An interim assessment of bleeding events in a prospective natural history study of hereditary hemorrhagic telangiectasia patients using a validated bleeding scale and a novel daily reporting instrument

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OVERVIEW

- A natural history (NH) study of adults with hereditary hemorrhagic telangiectasia (HHT) to characterize epistaxis and quality of life
- Interim analysis from patients enrolled between January and August 2025.
- Study supports design of a clinical trial investigating DIAG723, a novel bispecific ALK-1 and BMPRII agonist antibody in 2026

INTRODUCTION

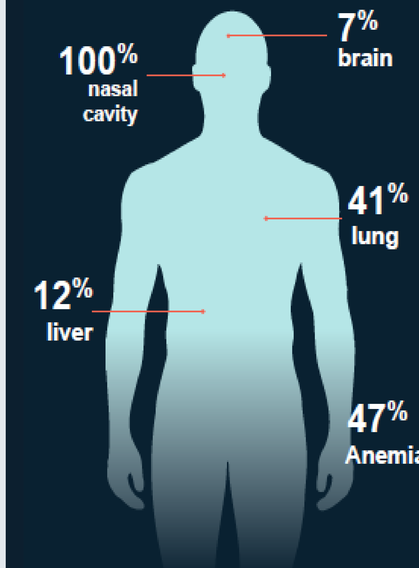
HHT is an inherited hematological disease characterized by arteriovenous malformations (AVMs) and recurrent bleeding in multiple vascular beds. There are no approved therapies for HHT. More than 90% of HHT patients have loss-of-function mutations in Endoglin (HHT1) or ALK1 (HHT2) genes. Recurrent epistaxis and gastrointestinal bleeding are common in HHT. This NH study of HHT provides important insights into various aspects of disease progression in the absence of available therapies. Data generated support design of clinical-trial endpoints and patient-reported outcome (PRO) instruments for a clinical trial with DIAG723, a novel disease-modifying therapy for HHT.

METHODS

A prospective natural history study of HHT patients with an Epistaxis Severity Score (ESS) at enrollment of ≥ 4 was jointly initiated by Diagonal Therapeutics, Inc. (Boston, MA) and Cure HHT (Monkton, MD) to evaluate various aspects of HHT disease progression. A novel PRO instrument – During My Day Diary (DMDD) – captured daily reported frequency, duration, and severity of epistaxis events as well as patient-reported quality-of-life data. Interim data are reported herein.

RESULTS

AVM Prevalence Reported by Patients

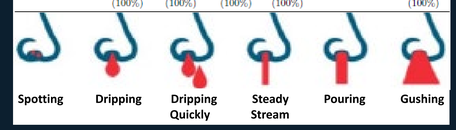


Baseline Patient Characteristics

Characteristic	N = 68
Age at time of Informed Consent	51 (41, 61)
Sex at birth	
F	53 (78%)
M	15 (22%)
Race	
Other	3 (4.5%)
White	64 (96%)
Unknown	1
Ethnicity	
HISPANIC OR LATINO	8 (12%)
NOT HISPANIC OR LATINO	60 (88%)

DMDD Epistaxis Severity

	M1, D1	M2, D1	M3, D1	M4, D1	Unscheduled Visit	Total
Severity Category						
Spotting	11 (31%)	224 (28%)	47 (14%)	0 (0%)	11 (24%)	293 (24%)
Dripping	6 (17%)	284 (35%)	145 (44%)	2 (40%)	13 (28%)	450 (37%)
Dripping Quickly	13 (36%)	174 (22%)	107 (32%)	1 (20%)	12 (26%)	307 (25%)
Steady Stream	4 (11%)	82 (10%)	28 (8.5%)	1 (20%)	10 (22%)	125 (10%)
Pouring	2 (5.6%)	33 (4.1%)	3 (0.9%)	1 (20%)	0 (0%)	39 (3.2%)
Gushing	0 (0%)	7 (0.9%)	1 (0.3%)	0 (0%)	0 (0%)	8 (0.7%)
Total	36 (100%)	804 (100%)	331 (100%)	5 (100%)	46 (100%)	1,222 (100%)



DMDD Epistaxis Duration

	M1, D1	M2, D1	M3, D1	M4, D1	Unscheduled Visit	Total
Response						
< 1 minute	2 (5.6%)	25 (3.2%)	9 (2.7%)	0 (0%)	0 (0%)	36 (3.0%)
1 - 5 minutes	14 (39%)	311 (39%)	100 (30%)	2 (40%)	16 (35%)	443 (37%)
6 - 15 minutes	8 (22%)	303 (38%)	156 (47%)	3 (60%)	10 (22%)	480 (40%)
16 - 30 minutes	8 (22%)	85 (11%)	56 (17%)	0 (0%)	9 (20%)	158 (13%)
> 30 minutes	4 (11%)	68 (8.6%)	9 (2.7%)	0 (0%)	11 (24%)	92 (7.6%)
Total	36 (100%)	792 (100%)	330 (100%)	5 (100%)	46 (100%)	1,209 (100%)

ESS vs During My Day Diary via ePRO Mobile App

ESS

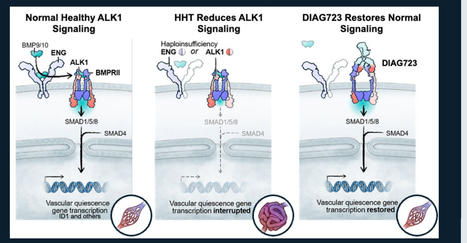
- Frequency: 60% with daily events
- Duration: 60% at 6-30 min/event
- Intensity: pouring/gushing in 41%
- Overall epistaxis severity:
  - 23% mild, 68% mod, 9% severe

During My Day Diary

- Frequency: 25/month
- Duration: 18 min/event
- Intensity:
  - Dripping quickly or steady stream 35%
  - Gushing or pouring 3.9%

DIAG723: Novel HHT Therapy

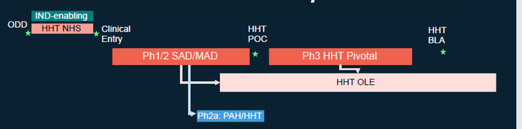
Bispecific Clustering Antibody



- Interim data is from enrollment between January and June of 2025: 94 adult HHT patients screened and 91 enrolled.
- Mean and median screening ESS were 5.3 (SD 1.5) and 5.5, respectively. ESS at 1 month showed 22.7% of population had mild disease (ESS ≤ 4), 68.0% moderate (4 < ESS ≤ 7), and 9.3% severe (ESS > 7). More than 60% of patients had daily epistaxis and 39% had several events daily. Epistaxis duration in 60% of patients was 6-15 minutes (37%) or 16-30 minutes (23%). Epistaxis intensity was typically pouring or gushing in 41% of patients.
- During My Day Diary: mean frequency of epistaxis was 25/month and mean duration 18 minutes/event. With a visual analog scale, epistaxis intensity pouring or gushing in 3.9% and dripping-quickly or steady-stream intensity in 35%.
- Daily-diary frequency, severity, and intensity of epistaxis at 3 months did not differ significantly from the 1-month timepoint.
- 41% of the patients reported having lung AVMs, 12% hepatic AVMs, and 7% brain AVMs, and 47% reported anemia in the last 3 mos. QoL assessments, nocturnal bleeding, and menstrual bleeding will be reported in the final analysis.

DIAG723 DEVELOPMENT

DIAG723 Clinical Development Plan



Phase 1 and 2 Clinical Trial

CONCLUSIONS

Here we report preliminary results of an ongoing natural history study of HHT patients with moderate-to-severe bleeding.

- Baseline ESS results and daily-diary reporting at 1 and 3 months were consistent, with daily bleeding events described by many in the population as frequently gushing or pouring.
- Diary-reported bleeding intensity was markedly lower than reported by ESS which required recall of intensity over a 1–3-month period.
- Final analysis will report patient bleeding events, QoL and impact of HHT on daily living to support interventional clinical trial and pivotal endpoint design to test novel therapeutics in the moderate-to-severe HHT population.

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