ERN-EuroBloodNet

Dissemination Pills

“Satisfy Trial (ERN-EuroBloodNet) : PROMs Selection Process. Associating PROMs in PKD in Clinical Trials”

Pilot in the framework of ERICA WP3

SPEAKER: Eduard van Beers

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European Reference Network | Hematological Diseases (ERN EuroBloodNet)

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- **Chair Sickle Cell Research Consortium and Registry (SCORE), the Netherlands**
- **Chair HOVON benign hematology working group**

Disclosures:

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RARE DISEASE High Burden, many diseases

7,000

Rare diseases exist and new ones are discovered each year

5% of rare diseases have FDA-approved treatments

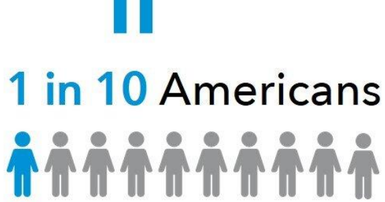
80% of rare diseases are inherited

Rare disease affects...

30 million people in the United States

=

1 in 10 Americans



30 million people in the European Union

350 million people worldwide

The vast majority of rare disease patients are **CHILDREN**

DRUG DEVELOPMENT not the solution

Global Status	Q3 2023	Q4 2023	Q1 2024	Q2 2024	Q3 2024
Preclinical	1,522	1,528	1,471	1,436	1,393
Phase I	256	270	301	314	318
Phase II	267	274	282	279	289
Phase III	30	33	35	34	35
Pre-registration	7	6	4	5	6
Total	**2,082**	**2,111**	**2,093**	**2,068**	**2,041**

CITELINE
a norstella company

American Society of Gene + Cell Therapy

DRUG REPURPOSING one of the solutions

- **Faster** Approval and Market Entry (Label extension is the best!)
- **Lower Development Costs**
- **Higher Success Rate**
- **Addresses Unmet Medical Needs Faster**
- **Lower Risk of Side Effects and Safer for Patients**
- **Environmental and Ethical Advantages**

Classical: thalidomide, senicapoc
Alternative: mitapivat, oncological product became benign hematology product

ASK FOR HELP:

- **Eurobloodnet** **pierre.fenaux@aphp.fr** **trial conduct /sponsorship**
- **Eurobloodnet** **e.j.vanbeers-3@umcutrecht.nl** **general tips directions in trialing**
- **EATRIS/ REMEDI4ALL** **https://remedi4all.org/** **regulatory advice**

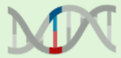
SATISFY Study design

Registration	• NCT05935202
Setup	• Investigator initiated, prospective, multicenter, single-arm phase 2 trial.
Locations	• Denmark and The Netherlands • Sibling study in Toronto, Canada
Sponsor	• Non-profit EuroBloodNet *Association*
Funding	• Agios Pharmaceuticals

SATISFY Eligibility

Key Inclusion Criteria

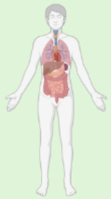
Membranopathy or CDAII



Genetically confirmed
ACMG class 3, 4, or 5

Age ≥18 years

Hb concentration:
<13.0 g/dL for males
<11.0 g/dL for females



Adequate organ function

Key Exclusion Criteria

PKLR

Pyruvate kinase deficiency
diagnosed with decreased PK activity or two pathogenic PKLR alleles

Blood transfusion within last 3 months or >5 units the last year

Significant medical comorbidity

Receiving hematopoietic stimulating agents

SATISFY Intervention

Primary objective

Safety
Type, incidence, severity and relationship of mitapivat to AE and SAE

Secondary objectives

Hemoglobin
≥1 g/dL increase
Average increase

Hemolysis
LDH, bilirubin, haptoglobin

Erythropoiesis
EPO, erythroferrone, sTfR

Health related quality of life
SF-36 v1
PKDIA

Spleen
Change in size in non-splenectomized

Exploratory objectives

Red blood cell
Lifespan
Metabolism
Membrane flexibility and stability

Iron metabolism
Hepcidin, ferritin, transferrin saturation
MRI: Hepatic and cardiac iron

PATIENT REPORTED OUTCOMES The basics

- The FDA and the National Institutes of Health define a PRO as ***"any report** of the status of a patient's health condition **that comes directly from the patient**, without interpretation of the patient's response by a clinician or anyone else"*
- HRQL is a **multidimensional concept** that represents an individual's general perception of the **physical, psychological, and social aspects** of their **life**
- It is a **subjective** rating
- **complements** traditional **measures of efficacy** such as survival and frequency of hospitalization

- Farrell AT, et al. Blood Adv. 2019. Dec 10;3(23):3982-4001

PATIENT REPORTED OUTCOMES QoL includes coping

Locked in syndrome-
rated his life as ‘9’

- **Coping**

‘response shift’ -> changes results

PATIENT REPORTED OUTCOMES Choosing a PRO

1. **Relevance to Disease Burden and Symptoms:**
   Select a PRO measure for clinically relevant symptoms and patient priorities (e.g., fatigue, pain, bleeding episodes, icterus (PKDIA!)).
2. **Regulatory and Scientific Validation**
   Choose a PRO measure that is validated and accepted by regulatory agencies (EMA/FDA) for use in hematological conditions or general chronic diseases.
3. **Feasibility and Patient Burden**
   Ensure the measure is easy to complete and minimizes patient burden.
4. **Sensitivity to Detect Treatment Effects**
   Consider measures that have established minimal clinically important differences (MCID) for similar conditions.
5. **Cross-Cultural Adaptability and Language Availability**
   Rare hematological diseases often require multi-national recruitment

For Energize: PKDIA and SF36

PATIENT REPORTED OUTCOMES Choosing a PRO: review literature

Table 1. Recommended end points and measures for PROs in SCD

Outcome/End point	Recommended measurement/tool(s)
Pain	
Intensity	For patients at least 8 y of age, an 11-point NRS or appropriately reproduced and administered VAS
Interference/impact	PROMIS Pain Interference measures for studies of adult, pediatric, or mixed age groups
	ASCQ-ME Pain Impact for adults or the Brief Pain Impact for adults
	PedsQL Pain Impact and Pain and Hurt for children
Behavior	PROMIS Pain Behavior domain for children and adults
Affect	
Depression/negative emotional impact	PedsQL SCD Module Emotions measure for children
	ASCQ-ME Emotional Impact measure for adults
	PROMIS Depression and Anxiety measures for more general measures of negative affect, particularly when mixed age samples are used
Fatigue	PROMIS or PedsQL Fatigue measures in children
	PROMIS Fatigue measure in adults
Function	
Emotional/social, physical, cognitive domains	Relevant domains of the PROMIS and ASCQ-ME in adults and PROMIS and PedsQL in children to measure emotional/social, physical, and cognitive function PRO domains
	The Canadian Occupational Performance Measure may be used to measure functional capacity that integrates self-report and expert interview
Occupational status	One item in PhenX for assessment of employment status and the more detailed WHO's Health and Work Performance Questionnaire to assess multiple factors related to work performance
Self-efficacy	Sickle Cell Efficiency Scale to measure self-efficacy in adolescents and adults with SCD

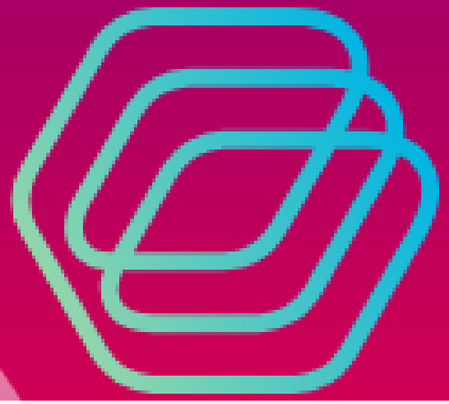
- Farrell AT, et al. Blood Adv. 2019. Dec 10;3(23):3982-4001

CONCLUSIONS

1. Investigator initiated trials are ideal for drug re-purposing/label extension in hematology
2. Eurobloodnet can help
3. Energize is an example of such a study
4. PRO's are important to incorporate in trials, but choose wisely
5. Collaborate and ….

Q&A e.j.vanbeers-3@umcutrecht.nl

Thank You!



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