Reviewer's report

Title: Pulmonary venous occlusion and death in pulmonary arterial hypertension: survival analyses using radiographic surrogates

Version: 1 Date: 19 December 2010

Reviewer: Michael Halank

Reviewer's report:

Takeda et al. in a prospective trial demonstrated, that typical radiological signs of PVOD are associated with poor survival.

Major point(s)

1.)
The authors concluded that radiologic abnormalities (adenopathy, ground-glass attenuation, thickening of septa) are directly related to venous occlusion of the pulmonary vessels.

But Montani et al. (Medicine 2008;87:220) demonstrated that PVOD with histological confirmation may be associated with normal CT and that radiological abnormalities on CT of the chest may be present in more than 15% of idiopathic PAH confirmed by histology.

In my opinion, for any correlation of pulmonary venous occlusion with survival, histological examinations are needed to confirm the diagnosis of PVOD.

As histological data are not available from this study, the manuscript actually assessed radiological abnormalities rather than pulmonary venous occlusion by itself. This should be referred to in the discussion section; and the wording of the title and the rest of the manuscript should be changed into “radiological abnormalities compatible to PVOD” instead of “pulmonary venous occlusion”.

2.)
From which results you conclude that antifibrotic drugs may benefit patients with CTD-associated PAH?

3.)
Please provide the PAH-causes for the 15 cases who did not survive. Did you observe any difference in mortality rates between the PAH-causes, as you suggest in your discussion (“This largely explains the difference in the survival rate between idiopathic PAH and CTD-associated PAH”). Otherwise this statement cannot be drawn from your study data.

4.)
Please check the significance levels given at page 11 lane 146/147. According to table 2, only 4/18 patients with IPAH but 14/19 patients with CTD-PAH showed
ground glass attenuation – this does not seem to fit into a significance level of 0.77.

5.) Ground glass attenuation and adenopathy are known indirect hints for a possible chronic thromboembolic pulmonary hypertension (CTEPH). Were perfusion/ventilation scans performed in all cases for excluding CTEPH as the cause of pulmonary hypertension?

6.) Please state whether two-sided p-values were used to assess significance (page 9 lane 127)

Minor point:
1.) The results section should be shortened, presenting the data in a more focused manner.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.