Response to: 'Correspondence on 'Risk of systemic lupus erythematosus after immune thrombocytopenia and autoimmune haemolytic anaemia: a nationwide French study" by Maquet *et al*

We thank Maquet *et al*[1] for their interest in our articles entitled 'Increased risk of systemic lupus erythematosus (SLE) in patients with autoimmune haemolytic anaemia (AIHA): a nationwide population-based cohort study'[2] and 'Risk of systemic lupus erythematosus in patients with idiopathic thrombocytopenic purpura (ITP): a population-based cohort study'.[3]

Maquet *et al*[1] estimated the cumulative incidence of SLE after incident primary ITP and AIHA in France. But they found that the cumulative incidence of SLE in France was significantly lower than our previous study results.[2 3] Therefore, we reassessed cumulative incidences stratified by age and sex to compare the data between Taiwan and France. Finally, our study[4] showed the 1-year/5-year cumulative incidences of SLE in adult patients with primary ITP (5.0%/10.7%) and adult patients with primary AIHA (11.6%/19.5%) in Taiwan were higher than in those in French ITP and AIHA cohorts (1.0%/1.9% and 0.5%/1.0%).[1] In addition, when we studied the primary AIHA cohort, we also found that the incidence of SLE was higher in patients aged <18 years than in those aged 18–45 years,[4] which was inconsistent with their study.[1]

Maquet *et al*[1] also commented that the numbers of patients with ITP and AIHA in our previous studies[2 3] were unexpectedly low compared with their study in France. In our previous studies, we only considered patients with ITP and AIHA if they had been hospitalised for at least one time with corresponding diagnoses.[2–4] Therefore, in the present study, we defined patients with ITP or AIHA as having at least three outpatient visits or one hospitalisation with a diagnosis of ITP or AIHA and having received therapy with corticosteroid and/or immunomodulatory agents within the first 6 months after the first diagnosis of ITP or AIHA. Using the 2003–2013 National Health Insurance Research Database, we collected eligible patients with newly diagnosed ITP or AIHA from 2005 to 2012 and excluded patients who had a diagnosis of SLE during inpatient or outpatient visits before the first date of ITP or AIHA diagnosis. The comparison groups for the ITP group and AIHA group included individuals who never had a diagnosis of ITP or AIHA during 2003–2013. Patients with SLE were defined as having at least three outpatient visits or one inpatient visit with SLE diagnosis (the International Classification of Diseases, Ninth Revision (ICD-9) code 710.0). Follow-up started on the date of the first diagnosis of ITP/AIHA and ended at SLE occurrence, withdrawal from the national insurance due to any cause such as death or leaving or end of the study (31 December 2013), whichever came first. We matched the AIHA group and non-AIHA group at a ratio of 1:20 for sex, age and year of the index date. Then, further propensity-score matching (PSM) was performed for the two groups at a ratio of 1:2 for the same selected comorbidities in our previous studies.[2 4] The ITP group and non-ITP group were selected using the same method.[3] Finally, after propensity-score matching, we identified 3179 patients with incident ITP/6358 individuals with no ITP and 914 patients with incident AIHA/1828 participants with no AIHA. We calculated incidences of SLE and conducted multivariable stratified analyses for the risks of SLE associated with ITP and AIHA using the conditional Cox model shown as HRs with 95% CIs (table 1).

As shown in table 1, the risks of SLE were increased in patients with ITP (HR, 135.91; 95% CI, 56.16 to 328.92) and in patients with AIHA (HR, 83.96; 95% CI, 31.03 to 227.21), which were higher than results from previous studies.[2 3] The ITP-associated SLE risk was consistently shown in those aged <65 years or women. No significant association between ITP and SLE risk could be demonstrated in those aged ≥65 years or men, given that no incident SLE cases were found in the corresponding control groups. The AIHA-associated SLE risk was consistently revealed in those aged <65 years and those aged ≥65 years. Although the magnitude of SLE risk associated with AIHA seemed higher in those aged <65 years (HR, 103.83) than in those aged ≥65 years (HR, 42.89), no significant interaction effect by the age group was found (p for interaction=0.376). The AIHA-associated SLE risk was statistically significant in women but no in men, given that no incident SLE case was found in men.

In conclusion, the present study showed that patients with incident ITP or AIHA receiving corticosteroid and/or immunomodulatory therapy at outpatient or inpatient setting had a markedly increased risk of SLE in Taiwan. Therefore, clinicians need to carefully monitor the laboratory indicators and symptoms associated with SLE during the follow-up process of patients with ITP or AIHA, especially in women and patients aged <65 years, in order to diagnose and treat SLE as soon as possible.

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Table 1 Multivariable stratified analyses for the risk of SLE associated with ITP or AIHA exposure in the propensity-score matched (1:2) populations

	ITP					AIHA				
	Non-ITP	ITP				Non-AIHA	AIHA			
	No. of events/total no. of patients (per 10^5 person months)		HR (95% CI)	P value	P for interaction	No. of events/total no. of patients (per 10^5 person months)		HR (95% CI)	P value	P for interaction
Overall	5/6358 (1.36)	307/3179 (197.44)	135.91 (56.16 to 328.92)	<0.001		4/1828 (3.96)	138/914 (357.31)	83.96 (31.03 to 227.21)	<0.001	
Age (years)					0.966					0.376
<65	5/4479 (1.82)	280/2246 (239.92)	124.33 (51.34 to 301.11)	<0.001		3/1100 (4.45)	122/552 (472.11)	103.83 (32.93 to 327.37)	<0.001	
≥65	0/1879 (0.00)	27/933 (69.61)	Cannot estimate	0.988		1/728 (2.96)	16/362 (125.19)	42.89 (5.41 to 339.81)	<0.001	
Gender					0.964					0.981
Female	5/4220 (1.97)	265/2110 (253.08)	118.62 (48.95 to 287.43)	<0.001		4/1130 (6.21)	109/565 (457.11)	68.09 (24.99 to 185.53)	<0.001	
Male	0/2138 (0.00)	42/1069 (82.71)	Cannot estimate	0.985		0/698 (0.00)	29/349 (196.26)	Cannot estimate	0.992	

AIHA, autoimmune haemolytic anaemia; ITP, immune thrombocytopenia; SLE, systemic lupus erythematosus.

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