PATH-HHT

ABOUT PATH-HHT

The PATH-HHT study is exploring the use of an oral medication called pomalidomide for the treatment of nosebleeds in HHT at about 11 research centers across the United States. Adults suffering from HHT with moderate to severe nosebleeds (epistaxis) who require iron infusions or blood transfusions are eligible. During the 6-month study, 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 nosebleeds after 24 weeks of treatment.

Secondary Objectives:

a) To determine the safety and tolerability of pomalidomide for the treatment of HHT
b) To determine if pomalidomide treatment improves quality of life in HHT
c) To determine whether there is a continued response to pomalidomide 12 weeks after treatment discontinuation
d) 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 109/L
4. WBC ≥ 2.5 x 109/L
5. INR ≤ 1.4 and normal activated partial thromboplastin time (aPTT)
6. Epistaxis severity score ≥ 3 measured over the preceding 3 months
7. Parenteral infusion of at least 250 mg of iron or 1 unit of blood transfusion in the preceeding 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

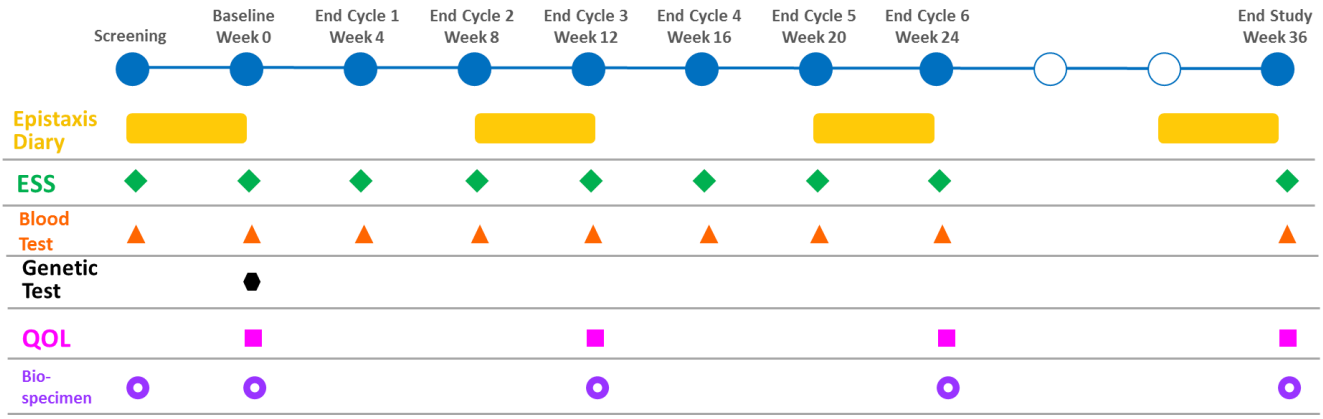
1. Women currently breast feeding or pregnant
2. Renal insufficiency, serum creatinine > 2.0 mg/dl
3. GI bleeding thought to be related to hepatic insufficiency, bilirubin > 2.0 or transaminases > 3.0x normal
4. Thalidomide or other Immunomodulatory imide drugs (IMiDs) treatment within previous 6 months
5. Prior treatment with bevacizumab (systemic or nasal) within previous 8 weeks
6. The use of octreotide or estrogens within the previous month
7. History of prior thromboembolism confirmed by venous ultrasound or other imaging modalities
8. Peripheral neuropathy, confirmed by neurologic consultation
9. Known underlying hypoproliferative anemia (i.e. myelodysplasia, aplastic anemia)
10. Currently enrolled in other interventional trials
11. Known hypersensitivity to thalidomide or lenalidomide.
12. Development of erythema nodosum as characterized by a desquamating rash
13. Known SMAD-4 mutation
14. Anything that in the investigator's opinion is likely to interfere with completion of the study

STUDY SITES

Site Number	Site Name	Phone Number
P01	Cleveland Clinic	216-445-2246
P02	Massachusetts General Hospital	857-242-0719
P03	UNC HHT Center of Excellence	919-966-2790
P04	UT Southwestern Medical Center	214-645-6493
P05	Johns Hopkins Medicine	410-502-3628
P06	University of California San Francisco Medical Center	415-514-8995
P07	University of Pennsylvania Perelman School of Medicine	215-573-0293
P08	Medical College of Wisconsin	414-805-7291
P09	University of Utah	801-213-3417
P10	Mayo Clinic	507-284-9259

SCHEDULE OF EVENTS

Total Study Duration: 9 months



STUDY COSTS

	Standard Of Care	**Research**
Study Drug		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