Risk of systemic lupus erythematosus in patients with idiopathic thrombocytopaenic purpura

We read the published article by Zhu *et al*¹ with great interest. In this population-based retrospective cohort study, the authors demonstrated that the patients with idiopathic thrombocytopaenic purpura (ITP) had a 26 times higher risk of new-onset systemic lupus erythematosus (SLE) compared with the control population. However, some concerns do exist and should be addressed.

First, thrombocytopaenia is known as a common clinical manifestation of SLE and can be the initial presentation in 5% of patients with SLE.^{2,3} The diagnosis of ITP is based principally on the exclusion of any known causes of thrombocytopaenia by history, clinical manifestations, physical examination, laboratory tests, bone marrow examination and so on.⁴ In the study, the search of patients with ITP was according to International Classification of Diseases, Ninth Revision, Clinical Modification code 287.3. In the setting of nationwide population, obviously, most patients with thrombocytopaenia initially see haematologists, rather than rheumatologists. Under the circumstances, some early stage of SLE patients with thrombocytopaenia as the only initial manifestation may be wrongly diagnosed as ITP and were included in ITP group in the study. Therefore, serious selection bias exists, which is, at least in part, attributable to the incredibly high HR. The authors should have checked the diagnosis of ITP before these patients were included in the ITP group. A potential solution is to exclusively include the patients with negative auto-antibodies at the time of ITP diagnosis. Second, only 0.19% of patients in the non-ITP group developed SLE during follow-up. In the context of extremely low incidence rates, a cohort design is deeply challenging and problematic and usually lead to poor robustness of estimates, embodied in the particularly wide 95% CI in the study (eg, 95% CI 13.7 to 46.0). Meanwhile, although the authors had controlled a range of baseline characteristics, several considerable risk factors strongly related to developing SLE still failed to be adjusted, for example, family history of SLE (or rheumatic diseases) in first-degree relatives and smoking.⁵ The presence of residual factors was acceptable in some situation, but the confounding bias caused by confounding factors could be amplified in the presence of extremely low incidence

rates and largely weakened the reliability of findings. In addition, we consider the time to the SLE for the two groups should be provided in the study.

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