Reviewer's report

Title: Effect of Roflumilast on Inflammatory Cells in the Lungs of Cigarette Smoke-Exposed Mice

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Reviewer: Guy G Brusselle

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Review manuscript “effect of roflumilast on inflammatory cells in the lungs of CS-exposed mice” by Martorana P. et al, BMC Pulmonary Medicine.

In the present manuscript the authors quantified in a thorough manner (i.e. the volume density) the accumulation of inflammatory cells (of both the innate and the adaptive immune system) in the lungs of chronic CS-exposed mice. Interestingly, they correlate these inflammatory cell volume density data with the development of pulmonary emphysema, and the influence of the treatment with roflumilast (which prevented emphysema at a high dose, but was ineffective at a low dose, as already described by the same group in the AJRCCM journal). These results are interesting, important and relevant.

Major compulsory revisions: None.

Minor essential revisions:
1) How specific is the immunodetection of dendritic cells by monoclonal antibody to fascin?
   Which subset of dendritic cells (DC) is detected? Myeloid DCs? Plasmacytoid DCs?

2) How specific is the immunohistochemistry (IHC) of CD4 for CD4+ T-lymphocytes? CD4 is not only expressed on T-lymphocytes, but also on some monocytes/macrophages. Please comment this limitation in the discussion (or perform double staining IHC).

3) How specific is the IHC of CD8 for CD8+ T-lymphocytes? CD8 (especially CD8a) is not only expressed on T-lymphocytes, but also on some NK and DC subsets. Same advice as in comment 3.

4) The discussion should be shortened; especially the last paragraph could be omitted.

Minor comments:
Introduction: Page 4: first paragraph: dendritic cells are listed as adaptive immune cells, but are also important as innate immune defence; in fact, dendritic cells are linking innate and adaptive immunity.
Methods: Page 5: second paragraph: please correct “Seven months after chronic exposure to …”, suggesting a seven month exposure-free interval, into “After chronic exposure to room air or cigarette smoke for seven months, …”

Discussion: Page 8: first sentence: please correct “Two are the main points of this study:”

Declaration of competing interests:

I declare that I have no conflict of interest with respect to this paper.