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athn transcends

ATHN Transcends: A Natural History Cohort Study of the Safety, Effectiveness, and Practice of Treatment in People with Non-Neoplastic Hematologic Disorders

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Background

The impact of the American Thrombosis and Hemostasis Network (ATHN) clinical research program has advanced knowledge and transformed the care provided to individuals affected by bleeding disorders, clotting disorders and other rare blood disorders. However, the administrative and financial burden of maintaining many studies at each collaborating site is overwhelming the resources of individual researchers and their sites. In order to address this concern, ATHN Transcends: A Natural History Cohort Study of the Safety, Effectiveness, and Practice of Treatment of People with Non-Neoplastic Hematologic Disorders was developed. The protocol design is based on successful cancer protocols run by industry as well as National Cancer Institute (NCI)-supported groups such as Children's Oncology Group.

Utilizing ATHN's secure and robust data infrastructure, ATHN Transcends allows clinical researchers from institutions of all sizes and with varying levels of financial and personnel resources to participate in the collection and analysis of data gathered assessing the safety, effectiveness, and practice of treatment of current and future therapies.

Rationale

In parallel with the growth of ATHN's clinical studies, the number of new therapies for all congenital and acquired hematologic conditions, not just those for bleeding and clotting disorders, is increasing significantly. Some of the recently FDA-approved therapies for congenital and acquired hematologic conditions have not yet demonstrated long-term safety and effectiveness beyond the pivotal trials that led to their approval. In addition, results from well-controlled, pivotal studies often cannot be replicated once a therapy has been approved for general use. It is imperative that clinicians and clinical researchers in the field of non-neoplastic hematology have a uniform, secure, unbiased, and enduring method to collect long-term safety and efficacy data. As emphasized in a recently published review, accurate, uniform, and quality national data collection is critical in clinical research, particularly for longitudinal cohort studies covering a lifetime of biologic risk.

Key advantages of an independent, non-manufacturer-based study conducted by the ATHN network of collaborators include:

1. The ability to observe participants on a variety of treatment regimens regardless of regimen dosing, frequency, or time of initiation.
2. The ability to observe participants on recently FDA-approved therapies as well as continued monitoring of well-established therapies.
3. The ability to enrich the ATHNdataset with participants affected by congenital and acquired non-neoplastic hematologic conditions and connective tissue disorders with bleeding tendency in addition to those participants affected by bleeding and clotting disorders.
4. The ability to be the initial cohort study involving all ATHN-affiliated sites to provide the infrastructure for all congenital and acquired hematologic disorders-related sub-studies in cooperation with other funders, including federal, foundation, academic, and industry sources.

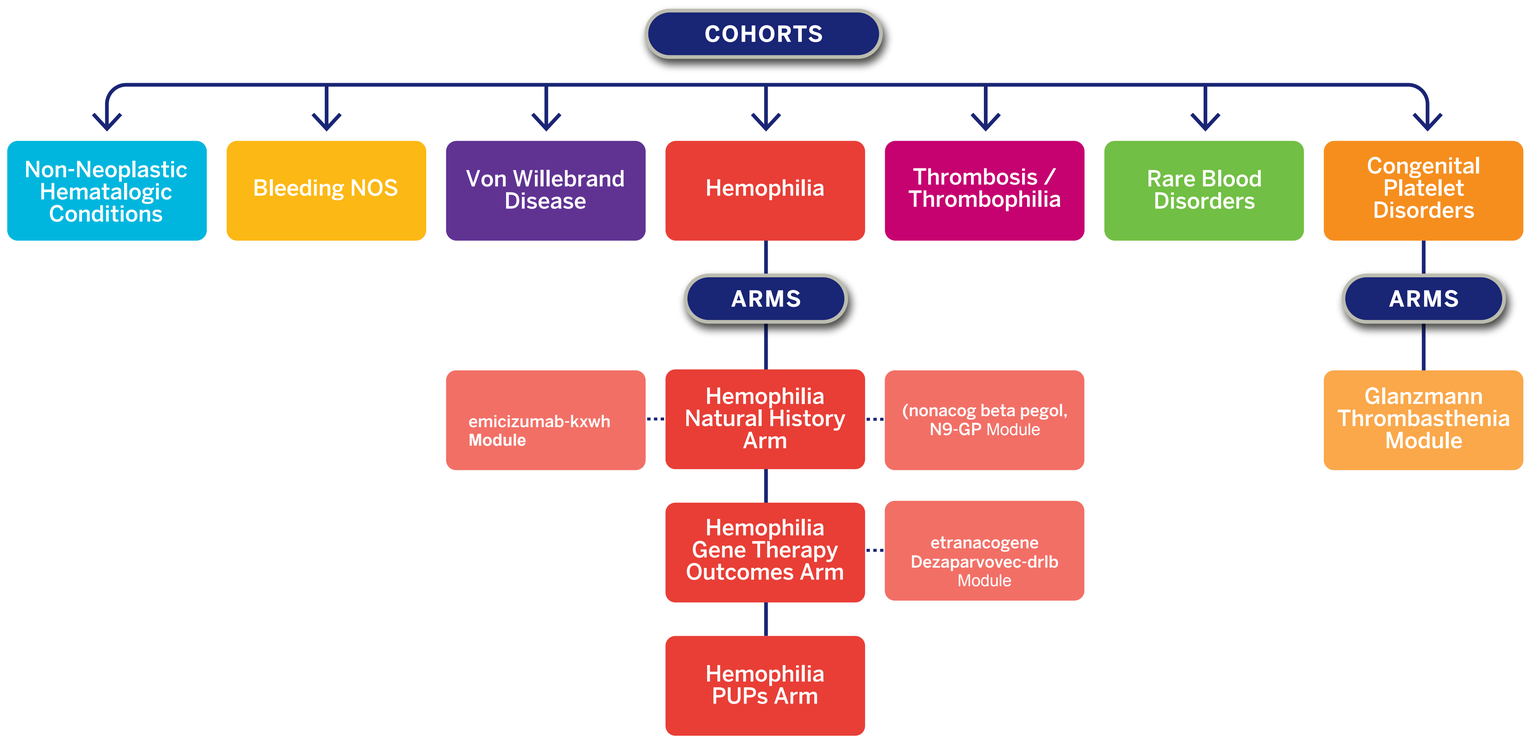
Objectives

Primary Objective:

To determine the safety of therapies used in the treatment of participants with congenital or acquired non-neoplastic blood disorders and connective tissue disorders with bleeding tendency. Safety will be measured by those events in the European Haemophilia Safety Surveillance (EUHASS).

Additional safety events of interest may be collected. These will be chosen from drug and intervention development profiles based on investigational studies, Food and Drug Association prescribing information, and emerging clinical and scientific observations.

Figure 1: ATHN Transcends Cohort Protocol Design



Secondary Objectives:

1. To establish a platform to support study arms and modules for participants with bleeding, clotting, other non-neoplastic blood disorders, and connective tissue disorders with bleeding tendency.
2. To describe medication dosing regimens in the above conditions.
3. To describe real-world effectiveness of therapies used in the above conditions, by evaluating:
   a. Health care utilization as measured by number and type of visits and hospitalizations per year
   b. Patient reported outcomes (PROs) as measured by the Patient Reported Outcomes Measurement Information System (PROMIS®) Profile 29/25/Parent Proxy, Global Adherence Rating (GAR) and EQ-5D-5L
   c. Goal attainment as measured by GOAL-Hem for those participants that opt into this measurement
4. To develop a biorepository for current and future research through the collection of biospecimens from every person enrolled on this protocol.
5. To describe bleeding events, changes in overall bleeding, and annualized bleeding rate (ABR) as measured by individual bleeding components, calculated per ISTH Bleeding Assessment Tool (ISTH BAT), and if applicable, the Pictorial Bleeding Assessment Chart (PBAC), for applicable diagnoses.

Methods

ATHN Transcends is a longitudinal, natural history, observational cohort study being conducted at approximately 150 ATHN-affiliated sites. Participants will be followed for a minimum of 15 years. Harmonized data elements will be collected at the time of enrollment, quarterly, annually, and ad hoc. Base data will be collected for all participants. Specific data will be collected for participants enrolled in cohort-specific arms and modules.

Each participant will be assigned to a single cohort: Hemophilia, Von Willebrand Disease, Congenital Platelet Disorders, Rare Disorders, Bleeding Not Otherwise Specified (NOS), Thrombosis/Thrombophilia, or Non-Neoplastic Hematologic Conditions.

Participants who meet the following inclusion criteria and none of the exclusion criteria are eligible for enrollment in the cohort study.

Inclusion Criteria:

1. Any age
2. Having a congenital or acquired non-neoplastic hematologic disorder; or
3. Having a bleeding phenotype as indicated by an age adjusted abnormal ISTH Bleeding Assessment Tool score with an unknown diagnosis; or
4. Connective tissue disorder with bleeding tendency as indicated by an age adjusted abnormal ISTH Bleeding Assessment Tool score.

Exclusion Criteria:

1. Does not qualify for inclusion in a cohort
2. Unable to give informed consent or assent
3. Unwilling to perform study procedures

Summary

ATHN Transcends has received central IRB approval and is currently being rolled out across participating ATHN Affiliates in the United States. Enrollment in ATHN Transcends can begin as soon as a site opens to enrollment.

Conclusion

The impact of ATHN's clinical research program has advanced knowledge and transformed the care provided to patients affected by these disorders. ATHN Transcends, a natural history cohort study spanning various non-malignant hematologic diagnoses with a design based on successful cancer protocols run by industry as well as National Cancer Institute (NCI)-supported groups such as Children's Oncology Group. Utilizing ATHN's secure and robust data infrastructure, ATHN Transcends allows clinical researchers from institutions of all sizes and with varying levels of financial and personnel resources to participate in the collection and analysis of data gathered assessing the safety, effectiveness, and practice of treatment of current and future therapies.