PATH-HHT

ABOUT PATH-HHT

The PATH study is exploring the use of an oral medication called pomalidomide for the treatment of nosebleeds in HHT at up to 15 research centers across the United States. Adults suffering from HHT with moderate to severe nosebleeds (epistaxis) who have anemia and/or require iron infusions or blood transfusions are eligible. During the 6-month study treatment period, patients might receive either pomalidomide or a matching placebo (sugar pill) in addition to their usual care.

PATH is funded by a grant from the National Heart, Lung and Blood Institute, and is led by researchers at the Cleveland Clinic and RTI International. Pomalidomide is an FDA-approved drug for the treatment of some cancers and is manufactured by Celgene.

You can also learn more about the study from the study website: https://path-hht.org

AIMS AND OBJECTIVES

Primary Objective: To determine efficacy of pomalidomide compared to placebo for the reduction in severity of epistaxis after 24 weeks of treatment.

Secondary Objectives: To determine the safety and tolerability of pomalidomide for the treatment of HHT; to determine if pomalidomide treatment improves quality of life in HHT; to determine whether a continued response to pomalidomide is evident 4 weeks after treatment discontinuation; to develop a biorepository for future studies to define biomarkers predictive of pomalidomide response and allow investigations into the biology of HHT and mechanisms of pomalidomide.

INCLUSION CRITERIA

1. Clinical diagnosis of HHT as defined by the Curacao criteria
2. Age ≥ 18 years
3. Platelet count ≥ 100 x 10^9/L
4. WBC ≥ 2.5 x 10^9/L
5. INR ≤ 1.4 and normal ± 2 sec activated partial thromboplastin time (aPTT), except for patients on a stable dose of warfarin or direct oral anticoagulants
6. Epistaxis severity score ≥ 3 measured over the preceding 3 months
7. Requirement for anemia (as determined by local laboratory normal ranges) or parenteral infusion of at least 250 mg of iron or 1 unit of blood transfusion in the preceding 24 weeks
8. Participants must agree to be registered and comply with the FDA mandated POMALYST REMS® program
9. Females of childbearing potential must adhere to the POMALYST REMS® pregnancy testing schedule

10. Ability to understand and sign informed consent

EXCLUSION CRITERIA

1. Women currently breast feeding or pregnant
2. Renal insufficiency, serum creatinine > 2.0 mg/dl
3. Hepatic insufficiency, bilirubin > 2.0 (or >4.0 for patients with Gilbert's syndrome) or transaminases > 3.0x normal
4. Thalidomide or other Immunomodulatory imide drugs (IMiDs) treatment within previous 6 months
5. Prior treatment with bevacizumab (systemic or nasal) within previous 6 weeks*
6. Prior treatment with pazopanib within previous 6 weeks*
7. The use of octreotide or oral estrogens within the previous month*
8. History of prior unprovoked thromboembolism confirmed by venous ultrasound or other imaging modalities
9. Peripheral neuropathy, confirmed by neurologic consultation
10. Known underlying hypoproliferative anemia (i.e. myelodysplasia, aplastic anemia)
11. Currently enrolled in other interventional trials
12. Known hypersensitivity to thalidomide or lenalidomide.
13. Development of erythema nodosum as characterized by a desquamating rash
14. Known SMAD-4 mutation, unless there has been a normal colonoscopy or no more than 5 small polyps removed within the previous 18 months
15. Anything that in the investigator's opinion is likely to interfere with completion of the study

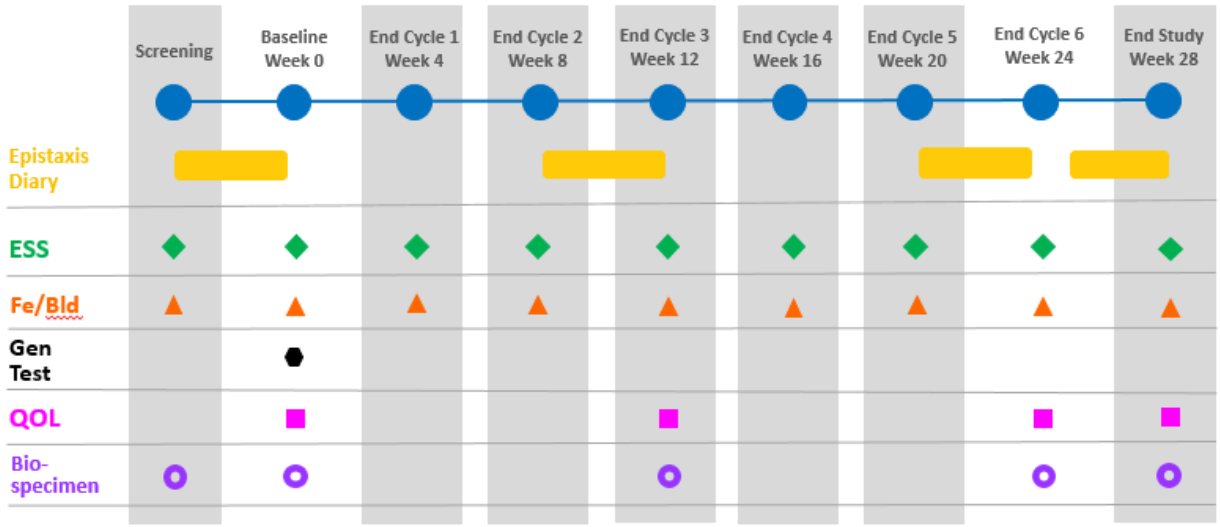
* Use of these treatments is not permitted during study participation.

STUDY SITES

Site Number	Site Name	Phone Number
P01	Cleveland Clinic	216-587-8718
P02	Massachusetts General Hospital	857-242-0719
P03	UNC HHT Center of Excellence	919-966-2790
P05	Johns Hopkins Medicine	443-974-8071
P06	University of California San Francisco Medical Center	415-353-9437
P07	University of Pennsylvania Perelman School of Medicine	267-326-1420
P08	Medical College of Wisconsin	414-805-7291
P09	University of Utah	801-928-3828
P10	Mayo Clinic	507-284-9259
P12	University of Florida	352-273-7503
P14	UCSD Hemophilia and Thrombosis Treatment Center	858-657-6437
P15	University of Minnesota	612-625-3278

SCHEDULE OF EVENTS

Total duration	8 months
# Study Visits	Total 9; **7/9** (gray shaded box in figure) can be completed remotely if safe for participant
ESS	Epistaxis Severity Score; a series of 6 questions to determine severity of nosebleeds
Epistaxis Diary	A phone app (or paper diary if unable to use app) to record details of nosebleed for a 4 week period
Fe/Bld	Laboratory tests, which include Complete Metabolic Panel, Complete Blood Count with Differential and Iron Studies
Genetic Test	Optional; test to include a panel of 6 genes that are known to be involved in HHT
Biospecimen	Optional; Sample collection for biorepository for future studies in HHT
QOL	Quality of Life questionnaires; a total of 26 questions to see how HHT influences various aspects of your life



STUDY COSTS

	Standard Of Care	**Research**
Study Drug	N/A	Provided by Study
Blood Test (CMP, CBC+DIFF, Iron Studies)	Billed to participant insurance	
Genetic Test	Billed to participant insurance, if private	Copays (private insurance) covered by study; Billed to study if insurance is federal
Epistaxis Diary Phone App		App available free of cost to study participants for study duration

IMPORTANT PRECAUTIONS

Pomalidomide is structurally similar to thalidomide, which is known to cause birth defects. Therefore, use of pomalidomide comes under the FDA-mandated REMS program, where patients are expected to **use effective birth control methods** in order to prevent pregnancy while taking pomalidomide. In addition**, females of child bearing potential are expected to undergo periodic pregnancy tests**.

CLINICALTRIALS.GOV

PATH is registered with clinicaltrials.gov. More information on the study design and status can be found here: https://www.clinicaltrials.gov/ct2/show/NCT03910244 or at https://path-hht.org/.