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ORIGINAL ARTICLE

Outcome of pretransplant melanoma after solid organ transplantation: an observational study

Marion Patras[1], Evelyne Decullier[2], Céleste Lebbé[3], Julie Delyon[4], Jacques Dantal[5], Christophe Legendre[6], Manal Mazloum[6], Aurélie Du Thanh[7], Feriel Boukari[8], Emmanuel Morelon[9], Denis Jullien[10], Jean Kanitakis[10] & Emilie Ducroux[10]

1 Université Claude Bernard Lyon 1, Lyon, France
2 Service d'Epidémiologie et Recherches Cliniques, Pôle de Santé Publique, Hospices Civils de Lyon, Lyon, France
3 AP-HP Dermatology, INSERM U976, Saint Louis Hospital, Université de Paris, Paris, France
4 Service de Dermatologie, Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis, Paris, France
5 Service de Néphrologie, Hôpital Universitaire de Nantes, Hôtel Dieu, Nantes, France
6 Service de Néphrologie et Transplantation, Assistance Publique-Hôpitaux de Paris, Hôpital Necker, Paris, France
7 Service de Dermatologie, Hôpital Universitaire de Montpellier, Montpellier, France
8 Service de Dermatologie, Hôpital Universitaire de Nice, Nice, France
9 Service de Néphrologie, Hôpital Universitaire Edouard Herriot, Hospices Civils de Lyon, Lyon, France
10 Service de Dermatologie, Hôpital Universitaire Edouard Herriot, Hospices Civils de Lyon, Lyon, France

Correspondence
Marion Patras, Hôpital Edouard Herriot, 5 Place d'Arsonval, 69003 Lyon, France.
Tel.: +33472110478
fax: +33472110323
e-mail: marion.patras@chu-lyon.fr

SUMMARY

The number of patients with a history of melanoma who are awaiting a solid organ transplantation (SOT) is increasing. Few recommendations exist on the timing to transplantation after melanoma diagnosis. The aim of this study was to assess the melanoma recurrence-free survival after pretransplant melanoma (PTM). We conducted a multicenter ambispective observational study. Organ transplant recipients (OTR) with a history of PTM and complete AJCC staging were included. Thirty-seven patients (predominantly men with a renal allograft) were included. Five melanomas were *in situ*, 21 stage IA, 4 stage IB, 5 stage II, and 2 stage IIIB. The median post-transplantation follow-up time was 4 years. Sixty-two percent of patients were followed up more than 2 years. Recurrence-free survival since melanoma reached 89.9%, but varied significantly according to AJCC staging ($P = 0.0129$). Three patients presented a recurrence. Despite the rather limited sample size and a wide range of follow-up, our findings concerning the recurrence-free survival appear reassuring for *in situ* and stage IA PTM; accordingly, we suggest that a waiting time to transplantation is not mandatory in patients with *in situ* or stage IA PTM, especially whenever SOT is urgently needed. Caution is, however, needed for patients with higher stage.

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Introduction

The increasing incidence of melanoma is well documented in the general population [1,2]. The number of solid organ transplantations (SOT) also regularly increases [3]. Consequently, the issue of the management of patients with a history of melanoma who require a SOT becomes increasingly frequent.

The outcomes of melanoma in the general population have been well documented. They depend on the stage of the disease [4], determined by Breslow thickness, and the presence of ulceration, lymph node involvement, and distant metastasis. SOT requires a lifelong immunosuppressive treatment (IST), which may worsen the prognosis of melanoma. Indeed, the outcome of melanoma in organ transplant recipients (OTR) seems to be significantly poorer, especially so for thicker tumors, compared with the general population [5–8].

There are a few series of OTR with pretransplant melanoma, either registry studies with many missing data concerning the melanoma, and a few series with complete data but very small patient sample size [5,8–13]. Therefore, these studies cannot provide reliable recommendations concerning the waiting time after melanoma diagnosis, according to the AJCC staging (American Joint Committee on Cancer) [4], after which SOT could be considered safe. Very recently, consensus expert opinion recommendations were published on this issue, but they were extrapolated from survival data in the immunocompetent population [14]. Up till now, such OTR need to be assessed on an individual basis, taking into account each patient's own risk and the consequences of not receiving SOT [15]. For reasons of chronic shortage of organs, it is important to allocate them to patients who will obtain the greatest benefit. We, therefore, conducted a multicenter, ambispective study on the outcomes of patients with pretransplant melanoma in order to assess the risk of recurrence and mortality caused by melanoma after SOT, so as to get insight into the necessity of respecting a waiting time between melanoma diagnosis and transplantation.

Materials and methods

Patients

Patients older than 18 years with pretransplant melanoma were included. Patients whose AJCC staging was not available were excluded.

Study design

We conducted a multicenter, ambispective observational study. Ethics approval was obtained on Feb 12, 2020, by the Paris Research Ethics Committee. Cases were identified by the French database in transplantation DIVAT with exhaustive extraction ("Données Informatisées et Validées en Transplantation", computerized and validated data in kidney transplantation), to which eight hospital centers participate, and by hospital Dermatologists (from the French group "Peau et Greffe d'Organe"—Skin and Organ Graft) involved in the management and follow-up of OTR.

Data collection

Investigators collected baseline data retrospectively, then follow-up data prospectively, on an electronic case report form over a 1-year period between 2019 and 2020. The data were retrieved from electronic medical or archived paper files from each center and from pathology laboratories. Missing values were retrieved with a questionnaire sent to the patients.

Patient characteristics included date of birth, gender, skin type (Fitzpatrick), hair color at age 20 years, eye color, and global sun exposure score (1 point for each of the following items: professional exposure, leisure outdoor, tanning bed use, and residence in a tropical zone). Skin history recorded the presence of atypical nevi and history of familial melanoma. Melanoma data included date of excision, tumor location, history of pre-existing nevus, histological type, Breslow thickness, ulceration, sentinel lymph node, AJCC 8 staging, and first treatment. Transplantation data included date, type of organ grafted, initial chronic IST, and at the latest consultation, rejection or graft lost. Data relating to the course included date and treatment of metastasis, date and cause of death, and date of the latest consultation.

Endpoints

The primary endpoint was melanoma recurrence-free survival since pretransplant melanoma. The secondary endpoints were recurrence-free survival since transplantation, recurrence-free survival since melanoma according to staging, melanoma outcome after transplantation, and matched case-control analysis with the RIC-Mel database.

Statistical analysis

Categorical variables were described in terms of frequency and percentages. The distributions of continuous variables were

described with median and range (minimum and maximum). For patients with two pretransplant melanomas, the thicker melanoma was considered for AJCC staging.

The recurrence-free survival was defined as the time from the first melanoma (or the SOT) to the date of melanoma recurrence, or until the latest follow-up date (whichever occurred first). Deceased patients were censored at the date of death. Survival curves and log-rank tests for comparison between stages were obtained using the Kaplan–Meier method.

A RIC-Mel data extraction was performed on January 07, 2021. For each case, we tried to match one to four controls on melanoma age (±5 years), gender, categorized Breslow ([0–0.5]; [0.5–1]; [1–2]; [2–4]; and >4), ulceration, year of melanoma (±20 years), and hospital center geographic latitude (north/south). Recurrence-free survivals were compared using Cox proportional hazards model for matched data. The SAS STATISTICAL software (V9.3) was used for all analyses.

Results

Study population

Fifty-eight patients with a history of pretransplant melanoma were identified (28 through the DIVAT database and 30 through hospital practitioners of the GPGO; Table 1). Thirty-seven OTR had a complete AJCC staging and were included in the study (Lyon: 11, Nantes: 9, Grenoble: 8, Paris: 5, Nice: 2, and Marseille and Montpellier: 1 each). Twenty-two patients (59%) were men. The mean global sun exposure score was 1.3. Three patients had a history of familial melanoma. The median time from diagnosis of melanoma to transplantation was 8.1 years (range, 0.2–18.4). Three of five stage 0 melanoma patients and 4 of 21 stage 1A melanoma patients had been transplanted <2 years after melanoma diagnosis. The median post-transplantation follow-up length was 4 years (range, 0.1–21.4). Twenty-three patients (62%, including 3 *in situ*, 13 stage IA, 5 stage II, and 2 stage IIIB) were followed over more than 2 years. The median time from melanoma diagnosis to the latest follow-up or death was 12.5 years (range, 1.4–28.4). The median patients' age at the latest follow-up was 63.9 years (range, 34–83) and the median age at death was 66.5 years (range, 39.2–77).

Table 1. Patients' characteristics.

	No. of patients (%)
Total	37 (100%)
Fitzpatrick's skin type	
Type I	1 (2.7%)
Type II	11 (29.7%)
Type III	11 (29.7%)
Type IV	1 (2.7%)
Type V	0
Type VI	0
NA*	13 (35.1%)
Hair color	
Black	5 (13.5%)
Brown	13 (35.1%)
Blond	4 (10.8%)
Red	3 (8.1%)
NA	12 (32.4%)
Eye color	
Brown	6 (16.2%)
Hazel	6 (16.2%)
Light	12 (32.4%)
NA	13 (5.1%)
Atypical nevi	
Yes	8 (21.6%)
No	17 (46%)
NA	12 (32.4%)

*NA = not available.

Data on melanomas

Thirty-four patients had one pretransplant melanoma and three patients had two pretransplant melanomas (Table 2). After transplantation, three patients developed a second melanoma in a different site from the primary tumor. Two of them were *in situ* (patients #34 and 24) and were diagnosed 1 and 5 years after transplantation, respectively. The third patient (#6) developed a stage IA melanoma 3 years after transplantation. The median age of patients at first melanoma diagnosis was 48 years (range, 23–53). The median Breslow thickness was 0.55 mm (range, 0–18). Patients #36 and 37, initially staged IB and IIA, developed before transplantation a local and a lymph node recurrence, 39 and 19 months after melanoma diagnosis, respectively, and were, therefore, upstaged to stage IIIB. Histologically, there were 24 (64.8%) superficial spreading melanomas, 3 (8.1%) *lentigo maligna* melanomas, 1 case each (2.7%) of acral lentiginous melanoma and nodular melanoma, and 4 cases each (10.8%) of unclassifiable or unknown type. Six pretransplant melanomas developed on pre-existing nevi. The melanomas were located on the legs (14), the back (7), the face (7), the arms (4), the chest, the skull, the genitalia, and the buttocks (one case each—in one case the localization was unknown).

Transplantation data

The median age of patients at transplantation was 57 years (range, 30–76); 30 of them (81.1%) had

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Table 2. Features of pre-transplant melanoma, transplantation data, and post-transplant outcome of our 37 patients.

AJCC	*N*	Year of melanoma	Age at melanoma	Breslow thickness (mm)	Ulceration	Sentinel lymph node	Time melanoma–transplantation*	Year of transplantation	Age at transplantation	Graft	Time* melanoma–latest FU‡	Time* transplantation–latest FU‡	Death
0	1	2013†	42	0	No	NP	1.2	2015	44	Kidney	5.3	4.0	No
	2	2018†	71	0	No	NA	0.4	2018	71	Kidney	1.4	1.0	No
	3	1989	37	0	No	NA	2.7	1991	54	Kidney	24.1	21.4	No
	4	2008	65	0	No	NP	1.5	2010	67	Kidney	11.6	10.1	No
	5	2010	45	0	No	NP	9.5	2019	54	Kidney	10.5	1.1	No
Total = 5			56.5 (37–71)	0	0		1.5 (0.4–9.5)		54 (44–71)		10.5 (1.4–24.1)	4.0 (1.0–21.4)	0
IA	6	1999†	57	0.7	No	NP	12.3	2011	69	Kidney	15.5	3.1	No
	7	2001†	44	0.5	Yes	NP	9.4	2010	53	Kidney	19.4	10	No
	8	2010†	55	0.2	No	NP	0.3	2011	56	Kidney	9.6	9.2	No
	9	2011†	27	0.65	No	NP	2.7	2014	30	Heart	8.9	6.2	No
	10	2015†	61	0.55	No	NP	1.7	2015	61	Liver	5.4	5.2	No
	11	2006†	48	0.4	No	NP	12.2	2018	60	Kidney	14.0	1.8	No
	12	2002	63	0.16	No	NP	1.8	2004	64	Kidney	7.1	5.4	Yes, unrelated
	13	1991	48	0.68	No	NA	18.4	2009	66	Kidney	28.4	10	No
	14	2012†	46	0.7	No	NP	5.7	2017	51	Kidney	7.7	2	No
	15	1999†	57	0.7	No	NP	12.3	2011	68	Kidney	19.2	6.9	No
	16	1995	47	0.3	No	NA	16.5	2011	53	Kidney	20.5	4	No
	17	1999	26	0.95	No	NA	8.1	2007	34	Kidney	15.8	7.6	No
	18	2007	47	0.54	No	NA	11.5	2018	57	Kidney	12.5	1	No
	19	2004	51	0.5	No	NP	3.2	2008	55	Lung	15.2	12	No
	20	2001	30	0.5	No	NP	16.4	2017	46	Kidney	19.5	3	No
	21	2004†	63	0.45	No	NP	15	2019	78	Kidney	16.1	1	No
	22	2013†	70	0.42	No	NP	6.1	2020	76	Kidney	6.3	0.1	No
	23	2009†	60	0.25	No	NP	0.3	2009	60	Liver	9.8	9.6	Yes, unrelated
	24§	2012†	50	0.65 + 0.55§	No	NP	6.9	2019	57	Kidney	7.8	0.9	No
	25	2012†	63	0.52	No	NP	8.4	2020	71	Kidney	8.6	0.1	No
	26	2002†	23	0.72	No	NP	18.1	2020	41	Kidney	18.2	0.1	No
Total = 21			48 (23–70)	0.5 (0.16–0.95)	1		8.5 (0.2–18.4)		57 (34–76)		14 (5.3–28.4)	4 (0.1–12)	2

Table 2. Continued.

AJCC	*N*	Year of melanoma	Age at melanoma	Breslow thickness (mm)	Ulceration	Sentinel lymph node	Time melanoma–transplantation*	Year of transplantation	Age at transplantation	Graft	Time* melanoma–latest FU‡	Time* transplantation–latest FU‡	Death
IB	**27**	**2012**†	**49**	**1.5**	**No**	**Negative**	**4.5**	**2017**	**54**	**Kidney**	**6.1**	**1.6**	**Yes, related**
	28	2005†	40	1.2	No	NP	15.1	2019	51	Kidney	15.1	0.5	No
	29	**2010**†	**57**	**1.1**	**No**	**NP**	**6.6**	**2016**	**62**	**Liver**	**6.6**	**0.6**	**Yes, related**
	30¶	2008	52	1.1 + 0¶	No	NP	12.3	2019	63	Kidney	12.3	1	No
Total = 4			50.5 (40–57)	1.15 (1.1–1.5)	0		8.6 (4.5–14.6)		58 (51–63)		9.4 (6.1–15.1)	0.8 (0.5–1.6)	2
IIA	31	1987†	43	2.2	No	NP	9	1991	47	Kidney–pancreas	9.0	5.7	Yes, unrelated
	32**	**1986**†	**26**	**2.0 + 0****	**Yes**	**NP**	**13.2**	**1991**	**31**	**Kidney**	**13.2**	**8.3**	**Yes, related**
	33	2017†	75	2.0	Yes	NA	2.5	2017	75	Kidney	2.5	2.1	Yes, unrelated
Total = 3			34.5 (26–75)	2 (2–2.2)	2		3.3 (0.3–4.9)		47 (31–75)		9 (2.5–13.2)	5.7 (2.1–8.3)	3
IIB	34	2002†	61	5.0	No	NA	8.8	2011	70	Kidney	17.7	8.9	No
IIC	35	1990†	50	18.0	Yes	NP	12.8	2003	63	Heart	23.8	11	Yes, unrelated
IIIB	36	2003†	43	1.95	No	Negative	9.4	2012	52	Kidney	16.5	7.1	No
	37	1998†	60	3.9	No	NA	13.9	2012	74	Kidney	20.9	7.0	No
Total = 2			51.5 (43–60)	2.9 (1.95–3.9)	0		11.6 (9.4–13.9)		63 (52–74)		18.7 (16.5–20.9)	7.1 (7–7.1)	0

Bold lines are for patients with postgraft recurrence.

* Time lapse in years.

†Excision with safety margins following guidelines.

‡Latest follow-up is the date of death or date of latest consultation.

§Patient 24 presented two pretransplant melanomas in 2012.

¶Patient 30 presented two pretransplant melanomas in 2008.

**Patient 32 presented two pretransplant melanomas (1986: stage IIA, 1991: in situ).

received a kidney transplant, 1 a kidney and pancreas, 3 a liver, 2 a heart, and 1 a lung transplant (Table 2). At induction, 17 patients (45.9%) received a T-cell-depleting treatment (antithymocyte globulins), 10 (27%) received basiliximab, and 1 patient received no treatment [relevant data were missing for 9 (24.3%) of the patients]. Initial IST contained a combination of calcineurin inhibitor (CNI), mycophenolate mofetil (MMF), and corticosteroids (CS) in two-thirds of cases, three patients received azathioprine (AZA) and 6 ciclosporine, and three patients had an mTOR inhibitor (mTORinh) from the beginning (everolimus). At the end date, the latest IST consisted of low-dose CNI and MMF in half of the cases. Fifteen patients were kept on low-dose CS. Six patients had an mTORinh (everolimus or sirolimus). Eight patients developed allograft rejection, which was treated by intravenous CS in all cases. Nine patients lost their graft after a mean post-transplantation delay of 7 years (range, 0.3–15.6). Following graft loss, five patients returned to dialysis and three patients (#3, 4, and 12 in Table 1) received a second transplant.

Outcomes of melanoma after transplantation

No recurrence was observed in the five patients with *in situ* melanoma and the 21 patients with stage IA melanoma, especially the four patients who were grafted within 2 years after melanoma diagnosis, for whom the minimum FU time post-transplantation was 5.2 years. Eight patients died, three of melanoma and five of unrelated causes (two sepsis, one autoimmune hepatitis, and two unknown; Table 2). Among the three patients who died of melanoma, two had stage IB, and one had stage IIA melanoma. Patient #27, with pretransplant melanoma stage IB (negative SLNB), presented a multimetastatic (lymph node, liver, lung, brain, and bone) recurrence 18 months postgraft and was treated by immunotherapy (nivolumab and ipilimumab) but died 1 month later. He had received a T-cell-depleting treatment induction. Patient #29, with pretransplant melanoma stage IB (SLNB not performed), presented a multimetastatic (lymph node, liver, lung, and bone) recurrence 4 months post-graft and died 4 months later without specific treatment. He had not received depleting induction treatment. Patient #32, with pretransplant melanoma stage IIA (SLNB not performed) presented a lymph node recurrence 7 years postgraft and was treated with lymph node dissection and interferon. Two years later, she presented liver and bone metastases, and died 16 months later without treatment. She had received a T-cell-depleting induction treatment.

Survival analysis

The recurrence-free survival since melanoma at 10 years reached 89.9% (Fig. 1). The recurrence-free survival curve since transplantation was similar. In our cohort, the recurrence-free survival varied significantly according to AJCC staging ($P = 0.0129$, Fig. 2).

RIC-Mel database

A total of 17 828 nontransplant patients with melanoma stages 0–I–II was extracted. The 9490 patients with missing data (stage, date, patient lost to FU, and patient with more than one melanoma) were excluded. The median Breslow thickness was 1.00 mm (range, 0–75). Seven melanomas (0.1%) were *in situ*, 3581 (42.9%) stage IA, 1745 (20.9%) stage IB, 1142 (13.7%) stage IIA, 928 (11.1%) stage IIB, and 565 (6.8%) stage IIC. The median age of patients at diagnosis was 61.8 years (range, 0–104). In this population, 1113 patients (13.3%) presented a recurrence with a median time-lapse of 1.72 years (0.1–28.4). The recurrence-free survival at 10 years was 100% in stage 0, 86.6% in stage IA, 64.1% in stage IB, and 46.5% in stage II.

Matched case–control analysis with the RIC-Mel database

Twenty-seven cases had at least one control, among which twenty cases had four controls. Among the 94 controls, 13 became metastatic with a median delay of 6 years (0.4–17.3); 5 melanomas (38.5%) were stage IA, 3 (23.1%) stage IB, 1 (7.7%) stage IIA, and 2 (15.4%) stage IIB. For two patients with stage I melanoma, the substatus was unknown. The recurrence-free survival at 10 years in controls reached 77.9%. The difference in recurrence-free survival between controls and cases (Fig. 3) was not statistically significant ($P = 0.5459$).

Discussion

We present a series of 37 patients with pretransplant melanoma and complete AJCC staging, which is, to our knowledge, the largest reported cohort of OTR with precise data on pretransplant melanoma. In our series, survival was reassuring for patients with *in situ* and stage IA melanoma, who had no tumor recurrence during the follow-up. By contrast, we observed three

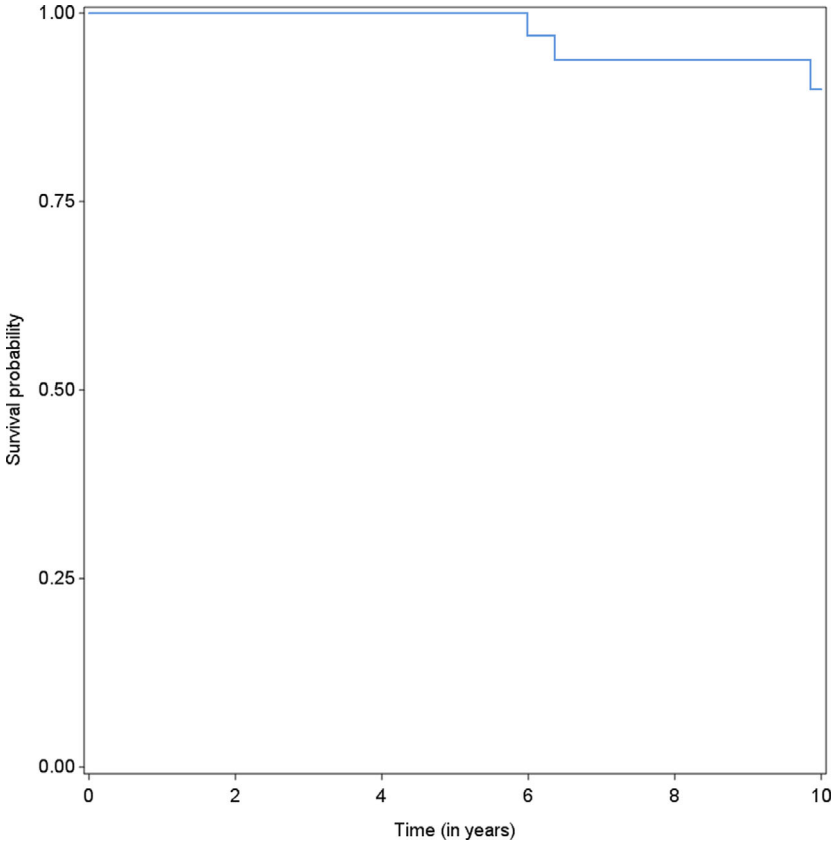

Figure 1 Recurrence-free survival since melanoma at 10 years.

melanoma recurrences among the 11 patients with higher-stage melanoma (IB-IIIB). Two of these recurrences occurred within the first 2 years after transplantation.

The immune system is involved in defense against cancer, especially via CD8+ and CD4+ T cells (which allow production of specific cytokines), as has been shown in the case of melanoma. The IST inhibits the proliferation of T cells [16]; consequently, OTR have a two- to fivefold higher risk of developing melanoma [6,17,18], and are more likely to be diagnosed with higher stages (II through IV) [19] compared with the general population. A higher melanoma-specific mortality has been shown for tumors with Breslow thickness >2 mm [8]. Data are not consistent for thinner (Breslow <2 mm) melanoma as most [6,7,20], but not all [21], studies have found an increased melanoma-specific mortality in OTR. Immunosuppression is more intense in the early period of the transplantation, aiming to avoid acute rejection, and may explain the rapid postgraft melanoma recurrence in two of our patients. Some studies exist on the outcome of pretransplant melanoma in OTR, but they are either small series or registry studies with several missing data [22–27]. The worst outcomes were reported by Penn in 1996 [9], who found a 19% recurrence rate of melanoma with an invariably lethal outcome; however, the stages of tumors in that study were not available. The largest study by Arron *et al.* in 2016 found an increased melanoma-specific mortality [13]. The study included 336 OTR with pretransplant melanoma, but did not use the AJCC staging. There were 112 *in situ* melanomas, 177 localized melanomas, 5 with regional metastasis, 2 with distant metastasis, and 40 of unknown stage. Six patients died of melanoma, but their initial staging was not available. Between 2008 and 2018, four reviews with precise staging data studied pretransplant melanoma [5,8,11,12]. A summary of these studies is presented in Table 3. They mentioned AJCC staging for 37 patients, but ulceration status was available for 15 patients only, thereby the substages are unknown. There were 15 *in situ* melanomas, 19 stage I melanomas, 1 stage III melanoma, and 2 stage IV melanomas. The follow-up period after transplantation varied between 0.5 and 15.7 years. No melanoma-specific mortality was reported among these patients. It should be noted that

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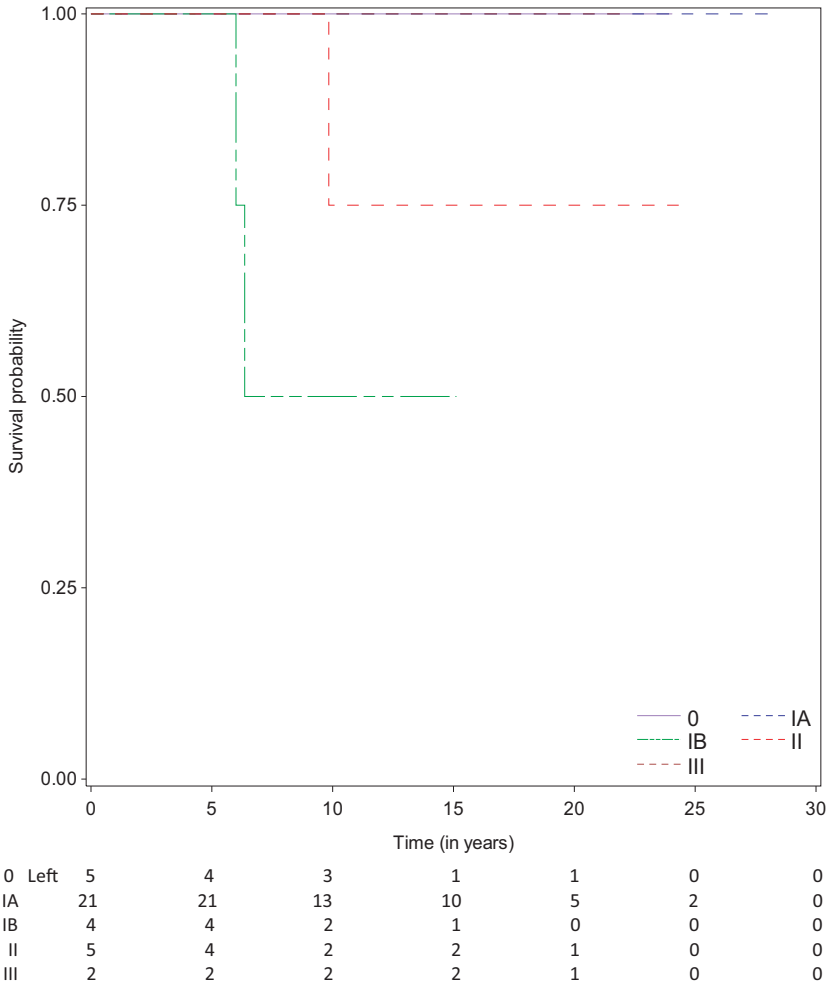

Figure 2 Recurrence-free survival since melanoma order to AJCC.

two patients with unavailable initial staging presented a recurrence.

A very recent publication reported a consensus expert opinion statement and proposed recommendations on the waiting time to transplantation after a pretransplant melanoma [14]. The proposed recommendations were based on overall survival by stage from AJCC database, considering the fact that if one accepts an 80% 5-year melanoma-specific survival as a threshold for transplantation, then all patients with pretransplant melanoma would be eligible to transplantation following tumor resection (except patients with disease stages IIIC, IIID, and IV); accordingly, they proposed no waiting time for *in situ* melanoma, and waiting times of 1 year for patients with stage IA melanoma, 1–2 years for patients with melanoma stage IB and IIA, 2–4 years for patients with melanoma stage IIB, IIC, and IIIB, and at least 5 years for patients with melanoma stage IIIC, IIID, or IV. These guidelines were extrapolated from the survival curve of immunocompetent patients (including patients treated specifically for melanoma); nevertheless, the safety of immunotherapy in OTR is concerning, as checkpoint inhibitors can activate alloreactive T cells that could trigger acute rejection (occurring in up to 37% of cases according to some studies) [28–30] and graft loss [31]. Furthermore, the initial staging of melanoma is reportedly higher in OTR who have a worse prognosis [17], as already discussed above.

Based on the 100% 5-year melanoma-specific survival, and on the reassuring outcome data in our study and in the literature, we suggest no waiting time for *in situ* melanoma, as already proposed [32]. Even though the sample size of stage 1A pretransplant melanoma patients in our study is rather limited (n: 21), with only 4 stage 1A patients with a melanoma to transplantation delay shorter than 2 years, considering also the 19 stage I melanoma patients from the literature with no pretransplant tumor recurrence, and also

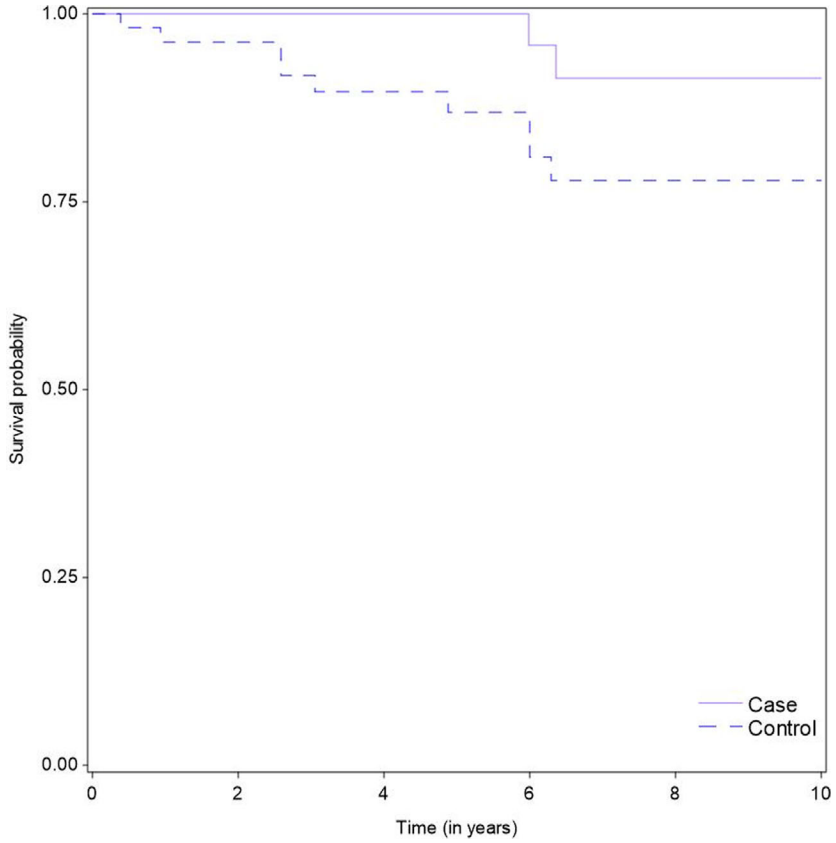

Figure 3 Recurrence-free survival in controls and cases.

the fact that stage IA melanoma seems to have the same prognosis in OTR as in the general population (as seen in the matched case–control analysis with RIC-Mel database and from the AJCC curve, 99% 5-year melanoma-specific survival), we believe that a waiting time is not mandatory for patients with stage IA pretransplant melanoma, especially whenever SOT is urgently needed. For higher stages, we believe that caution is necessary. Study of additional patients with adequate follow-up is needed in order to establish firm guidelines about the appropriate waiting time before transplantation.

Only one of our two stage IB melanoma patients with quick postgraft recurrence had a SLNB, which proved negative. It is possible that the other stage IB melanoma patient, for whom SLNB was not performed and who presented a recurrence 4 months after transplantation, was in fact initially stage III; therefore, for transplant candidates with melanoma, SLNB should be considered, even for stage I tumors, as a negative result would support the absence of waiting time before transplantation [32,33].

Two of our three patients with postgraft recurrence had received a T-cell-depleting treatment. Although the small number of such patients does not allow firm conclusions to be drawn, this observation is consistent with the contention that patients who have received T-cell-depleting treatments are at increased risk of cancer [34], namely secondary skin cancer after retransplantation [35].

In our series, very few patients received mTORinh as IST. mTOR plays a pivotal role in the control of cell growth and proliferation and is an important target of anticancer drugs [36]. mTORinh have shown some efficacy in melanoma [37]; however, the role of mTORinh on melanoma progression still remains unclear [38].

In our series, 24% of patients had a history of graft rejection, contrasting with a mean rate of around 10% [39]. This means that either our patients were very immunized or that their IST was very low, probably because of their history of melanoma.

Although our cohort contains melanoma of various stages, the total number of patients is somewhat limited and only 4 of 21 stage IA melanoma patients were

Table 3. Reported data of pretransplant–melanoma in literature.

Study	AJCC available/ total sample	Breslow thickness (mm) Number					Ulceration			AJCC						Time* melanoma–transplant	Time* transplant–last FU	Recurrence	Time-lapse transplant–recurrence	Melanoma-specific mortality
		0	≤0.75	0.76–1.50	1.51–3.00	>3.00	NA	Yes	No	NA	0	I	II	III	IV	NA				
Puza *et al.* 2018 [14]	12/12	6	4	1	0	0	1	0	10	2	6	6	0	0	0	0	4.13 (1.1-13.3)	2.8 (NA)	0	0	0
Brewer *et al.* 2011 [6]	13/61	5	5	5	1	1	44	0	5	56	5	6	0	1	1	48	4.5 (0.1-12.5)	NA	2†	NA	0
Dapprich *et al.* 2008 [13]	10/12	Median Breslow 0.35 (0–2.00)‡						NA	NA	12	4	5	0	0	1	2	3.8 (0.1–18.4)	3.5 (0.5–15.7)	0	0	0
Matin *et al.* 2008 [12]	2/9	0	2	2	1	1	3	NA	NA	9	0	2	0	0	0	7	7.8 (0.4–32.5)	5 (0.5–10.2)	0	0	0

*Median (range) in years.
†AJCC staging was not available for the recurrences.
‡Details on Breslow thickness were not available.

transplanted within 2 years after melanoma, facts that do not allow to draw firm conclusions and guidelines. We had to exclude 14 patients with pretransplant melanoma because of AJCC missing data, namely for old cases or deceased patients (six deaths were unrelated to melanoma). The follow-up after transplantation was also not very long, although it varied considerably, namely for stage IA patients where our main recommendation lies, especially since melanoma is prone to late recurrences. Another limitation of our study is its partial retrospective nature. Also of note, most of our patients were kidney transplant recipients; therefore, extrapolation to other types of SOT should be made with caution. Regarding the RIC-Mel analysis, we were limited by year of melanoma diagnosis (the RIC-Mel base was more recent than ours) and by latitude. Therefore, not all of our patients had a closely matched control.

In conclusion, as far as we know, our study reports the largest population of OTR with pretransplant melanoma and precise data on tumor staging. The recurrence-free survival appears reassuring in patients with *in situ* and stage IA pretransplant melanoma, even though the sample size in our study is rather limited with a wide variation in the follow-up. We suggest that a waiting time to transplantation is not mandatory in patients with *in situ* and stage IA pretransplant melanoma, especially whenever SOT is urgently needed. Caution is, however, needed for patients with higher stage. Collection of additional cases of OTR with pretransplant melanoma and a longer follow-up will hopefully help to establish more precise guidelines on the waiting time before transplantation in this specific setting.

Authorship

MP: participated in the performance of the research and writing of the paper. ED: participated in the writing of the paper, contributed new reagents or analytic tools, and participated in data analysis. CL: participated in research design. JD: participated in research design. JD: participated in the performance of the research. CL: participated in the performance of the research. MM: participated in the performance of the research. ADT: participated in the performance of the research. FB: participated in the performance of the research. EM: contributed new reagents or analytic tools. DJ: participated in research design. JK: participated in the writing of the paper and contributed new reagents or analytic tools. ED: participated in research design, participated in the performance of the research, and participated in the writing of the study.

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Conflicts of interest

The authors declare no conflicts of interest.

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