rate calculated using survival analysis techniques was 5.1% for recurrent tumors (95% CI, 2.3%-11.0%) vs 3.4% for primary tumors (95% CI, 2.4%-4.6%) (P=.18). The Figure depicts Kaplan-Meier curves of tumor recurrence for primary and recurrent tumors.

Discussion. To our knowledge, this study is the largest prospective cohort study in the United States examining long-term re-recurrence of recurrent BCCs and SCCs treated with the 3 most common treatments. Tumors in the treatment groups differed in severity, and given the small number of recurrences overall we cannot compare effectiveness after different therapies or adjust for other risk factors. The results suggest, however, that overall re-recurrence rates of already recurrent BCCs and SCCs treated in the community may be less than conventionally believed.

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Nonmelanoma Skin Cancer in Organ Transplant Recipients: Increase Without Delay After Transplant and Subsequent Acceleration

Organ transplant recipients (OTRs) have a 60- to 250-fold increased risk for cutaneous squamous cell carcinoma (SCC) and a 10-fold increased risk for basal cell carcinoma (BCC).1 It is still unclear, however, how fast after transplant these tumors arise. To develop risk-adjusted clinical follow-up in OTRs, we investigated the incidence of first and subsequent nonmelanoma skin cancers (NMSCs) in OTRs.
Methods. Following approval by the local ethical committee, clinical information from 225 OTRs who underwent transplant at the University Hospital Zurich, Zurich, Switzerland, with complete follow-up in a special consultation for OTRs at the Department of Dermatology for at least 8 years after transplant was retrieved from medical charts. None of these patients had NMSC before transplant. In addition, clinical information from 10028 NMSCs in immunocompetent control patients was retrieved from the dermatohistopathology archive database, and clinical information from medical charts was also retrieved in a subset of 10 immunocompetent patients with multiple SCC or BCC. Histological diagnoses of NMSC were all made by board-certified dermatopathologists. GraphPad Prism software v5.0 (GraphPad) was used for statistical analysis. \( P < .05 \) was considered significant.

Results. The mean (SD) age at transplant was 41.99 (14.3) years \((n = 255)\) (eFigure 1A; http://www.jamaderm.com). Transplanted organs included 130 kidneys, 53 livers, 35 lungs, and 7 hearts (eFigure 2).

Of 225 OTRs, 24 (10.7%) developed 1 SCC or more and 17 (7.6%) developed 1 BCC or more within 8 years (Figure 1A). Cumulative incidence of the first NMSC rose linearly and without delay after transplant and was
similar between SCC and BCC (P=.18, log-rank test) (Figure 1B).

Squamous cell carcinoma in OTRs developed earlier (mean [SD] years, 56.2 [15.5]; SCC, n=53) than in immunocompetent controls (73.9 [12.9] years; SCC, n=253; P <.01, t test). Similarly, BCC occurred earlier in OTRs (58.8 [15.2] years; BCC, n=35) than in immunocompetent patients (67.2 [14.1] years; BCC, n=7497; P <.01) (eFigure 1B).

Total annual numbers of NMSC were variable without an upward or downward trend and with a mean of 6.6 SCCs (2.9%) and 4.4 BCCs (1.9%) per year (Figure 2A and B). An analysis of organ transplant groups revealed a trend toward earlier occurrence of SCC in the strongly immunosuppressed heart and lung OTRs (combined, n=42) compared with the less immunosuppressed liver and kidney OTRs (combined, n=183) (heart and lung OTRs, 7 SCCs in years 1-4 and 4 SCCs in years 5-8; kidney and liver OTRs, 16 SCCs in years 1-4 and 26 SCCs in years 5-8; P=.18, Fisher exact test) (Figure 2A and B).

Of interest, subsequent NMSC in OTRs with several NMSCs showed accelerated carcinogenesis: In OTRs with multiple SCC (n=5), the first SCC developed after a mean (SEM) of 36.6 (9.4) months, whereas the second SCC occurred after only another 4.0 (1.3) months (P=.008, Kruskal-Wallis with Dunn post hoc test). In control immunocompetent patients with multiple SCCs (n=10), the time interval to a second, third, or fourth SCC remained constant (Figure 2C). Organ transplant recipients with multiple BCCs (n=4) had a first BCC after a mean (SEM) of 47.5 (6.8) months and the second BCC already after another 12.5 (1.0) months (P=.048) (Figure 2D). There was a trend toward shorter time intervals in OTRs than in immunocompetent patients from the first to second SCC (4.0 [1.3] vs 12.5 [3.74] months; P=.14), from the second to third SCC (6.0 [2.3] vs 10.6 [1.92] months; P=.16) (Figure 2C); and from the first to second BCC (12.5 [0.96] vs 20.0 [3.63] months; P=.23) (Figure 2D).

Discussion. We aimed to determine how fast after organ transplant the incidence of NMSC increases. Age at time of transplant and at occurrence of NMSC in our cohort compared well with published data.1

While some previous publications reported a linear increase of the NMSC cumulative incidence,2 others indicated a low or even unchanged risk in the first years, followed by a marked increase after 5 to 10 years.3 Our study demonstrated a linear increase of the cumulative incidence of first SCC and BCC without delay after transplant and a constant accrual of total annual SCC and BCC over the first 8 years.

Several other studies have described an increased risk for subsequent NMSC in OTRs, reporting a cumulative 3-year incidence for a second NMSC ranging between 22% and 52%.4,5 Herein, we demonstrated that the risk for subsequent NMSC in OTRs was not only increased overall but also accelerated with intervals shrinking between the first and subsequent NMSC. Even though OTRs received skin checks more frequently after a first NMSC, we do not believe that earlier detection of subsequent NMSC in OTRs accounted for that acceleration because clinically and histologically first NMSC had similar tumor stages at the time of diagnosis as subsequent NMSC and because a trend toward shorter time intervals in OTRs was observed not only from first to second but also from second to third NMSC. Nonmelanoma skin cancers after transplant should be considered a marker for increased subsequent NMSC risk in OTRs and be integrated into the clinical algorithms for the follow-up in OTR specialty clinics.

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