European Journal of Cancer 96 (2018) 111–114

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Letter to the Editor

Checkpoint blockade after kidney transplantation

Mathieu Lesouhaitier [a], Caroline Dudreuilh [b,c], Mathilde Tamain [d,e], Nada Kanaan [f], Elodie Bailly [g,h], Delphine Legoupil [i], Clement Deltombe [j], Peggy Perrin [k], Guillaume Manson [m], Cécile Vigneau [a,l,1], Roch Houot [m,n,*,1]

[a] CHU Pontchaillou, Division of Nephrology, Rennes, France
[b] Department of Nephrology and Renal Transplantation, Institut Francilien de Recherche en Néphrologie et Transplantation (IFRNT), Groupe Hospitalier Henri-Mondor/Albert-Chenevier, AP-HP (Assistance Publique-Hôpitaux de Paris), Créteil, France
[c] DHU (Département Hospitalo-Universitaire), VIC (Virus-Immunité-Cancer), Université Paris-Est-Créteil (UPEC), IMRB (Institut Mondor de Recherche Biomédicale), Equipe 21, INSERM U 955, Créteil, France
[d] Division of Nephrology, CHU Clermont-Ferrand, Clermont-Ferrand, France
[e] Université Clermont Auvergne, Clermont-Ferrand, France
[f] Division of Nephrology, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium
[g] Department of Nephrology and Kidney Transplantation, University Hospital of Tours, France
[h] Université François Rabelais, Tours, France
[i] Division of Dermatology, Hôpital Morvan, CHU BREST, France
[j] Institute for Transplantation, Urology and Nephrology (ITUN), Nantes University Hospital, Nantes, France
[k] Nephrology-Transplantation Department, University Hospital, Strasbourg, France
[l] Univ Rennes, Inserm, EHESP, Irset (Institut de Recherche en Santé, Environnement et Travail) - UMR 1085, Rennes, France
[m] CHU Pontchaillou, Department of Hematology, Rennes, France
[n] INSERM, U1236, Rennes, France

Received 15 March 2018; accepted 17 March 2018

Dear Editor,

Immune checkpoint inhibitors (CPIs) have opened a new era in the treatment of cancer, and their indications are increasing rapidly. To date, these CPIs include anti-CTLA4 (ipilimumab), anti-Programmed Death 1 (PD1) (nivolumab, pembrolizumab) and anti-Programmed Death-Ligand 1 (PD-L1) (atezolizumab, avelumab, durvalumab) antibodies (Abs). Solid organ transplant recipients have a higher risk of neoplastic complications because of immunosuppressive treatments and oncogenic viral infections [1]. Thus, cancer has now become the second cause of death among transplant patients [2]. However, data are lacking regarding the use of CPI in these transplant patients because they were excluded from clinical trials because of the theoretical risk of organ

* *Corresponding author*: Department of Hematology, CHU Rennes, 2 rue Henri Le Guilloux, 35033 Rennes Cedex 9, France. Fax: +33 (0)2 99 28 41 61.
E-mail address: roch.houot@chu-rennes.fr (R. Houot).
[1] Equal contribution.

https://doi.org/10.1016/j.ejca.2018.03.019

rejection [3–5]. Only a few isolated cases of CPI use in transplant recipients have been reported in the literature so far (reviewed in [6]). Therefore, although there is a clear medical need, the possibility of using these new therapies in transplant patients with cancer remains largely unknown. Here, we report a series of seven kidney allograft recipients treated with CPI for cancer.

Patients were identified through the network of kidney transplant teams in France and Belgium. The study was approved by the institutional review board of Rennes University Hospital (N°17.07). Clinical and biological characteristics of the patients as well as their outcomes were retrospectively collected by the physicians in charge of the patient.

Overall, we identified nine cases of patients with kidney transplant and cancer treated with CPI in France and Belgium. One patient was excluded because he died 2 d after the first injection of CPI and another one because he experienced a haemorrhagic shock 4 d after the beginning of CPI. The characteristics of the seven remaining patients are summarised in Table 1. Patients were treated with anti-CTLA4 (N = 1) or anti-PD1/PD-L1 (N = 6) Abs for melanoma (N = 4), non-small-cell lung cancer (N = 2) or Merckel cell carcinoma (N = 1). None of the patients had experienced graft rejection before CPI treatment. After CPI initiation, three of seven patients (43%) experienced graft rejection, which occurred at a median time of 2 months (range: 1–3 months) after the first infusion of CPI. Graft rejection was managed with CPI discontinuation and steroids in all patients. Two of the three patients with graft rejection experienced graft loss. Only one patient (14%) experienced an objective (partial) response of his cancer which lasted for 3 months. Three of four patients who did not experience graft rejection discontinued CPI because of the absence of response. Five of the seven patients died, all of them because of cancer Fig. 1. Three patients presented at least one immune-related adverse event (three gastrointestinal disorders and one cytopenia). Two of them had steroid therapy at the time of the IRAE.

Kittai *et al.* reviewed all the cases previously reported in the literature (N = 12) regarding patients with organ transplantation treated with CPI [6]. In their study (nine kidney, two liver and one heart transplant recipients), graft rejection occurred in four of 12 patients (33%), all in

Table 1
Patients' characteristics and outcome.

Patient	Gender	Age	Time from transplantation to CPI (years)	Malignancy	CPI (number of doses)	Immunosuppression while on CPI	Graft rejection (time after the first injection)	Treatment of rejection	Graft survival if rejection	Cancer response
1	Male	57	2.25	Non-small cell lung carcinoma (adenocarcinoma)	Nivolumab (5)	Steroids mTOR inhibitor	No	–	–	No[c]
2	Male	70	8.75	Melanoma	Pembrolizumab (4)	Steroids Mycophenolate mofetil	No	–	–	Yes[a,b]
3	Male	72	3.5	Merckel cell carcinoma	Avelumab (8)	Streoids mTOR inhibotor	No	–	–	No[c]
4	Female	68	0.75	Melanoma	Ipilimumab (4)	Steroids Mycophenolate mofetil mTOR inhibitor	No	–	–	No[c]
5	Male	64	6	Non-small cell lung carcinoma (adenocarcinoma)	Nivolumab (9)	Tacrolimus Mycophenolate mofetil	Yes (3 months)	Stop CPI Pulse steroids therapy Increase Tacrolimus residual	No	No[c]
6	Male	73	1.25	Melanoma	Nivolumab (2)	Tacrolimus Mycophenolate mofetil	Yes (1 month)	Stop CPI Pulse steroids therapy	No	No[c]
7	Male	85	27.6	Melanoma	Pembrolizumab (2)	Ciclosporine	Yes (2 months)	Stop CPI Pulse steroids therapy	Yes	No[b]

CPI, checkpoint inhibitor; mTOR, mammalian target of rapamycin: PR, Partial Response.
[a] PR which lasted for 3 months;
[b] Patients still alive at the time of publication;
[c] Patients dead at the time of publication.