WFH Gene Therapy Registry

February 2021

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WORLD FEDERATION OF HEMOPHILIA
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GTR Oversight

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OVERSIGHT

- Steering Committee
- Scientific Advisory Board
- Industry Consortium
- Patient Advisory Group

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GTR STEERING COMMITTEE

Name	Affiliation
Barbara Konkle	Chair , WFH WBDR SC Co-Chair
Glenn Pierce	WFH VP Medical
Mike Recht	ATHN
Bindu George	FDA Liaison
TBD	EMA Liaison
Vanessa Newman	Industry - Biomarin
Ian Winburn	Industry - Pfizer
Bartholomew Tortella	Industry - Spark
Eileen Sawyer	Industry - Uniqure
Cary Clark	ISTH
Johnny Mahlangu	ISTH
Flora Peyvandi	ISTH
Lindsey George	Leader in the field, Children's Hospital of Philadelphia
Len Valentino	NHF
Steve Pipe	NHF, MASAC
Wolfgang Miesbach	EAHAD
Declan Noone	Patient advocate, EHC
Mark Skinner	Patient advocate, coreHEM, PROBE
Alfonso Iorio	WFH WBDR SC Co-Chair
Donna Coffin	WFH Staff
Mayss Naccache	WFH Staff

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GTR SCIENTIFIC ADVISORY BOARD

Position	Representative
Chair, WFH Gene Therapy Registry Steering Committee	Barbara Konkle
VP Medical, WFH	Glenn Pierce
ISTH	Flora Peyvandi
EAHAD	Wolfgang Miesbach
NHF MASAC	Steve Pipe
EHC Medical Advisory Group	Mike Makris
Patient advocate	Brian O'Mahony
Patient advocate	Mark Skinner

Support staff

Position	Representative
Director, Research & Public Policy, WFH	Donna Coffin
Gene Therapy Program Manager, WFH	Mayss Naccache

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INDUSTRY CONSORTIUM

Name	Affiliation
Barbara Konkle	Chair, WFH Gene Therapy Registry Steering Committee
Glenn Pierce	VP Medical, WFH
Vanessa Newman	Biomarin
Ian Winburn	Pfizer
Bartholomew Tortella	Spark
Eileen Sawyer	uniQure

Support staff

Position	Representative
Director, Research & Public Policy, WFH	Donna Coffin
Gene Therapy Program Manager, WFH	Mayss Naccache

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PATIENT ADVISORY BOARD

Name	Country
Bradley Rayner	South Africa
Brendan Hayes	USA
Brian O'Mahony	Ireland
David Page	Canada
Laurence Woollard	UK
Mark Skinner	USA

Support staff

Position	Representative
Director, Research & Public Policy, WFH	Donna Coffin
Gene Therapy Program Manager, WFH	Mayss Naccache

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Protocol & Core Data Set

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WFH GENE THERAPY REGISTRY

- Prospective, observational, and longitudinal registry.
- Goal: Data collection on all patients who receive gene therapy for hemophilia, via clinical trials and post-marketing
- Worldwide

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PROTOCOL DEVELOPMENT

- Protocol developed with
  - Input from multi-stakeholder Steering Committee
  - CHMP EMA provided Scientific Advice
  - FDA provided comment and feedback

- Core Data Set
  - Published in JTH, open access

Konkle BA, Pierce GF, Coffin D, Naccache M, Clark C, George LA, Iorio A, O'Mahony B, Pipe S, Skinner MW, Watson C, Peyvandi F, Mahlangu JN, for the ISTH subcommittee on Factor VIII, Factor IX and rare bleeding disorders. Core data set on safety, efficacy and durability of hemophilia gene therapy for a global registry: communication from the SSC of the ISTH. *J Thromb Haemost*. 2020 Oct. https://doi.org/10.1111/jth.15023

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GTR OBJECTIVES

- Primary objective:
  - to determine the long-term safety of factor VIII and factor IX gene therapies in patients with hemophilia.

- Secondary objectives:
  - to determine the long-term efficacy and the durability of factor VIII and factor IX gene therapies in patients with hemophilia;
  - to assess long-term quality of life (EQ-5D-5L) and burden of disease (PROBE) post gene-therapy infusion.

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CORE DATA SET

- Sections included:
  - Demographics & Diagnosis
  - Medical/Clinical History
  - Gene Therapy Infusion Details
  - Safety Data
  - Efficacy Data
  - Patient Reported Outcome Measures
  - Mortality

Konkle BA, Pierce GF, Coffin D, Naccache M, Clark C, George LA, Iorio A, O'Mahony B, Pipe S, Skinner MW, Watson C, Peyvandi F, Mahlangu JN, for the ISTH subcommittee on Factor VIII, Factor IX and rare bleeding disorders. Core data set on safety, efficacy and durability of hemophilia gene therapy for a global registry: communication from the SSC of the ISTH. *J Thromb Haemost*. 2020 Oct. https://doi.org/10.1111/jth.15023

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DEMOGRAPHICS & DIAGNOSIS

Demographics
Enrolment date
Date of birth
Sex at birth
Country of residence
Race
HTC for GT administration
HTC for follow-up data

Diagnosis
Hemophilia Type
Severity
Year of diagnosis
Baseline factor level
DNA Variant

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MEDICAL HISTORY

Medical/Clinical History
Family history of hemophilia
Factor VIII or IX inhibitor?
Was patient on prescribed prophylaxis at time of GT?
Number of exposure days of factor replacement therapy prior to gene therapy infusion?
AAV Neutralizing Antibodies to product received (prior to infusion)
Test methodology
Date of test
Result
Titre (if recorded)
Concomitant medication
Any concomitant medication (prescription, over the counter (OTC), herbal medications, and supplements)?
Alcohol consumption

Pre-existing / co-morbidities (select all that apply)
Thromboembolic event(s)
Autoimmune disorders
History of cancer (any)
HIV-positive
Liver related medical history
Pre-existing liver disease
History of hepatitis C infection
History of hepatitis B infection
Liver assessment in the last 2 years

GENE THERAPY INFUSION DETAILS

Vector infusion details
Vector product
Batch number
Lot number
Date of infusion
Dose – total vector genomes
Dosing weight (kg)
Vector genomes/kg
Complications at time of infusion (24 hours)
Complications during the following 2 weeks

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SAFETY DATA

Safety fields
Adverse events of special interest • Adverse event (FVIII inhibitors, FIX inhibitors, Thromboembolic events, Autoimmune disorders, Malignancies, Liver disease, Other) • Date of onset • Date of resolution • Description
Inhibitors tested against FVIII/FIX
Liver function tests • ALT • AST • Bilirubin • Other
If elevated enzymes: are there alternative diagnoses?
Has patient been diagnosed liver disease?

Safety fields
Liver biopsies?
Have you received non-vector related immunosuppressive therapy since last follow-up?
Onset of any other new co-morbidities

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EFFICACY DATA

Efficacy fields
Bleeding events • Date • Reason • Treatment • Location
FVIII/FIX activity level test *ability to enter >1 test result
Use of any hemostatic treatment (factor, emicizumab, other) • Date • Drug • Dose, units • Frequency
Any change in concomitant medications since last visit (prescription, over-the-counter (OTC), herbal medications, and supplements)?

Surgeries
Surgeries • Type • Date • Severity • Factor use • Bleeding complication

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PATIENT REPORTED OUTCOME MEASURES

Patient Reported Outcome Measures
EQ-5D-5L
PROBE

MORTALITY

Mortality
Date of death
Death related to gene therapy
Primary cause of death

DATA COLLECTION SCHEDULE

Data will be collected at:

- Baseline/Infusion
- Follow-up visits
  - Month 3, 6, 12, 18, 24
  - Annually thereafter

Implementation

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IMPLEMENTATION

Implementation

- Individual HTCs
  - Outreach to individual HTCs has began
- Linking with existing registries
  - USA (ATHN)
  - European registries if possible

Clinical trial patients

- Working with companies to determine process to obtain clinical trial data/enroll participants once trial completed
- Recruit previous clinical trial participants 1999-2005 (N=40)

DATABASE DEVELOPMENT & LAUNCH

Consent & Ethics

- Every patient enrolled must provide written informed consent
- Each HTC participating must obtain ethics approval from their local IRB

Timeline

- Database ready to receive data in mid-2021

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WFH GTR HTC EDUCATIONAL PROGRAM

In development:

- HCP and Data Manager GTR Readiness Program
  - Training modules, resources and guides (On-line Learning Series, user guide, webinars, virtual & in-person training sessions and meetings)

- PWH GTR Readiness Program

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ADVANTAGES OF PARTICIPATION

Advantages include:

- Per patient funding for data entry
- Data visualization (patient summary, data dashboard, etc.)
- Contributing critical data on benefits and risks of gene therapy in hemophilia

THANK YOU

For more information contact us at:

gtr@wfh.org

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