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# Treating critically ill anaemic patients with erythropoietin: why not?

Sigismond Lasocki<sup>1\*</sup> Antoine Kimmoun<sup>2</sup>, Gerald Chanques<sup>3</sup>, Lionel Velly<sup>4,5</sup> and Frédéric Pène<sup>6</sup>

Dear Editor,

We read with great interest the clinical practice guidelines on transfusion strategies recently published in the journal [1]. Although it followed a well designed and robust methodology, we are concerned by the recommendation against the use of erythropoietin (EPO, with or without iron) in critically ill patients. Following a similar methodology, we ended up with different conclusions in our national guidelines under the aegis of the French society of anaesthesiology and critical care (SFAR) and the French intensive care society (SRLF) [2, 3]. Indeed, recent meta-analyses report a decrease in red blood cell transfusion and a reduction in mortality (relative risk for hospital mortality 0.82, 95% CI 0.71–0.94,  $p=0.006$ ,  $I^2=0.1\%$ ) [4], without evidence for increased morbidity, neither for thromboembolic events nor for cardiovascular complications [4, 5]. This is why we recommended the use of erythropoietin to treat anaemia in the critically ill patients. Because the use of EPO is not widely admitted for critically ill patients and because morbidity is not well described in all the randomized controlled trials (RCTs), we choose to downgrade the recommendation to a grade 2 level (optional recommendation). We also mentioned that anaemic and trauma patients may draw a greater benefit from this treatment because the evidence of a reduction in mortality comes mainly from these subpopulations. We agree that one should remain cautious about the potential risk of adverse event (mainly thrombosis), and we also recommended to target reasonable haemoglobin levels (not higher than 12 g/dl), since higher targets are associated with worse outcomes

**Table 1 Hospital cost for 40,000 UI of epoietin alpha and estimated cost for “one saved life”**

	Cost for 40,000 UI epoietin alpha <sup>a</sup>	Estimated cost for one life saved <sup>b</sup> (K€)
Australia	AUD 965 (€ 588) (Cost for the patient: AUD 41 or 6.6 = € 25 or 4)	65.2
Canada	CDN 426 (€ 296)	32.8
Denmark	€ 400	44.4
France	€ 61	6.8
Germany	€ 35	3.9
Italy	€ 120	13.3
Spain	€ 49	5.4
UK	£ 193 (€ 222)	11.3
USA	USD 685 (€ 632)	70.1
Mean cost	€ 267	13.7

<sup>a</sup> Costs of epoietin (mostly biosimilars) were obtained from one hospital in each country and may vary across the country.

<sup>b</sup> This cost was estimated using the data from the published meta-analysis from Litton et al. showing that 37 patients had to be treated to save one life (using the reported hospital mortality) [4] and assuming that patients received a mean of 3 injections (estimated cost =  $37 \times 3 \times$  cost of 1 injection).

in patients with chronic kidney disease [2, 3]. In addition, it has to be emphasized that iron deficiency was treated in most of the large RCTs evaluating erythropoietin, making it difficult to decipher the results of studies addressing the interest of erythropoietin alone or of erythropoietin + iron. The main reason advocate by the ESICM expert panel against the use of erythropoietin is the cost of the product [1]. Nowadays, due to the arrival of biosimilars in the market in most countries, costs of erythropoietin have dramatically decreased and the estimated “price” for saving one life is quite fair in most of the places, being as little as 3900 € in Germany (see Table 1). Efforts should probably be made at the European level to

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reduce the cost of erythropoietin where it remains high. We thus believe that erythropoietin should be considered to limit transfusion and improve outcome in critically ill patients. This is in agreement with the European Guidelines, indeed, the experts stated at the end of their argumentation that “At the same time, given the lack of signal for harm, some clinicians and ICUs may reasonably choose to adopt EPO, if sufficient resources exist for implementation” [1]. A new large randomized controlled trial is thus required to provide definite conclusions on the current benefit–risk balance of this treatment, in all ICU patients.

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#### Compliance with ethical standards

#### Conflicts of interest

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