Reviewer’s report

Title: Serum VEGF levels are related to the presence of Pulmonary Arterial Hypertension in Systemic Sclerosis

Version: 1 Date: 12 August 2008

Reviewer: Cecilia Calabrese

Reviewer’s report:

In the present study the authors detected significantly higher serum VEGF levels in patients affected by SSc with PAH compared to those without PAH and to control subjects. Furthermore they found a positive correlation of sVEGF levels both with PAH and MRC dyspnea score and a negative correlation between sVEGF levels and DLCO. The methods seem appropriate and well described and the data are sound.

Major Compulsory Revisions

1) The question posed by the authors is not well defined. The main aim of the study is to determine serum VEGF levels in patients with SSc and to evaluate whether those levels are different in patients with and without PAH not secondary to a lung interstitial involvement of the disease. Furthermore, the authors will evaluate the relationship between VEGF levels and several clinical and functional parameters.

2) In the discussion the authors state that “further prospective studies are needed to investigate whether the worsening in sPAP is followed by increases in serum VEGF levels” and they conclude that “our findings suggest that serum VEGF levels may be used as a predictor of sPAP in patients with SSc”. The authors should better clarify their hypothesis on the role of VEGF in the pathogenesis of PAH in patients with SSc.

3) Patients with SSc and PAH have significantly lower DLCO compared to those without PAH. Is there a significant difference in arterial oxygen partial pressure between the two groups of patients? Measurements of PaO2 and PaCO2 should be presented in table 1. Considering the potential role played by chronic hypoxia in inducing VEGF expression the authors should discuss this aspect in patients affect by SSc with and without PAH.

4) Is the effect of sVEGF level on the clinical and functional parameters mediated by the increase in PAH? Is there a correlation of sPAP both with MRC dyspnea score and DLCO?

5) Some patients of the group with PAH showed an overlap in sVEGF levels with others of the group without PAH. Have these patients other characteristics that could explain the increase in PAH? In any case it could be very interesting to strictly monitor those patients who have not developed PAH.
Minor Essential Revisions

1) On page 15 “It has also been reported” instead of “It has been also reported”

2) On page 17 the statement “Additionally, in severely hypoxic rats treated with an flk-1 inhibitor, the development of more marked PH accompanied by a marked increase in endothelial cell proliferation in the pulmonary artery[32]” is not clear

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests