the transplanted patients die (for any reason)?	Overall (N = 7)
3j. S1 What were the contributing causes of death?	
Malignancy	3 (43%)
Rejection	4 (57%)

= 1 [10%]), and did not know or do not recall (n = 1 [10%]) (Table 2). On estimation of how many of these patients lost their grafts or died because of severe rejection, six (60%) responded 1–3, one (10%) 3–5, none (0%) >5, and three (30%) did not know or did not recall (Table 2). There was no statistically significant difference between rejection occurrence and the different time durations between the last dose of immunotherapy and transplant (p = 0.35). In comparison with an average transplant patient, respondents felt that the graft survival in these patients was the same (n = 21 [55%]), worse (n = 2 [5%]), or had not followed them for enough time to make the determination (n = 14 [37%]) (Table 2).

3.1.6.2. Death. The respondents were aware of such patients dying (for any reason) in seven (18%), whereas twenty-seven (71%) reported no, and four (11%) could not recall or did not know (Table 2). The contributing causes of death in patients who died included malignancy (n = 3 [43%]) and rejection (n = 4 [57%]) (Table 2). In comparison with an average transplant patient, respondents felt that the patient survival in these patients was the same (n = 18 [47%]), worse (n = 3 [8%]), or had not followed them for enough time to make the determination (n = 16 [42%]) (Table 2).

4. Discussion

This study provides preliminary insights into the attitudes towards and experiences with SOT after immunotherapy for cancer. Over half of the respondents (62%) considered offering an organ transplant to a patient with a previous history of immunotherapy for cancer. More than one-third (34%) were aware of recipients receiving immunotherapy for cancer before organ transplantation. Moreover, some patients are being denied listing transplantation based on prior immunotherapy exposure. Over the last few years, there has been an increasing trend in the number of transplant recipients who were aware of who received immunotherapy for cancer before their transplant. Lastly, the majority (75%) of respondents reported an absence of institutional policies for the clinical management of these patients. Taken together, this study highlights that this represents a clinical scenario for which outcomes should be further clarified, and that consensus guidelines are necessary to inform future clinical management in these patients, especially as immunotherapy for cancer is likely to increase in the coming years.

Most of the immunotherapy used in cancer has been for advanced or metastatic disease [6]. However, there is likely to be an increased use in the neoadjuvant and curative-intent setting in the future, with ongoing studies in non-small cell lung cancer, bladder cancer, hepatocellular carcinoma (HCC), melanoma, head and neck squamous cell cancer, breast cancer, esophageal cancer, gastroesophageal cancer, pancreatic cancer, colorectal cancer, and sarcoma. Cancer immunotherapy has been studied in the post-transplant setting, where the indications have been mostly for metastatic melanoma or HCC [6,7]. In this setting, Miao et al. found that the use of mTOR and calcineurin inhibitors may help to reduce the occurrence of host-versus-graft response, one of the feared complications of immunotherapy in both the pre- and post-transplant settings [5,7]. Such information may be helpful for the development of guidelines for patients who have received cancer immunotherapy in the pre-transplant setting.

The optimal timeframe between cancer immunotherapy exposure and solid organ transplantation remains to be clarified and may be in part guided by the half-life of the agent used. Within this context, the target occupancy of PD-1 persists significantly longer than the half-life of the drug. In the case of nivolumab, PD-1 saturation was found on circulating lymphocytes for up to 100 days after a single 10-ml/kg dose, despite the half-life at that dose being 27-days [8–10]. Rejection represents a major concern in the transplant setting after previous immunotherapy and warrants further investigation. In the context of our survey, the 7 respondents who reported any death in their transplanted patients, rejection was the contributing cause in 4 (57%). Nordness et al. described a case of fatal hepatic necrosis when the timeframe between nivolumab cessation and the transplant was eight days [4]. In contrast, Schwacha-Eipper et al. reported no organ rejection when the timeframe was six weeks [2]. Schnickel et al. recently reported their single-center experience with pre-liver transplant use of nivolumab in five patients [11]. None of their patients who underwent liver transplant beyond three months from the last dose of nivolumab experienced biopsy-proven acute cellular rejection [11].

Liver cancer was the most common indication for immunotherapy receipt among the respondents who reported experience with organ transplant after immunotherapy receipt for cancer, and the most common type of immunotherapy used was an immune checkpoint inhibitor. Tabrizian et al. recently reported the largest single-institution series (nine patients) of patients who received anti-programmed cell death protein 1/programmed death ligand 1 (PD-1/PD-L1) checkpoint

inhibitor for HCC before liver transplant between 2017 and 2020 [12]. In this series, 89% ($n = 8$) received their last dose of nivolumab within four weeks of transplantation [12]. The group reported no allograft rejections, graft losses, tumor recurrences, or post-transplant deaths at a median follow-up of 16 months (range 8–23) [12]. After noting that liver transplantation can be performed safely if at least three months have elapsed since final checkpoint inhibitor treatment, Schnickel et al. have altered their peritransplant protocol based on their recent case series to include a 3-month waiting period before transplant [11]. Moreover, they also screen for donor-specific antibodies and thymoglobulin induction after having observed high levels of DSA that persisted despite plasmapheresis and rituximab treatment in one of their early patients [11]. The reason for this is speculated to be due to the PD-1 expression of B cells, resulting in increased antibody production after checkpoint inhibitor therapy [13]. Though these results can be interpreted with cautious optimism, it offers early insight that transplantation may be feasible in select circumstances after previous immunotherapy receipt for cancer.

4.1. Limitations

This study is limited by its survey design, subject to recall bias, and lack of detailed clinical information, including immunosuppression protocols used. This study aimed to offer insights into attitudes and whether institutional clinical guidelines exist and initiate a discussion on the topic of cancer immunotherapy before SOT. As such, the study cannot reliably evaluate post-transplant outcomes or report the specifics of cancer immunotherapy regimens used, or verify the accuracy of the impressions regarding patient outcomes. This will be assessed through a retrospective multicenter case series, which is currently ongoing. Moreover, nuances exist in the clinical management of various immunotherapy-treated cancer patients such as those with hematologic malignancies and primary hepatic malignancies, which will likely need to be considered separately in future consensus guidelines. In addition, there is potential for non-response bias. In addition, the surveys were distributed mainly through members of liver transplant communities. Although there is often overlap in the transplanted abdominal solid organs (liver, kidney, pancreas, and intestine), there is a limited representation of non-abdominal organs, such as the heart and lung transplants. Owing to the aforementioned reasons, there is a potential for overrepresentation of liver transplant recipients in this survey. Nonetheless, cancer immunotherapy used for curative intent is most likely related to the treatment of HCC in the transplant setting, as most other cancer immunotherapy indications have been for advanced or metastatic malignancies. Consequently, the attitudes and experiences reported may not be reflective of all transplant programs and settings globally. Nonetheless, this is the first survey of its kind and offers preliminary insight into attitudes and experiences with SOT after immunotherapy receipt for cancer in an international setting.

5. Conclusion

The information collected provides the first impression of the contemporary global transplant community's experience and approach towards patients receiving immunotherapy before SOT. The international transplant community is receptive towards transplanting transplant candidates who have previously received immunotherapy for cancer, although experience in this setting is still limited. In this context, more centers have started to offer SOT to patients with a history of immunotherapy for cancer in recent years. However, institutional guidelines for this clinical setting are lacking. Given the absence of institutional guidelines for pre-transplantation in the setting of previous cancer immunotherapy, the outcomes remain unclear. Therefore, a future multi-institutional study of outcomes following transplantation in patients previously treated with immunotherapy is ongoing. Clarification of outcomes and risk factors for adverse post-transplant outcomes is necessary to develop clinical practice guidelines and improve patient outcomes, particularly because immunotherapy for cancer is likely to increase in the coming years.

Author contribution

TI: Conception of the project, literature review, data analysis, interpretation of results, and writing of the manuscript.

MC: Conception of project, interpretation of results, write up of the manuscript.

DA: Conception of project, interpretation of results and write up of the manuscript.

GS: Conception of project, interpretation of results, and writing of manuscript.

All authors have given final approval for this manuscript to be submitted to *Transplant Immunology*.

Disclosures

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Category

Short report.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.trim.2022.101637.

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