

Response Letter:

The authors gratefully acknowledge the constructive and helpful suggestions made by the reviewers.

The manuscript has been revised according to their advice.

The following revisions have been made:

Reviewer 00729478: No revisions demanded.

Reviewer 00013033:

1. The paper is way too long please shorten and better focus.
We made several abridgements, reducing the word count of the main body (introduction to conclusion) from 4434 to 3649.
To do this we focussed more on gastrointestinal cancers, however solid data on gastrointestinal cancer patients with regard to VTE are very rare.
2. Reference style should be adjusted.
Has been done.
3. Please add a table with 5-6 bullet points as main take home messages.
With pleasure we followed this suggestion and included a new table (Table 6).

Reviewer 01992073

„The manuscript by Riess and colleagues is an interesting review of primary prevention and treatment of venous thromboembolic events (VTE) in patients with gastrointestinal (GI) cancers. Overall, the article is potentially interesting and worthy of consideration. However, although the Authors declare their intention of focusing on VTE management in GI cancers, the paper is centered on cancer patients in general. Thus, the innovative aspect of the article (the focus on GI tumors) is completely lost, endangering its novelty and publishing priority. As GI cancers are a miscellanea of cancer types with different VTE rates, I would have expected **a more detailed scrutiny of the available evidences on different GI cancer types**. Not all guidelines, for example, recommend thromboprophylaxis for pancreatic cancer; all agree on the need to treat high risk tumors, **but stomach cancer (high risk in the Khorana score) is never referred to**. The situation is even more confusing for colorectal cancer that, although previously considered as “low-risk”, could be probably **classified as intermediate (Thromb Res 2015; 135: 472-478)**. A thorough discussion of these or similar issues would have greatly increased the significance of the manuscript. The English form needs to be improved for clarity and grammar. **References are not up-to-date**, some are duplicated (Ref. # 32 is the same as # 81) and some relevant articles are missing. For example, authors report on the implementation of Khorana score using laboratory variables, but they completely overlooked a similar approach that used drugs to improve VTE risk prediction (**the Protecht score**). Furthermore, the **recent guidance from the SSC of the ISTH on the use of Khorana score to classify high risk patients who may benefit from thromboprophylaxis should be cited, as it should the recent review on pro and cons of NOACs by Verso et al. (Intern Emerg Med 2015; 10:651-656)**. Reference format and authors’ name correctness should be also checked.“

We absolutely agree, that only very few studies are available which deal with VTE, VTE prevention and VTE treatment in patients with GI cancers. VTE rates in different GI cancers differ widely, most likely according to different cancer stages and other, patient- or treatment-related characteristics in addition to the specific type of GI cancer. In the revised manuscript we provide more numerical data on incidence.

Despite the fact that gastric cancer is considered „high risk“ in the Khorana score, we are not aware of relevant results or subgroup analyses with regard to VTE prevention or VTE therapy in patients with cancer of the stomach.

With regard to prevention and treatment, we agree that the situation for specific GI cancer types is confusing. With very rare exceptions, high grade evidence on which to base specific recommendations for most cancers – and this is also true for GI cancers – is lacking. This is reflected in the variable guideline statements. In most cases recommendations for patients with GI cancers must be derived from studies investigating a heterogeneous collective of cancer patients, including patients with GI cancers. Some of these studies report subgroup analyses including GI cancers. We update Table 3 with the results from the PROTECHT study, where results for GI cancers are also available.

The Protecht score, the meta-analysis from Verso et al. and the SCC guidance have been included.

The reference format and authors names have been checked.

The English has been checked. We gratefully acknowledge the help of Sue Trevis, Canberra, a native English co-worker.