leprosy, but its immunomodulatory effects have also been demonstrated in other mycobacterial infections such as pulmonary tuberculosis, human immunodeficiency infection and malignant neoplasms of the head, neck, bladder, and lung.1-3 Our research team has previously reported an 88.9% cure rate with Mw vaccine in genital warts.4

The exact mechanism of the wart clearance with Mw vaccine is yet to be studied. The strong proinflammatory signals against Mw attract antigen-presenting cells with production of helper T-cell type 1 cytokines and activation of cytotoxic and natural killer T cells that probably also recognize and process low-profile human papillomavirus particles in the infected tissue.5 The strong adaptive immune response clears not only treated lesions but also distant lesions. Mw vaccine appears to be an effective immunotherapy for extensive and multiple cutaneous warts, and it should be further evaluated in randomized controlled trials.

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Recurrent After Treatment of Cutaneous Basal Cell and Squamous Cell Carcinomas in Patients Infected With Human Immunodeficiency Virus

Cutaneous basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), collectively called nonmelanoma skin cancer (NMSC), are the most common primary malignant neoplasms, yet recurrence after treatment is unusual.1 With modern antiretroviral therapy, NMSC is also the most frequent cancer in persons infected with human immunodeficiency virus (HIV),2 but recurrence rates in this population are largely unknown.3 We followed a large prospective cohort of patients with NMSC to determine tumor recurrence rates and found unexpectedly high recurrence among the HIV-infected patients.

Methods. This study was approved by the committee on human research, University of California, San Francisco, and details of this study have been described elsewhere.1 Briefly, eligible patients were those with primary NMSC diagnosed in 1999 or 2000 at a university-based practice and its affiliated Veterans Affairs Medical Center. Data were collected via medical records, patient survey, and blinded physical examination, and patients were followed up for a median (interquartile range [IQR]) of 7.3 (3.1-8.7) years after treatment. Given the prevalence of human papilloma virus–associated genital SCCs among HIV-infected patients, tumors located in the genital area were excluded from all analyses.

We compared groups by the χ2 test for categorical characteristics and Wilcoxon rank sum test for continuous characteristics. Cumulative incidence of tumor recurrence over time was displayed using Kaplan-Meier plots. We also constructed a series of Cox proportional hazard models to calculate unadjusted and adjusted 5-year recurrence rates and hazard ratios (HRs). Because of the limited number of recurrences, we forced HIV status and treatment type (categorized as conservative [destruction, topical, or none] or aggressive [excisional or Mohs surgery]) into the adjusted models then applied a forward stepwise selection based on AIC (Akaike Information Criterion) within the entire sample and each histological subtype (BCC and SCC). Potentially selected variables were those significant in bivariate analyses, including age, history of prior NMSC, multiple NMSCs at enrollment, tumor location in the H-zone of the face—a high-risk area for recurrence—histologic type, histologic invasiveness, and number of annual visits to a dermatologist throughout the follow-up period. Unadjusted analyses were repeated in an SCC subset matched at a 1:5 ratio, HIV-infected to HIV-uninfected, on age, sex, and tumor body location. Statistical analyses were performed using R statistical software, version 2.13.

Results. Of the 1534 nongenital NMSCs that occurred among 1202 patients, 50 were primary tumors in 34 HIV-infected patients. Compared with HIV-uninfected patients, HIV-infected patients were younger (median ages,
50.5 vs 70.0 years) \( (P < .001) \) and had tumors of similar size and histopathologic characteristics that were, however, less likely to be located in the H-zone (22% \( [n = 11] \) vs 37% \( [n = 549] \) \( (P = .05) \). Tumors in HIV-infected patients were more often treated with destructive or topical therapies (54% \( [n = 27] \) vs 29% \( [n = 430] \) ) than surgical treatments (44% \( [n = 22] \) vs 71% \( [n = 1054] \) ) \( (P < .001) \), and HIV-infected patients visited the dermatologist more frequently (median [IQR] number of annual visits, 2.1 [1.0-3.5] vs 1.5 [0.5-3.0]) \( (P < .001) \). At enrollment, the median (IQR) duration of HIV infection was 11.0 (9.5-15.0) years. Thirty-one of the 34 HIV-infected patients took approved highly active antiretroviral therapy (91%).

Overall 5-year tumor recurrence rates after treatment were 2.9% in HIV-uninfected patients and 13.8% in HIV-infected patients \( (HR, 3.1; P = .005) \) \( (\text{Table}) \). Rates were statistically significantly higher for the 376 SCCs \( (\text{Figure}) \). Among SCCs, HIV infection was highly predictive of tumor recurrence in both unadjusted \( (HR, 9.5; P = .004) \) and multivariate models \( (HR, 9.6; P < .001) \), including tumor location in the H-zone of the face, histologic invasiveness, and treatment type. Unadjusted results were consistent in the matched SCC sample.

Median (IQR) CD4 counts and viral loads averaged from time of diagnosis to the end of follow-up were 449/\( \mu L \) (301/\( \mu L-674/\( \mu L \)) and 500/mL (0/mL-27 990/mL), respectively. There was no relationship between recurrence and CD4 count or viral load.

Of note, no recurrences occurred among 51 tumors in patients who had received organ transplants.

Comment. Patients with HIV and nongenital SCCs had higher rates of recurrence after treatment, despite being relatively young with well-controlled HIV. Treatment choices or frequency of follow-up may have contributed to these results, but immune surveillance \( ^4 \) or advanced immunosenescence \( ^5 \) are likely also important. That recurrence did not occur in organ transplant patients or relate to CD4 count suggests that immunosuppression alone is not a sufficient explanation. If replicated, these findings support specific monitoring of HIV-infected individuals with cutaneous NMSC and determination of optimal therapy for primary tumors.

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We read with great interest the recent study in this journal by Brauer et al1 and congratulate them for carrying out a well-designed pilot study of a picosecond laser for tattoo removal. In particular, we applaud the authors for demonstrating the potential of these lasers to remove multicolored tattoos, which often prove to be more challenging to remove than traditional black tattoos with current ns-nano second technology. While it is exciting to read about a new commercially available device, the use of a picosecond laser for tattoo removal is not novel. Over a decade ago, several key studies that were not cited by Brauer et al1 fully set the stage for their work. The Wellman Center for Photomedicine2 at Massachusetts General Hospital and Harvard Medical School pioneered the use of picosecond lasers for tattoo treatment over 14 years ago in a landmark human pilot trial comparing picosecond and nanosecond pulsed lasers using pulse durations shorter than those used in the study reported by Brauer et al.1 Herd et al2 also reported an animal study showing superiority of a picosecond titanium:sapphire laser over the Q-switched alexandrite laser in removing tattoo pigments.

The case for picosecond lasers is based largely on the theory of selective photothermolysis.3 Most of the common tattoo ink particles have a particle size of about 0.1 μm, corresponding to a thermal relaxation time of under 10 nanoseconds. Thus a laser with a subnanosecond pulse width, such as a picosecond laser, was long ago expected, and shown without doubt to be more effective than the current commercially available Q-switched nanosecond laser technology.

However, while we have known about the potential for picosecond lasers to improve our ability to remove tattoo particles for over a decade, the availability of these devices was hampered by an inability to produce a commercially viable and stable version of a picosecond laser. Recently, Izikson et al4 reported the safety and effectiveness of the same picosecond laser used in the study reported by Brauer and coworkers1 in an animal model. While the report by Brauer et al supports the potential for picosecond lasers in treating unwanted tattoos, it failed to cite these key initial studies that have paved the way for picosecond laser in tattoo removal and offer a more detailed description and analysis of the phenomenon.