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Drug for fungal infections in lung transplant recipients increases risk for cancer, death

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Voriconazole, a prescription drug commonly used to treat fungal infections in lung transplant recipients, significantly increases the risk for skin cancer and even death, according to a new study by UC San Francisco researchers. The team recommends physicians consider patient-specific factors that could modify the drug's risks and benefits, when providing care.

Their study appears online Sept. 3, 2015, in the *American Journal of Transplantation*.

"It is important for physicians to be aware of the impact of voriconazole on these outcomes," said senior author Sarah Arron, MD, PhD, associate professor of dermatology and director of the UCSF High Risk Skin Cancer Clinic. "We recommend that all providers counsel lung transplant recipients on skin cancer risk and photoprotection in addition to scheduling routine skin cancer screening with a trained dermatologist after transplantation. Lung transplant programs should also consider patient-specific risk factors when deciding on the type, dose and duration of antifungal prophylaxis regimens."

Skin cancer is the most common malignancy following solid organ transplants, primarily due to immunosuppression, with recipients experiencing a greater than 65-fold increased risk of developing cutaneous squamous cell carcinoma (SCC) compared to the general population. These carcinomas are aggressive and can lead to numerous lesions, resulting in multiple debilitating surgeries and increased risk of

death.

Lung transplant recipients are particularly susceptible to SCC due to older age at transplant and more intensive immunosuppression. They also have high rates of fungal infections after transplant, which can result in significant morbidity and mortality.

First approved in 2002, voriconazole is used to prevent and treat invasive fungal infections like those caused by the *Aspergillus* fungi, especially in patients with compromised immune systems such as following a lung or other organ transplant. The *Aspergillus* fungi can cause aspergillosis, a variety of diseases often occurring in people with healthy immune systems but having an underlying illness such as tuberculosis or chronic obstructive pulmonary disease (COPD).

However, SCC is a serious side effect of voriconazole, which has no clear guidelines for prophylaxis regimens despite its widespread use.

In their study, Arron and her colleagues evaluated all UCSF single-lung, double-lung or heart-lung transplant recipients receiving a transplant between October 1991 and December 2012. These 455 individuals were analyzed for voriconazole exposure and its impact on SCC, *Aspergillus* colonization, invasive aspergillosis and all-cause mortality.

The researchers found that voriconazole exposure resulted in a 73 percent greater risk for SCC, with each additional 30-day exposure increasing the risk by 3 percent.

Further, the drug significantly reduced the risk of *Aspergillus* colonization, especially in the first year after transplant, but not aspergillosis. It also reduced all-cause mortality among those transplant recipients who developed *Aspergillus* colonization but had no significant impact on those without colonization.

"Among lung transplant recipients with risk factors for SCC, including those with older age, male sex and white race or those in whom prolonged voriconazole administration may not have clear benefit, transplant physicians should consider limiting exposure to high doses of voriconazole or using alternative pharmacologic options that do not pose an increased risk for SCC," said lead author Matthew Mansh, MD, who did the work as a doctoral student at Stanford University that included a research year in the UCSF Department of Dermatology.

Provided by University of California, San Francisco