Reviewer’s report

Title: Use of ivacaftor in late diagnosed Cystic Fibrosis monozygotic twins heterozygous for F508del and R117H-7T – a case report

Version: 0 Date: 15 Dec 2018

Reviewer: Massimo Conese

Reviewer’s report:

This manuscript brings the attention of the scientific community of pulmonologists on the variability of clinical presentation and response to the so-called personalized medicine even between monozygotic twins.

However, the authors have not discussed at all which factors may have determined this difference.

Focusing on the ivacaftor therapy outcome:

1) The pulmonary less affected twin sister showed improvement in lung function with an increase in FEV1. Can it be that the residual function in CFTR may have allowed to have a better response than the other twin? And if this is possible, which factors may be at work here? Did the worst patient have any viral infections? Is she a smoker? Besides antibiotics, which other therapies were they subjected to?

2) Ivacaftor therapy response in individuals with G551D allele was found to be associated with polymorphism in SLC26A9, an anion channel expressed by epithelial cells (Strug LJ, Gonska T, He G, et al. Cystic fibrosis gene modifier SLC26A9 modulates airway response to CFTR-directed therapeutics. Hum Mol Genet. 2016 Oct 15;25(20):4590-4600). Said this, may it possible that epigenetic changes have altered SLC26A9 expression in one of the twin?

Minor

The two tables may be well merged into one.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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