ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

ORIGINAL RESEARCH

Immune checkpoint blockers in solid organ transplant recipients and cancer: the INNOVATED cohort

J. Remon[1*], E. Auclin[2], L. Zubiri[3], S. Schneider[4], D. Rodriguez-Abreu[5], N. Minatta[6], O. Gautschi[7], F. Aboubakar[8], E. Muñoz-Couselo[9], T. Pierret[10], S. I. Rothschild[11,12], F. Cortiula[13], K. L. Reynolds[3], C. Thibault[2], A. Gavralidis[3,14,15], N. Blais[16], F. Barlesi[1], D. Planchard[1] & B. M. D. Besse[1]

[1]Paris-Saclay University, Department of Cancer Medicine, Gustave Roussy, Villejuif; [2]Department of Cancer Medicine, Hôpital Européen Georges-Pompidou, Paris, France; [3]Massachusetts General Hospital Cancer Center, Division of Hematology/Oncology, Department of Medicine, Massachusetts General Hospital, Boston, USA; [4]Department Pneumology, Hôpital de Bayonne, Bayonne, France; [5]Medical Oncology Department, Complejo Hospitalario Universitario Insular-Materno Infantil de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain; [6]Department of Oncology Hospital Italiano Buenos Aires, Buenos Aires, Argentina; [7]Department of Cancer Medicine, University of Berne and Cantonal Hospital of Lucerne, Lucerne, Switzerland; [8]Department of Pneumology, Cliniques Universitaires Saint Luc, Brussels, Belgium; [9]Department of Oncology, Hospital Vall d'Hebron de Barcelona, VHIO Vall d'Hebron Institute of Oncology, Barcelona, Spain; [10]Department of Pneumology, CHU Grenoble Alpes, Grenoble, France; [11]Medical Oncology Department, University Hospital Basel, Basel; [12]Division Oncology/Hematology, Department of Medicine, Cantonal Hospital Baden, Baden, Switzerland; [13]Department of Oncology, University Hospital of Udine, Udine, Italy; [14]Division of Hematology/Oncology, Department of Medicine, Massachusetts General Hospital, Boston; [15]Salem Hospital, Salem, USA: [16]Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, Canada

Available online 22 April 2024

Background: Patients with solid organ transplant (SOT) and solid tumors are usually excluded from clinical trials testing immune checkpoint blockers (ICB). As transplant rates are increasing, we aimed to evaluate ICB outcomes in this population, with a special focus on lung cancer.

Methods: We conducted a multicenter retrospective cohort study collecting real data of ICB use in patients with SOT and solid tumors. Clinical data and treatment outcomes were assessed by using retrospective medical chart reviews in every participating center. Study endpoints were: overall response rate (ORR), 6-month progression-free survival (PFS), and grade $\geq$3 immune-related adverse events.

Results: From August 2016 to October 2022, 31 patients with SOT (98% kidney) and solid tumors were identified (36.0% lung cancer, 19.4% melanoma, 13.0% genitourinary cancer, 6.5% gastrointestinal cancer). Programmed death-ligand 1 expression was positive in 29% of tumors. Median age was 61 years, 69% were males, and 71% received ICB as first-line treatment. In the whole cohort the ORR was 45.2%, with a 6-month PFS of 56.8%. In the lung cancer cohort, the ORR was 45.5%, with a 6-month PFS of 32.7%, and median overall survival of 4.6 months. The grade 3 immune-related adverse events rate leading to ICB discontinuation was 12.9%. Allograft rejection rate was 25.8%, and risk of rejection was similar regardless of the type of ICB strategy (monotherapy or combination, 28% versus 33%, $P = 1.0$) or response to ICB treatment.

Conclusions: ICB could be considered a feasible option for SOT recipients with some advanced solid malignancies and no alternative therapeutic options. Due to the risk of allograft rejection, multidisciplinary teams should be involved before ICB therapy.

Key words: solid-organ transplant, cancer, immune checkpoint inhibitors, allograft rejection, lung cancer

INTRODUCTION

Solid organ transplant (SOT) improves patient survival and quality of life in those with end-stage organ disease, significantly impacting public health and socioeconomic burden of organ failure.[1,2] Kidney transplants are the most common (62%), followed by liver (23%), heart, and lung (both ~6%).[1,3]

While SOT outcomes have dramatically improved over time, chronic immunosuppressive therapy in SOT patients increases the risk of cancer compared with an age- and sex-matched general population.[4,5] Cancer represents a major adverse outcome in SOT recipients, and is the second leading cause of mortality in these patients.[6]

Immune checkpoint blockers (ICBs) have become the standard treatment of several cancer types, and the

*Correspondence to: Dr Jordi Remon, Paris-Saclay University, Department of Cancer Medicine Gustave Roussy, 114, rue Edouard Vaillant, 94805 Villejuif, France. Tel: +33-(0)1-42-11-42-11

E-mail: JORDI.REMON-MASIP@gustaveroussy.fr (J. Remon).

spectrum of patients with cancer who may benefit from this therapeutic strategy is expanding, as well as the new combinations of ICBs with other agents.[7,8] Most registrational clinical trials, however, have excluded SOT patients due to concerns about ICBs potentially triggering allograft rejection and the possible contribution of immunosuppressive drugs to reducing the antitumor activity of ICBs.[9] Although the number of patients with SOT is increasing over time,[1] data to inform clinicians about the outcome and safety profile of ICBs in this population are limited. Therefore, we initiated the INNOVATED (ImmuNe checkpoint iNhibithors outcome sOlid organ transplant recipients with cancer eVAluated in an inTErnational Database) project, which is a retrospective database collecting real-world data to evaluate the efficacy and toxicity of ICBs in this population. Indeed, we attempt to assess this data in the subgroup of patients enrolled in the INNOVATED project with non-small-cell lung cancer (NSCLC) since no previous data in this subset have been reported.

METHODS

This is a multicentric cohort study that includes adult SOT recipients with a diagnosis of advanced solid cancer and treated with ICB (either in monotherapy or combination according to physician's criteria), from August 2016 to October 2022, regardless of the treatment line. Clinical data and treatment outcomes were collected through retrospective medical chart reviews in each participating center. Institutions from around the world were invited to collaborate via email. The data were collected in a REDcap database, and the last update was carried out in December 2022. The study was approved by the Institutional Review Board of the Gustave Roussy Cancer Center (France). All surviving patients were informed about the data collection.

The following endpoints were assessed: (i) overall response rate (ORR), (ii) disease control rate (DCR), (iii) progression-free survival (PFS), (iv) overall survival (OS), (v) 6- and 12-month PFS and OS, (vi) grade $\geq$3 immune-related adverse events (ir-AEs), and (vii) allograft rejection rate.

All outcome data were assessed by the local investigator. PFS was defined as the time interval between the date of ICB therapy initiation and the date of disease progression or death, whichever occurred first. OS was defined as the time interval between the date of ICB treatment initiation and the date of death. ORR at each center was assessed using RECIST 1.1 criteria.

Descriptive statistics of patients' demographics and clinical characteristics for both allograft type and cancer were reported as frequencies (proportions) for categorical variables and median [interquartile range (IQR)] for continuous variables. PFS and OS were calculated with the Kaplan–Meier method and compared with the log rank test. All analyses were carried out using R (version 3.6). No power analysis was conducted to calculate the sample size, as the aim was descriptive in nature, focusing on estimation rather than hypothesis testing.

RESULTS

Patients' characteristics

The cohort included a total of 31 patients. Table 1 summarizes population characteristics. Median age was 61 years, with 68% being males. The majority of patients had kidney SOT (98%). The identified solid cancer included lung cancer (n = 11 patients, 36%), melanoma (n = 6, 19.4%), genitourinary cancer (n = 4, 13.0%), gastrointestinal cancer (n = 2, 6.5%), and other tumors (n = 8, 26%). Tumors with programmed death-ligand 1 (PD-L1) expression accounted for 26%, while the PD-L1 status remained unknown in 15 cases. The majority of patients (71%) received ICB as first-line treatment, and ICB was prescribed either as monotherapy (81%) or in combination strategies (19%). Baseline characteristics were similar in the lung cancer cohort (N = 11, Table 1), with a higher percentage of patients receiving ICB plus chemotherapy (n = 3, 27%) compared with the whole cohort (n = 3, 9.5%).

The median time from transplant to ICB initiation was 12.3 years (IQR, 7.4-18.2 years) years. One-third of the patients had a previous history of allograft rejection before starting ICB. Immunosuppressant therapy was modified before ICB initiation in 46.7% of patients, with a decrease in 69.2% of cases. Additionally, 37.5% of patients were receiving steroids at baseline (Supplementary Table S1, available at https://doi.org/10.1016/j.esmoop.2024.103004).

In the lung cancer cohort, a previous allograft rejection was reported in 9.1% of cases. Some 60% of patients modified their immunosuppressant therapy, with an increase in 67% of cases, and 45.5% receiving steroids at baseline (Supplementary Table S2, available at https://doi.org/10.1016/j.esmoop.2024.103004). In the study, the dose of steroids was not collected.

Outcome during treatment with immune checkpoint inhibitors

In the whole cohort, the ORR to ICB therapy was 45.2% (N = 14), and the DCR was 58.1% (N = 18), with 13 patients experiencing progression under ICB as the best response. The median duration of treatment was 2.8 months (range:1.5-10.7 months).

After a median follow-up of 30.6 months, the median PFS and OS were 7.2 months [95% confidence interval (CI) 2.4-not reached [NR) and 8.6 months (95% CI 4.6-NR), respectively. The 6-month PFS and OS were 53.8% and 62.7%, respectively (Figure 1), whereas the 12-month PFS and OS were 46.6% and 47.9%, respectively. The PFS according to tumor type is reported in Figure 2.

In the exploratory subgroup analyses, there were no significant differences in PFS and OS based on the tumor type, treatment line, PD-L1 expression, and ICB strategy (Supplementary Table S1, available at https://doi.org/10.1016/j.esmoop.2024.103004).

In the lung cancer cohort, the ORR and DCR were 45.5% and 54.5% (4 partial response, 1 complete response, 1

Table 1. Patients' characteristics.

Characteristic	Whole cohort	Lung cancer subgroup
	N = 31 (%)	*N* = 11 (%)
Median age (years)	61 (57-70)	64.8 (60.5-70)
Female/male	10 (31)/21 (68)	3 (27)/8 (73)
Never smokers	15 (48.4)	2 (18.2)
ECOG PS: 0/1/2	6 (20)/17 (56.7)/7 (23.3)	1 (9.1)/4 (36.4)/6 (54.5)
Allograft kidney/lung	30 (98)/1 (2)	11 (100)/0
Previous rejection	10 (32.3%)	2 (18.2%)
Median time from transplant to cancer diagnosis, years (IQR)	8 (4.2-13)	9 (5.5-13.5)
Cancer type		
Lung	11 (36)	11 (100)
Melanoma	6 (19.4)	—
Genitourinary	4 (13.0)	—
Gastrointestinal	2 (6.5)	—
Other	8 (26)	—
Metastatic sites		
Brain	1 (3.2)	0
Liver	8 (26)	3 (27.3)
Bone	9 (29)	3 (27.3)
Lung	14 (45)	6 (54.5)
PD-L1 expression		
Positive/negative/UK	8 (26)/8 (26)/15 (48)	4 (36)/5 (45)/2 (18)[a]
Line of treatment with ICB		
1st/2nd and beyond	22 (71)/8 (26)	7 (63)/3 (30)
ICB type		
Monotherapy	25 (81)	8 (73)
PD-L1	4 (16)	8 (100)
PD-1	19 (76)	—
Not defined	2 (8)	—
Dual immunotherapy	3 (9.5)	—
ICB + chemotherapy	3 (9.5)	3 (27)

Dual immunotherapy, anti-PD(L)-1 plus anti-CTLA4. ECOG PS, Eastern cooperative oncology group performance status; ICB, immune checkpoint blockers; IQR, interquartile range; PD-1; programmed cell death protein 1; PD-L1, programmed death-ligand 1; UK, unknown.

[a]In the non-small-cell lung cancer (NSCLC) subgroup, out of four tumors with PD-L1 expression (22C3 clone), the rates were: 60%, 30%, and 5% for each of the remaining two other cases, respectively.

stable disease), respectively, and 5 (45%) progressive disease. The median treatment duration was 2.2 months (range: 0.3-3.4 months). After a median follow-up of 33.8 months, the median PFS and OS were 4.0 and 4.6 months, respectively, with a 6-month PFS and OS of 32.7% and 42.2%, respectively (Figure 1).

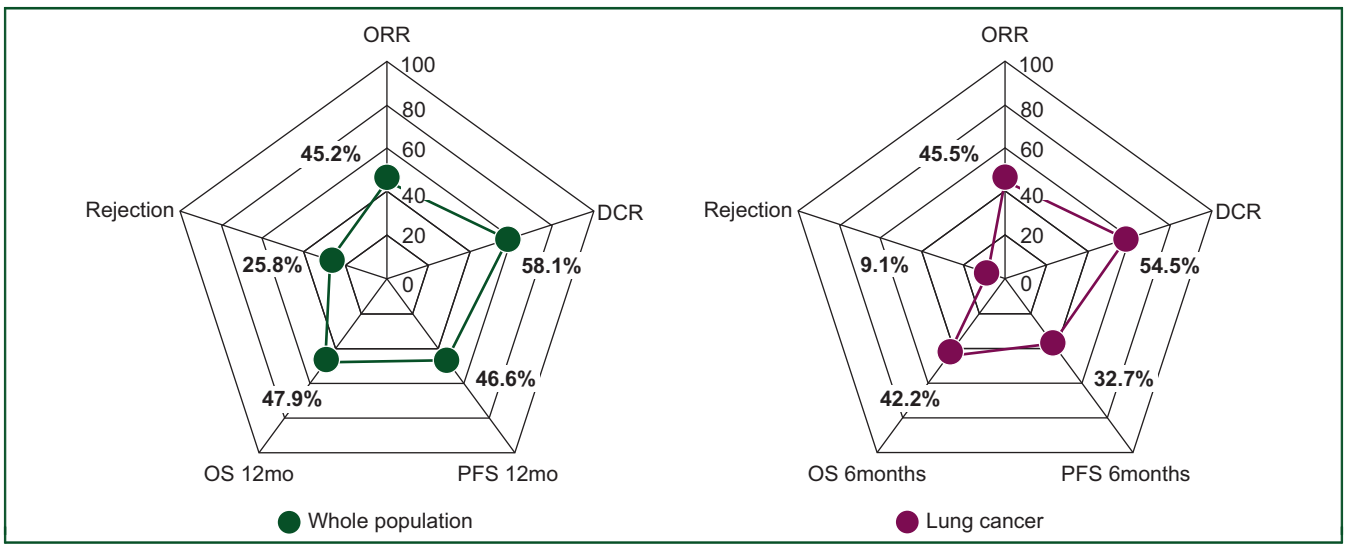

Figure 1. Data outcome (ORR, reported in percentage; DCR, reported in percentage; 6-month PFS, 6-month OS) and rejection rate in the whole cohort and in lung cancer patients.

DCR, disease control rate; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.

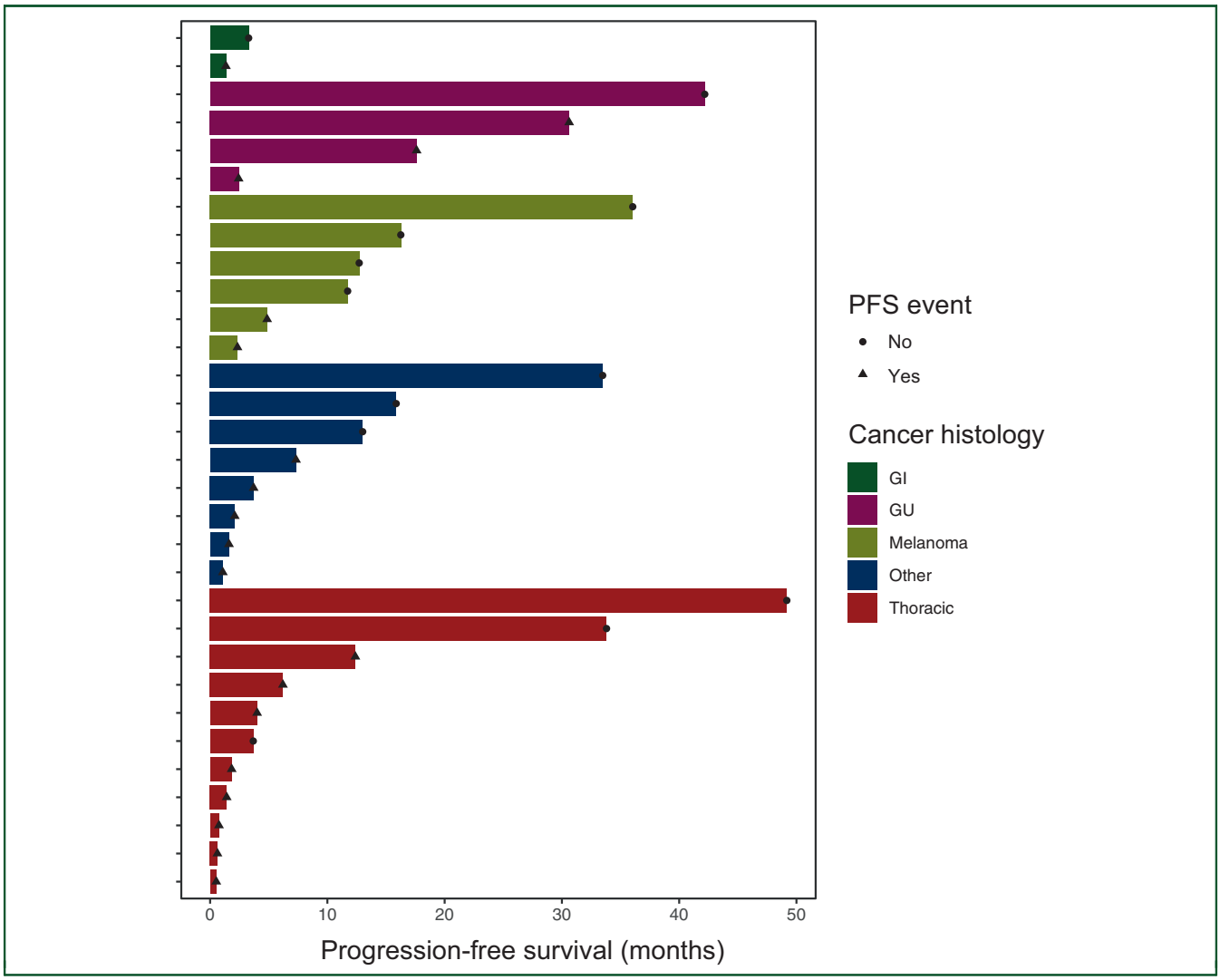

Figure 2. Progression-free survival (PFS) by each patient enrolled according to the tumor type.
GI, gastrointestinal; GU, genitourinary.

Toxicity and allograft rejection

Grade 3 ir-AEs occurred in 12.9% of patients, including colitis ($N = 3$) and pneumonitis ($N = 2$). Irrespective of rejection, ir-AEs led to the discontinuation of ICB in four patients. Disease progression, however, was the primary reason for discontinuation of ICB in 68.4% of patients followed by 21% who discontinued as a consequence of ir-AEs (Table 2).

The occurrence of grade 3 ir-AEs was higher in patients who responded to ICB therapy compared with non-responders (21.4% versus 5.9%, $P = 0.30$), and they occurred in patients without modifications to immunosuppressive therapy. Data about ICB rechallenge were only available in 26 out of 31 patients, and 3 patients out of 26 (11.5%) were rechallenged with an ICB. In two of these rechallenged cases, ICB was resumed after ir-AE resolution, and in the third case, ICB treatment was discontinued after the ir-AE and later resumed due to disease progression. In the lung cancer cohort, 1 out of 10 patients (9.1%) experienced a grade 3 ir-AE (colitis), and no patients were rechallenged in this cohort.

Table 2. Reasons for discontinuation of immune checkpoint blockers.

Reason for ICB stop	Allograft rejection	2 (10.5%)
	Ir-AE (not including rejection)	4 (21.1%)
	Progression	13 (68.4%)
	Missing	13

ICB, immune checkpoint blockers; Ir-AEs, immune-related adverse events.

In the whole cohort, the allograft rejection rate was 25.8% ($N = 8$), with 50% having a biopsy-proven rejection, although PD-L1 expression in the allograft organ was not available. Allograft rejection occurred after a median of 2.04 months (min 0.7-max 7.0 months) following ICB initiation, and 88% resulted in allograft loss. No patients died due to allograft rejection. In the lung cohort, the allograft rejection rate was 9.1% (1/11).

Allograft rejection risk was independent of ICB line ($P = 0.16$), response to ICB ($P = 0.7$), as 37.5% of the patients with allograft rejection had an objective response under ICB

therapy; previous rejection history [5 rejections out of 21 in patients with no history of rejection (23.8%); and 3 rejections out of 10 in patients with a previous history of rejection (30%), $P = 1.0$], ICB as monotherapy or in combination (28% versus 33%, $P = 1.0$) and modification of immunosuppressive therapy [3 out of 16 (19%) in patients without modification, 5 out of 14 (36%) in patients with modification, $P = 0.42$]. Among patients who modified the immunosuppressant strategy, however, zero out of four patients experienced rejection when immunosuppression was increased, while four out of nine had rejection when immunosuppression therapy was decreased, although the difference was not statistically significant ($P = 0.15$).

DISCUSSION

The INNOVATED database supports the consideration of ICB as a feasible option for SOT recipients facing life-threatening advanced malignancies with no other therapeutic oncologic alternatives. This potential benefit is tumor-dependent, however, being less clinically meaningful for patients with NSCLC. ICB therapy was associated with tumor response, and the percentage of grade 3 ir-AEs mirrors the data reported in the general population. Nevertheless, safety of ICB in this population may be limited by the risk of allograft rejection in up to one-third of patients within the first 8 weeks following ICB initiation, leading to allograft loss in almost all cases. Therefore, ICB strategy should be individualized and preceded by a detailed discussion of all associated risks. Despite this risk, patients appear to be willing to test ICB strategies, as even patients with previous history of rejection accepted to be treated with ICB, and only 30% experienced a new rejection.

ICB therapy has transformed the treatment landscape and outcomes for patients with cancer. Registrational phase III trials involving ICB, however, have excluded individuals with SOT. There is an urgent need for outcome and safety data concerning the use of ICB in this population, given that ICB has become a vital component of contemporary oncology treatment protocols, and SOT rates are continually on the rise.[1]

The outcome data from INNOVATED aligns with findings from recent systemic reviews (ORR: 39.6%, PFS: 4.75 months, OS: 9.0 months),[9-11] as well as in institutional experiences,[12] and multicenter studies.[13] Indeed, initial data from prospective studies in patients with kidney SOT and cutaneous cancers treated with ICB reported response rate ranging from 30% to 50% and median PFS from 7.9 months to 22.5 months.[14,15] These findings support ICB as a potential therapeutic strategy for patients with SOT and cancer, potentially leading to improved outcomes compared with patients not receiving ICB.[13] Nevertheless, this benefit is not uniform across all tumor types, raising a challenging question: identifying the specific subgroup of patients with SOT and solid cancer who would benefit most from ICB treatment. Despite exploratory subgroup analyses in INNOVATED not revealing significant differences in survival, even when considering different tumor types, it is crucial to interpret these findings with caution. The limited number of patients in most subgroups and the heterogeneous population included in the database warrant careful consideration of these data.

Lung cancer is reported as the most common cause of cancer death in SOT recipients,[6] and ICB is strategic in the therapeutic strategy of NSCLC.[16] ICB treatment in this population, however, is challenging as there are no specific guidelines. In a recent survey, only some physicians (21%) would consider treating kidney transplanted patients with NSCLC, but only a few (5%-9%) would consider treatment within other organ transplants (heart, lung, liver), and only 14% had prescribed ICB to this population in daily practice.[17] In advanced NSCLC, the ICB as second- or first-line treatment has reported a 6-month PFS ranging from 35% to 50% and a 6-month OS of 70%.[18-21] In INNOVATED, the 6-month PFS in patients with lung cancer aligns with the data reported in the phase III trials. OS data, however, remain limited and probably not clinically meaningful. Several factors could explain this, including the transitory effect of ICB in this population, the poorer prognosis of lung cancer in SOT patients when compared with non-transplant patients with lung cancer,[6,22] and higher increases in immunosuppression therapy and higher doses of steroids at the time of ICB initiation, which could potentially diminish the efficacy of ICB therapy by blunting cancer immune response.[23] While PD-L1 expression stands as a robust predictive biomarker in NSCLC, it is noteworthy that in the INNOVATED database, nearly half of the patients with NSCLC exhibited a PD-L1-negative tumor. Moreover, only one patient had a tumor with PD-L1 expression $\geq$50%.

The potential benefits of ICB therapy in SOT patients with solid tumors must be carefully balanced with safety considerations before the widespread application of this strategy in daily clinical practice. The allograft rejection rate in INNOVATED was substantially lower than previous studies,[9,12,13] suggesting a potential improvement in patient selection and clinical management in recent years. This risk, however, still occurs in up to one-third of patients. Therefore, close monitoring should be carried out, specially within the first 2 months after ICB initiation, with potential adjustments to immunosuppressive treatment and control strategies moving forward. Some authors have reported that a prior history of allograft rejection is associated with a higher risk of rejection after ICB therapy. In contrast, treatment with at least one immunosuppressant drug, other than corticosteroids, a higher number of immunosuppressant agents at the time of ICB initiation and use of anti-PD-L1 treatment (versus anti-programmed cell death protein 1, PD-1) were all associated with a lower risk of graft rejection.[9,13] The evidence remains limited, however, and in INNOVATED, the risk of rejection was independent of prior history of rejection, response to ICB treatment, type of ICB strategy (monotherapy or combination), and immunosuppressant treatment modifications. Notably, no patient with increased immunosuppressant therapy had rejection. Whether adjustments to immunosuppression therapy, ICB strategy, or both, induce organ rejection is challenging to

determine from our study due to the sample size. A recent phase I trial reported that maintaining baseline immunosuppression might not negatively impact ICB efficacy and could potentially reduce the risk of allograft rejection mediated by ICB therapy.[24] Similarly, the use of mammalian target of rapamycin (m-TOR) inhibitors as immunosuppressant therapy seems protective for the allograft rejection.[11,15] Finally, some recent evidence suggests that among patients with kidney SOT and cancer treated with ICB, the increase in donor-derived cell-free DNA levels could be an early potential predictor of allograft rejection.[14]

Our cohort has several limitations. It is exploratory, retrospective, and characterized by a small sample size, which limits our ability to adjust for various confounders in multivariable analyses for both efficacy and the risk of graft rejection. Furthermore, the majority of the patients had kidney transplants, preventing us from extrapolating our findings to other SOT recipients. Additionally, the assessment of ORR was conducted by the investigators, which leaves open the possibility of overestimation of the results. Not all patients with rejection underwent biopsy confirmation, which reduces the accuracy of the diagnosis of rejection. Due to constrains of sample size and heterogeneity, we could not draw definitive conclusions regarding optimal patient selection and immunosuppressive management before and during ICB therapy. Nevertheless, despite these limitations, our cohort provides valuable real-world data that may contribute to the existing evidence. Importantly, several ongoing clinical trials are exploring ICB administration in SOT recipients with cancer (NCT03966209, NCT04721132). These trials hold the potential to further establish the efficacy and safety of ICB treatment in SOT recipients.

In conclusion, ICB could be considered a feasible option for kidney transplant recipients with some life-threatening advanced malignancies and no other therapeutic oncologic alternatives are available, where ICB treatment has been shown to be associated with tumor response. ICB strategy should be individualized on a case-by-case basis, however, and preceded by a detailed discussion of all associated risks. A careful selection and monitoring of patients, and tailoring of immunosuppression therapy in close collaboration with transplant experts are critical.

FUNDING

None declared.

DISCLOSURE

JR reports receipt of grants/research support: Merck Sharp & Dohme (MSD), AstraZeneca (EORTC), Sanofi (EORTC). Honoraria or consultant fees: advisory boards (all institution): AstraZeneca, EDIMARK. Sponsored research (all institution): Merck other support/potential conflict of interest: speaker educationals/webinars: AstraZeneca, Sanofi, Takeda, Roche, Janssen. Other (non-financial): secretary of EORTC-LCG.

EA reports advisory from: Amgen, Sanofi-Genzyme.

LZ reports consultant from Merck, GlaxoSmithKline (GSK).

DRA reports honoraria for lectures from: MSD, Roche, Bristol-Myers Squibb (BMS), Novartis, Takeda, Lilly, AstraZeneca. Travel from: Roche, MSD, Novartis, Sanofi. Advisory board from: MSD, Regeneron, BMS, GSK, Lilly.

JM reports advisory from: Pfizer, Takeda, AstraZeneca, MSD, Merck, Bayer.

SIR reported grants to institution Amgen, AstraZeneca, Bayer, BMS, Boehringer-Ingelheim, Eli Lilly, Janssen, Merck KG, MSD, Novartis, Otsuka, Pfizer, PharmaMar, Roche Pharma, Roche Diagnostics, Takeda. Others: vice president of: Swiss Group for Clinical Cancer Research (SAKK).

FB reports institutional grants from: AbbVie, ACEA, Amgen, AstraZeneca, Bayer, BMS, Boehringer—Ingelheim, Eisai, Eli Lilly Oncology, F. Hoffmann—La Roche Ltd, Genentech, Ipsen, Ignyta, Innate Pharma, Loxo, Novartis, Medimmune, Merck, MSD, Pierre Fabre, Pfizer, Sanofi-Aventis, and Takeda.

DP reports honoraria from: AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Merck, Novartis, Pfizer, prIME Oncology, Peer CME, Roche, Janssen, AbbVie. Consulting/advisory from: AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly, Merck, Novartis, Pfizer, prIME Oncology, Peer CME, Roche, Janssen, AbbVie. Clinical trial as investigator from: AstraZeneca, BMS, Boehringer Ingelheim, Eli Lilly, Merck, Novartis, Pfizer, Roche, Medimmune, Sanofi-Aventis, Taiho Pharma, Novocure, Daiichi Sankyo. Travel/accommodation from: AstraZeneca, Roche, Novartis, Pfizer.

BMDB reports sponsored research at Gustave Roussy Cancer Center from 4D Pharma, AbbVie, Amgen, AstraZeneca, BeiGene, Blueprint Medicines, Celgene, Cergentis, Chugai Pharmaceutical, Da Voltera, Daiichi-Sankyo, Eli Lilly, Ellipse Pharma, Eisai, F-Star, Genmab, Genzyme Corporation, GSK, Hedera Dx, Inivata, Ipsen, Janssen, MSD, Onxeo, OSE Immunotherapeutics, Pfizer, PharmaMar, Roche-Genentech, Sanofi, Socar Research, Tahio Oncology, Takeda, Tolero Pharmaceuticals, Turning Point Therapeutics.

All other authors have declared no conflicts of interest.

REFERENCES

1. Vanholder R, Domínguez-Gil B, Busic M, et al. Organ donation and transplantation: a multi-stakeholder call to action. *Nat Rev Nephrol*. 2021;17:554-568.
2. Chen H-F, Ali H, Marrero WJ, Parikh ND, Lavieri MS, Hutton DW. The magnitude of the health and economic impact of increased organ donation on patients with end-stage renal disease. *MDM Policy Pract*. 2021;6:23814683211063418.
3. Available at https://www.transplant-observatory.org/summary/. Accessed April 1, 2024.
4. Vajdic CM, van Leeuwen MT. Cancer incidence and risk factors after solid organ transplantation. *Int J Cancer*. 2009;125:1747-1754.
5. Engels EA, Pfeiffer RM, Fraumeni JF, et al. Spectrum of cancer risk among US solid organ transplant recipients. *JAMA*. 2011;306:1891-1901.
6. Acuna SA, Fernandes KA, Daly C, et al. Cancer mortality among recipients of solid-organ transplantation in Ontario, Canada. *JAMA Oncol*. 2016;2:463-469.

7. Marcus L, Lemery SJ, Keegan P, Pazdur R. FDA approval summary: pembrolizumab for the treatment of microsatellite instability-high solid tumors. *Clin Cancer Res*. 2019;25:3753-3758.
8. Marcus L, Fashoyin-Aje LA, Donoghue M, et al. FDA approval summary: pembrolizumab for the treatment of tumor mutational burden-high solid tumors. *Clin Cancer Res*. 2021;27:4685-4689.
9. d'Izarny-Gargas T, Durrbach A, Zaidan M. Efficacy and tolerance of immune checkpoint inhibitors in transplant patients with cancer: a systematic review. *Am J Transplant*. 2020;20:2457-2465.
10. Fisher J, Zeitouni N, Fan W, Samie FH. Immune checkpoint inhibitor therapy in solid organ transplant recipients: a patient-centered systematic review. *J Am Acad Dermatol*. 2020;82:1490-1500.
11. Rünger A, Schadendorf D, Hauschild A, Gebhardt C. Immune checkpoint blockade for organ-transplant recipients with cancer: a review. *Eur J Cancer*. 2022;175:326-335.
12. Abdel-Wahab N, Safa H, Abudayyeh A, et al. Checkpoint inhibitor therapy for cancer in solid organ transplantation recipients: an institutional experience and a systematic review of the literature. *J Immunother Cancer*. 2019;7:106.
13. Murakami N, Mulvaney P, Danesh M, et al. A multi-center study on safety and efficacy of immune checkpoint inhibitors in cancer patients with kidney transplant. *Kidney Int*. 2021;100:196-205.
14. Schenk KM, Stein JE, Chandra S, et al. Nivolumab (NIVO) + tacrolimus (TACRO) + prednisone (PRED) +/− ipilimumab (IPI) for kidney transplant recipients (KTR) with advanced cutaneous cancers. *J Clin Oncol*. 2022;40:9507. 9507.
15. Hanna GJ, Dharanesswaran H, Giobbie-Hurder A, et al. Cemiplimab for kidney transplant recipients with advanced cutaneous squamous cell carcinoma. *J Clin Oncol*. 2024;42(9):1021-1030.
16. Hendriks LE, Kerr KM, Menis J, et al. Non-oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2023;34:358-376.
17. Castelo-Branco L, Morgan G, Prelaj A, et al. Challenges and knowledge gaps with immune checkpoint inhibitors monotherapy in the management of patients with non-small-cell lung cancer: a survey of oncologist perceptions. *ESMO Open*. 2023;8:100764.
18. Herbst RS, Giaccone G, de Marinis F, et al. Atezolizumab for first-line treatment of PD-L1-selected patients with NSCLC. *N Engl J Med*. 2020;383:1328-1339.
19. Mok TSK, Wu Y-L, Kudaba I, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial. *Lancet*. 2019;393:1819-1830.
20. Herbst RS, Garon EB, Kim D-W, et al. Five year survival update from KEYNOTE-010: pembrolizumab versus docetaxel for previously treated, programmed death-ligand 1-positive advanced NSCLC. *J Thorac Oncol*. 2021;16:1718-1732.
21. Borghaei H, Gettinger S, Vokes EE, et al. Five-year outcomes from the randomized, phase III trials CheckMate 017 and 057: nivolumab versus docetaxel in previously treated non-small-cell lung cancer. *J Clin Oncol*. 2021;39:723-733.
22. Chen LN, Spivack J, Cao T, et al. Characteristics and outcomes of lung cancer in solid organ transplant recipients. *Lung Cancer*. 2020;146:297-302.
23. Arbour KC, Mezquita L, Long N, et al. Impact of baseline steroids on efficacy of programmed cell death-1 and programmed death-ligand 1 blockade in patients with non-small-cell lung cancer. *J Clin Oncol*. 2018;36:2872-2878.
24. Carroll RP, Boyer M, Gebski V, et al. Immune checkpoint inhibitors in kidney transplant recipients: a multicentre, single-arm, phase 1 study. *Lancet Oncol*. 2022;23:1078-1086.