

Detailed Responses to the Reviewer's Comments

Dear Editor and Reviewers,

Many thanks for your constructive comments on our manuscript submitted to the World Journal of Clinical Cases. We would like to express our sincere appreciation to you. The detailed responses to the reviewers' comments are presented below.

Best,

Jinling Chen

May 29, 2021

The **comments** from reviewers and the corresponding **responses** are in **black** and **blue** respectively.

Comments from the reviewers:

Comment #1:

Could there be other factors such as smoking/ excessive alcohol intake/ drug consumption that may have contributed to the disease?

Response: The exact cause of pulmonary lymphangiomyomatosis is unknown now. More studies put forward that it was related with tuberous sclerosis. However, medical history of the patient in this report has no factors such as smoking/ excessive alcohol intake/ drug consumption.

Comment #2:

Are there other treatment options to consider other than Sirolimus? How was this treatment chosen?

Response: Lymphangiomyomatosis (LAM) is an uncommon disease which is associated with tuberous sclerosis (TSC). TSC is an inherited autosomal dominant

disease caused by mutations in TSC1 (hamartin) and TSC2 (tuberin) genes. Mutations in the TSC1 and TSC2 tumor suppressor genes cause hyperactivation of the mTORC1 (mammalian target of rapamycin complex 1), developing neoplastic lesions called hamartoma in numerous organs, such as the brain, skin, kidneys, and lungs. Sirolimus is an mTOR (mammalian target of rapamycin) inhibition, which was proved as an effective therapy of TSC-LAM including improvement of lung function or progress of angioliomyolipoma. This patient has no other better treatment options for her genetic abnormality. Thus, we chose the Sirolimus for her treatment.

Comment #3:

How are you planning to follow-up the patient?

Response: We follow up the patient regularly during Sirolimus treatment, including ultrasound and lung function evaluation every three months, CT every six months.

We have added this part into the revised manuscript.