Response

To the Editor:

We thank Peled and Dau for their comments on the 2018 CHEST guidelines.1 We agree with their concern regarding the cost of reversal agents and inappropriate utilization. The major advance of non-vitamin K antagonist oral anticoagulants is that they are vastly safer than vitamin K antagonists with respect to life-threatening or fatal bleeding without an antidote. Therefore, reversal agents (both nonspecific and specific) will be needed infrequently and should be used sparingly. We also agree that the lack of a clinical trial directly comparing prothrombin complex concentrates (PCCs) with specific reversal agents in the setting of life-threatening bleeding limits the ability to make strong recommendations regarding the superiority of one strategy over the other, which is why the statement regarding this topic in the 2018 CHEST guideline was made as an expert consensus opinion.

We disagree, however, with their statement that the data supporting PCCs and andexanet are equivalent. There are two criteria when evaluating reversal agents: do they normalize the laboratory coagulation abnormalities and, most importantly, is there evidence that they improve clinical outcomes? PCCs have demonstrated variable ability to normalize coagulation parameters in healthy volunteers, whereas andexanet leads to near complete normalization of coagulation parameters in actual bleeding patients. Peled and Dau do make the important point that normalizing a laboratory test is only a surrogate for what we really care about, which is improving the prognosis of patients who present with life-threatening bleeding. However, in this regard, PCCs again fall short of andexanet. They cite a real-world study by Majeed et al2 that included 84 patients with a major bleed from Sweden treated with PCCs where the 30-day mortality was 32%. In a prospective cohort study in nine Canadian hospitals, 66 patients on apixaban or rivaroxaban suffering a major bleed were treated with PCCs, with 14% mortality by 30 days, and 8% had major thromboembolic events.3 The international Andexanet Alfa, a Novel Antidote to the Anticoagulation Effects of FXA Inhibitors (ANNEXA-4) trial enrolled 352 patients with major bleeding treated with andexanet, and the 30-day mortality was only 14%.4 The cost-benefit analysis of available treatments is critical in any health-care ecosystem. For patients who truly present with life-threatening non-vitamin K antagonist oral anticoagulant-associated bleeding, we felt the opportunity to save more lives warrants preference of specific reversal agents over PCCs.

Gregory Y. H. Lip, MD
Birmingham, England
Christian T. Ruff, MD, MPH
Boston, MA
Lisa Moores, MD, FCCP
Bethesda, MD
on behalf of the 2018 CHEST Guideline Expert Panel

Affiliations: From the Liverpool Centre for Cardiovascular Science (Dr Lip), University of Liverpool, and Liverpool Heart and Chest Hospital, Liverpool, England; the Aalborg Thrombosis Research Unit (Dr Lip), Department of Clinical Medicine, Aalborg University, Aalborg, Denmark; the Cardiovascular Medicine Division (Dr Ruff), Brigham and Women’s Hospital, Harvard Medical School; and the F. Edward Hebert School of Medicine (Dr Moores), The Uniformed Services University of the Health Sciences.

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Correspondence to: Gregory Y. H. Lip, MD, West Derby St, Liverpool, L7 8TX, England; e-mail: gregory.lip@liverpool.ac.uk

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References


The New CHEST Guidelines on Antithrombotic Therapy for Atrial Fibrillation Should Consider Recent Data on Rivaroxaban

To the Editor:

We are writing regarding the recently updated CHEST guidelines (November 2018) on antithrombotic therapy for atrial fibrillation (AF). These guidelines recommend the use of non-vitamin K antagonist oral anticoagulants (NOACs) over vitamin K antagonists for the prevention of stroke in patients with AF. However, a recommendation specifically to use