Reply to the comment on: Impact of early immuno-suppressive therapy on pulmonary arterial hypertension in systemic sclerosis: a single-centre real-world study

Sirs,

We thank Dr Bakay for highlighting clearly the potential significance of our findings and need for further research to fully understand the impact of immunosuppression in systemic sclerosis associated pulmonary arterial hypertension (1).

The reported protective effect of early mycophenolate treatment on pulmonary arterial hypertension (PAH) development is intriguing and aligns with the accepted concept of interplay between vasculopathy, fibrosis, autoimmunity, and inflammation in systemic sclerosis, where targeting one component may influence the others. Early initiation of mycophenolate is already recognised as pivotal for achieving meaningful responses in skin fibrosis and interstitial lung disease (2). It would be valuable to further investigate its potential role in preventing PAH among patients who, under current recommendations, might not otherwise receive mycophenolate. Such an evaluation would require a long-term prospective study. Since PAH typically arises late in the natural history of the disease and higher risk cases can be identified, a 'prevention of progression paradigm' could be explored.

Equally interesting was the observation of a protective effect of hydroxychloroquine in patients with established PAH, even after adjusting for baseline pulmonary haemodynamic and background vasodilator therapy. This finding raises the possibility that hydroxychloroquine may help restore pulmonary vascular homeostasis, consistent with its direct effects on endothelial and smooth muscle cells (3).

Finally, we thank Dr Bakay for underscoring the limitations of our study, which is presented as hypothesis-generating. We hope that it will give impetus to future research.

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