

CDISC Implementation on Haemophilia Trial Data

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Disclaimer



The information contained in this presentation is provided for informational purposes only. And is based on Larix's SDTM approach of handling Haemophilia data.



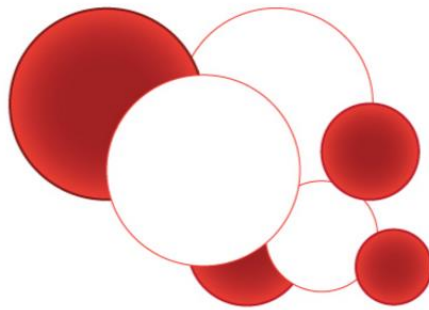
AGENDA



- About Haemophilia
- Introduction to Haemophilia trial data
- Our approach to implementing CDISC models on this trial data
- Challenges and important considerations around data structure / mapping
- Conclusion

UNDERSTANDING

HAEMOPHILIA



- Haemophilia is a group of hereditary genetic disorders that impairs the body's ability to control blood clotting.
- Haemophilia is carried on the X chromosome and is called an X linked genetic disorder and occurs more commonly in males than in females.
- Mutations in the FVIII gene cause Haemophilia A. Mutations in the FIX gene cause Haemophilia B.

Type	Inheritance	Cause	Frequency
Haemophilia A	X linked recessive	Factor VIII	80%
Haemophilia B	X linked recessive	Factor IX	15%

Management and Treatment

No cure for Haemophilia.

But a number of treatments exist.

- ✓ Plasma and whole blood transfusions
- ✓ Factor replacement (Prophylaxis or On-demand) – Intravenous infusions of the deficient clotting factor
- ✓ Gene therapy : Replacement of/Addition to a defective gene sequence with a corrected version to eliminate disease for the lifetime of the patient
- ✓ Preventive exercises



TREATMENT & CARE

Introduction to Haemophilia trial data – an Example

Trial data consists of general data

- Demographics (DM),
- Inclusion/Exclusion criteria (IE),
- Exposure (EX),
- Surgical history (MH),
- Adverse events (AE),
- Vital signs (VS) etc.

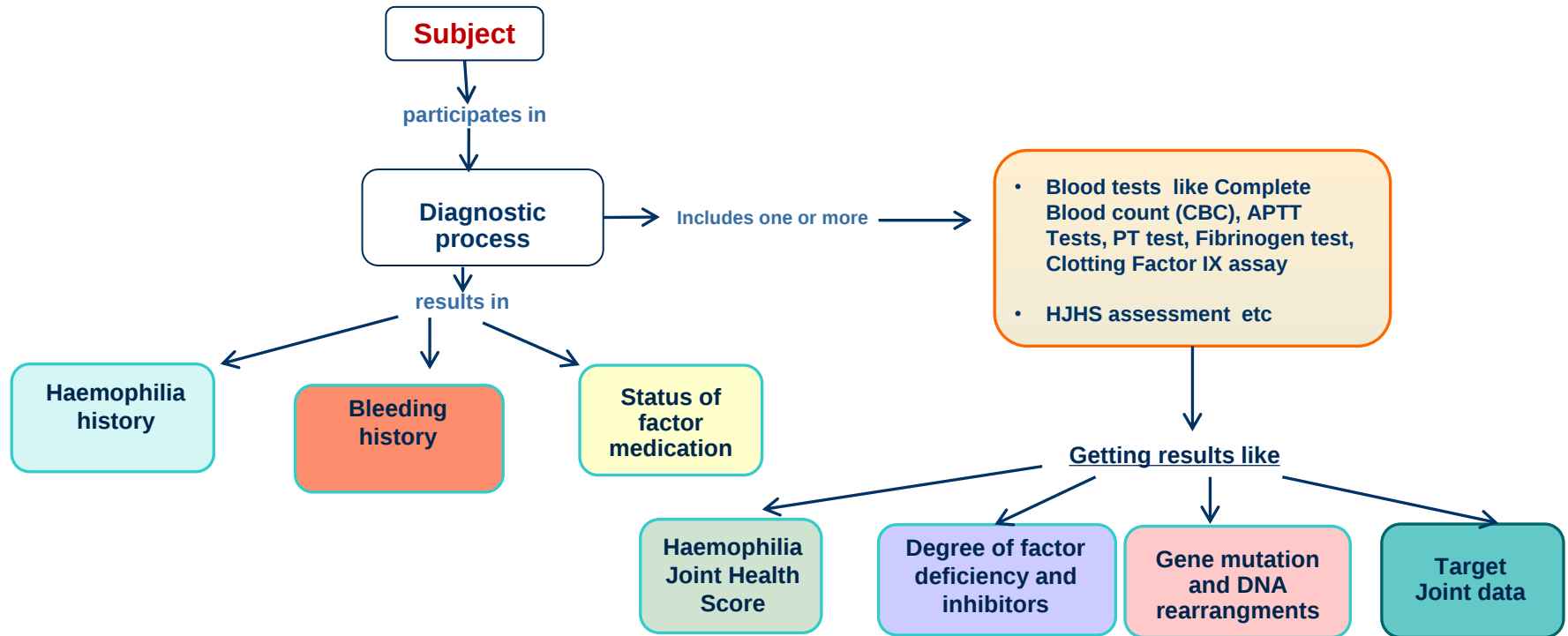
but in addition to this we also encounter c



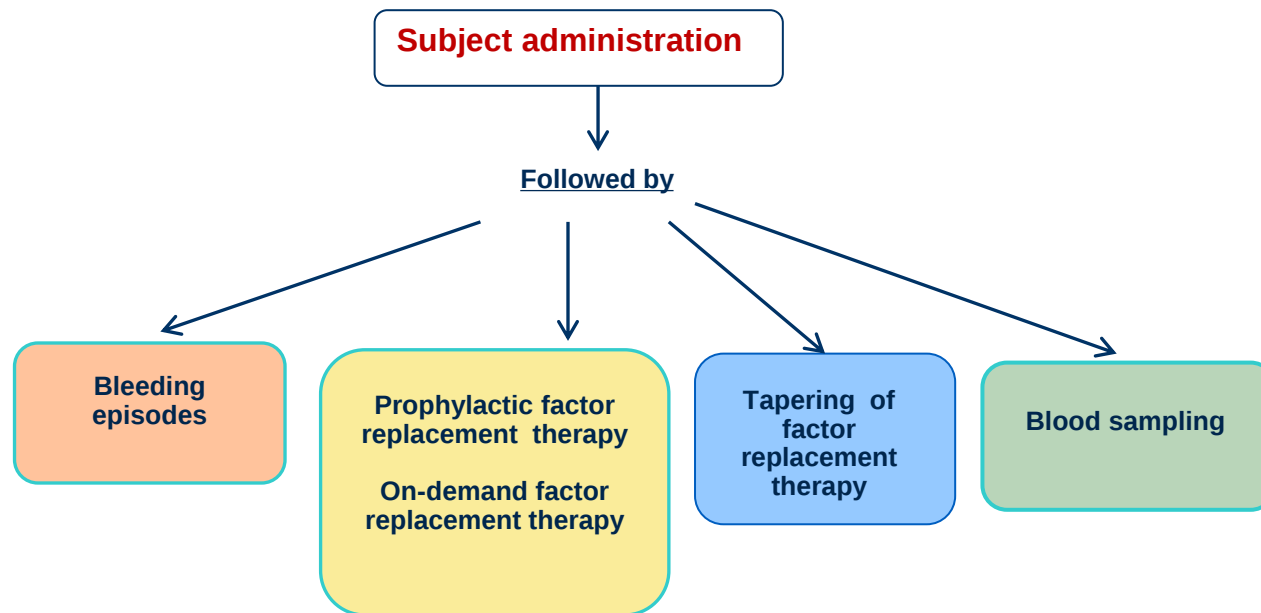
Most commonly collected Haemophilia data

- Haemophilia Joint Health Score (HJHS)
- Factor Gene mutation and gene sequencing analysis (FGM)
- Haemophilia history
- Degree of factor deficiency and inhibitors
- Bleeding episodes
- Target Joints
- Prophylactic or On-demand factor Replacement Therapy
- Tapering of prophylactic replacement therapy
- History and Status of factor medication and Bleeding
- Diagnosis and Laboratory data

Stages and processes – Screening and Inclusion



Stages and processes - Treatment



An approach of mapping Haemophilia data to SDTM



Haemophilia Data

Bleeding History

A physician administered standard questionnaire for history taking and bleeding score assignment

Examples: Number of episodes, Duration, Spontaneous?, Location, Type of Bleeding

FINDINGS



SDTM

Questionnaires Domain (QS) when QSCAT="BLEEDING HISTORY"

QRS controlled terminology does not cover some of the above questionnaires, hence used the custom terminology for QSTESTCD, QSTEST, QSORRES

Haemophilia disease related History

Questions related to disease diagnosis history prior to the trial participation

Examples: Diagnosed date, Factor activity level, Degree of deficiency, Any of family members has factor inhibitors? etc

FINDINGS



Custom Domain (XH) for Haemophilia History based on *Findings* observation class. We followed SDTM IG rules for creating custom domain.

Haemophilia Data

Status of factor medication and Bleeding

Medication prior to Trial start.

Examples: Treatment, Form, Frequency, Start date, Stop date, Ongoing, Dose, Number of treatment requiring bleeding episodes

INTERVENTIONS



SDTM

CM, MH and Supplementary domains

Factor medication data placed into CM, SuppCM e.g. with CMCAT ="PRIOR FACTOR MEDICATION" and CMSCAT = XXXX.

Prior bleeding episodes data are placed into MH, SuppMH with MHCAT/MHSCAT = XXX/YYY. If relevant: Link episodes with medications in RELREC

Target Joint data

Target joint is the joint having four bleeds into the same joint in a six-month time period.

Examples: Any Target joints?, Location, Laterality etc

FINDINGS



Findings About Domain (FA)

NOTE: Custom terminology for FATESTCD, FATEST

Haemophilia Data

Haemophilia Joint Health Score

The HJHS is a physical examination assessment tool sensitive enough to pick up the subtle early signs of joint damage

FINDINGS



SDTM

Findings About Domain

NOTE: Custom terminology for FATESTCD, FATEST

(or)

Questionnaires Domain (QS)

when QSCAT="HJHS"

Examples of HJHS data:

Hemophilia Joint Health Score 2.1 - Summary Score Sheet

	Left Elbow		Right Elbow		Left Knee		Right Knee		Left Ankle		Right Ankle	
Swelling		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Duration (swelling)		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Muscle Atrophy		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Crepitus on motion		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Flexion Loss		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Extension Loss		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Joint Pain		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Strength		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Joint Total												

Sum of Joint Totals

+

NE = Non-Evaluable

Global Gait Score

(☐ NE included in Gait items)

HJHS Total Score

=

Haemophilia Data

Bleeding episodes

Patient evaluation of treatment for a bleeding in e-diary

Examples: Start date, time of Bleed, Stop date, time of bleed, Location, Circumstances of bleed, Action taken, Treatment, Severity of Bleeding etc

EVENTS



SDTM

CE, SuppCE when CECAT=
"BLEEDING EPISODE"

Prescribed factor replacement therapy

Replacement therapy may be administered through on-demand or prophylaxis regimens.

Examples: Medication name, dose, units, frequency, Start, Stop date, On-going

INTERVENTIONS



CM, SuppCM when CMCAT=
"PRESCRIBED FACTOR REPLACEMENT
THERAPY DURING TRIAL"

Haemophilia Data

Tapering of replacement therapy

Gradually reducing the amount of a drug when stopping it abruptly would cause unpleasant withdrawal symptoms.

Examples: Did tapering start? If No, reason for not tapering; Date of initiating the tapering; Reason for the date chosen



SDTM

SuppCM in relation to prescribed factor replacement therapy records in CM

Prophylactic factor Replacement Therapy and On-demand factor Replacement Therapy data

Subject filled information about taking the factor infusions relating to the Bleeding episodes or Regular medications

Examples: Name of infusion product, dose, form, Start date and time etc

EVENTS



CM and SuppCM when
CMCAT="PROPHYLACTIC INFUSION" or
CMCAT = "ON-DEMAND INFUSION"

Haemophilia Data

Diagnosis and Laboratory data

Factor activity, Factor inhibitors, CBC, aPTT, PT, Clotting factor assays, mutations and DNA rearrangements etc , other than general Chemistry, Hematology, Urinalysis data

FINDINGS

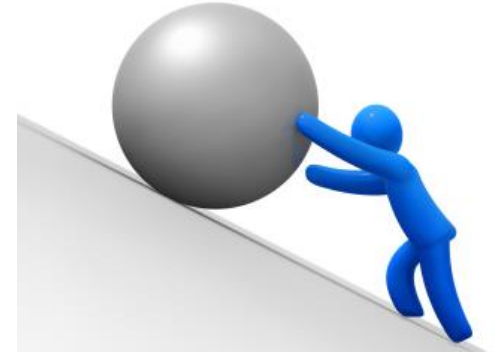


SDTM

LB and SuppLB

NOTE: SDTM controlled terminology doesn't cover the some of the Lab test names, hence used the custom terminology for LBTESTCD, LBTEST

Challenges and important considerations



- Handling the Haemophilia disease related history data
Will it go into FA or SUPPMH or XH (custom) ????
- Handling the Bleeding history data
Will it go into QS or SUPPMH or XB (custom)????
- Tapering of factor replacement dose
Will it be placed in SUPPCM or any (custom) domain????
- Handling disease related Laboratory tests as they are not part of controlled terminology.

Conclusion

Haemophilia could be considered as candidate for a Therapeutic Area Standards User Guide development.

Overall, these are exciting times for Haemophilia clinical trials and likelihood of further clinical successes in the near future.

A day will come when a person with haemophilia will go to a treatment center and leave without haemophilia.



References

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