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Pomalidomide for Epistaxis in Hereditary Hemorrhagic Telangiectasia

Atieh Modarresi Ph.D., D.Pharm.,[1] Catherine Rennie PhD FRCS,[2] Claire L. Shovlin PhD FRCP[1*]

**Corresponding author: c.shovlin@imperial.ac.uk*

[1] National Heart and Lung Institute, Imperial College London; London, UK; [2] Imperial College Healthcare NHS Trust, London; London, UK

We read with interest the results of pomalidomide for epistaxis in hereditary hemorrhagic telangiectasia.[1] There is a clear unmet need for oral agents where topical approaches, and other oral randomised controlled trial-supported therapies such as tranexamic acid and tamoxifen have been insufficient.[2] Monoclonal antibodies to vascular endothelial cell growth factor (bevacizumab and biosimilars) are widely used,[2] but intravenously administered with attendent limitations. The first-generation immuno-modulatory drug, thalidomide, found a role in HHT, and pomalidomide was expected to have better safety profiles.

Overall, reported efficacy was modest, and stated to be similar in *ENG* and *ACVRL1* genotypes.[1] Patients with HHT usually display variable responses to treatments and it would help to know if some participants were 'better' responders to pomalidomide. This is particularly important as accumulating clinical[3] and laboratory[3,4] data indicate the type of pathogenic gene variant may explain a proportion of variability, both for epistaxis severity, and in the magnitude of individual responses to therapies.[3] To help position pomalidomide (*Figure 1*), data on reponse variability, and any relationships with HHT sub-genotypes, would be valuable additions.

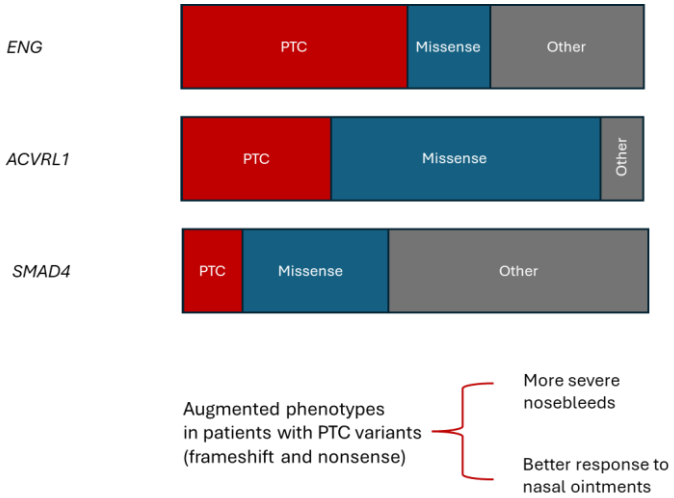


Figure 1: Major genes for hereditary haemorrhagic telangiectasia, and proportional representation of molecular subtypes. Further molecular detail is provided by Bernabeu-Herrero and colleagues.[3] The data suggesting medication efficacy and adverse events differ between genotypes is summarised elsewhere.[5] PTC, premature termination codon (frameshift and stop gain variants).

References

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The authors declare no conflict of interest. The use of MEK1 inhibitors for treatment of HHT bleeding is the subject of a patent application by Imperial College London