

Peer review file

Article information: <http://dx.doi.org/10.21037/jtd-20-2462>

Reviewer A

This paper provides a meta-analysis of studies undertaken to look at links between lung cancer and SLE. It uses a technique called Mendelian randomization that I am not familiar with, but concludes, as several others (though not all groups) have done that lung cancer is increased in SLE.

Clearly great care has been taken to include appropriate studies and analyze the cancer link carefully. I do though have several comments/ concerns

1) While clearly of interest the authors need to put these findings in more context. In my own group of around 700 SLE patients followed for >30 years the numbers of patients who died from lung cancer is small (around half a dozen). Thus the authors need to emphasize that the absolute numbers of SLE patients who are dying from lung cancer is small even if, as they report, the relative risk is increased.

Reply 1: Thank you for your comments. We have modified our text as advised.

Changes in the text: Page 26, line 509 to line 512.

2) In studies of these kinds the authors have to rely on the veracity and completeness of the original reports. To what extent do they feel able to say with confidence that a) the individual reports did a good job of selecting appropriate patients eg which SLE criteria (there are now 4 sets!) did patients meet - this information should be included in their review b) how good a job did the original authors do of capturing smoking and drug exposure data

Reply 2: Thank you for your comments. We have modified our text as advised.

Changes in the text: Page 8, line 133 to line 139

3) they refer to some SLE patients being genetically predicted, but its very heterogeneous nature (and the fact even among identical twins the concordance is only 25%) implies that another term perhaps 'genetically predisposed or inclined' would be

more accurate.

Reply 3: Thank you for your comments. We have modified our text as advised.

Changes in the text: Page 5, line 77; Page 6, line 90; Page 6, line 93; Page 10, line 169; Page 10, line 173; Page 20, line 388; Page 20, line 390; Page 21, line 405; Page 22, line 416; Page 23, line 453; Page 24, line 458; Page 49; Page 50.

4) A small error in the Discussion is that cyclosporin is in fact rather rarely used to treat SLE patients, it is not a main treatment. for SLE

Reply 4: Thank you for your comments. We have modified our text as advised.

Changes in the text: Page 25, line 487 to line 488.

5) Although I do congratulate the authors on their English usage in general the paper does need to be checked for a number of corrections eg in the Introduction it should be 'evidence' not 'evidences' and pulmonary 'lesions' not 'lesion'.

Reply 5: Thank you for your comments. We have modified our text as advised.

Changes in the text: Page 7, line 111; Page 8, line 126; Page 21, line 411.

Reviewer B

I am impressed that the manuscript attempts to inform the interested readers on an important topic of the relationship between autoimmunity and malignancy and has potential to change the perceptions in the management of patients. The authors are consisted in the methodology, particularly employing the Mendelian Randomization (MR) unlikely to be affected by confounding or reverse causation. The sentence structure and flow is acceptable and the manuscript has almost nil grammatical errors. I feel the manuscript can be accepted for publication as it is, although I would like the authors to correct 'resent' to 'recent' in line 84.

Reply 1: Thank you for your comments. We have modified our text as advised.

Changes in the text: Page 7, line 115