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Pomalidomide in Hereditary Hemorrhagic Telangiectasia

A PLAIN LANGUAGE SUMMARY

Based on the NEJM publication: Pomalidomide for Epistaxis in Hereditary Hemorrhagic Telangiectasia by H. Al-Samkari et al. (published September 19, 2024)

In this trial, researchers evaluated the efficacy and safety of pomalidomide, a thalidomide derivative, in treating hereditary hemorrhagic telangiectasia (HHT).

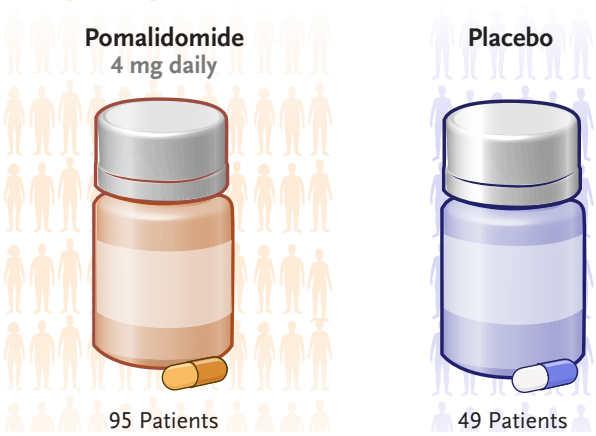
HHT is the second most common inherited bleeding disorder. The primary clinical manifestation is epistaxis that results in iron-deficiency anemia and reduced health-related quality of life.

WHY WAS THE TRIAL DONE?

No treatments for HHT are approved in the United States or Europe. Thalidomide, an immunomodulatory drug that might have efficacy in HHT, is associated with serious toxic side effects. Whether pomalidomide, a thalidomide derivative, has efficacy in treating HHT along with a more favorable safety profile is unknown.

HOW WAS THE TRIAL CONDUCTED?

144 patients were assigned to receive pomalidomide at a dose of 4 mg daily or matching placebo for 24 weeks. The primary outcome was the change in the Epistaxis Severity Score (range, 0 to 10, with higher scores indicating worse bleeding) from baseline through week 24. A reduction of 0.71 points or more is considered clinically significant.



PATIENTS

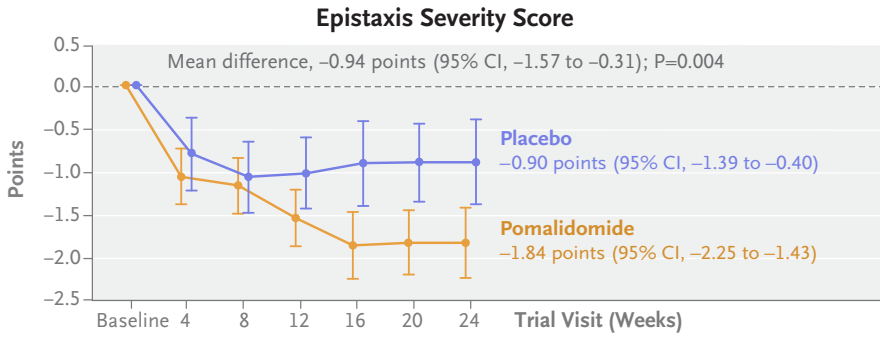
WHO	144 adults Mean age: 58.8 years
CLINICAL STATUS	A definite diagnosis of HHT as defined by the Curaçao criteria Epistaxis Severity Score of at least 3 within the 3 months before screening Anemia at screening or iron infusions or red-cell transfusions in the previous 6 months

TRIAL DESIGN

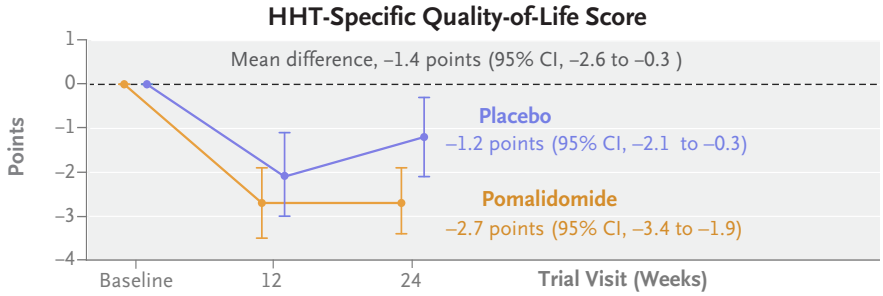
- DOUBLE-BLIND
- RANDOMIZED
- PLACEBO-CONTROLLED
- 11 U.S. SITES

RESULTS

At 24 weeks, the reduction in the Epistaxis Severity Score was significantly greater in the pomalidomide group than in the placebo group.



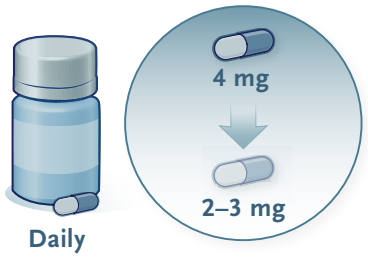
The HHT-specific quality-of-life score (a key secondary outcome) decreased by 2.7 points with pomalidomide as compared with 1.2 points with placebo (higher scores indicate more limitations).



Among adverse events of special interest, constipation, neutropenia, and rash were common and occurred more often with pomalidomide than with placebo.

DOSE REDUCTION

Dose reductions to 3 mg or 2 mg were allowed if toxic effects occurred.



Doses were reduced in 37% of pomalidomide recipients, as compared with 4% of placebo recipients.

LIMITATIONS AND REMAINING QUESTIONS

- Evidence of efficacy based on changes in the Epistaxis Severity Score led to early trial termination, which resulted in a lower number of patients than the planned sample size, thus affecting the power for secondary outcome analyses.
- Lower doses of pomalidomide might have had similar efficacy with fewer toxic effects.
- Black patients were underrepresented.

CONCLUSIONS

Among patients with HHT, pomalidomide reduced epistaxis severity and appeared to improve disease-specific quality of life, with no unexpected safety signals.

LINKS: FULL ARTICLE | NEJM QUICK TAKE

FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT03910244

Trial funding: National Heart, Lung, and Blood Institute

Full citation: Al-Samkari H, Kasthuri RS, Iyer VN, et al. Pomalidomide for epistaxis in hereditary hemorrhagic telangiectasia. N Engl J Med 2024;391:1015-27. DOI: 10.1056/NEJMoa2312749