

From the authors:

We are grateful to B.G. Baldi and colleagues for their interest in our paper [1]. We agree that based upon our own, as well as the author's, data that doxycycline cannot currently be recommended as a therapy to reduce a decline in lung function in patients with lymphangioleiomyomatosis (LAM). As the authors pointed out, in our randomised placebo-controlled study, the two groups had slightly differing baseline lung-function values, which may have led to the differences in the rate of progression of LAM and possibly the response to doxycycline [1]. However, the lack of effect on any study endpoint suggests that doxycycline is unlikely to be helpful for the majority of patients. In B.G. Baldi's study, 41 patients received doxycycline in an open-labelled manner, 31 patients completed 1 year of therapy and were then divided into those with a fall in forced expiratory volume in 1 s (FEV₁) or those whose FEV₁ did not fall, termed "nonresponders" and "responders" respectively, with responders tending to have a better baseline lung function [2, 3]. Although, these data would be consistent with B.G. Baldi's contention that patients with mild disease may respond to doxycycline, whereas those with more advanced disease do not. This idea would require testing in a randomised placebo-controlled trial of patients with early or mild disease, as it is also possible that doxycycline does not affect lung function decline in LAM and these observations are due to the variable rate of disease progression in LAM patients. Interest in the efficacy of doxycycline as a metalloproteinase inhibitor in LAM must also be tempered by the modest effect on matrix metalloproteinase (MMP) levels in LAM-derived cell supernatants [4] and serum levels of MMP-2 and MMP-9 in LAM [1, 3]. Similarly, the suggestion that doxycycline may work in synergy with other therapies will further need formal testing.

In the absence of responsive biomarkers for disease activity, endpoints for clinical trials rely upon lung function, making randomised controlled trials in a rare disease difficult to perform in a single country and also expensive. It is important for patients that biomarkers are developed allowing screening of potential therapies before embarking on large, definitive studies.



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At present the use of doxycycline to show progression of LAM is not supported by clinical trial evidence <http://ow.ly/tJFqN>

Simon R. Johnson^{1,2}, William Y.C. Chang¹, Anne E. Tattersfield¹, Sarah Lewis³, Maruti Kumaran⁴ and Jennifer L. Cane¹
¹Division of Therapeutics and Molecular Medicine, University of Nottingham, Nottingham, ²National Centre for Lymphangioleiomyomatosis, Nottingham University Hospitals NHS Trust, Nottingham, ³Division of Epidemiology and Public Health, University of Nottingham, Nottingham, and ⁴Dept of Radiology, Nottingham University Hospitals NHS Trust, Nottingham, UK.

Correspondence: S.R. Johnson, University of Nottingham, Queens Medical Centre, C floor, South block, Nottingham, NG7 2UH, UK. E-mail: simon.johnson@nottingham.ac.uk

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