New Medications Offer Hope For The Scourge Of Malaria

Universisty of Nebraska Medical Center
University of Nebraska Medical Ctr

The stakes are immense. Worldwide, more than 300 million new cases of malaria are diagnosed each year, and more than 1 million people die from it, according to the World Health Organization (WHO). Young children and expectant mothers are especially at risk.

An enormous problem: The parasites that cause malaria have developed resistance to long-effective medications. The best drugs currently available are derived from artemisinin, a Chinese herbal medicine that's extracted from the bark of sweet wormwood. It's costly, its supply is limited and it requires frequent doses.

Jonathan Vennerstrom, Ph.D., a professor at the University of Nebraska Medical Center, is hoping to change that by developing a synthetic version of artemisinin, one that can be more effective, easier to administer and manufactured in large quantities at lower cost.

In research supported by a small grant from WHO, Vennerstrom, Yuxiang Dong, Ph.D., and other Nebraska colleagues were able to synthesize a peroxide-based drug that acted like artemisinin by producing a chemical reaction that

ultimately leads to the death of the parasite.

Projects of the Year

With promising results, they approached Medicines for Malaria Venture (MMV), a nonprofit foundation based in Switzerland. MMV provided funding and formed an international team involving scientists at Nebraska, Monash University in Australia and the Swiss Tropical and Public Health Institute.

The first drug candidate, OZ277, was declared MMV's Project of the Year in 2002 and was licensed to Ranbaxy Laboratories in India for development. In 2004, the team published its results in Nature.

Still, team members thought they could do better. For one thing, OZ277 requires three doses over three days.

> *For reduced costs, improved patient compliance and easier distribution, the researchers envisioned a second generation that could work in one dose.*

OZ439, a potential single-dose drug candidate that remains effective for much longer than OZ277, became MMV's Project of the Year for 2006. The lead innovators include Vennerstrom and Dong at Nebraska; Susan Charman, Ph.D., and Bill Charman, Ph.D., at Monash; Sergio Wittlin, Ph.D., at the Swiss Institute; and Hugues Matile, Ph.D., at Hoffman-La Roche Ltd. The team published its results in the Proceedings of the National Academy of Sciences in February 2011.

Vennerstrom tends to be cautious about predicting success. However, OZ277 could be available for use by the end of 2011. The new drug, OZ439, is in Phase IIa trials now in Bangkok and hopefully will be available in several years.

This story was originally published in 2011.

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