



RESEARCH NEWS

Experimental drug seems very effective for frequent menopausal hot flashes

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An experimental drug has been found to cut the number of menopausal hot flashes by almost three quarters in an early trial reported in the *Lancet*.¹

The trial, funded by the UK Medical Research Council and the National Institute for Health Research, tested a neurokinin 3 receptor antagonist (MLE4901), originally developed by AstraZeneca and licensed to Millendo Therapeutics, in women who experienced severe flushing as a menopausal symptom.

Postmortem studies of brain tissue from post-menopausal women have shown that it contains elevated levels of neurokinin B, and researchers at Imperial College London have found that giving neurokinin B to younger women in a temperature controlled room causes flushing. The researchers at Imperial College therefore wanted to test whether blocking the action of neurokinin B could be a potential treatment for menopausal flushing.

The team recruited 28 women aged 40 to 62 who experienced seven or more hot flashes a day and who had not had a period in at least 12 months, for a phase II, randomised, double blind, placebo controlled trial.

The women were randomly split into two groups. Women in the first group received an 80 mg daily dose of MLE4901 (40 mg twice daily) for four weeks, and then their pills were switched to a placebo for another four weeks. Those in the second group received the placebo treatment for the first four weeks and were then switched to the active treatment.

On average, women experienced 45% fewer hot flashes a week (95% confidence interval 22% to 67%) during the four week treatment period with the compound MLE4901 than when taking placebo (intention to treat adjusted means: placebo 49.01 (40.81 to 58.56) v MLE4901 19.35 (15.99 to 23.42); P<0.001). The adjusted (least squares) estimate of percentage change from baseline in the weekly number of hot flashes was -28% (-17% to -39%) with placebo and -73% (-61% to -84%) with MLE4901.

Compared with placebo, MLE4901 also reduced hot flush severity by 41% (32% to 49%) (placebo 5.70 (5.09 to 6.38) v MLE4901 3.27 (2.92 to 3.66); P<0.001). Also, women taking MLE4901 reported that their symptoms were less bothersome and interfered less with sleep.

Waljit Dhillon, a National Institute for Health Research professor at the Department of Medicine at Imperial College, said, "If a woman is having more than seven flushes a day and the drug is getting rid of three quarters of them, that's pretty life changing. For day to day living and work, that's a significant impact on quality of life. If we can reduce flushing by 73% it's a game changer for those patients."

He added that a lot of women choose not to take hormone replacement therapy because it is oestrogen based. "This new drug is a pill which blocks the NK3 receptor, so it won't have the side effects associated with oestrogen," said Dhillon.



1 Prague JK, Roberts RE, Cominos AN, et al. Neurokinin 3 receptor antagonism as a novel treatment for menopausal hot flashes: a phase 2, randomised, double-blind, placebo-controlled trial. *Lancet* 2017; published online 3 Apr. doi:10.1016/S0140-6736(17)30823-1.

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