# Use of Sirolimus in Patients with Lymphangioleiomyomatosis on Waiting Lists for Lung Transplant: An International Survey of Practice

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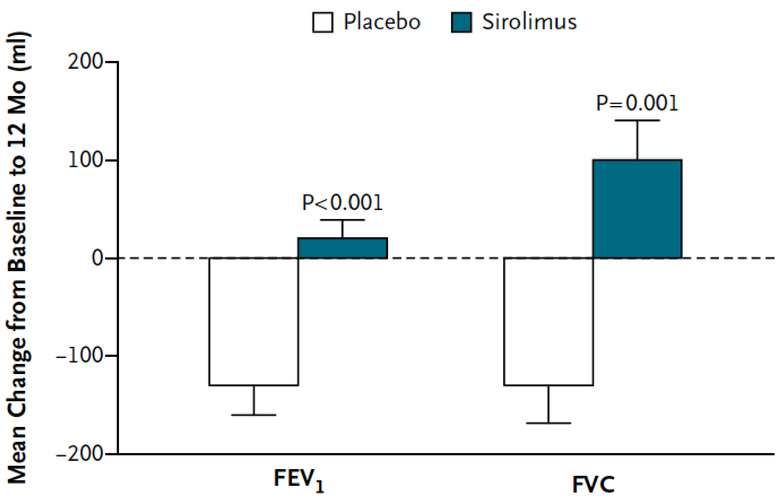
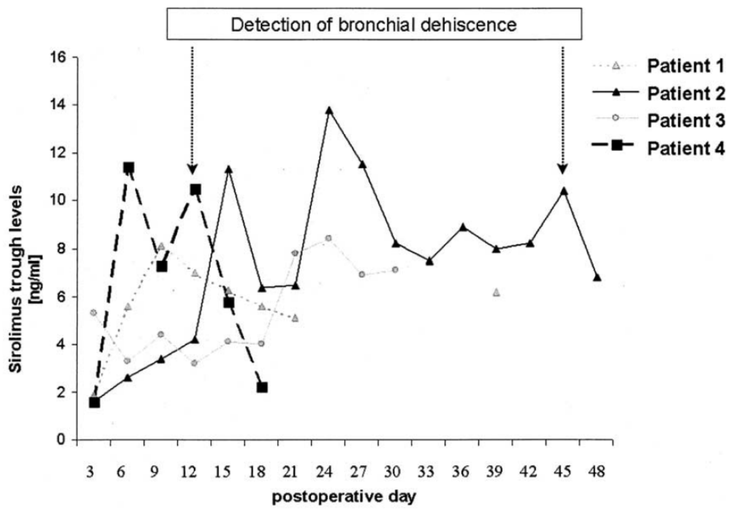
## Introduction

A pivotal study (published in 2011) proved that women with lymphangioleiomyomatosis (LAM) receiving inhibition of the mammalian target of rapamycin (mTOR) with sirolimus had slowing of lung function decline[1]. Use of mTOR inhibitors (sirolimus or everolimus) is now standard and ubiquitous in management of LAM[2] and withdrawal can result in precipitous decline. However, use of sirolimus immunosuppression immediately after lung transplant (LTX) has has been shown to be associated with bronchial dehiscence resulting in patient deaths from 4-6 months post LTX[3,4]. Many lung LTX programs prohibit use of mTOR inhibitors while on the waiting list, often resulting in resumption of lung function decline.

An alternative strategy, allowing mTOR inhibitor use up until the time of LTX, has been proposed. In this scenario, sirolimus washes out within a week, long before the critical period for anastomotic healing. However it is not known how widely this is adopted.




Reference 1 -- Efficacy and Safety of Sirolimus in Lymphangioleiomyomatosis



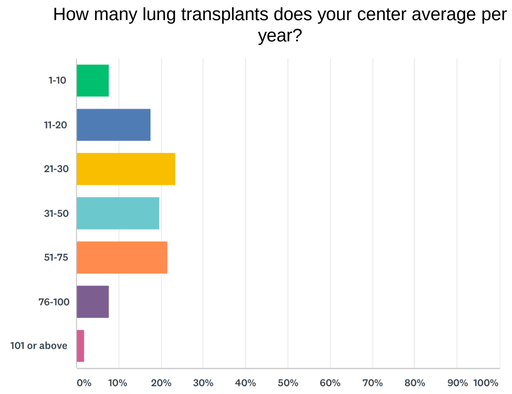

Reference 4 -- Airway Anastomosis Complications in De Novo Lung Transplantation With Sirolimus-Based Immunosuppression

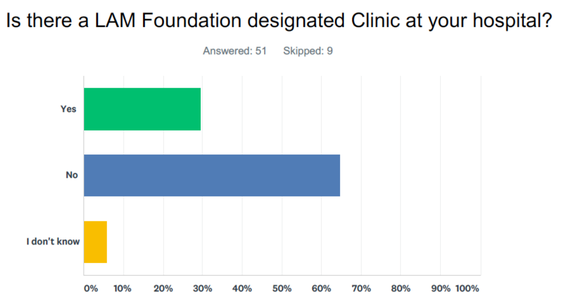
## Methods

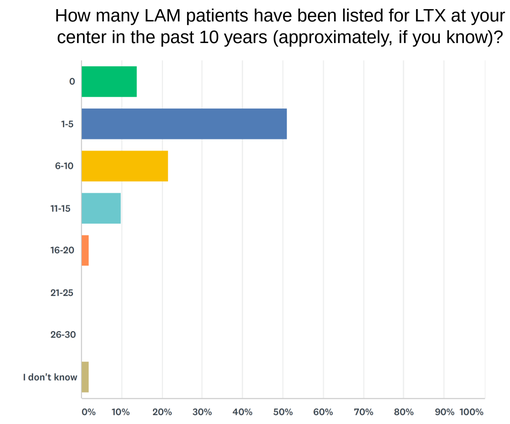
With support of the ISHLT Pulmonary Council, an online survey (Survey Monkey™) was sent to pulmonologists at 123 LTX programs identified from the ISHLT database to query center policies on mTOR inhibitor use in LAM patients on the waitlist.

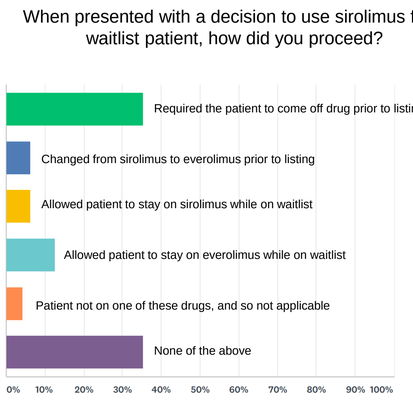
## Results

There was a 41.5% (51/123) response rate, with 43.1% of these coming from outside of North America. 82.4% stated that a patient with LAM had ever been listed at their center – albeit few at each – as only one-third of programs had listed more than 5 LAM patients in over the past ten years. 62.5% stated that their program had been confronted with a decision about whether to allow a listed patient with LAM to continue on an mTOR inhibitor up until LTX.

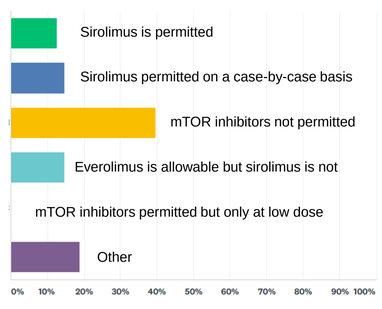



A majority (60.8%) of programs have a formal policy about this matter.




35.4% of respondents stated that they had required the patient to come off of the drug prior to listing, yet 25% allowed a patient to stay on sirolimus or everolimus up until the time of transplant, and 39.6% had not confronted this issue. Of the 13 centers reporting a LTX in patients on an mTOR up till the time of transplant, all reported a favorable outcome and none declared any adverse consequences of having used mTOR therapy up until LTX.

Some respondents noted that local allocation policies allow for mTOR to be stopped and the patient to be prioritized for transplant in a short time frame or that the drug was stopped once the patient became “high” on the list.

## Conclusion

Although controversy exists regarding whether mTOR inhibitors can be safely continued during waitlist time, this survey demonstrates that continuation the drugs has been successful in many centers. A more detailed assessment of outcomes of these particular patients is planned.

## References

1. McCormack FX et al. N Engl J Med 2011;364:1595-606
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3. King-Biggs MB et al. Transplantation 2003;75(9):1437-43
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