Dear Professor Catia Cornacchia,

Please consider our manuscript submission entitled Whole lung lavage combined with Granulocyte-macrophage colony stimulating factor inhalation for an adult case of refractory pulmonary alveolar proteinosis for publication as a Case Report in the BMC pulmonary medicine. This is the revised version of our article. I have re-edited my manuscript according to the reviewer suggestions. Response to the reviewers will be attached in the second part of this cover letter. Language throughout the revised version of this manuscript has been copyedited by a native english speaker in USA.

Pulmonary alveolar proteinosis (PAP) is a rare yet potentially treatable disease that is characterized by accumulation of periodic acid Schiff (PAS) positive lipoproteinaceous substance in the alveoli due to impaired surfactant metabolism. There are few treatment options for patients with symptomatic PAP. Whole lung lavage (WLL) is the first-line treatment for patients with symptomatic PAP. However, significant proportions of patients require multiple WLLs, or do not respond to treatment with WLL. Other treatment options such as GM-CSF supplementation and plasmapheresis, have been introduced. However, treatment of severe refractory cases is still a major challenge for clinicians, in which combination therapy instead of monotherapy maybe a better choice. Here we describe an adult case of severe refractory PAP successfully treated with WLL in combination with sequential GM-CSF inhalation therapy.

These findings have important implications for physicians treating this population of patients. Again we emphasize the fact that there are only a few well-established treatment options for these patients. Here we describe a case of successful treatment of refractory adult PAP with WLL and rhGM-CSF combination therapy. For severe refractory PAP, bilateral WLL combined with sequential GM-CSF supplementation could be an excellent treatment option. We believe our findings will be of broad interest to your general readership and have
direct implications in the field for treating patients with PAP.

This paper has not been submitted elsewhere. It is not under review or published previously. All of the authors are aware of and approve of the manuscript being submitted to your journal. There is no conflict of interest among them. Written informed consent for publication of her clinical details and clinical images was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal. I’ll attach it in the third part in this letter. I’ll also mail it to the Editor-in-Chief. Your kind assistance and consideration of our manuscript is highly appreciated. We thank you for your time.

Sincerely yours,
Hui Huang
Peking Union Medical College Hospital, Beijing, China

Respondse to the reviewers:

Dear Professor Low,

Thank you very much for your pertinent and impressive suggestions. It was very kind of you to review our article. I will keep you suggestions in mind as I revise my manuscript.

Explanations for minor essential revisions:

1. Thank you for your suggestion. I’ll re-edit it according to your suggestion in our revised version.

2. Thank you for your suggestion. It’s a very good idea. What a pity for us! Although we have preserved her replaced fluid during the every plasmapheresis in our refrigerator in -80#, we just have preserved her serum before the first plasmapheresis, after her last plasmapheresis and at the last follow-up. The replaced fluid during the every plasmapheresis might not standardized easily for us. We think the differences of serum GM-CSF antibody between these three points might not have useful implication. We’ll do better in the future.

3. I’ve added some explanation in the revised version.

Sincerely yours,
Hui Huang
Peking Union Medical College Hospital, Beijing, China

Dear professor Agarwal,

Thank you very much for your pertinent and impressive suggestions. I have re-edited my manuscript according to your suggestions in the revised version.

Sincerely yours,
Hui Huang
Peking Union Medical College Hospital, Beijing, China