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The Authors Reply: We have read the letter to the editor by Hugo and Eliseo.[1] Although all erythropoiesis-stimulating agent (ESA) products have potential immunogenicity, we do not think that induction of the recombinant erythropoietin antibody seems to be a class effect of ESA. Combe *et al.*[2] and Singh[3] have investigated biosimilar erythropoietins and showed tremendously different characteristics from one product to another, most likely resulting from the complexity of recombinant protein manufacturing. Thus, the stringent regulations and pharmacovigilance of each individual product is mandatory to ensure patients' safety.

All follow-up on recombinant erythropoietins in Thailand has been licensed with limited nonclinical/clinical data and without quality data, which makes it difficult to define these products as biosimilar by EMEA definition.[4] The registration of these products was licensed by generic chemical drug paradigm, and pharmacovigilance was not required. The Thai Food and Drug Administration (FDA) has now been revising the regulation including the license revision. On reviewing the data with the Thai FDA, we found that the pharmacovigilance plan of follow-up on recombinant erythropoietins in Thailand has never been submitted by any pharmaceutical industries. Pharmacovigilance is a proactive, well-planned action formally submitted to the regulator to monitor drug-related problems that may not be evidenced during the pre-marketing period. The Thai ESA registry has been initiated by Thai FDA and scientific societies, not the pharmaceutical industries, aiming to provide more precise risk of the immunogenicity.

Although aplastic anemia has been reported with higher incidence in Thailand compared with the West, this background has no link to the pathogenesis of anti-recombinant erythropoietin-associated pure red cell aplasia. The induction of neutralizing antibody of recombinant erythropoietins causes maturation arrest of erythroblasts and consequently pure red cell aplasia, whereas environmental toxin exposure causes damage of hematologic stem cells, resulting in pancytopenia and thus aplastic anemia.

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Hemodialysis vs. peritoneal dialysis in chronic heart failure: getting to the heart of the matter

To the Editor: REIN registry data published by Sens *et al.*[1] imply a survival benefit for hemodialysis (HD) in end-stage renal disease patients with chronic heart failure (CHF) condition when starting HD or peritoneal dialysis (PD). However, concerns relate to the correct CHF characterization in this study. Besides the nephrologist's judgment and a crude New York Heart Association (NYHA) classification (combined class NYHA III–IV), the degree of CHF remains unclear. Specifically, echocardiographic parameters of systolic or diastolic cardiac function were not provided. Second, CHF diagnosis was not ascertained at least one more time after dialysis onset. Thus, initial overhydration due to renal failure mimicking CHF cannot be ruled out. Third, no differentiation was made between valvular and non-valvular CHF. Finally, no specific NYHA class differentiation, i.e., the presence of NYHA class III or IV, was provided. When using the combination of NYHA III–IV, more PD patients may belong to NYHA IV and, vice versa, more HD patients may belong to NYHA III, which may represent an additional confounding issue. The prognosis for NYHA class-III or class-IV patients is quite different.[2] Thus, the combination of NYHA III–IV may have obscured a survival benefit for either dialysis modality. Unfortunately, neither brain natriuretic peptide (BNP) nor NT-proBNP, surrogates of CHF, was determined. BNP could have provided additional information on cardiorenal syndrome when interpreted over time after onset of dialysis.[3] Until proven otherwise, the main outcome, survival, may have been confounded by more severe CHF in terms of more NYHA class-IV patients in the PD group.

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2. Muntwyler J, Abetel G, Gruner C *et al.* One-year mortality among unselected outpatients with heart failure. *Eur Heart J* 2002; **23**: 1861–1866.
3. Chazot C, Vo-Van C, Zaoui E *et al.* Fluid overload correction and cardiac history influence brain natriuretic peptide evolution in incident haemodialysis patients. *Nephrol Dial Transplant* 2011; **26**: 2630–2634.