

Ataxia Global Initiative

Holm Graessner on behalf of AGI

EuroAtaxia
18 June 2021



The road towards molecular therapies for ataxias



Laying the groundwork

- genes and mechanisms
- rating scales
- longitudinal cohorts

Trial readiness

- trial ready cohorts
- biomarker development
- regulatory acceptance of outcome measures

Preclinical drug development

clinical trials



ATAXIA GLOBAL INITIATIVE

worldwide platform for clinical research in ataxias

- Cohort aggregation
- Harmonization of biomarkers and outcome measures
- Education and training
- Multicentre trial readiness services

coordination,
standardization &
joint projects

expertise &
knowledge

content
input

Patient Data

cohorts, registries & natural history studies

study networks

single site studies



NAF CRC-SCA



BIGPRO
Brazil

TREAT-ARCA



anonymized
data



- Regulatory qualification of outcome measures and biomarkers
- Trial simulation
- Clinical data standards

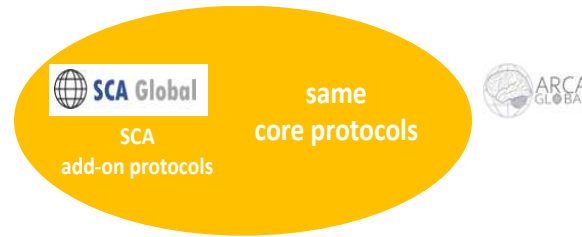
Harmonization of biomarkers and outcome measures



Standardization working groups



- **consensus among ataxia investigators** in the field on a global scale
- **common core of cross-center harmonized assessment protocols & SOPs** for each domain



#1	Clinical outcomes & registries	
#2	Molecular biomarkers & biosampling	
#3	MR biomarkers	
#4	Digital-motor biomarkers	
#5	Model systems & preclinical trials	
#6	Next-generation genomics and platforms	
#7	Policy and patient organization engagement	

Harmonization of biomarkers and outcome measures

- tight cooperation with the **Critical Path to Therapies for the Ataxias (CPTA)** initiative of **C-PATH**
- to achieve regulatory acceptance of biomarkers and outcome measures



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CRITICAL PATH
INSTITUTE

Harmonization of biomarkers and outcome measures

Development of improved and regulatory accepted outcome measures:

SARA Global

- Criticism of SARA concerns **clinical meaningfulness** of single items and **metric properties** of the scale
- Development of SARA Global in three steps:
 - Detailed data-driven **analysis**
 - **Design** of modified scale
 - **Validation**

Rater: _____ date: _____ patient: _____

Scale for the assessment and rating of ataxia (SARA)

1) Gait	2) Stance
Proband is asked (1) to walk at a safe distance parallel to a wall including a half-turn (turn around to face the opposite direction of gait) and (2) to walk in tandem (heels to toes) without support.	Proband is asked to stand (1) in natural position, (2) with feet together in parallel (big toes touching each other) and (3) in tandem (both feet on one line, no space between heel and toe). Proband does not wear shoes, eyes are open. For each condition, three trials are allowed. Best trial is rated.
0 Normal, no difficulties in walking, turning and walking tandem (up to one misstep allowed)	0 Normal, able to stand in tandem for > 10 s
1 Slight difficulties, only visible when walking 10 consecutive steps in tandem	1 Able to stand with feet together without sway, but not in tandem for > 10s
2 Clearly abnormal, tandem walking >10 steps not possible	2 Able to stand with feet together for > 10 s, but only with sway
	3 Able to stand for > 10 s without support in natural

Meetings, education and training

Organizing and hosting **international meetings and conferences** to update and educate the field on key issues

April 2018	SCA Global inauguration (AIM Meeting, Philadelphia)
March 2019	1 st SCA Global Meeting in Las Vegas / ARCA Global Inauguration
Oct 2020	SCA Global & ARCA Global Online Conference
22+23 Nov 2021	Ataxia Global Initiative Online Workshop
March 2022	Ataxia Global Initiative Conference (Orlando)

Ataxia Global Initiative Online Workshop

	(Berlin time)	
22 Nov 2021	14:00-15:35	Session 1: Genetics & New Targets/Pathways
	15:40-17:15	Session 2: Business meeting
23 Nov 2021	19:30-21:05	Session 3: Biomarkers and natural history
	21:10-22:40	Session 4: Therapy

Keynote	Karl Broich
WG3: MR Biomarkers	Gülin Öz
Project: retinal degeneration as a biomarker in ataxias	José Luiz Pedroso
Project: Fluid biomarkers in SCA1	Puneet Opal
Project: PROSPAX cohort	Rebecca Schüle
Project: PAHAN survey	Laura Jardim

Meetings, education and training

Organizing and hosting **international meetings and conferences** to update and educate the field on key issues



2019 Las Vegas Meeting

Education and training

Providing a platform for young investigators



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About the Young Investigator Initiative (YII)

Young Investigators

- About the Young Investigator Initiative (YII)
- Education and Training
- Members of the Young Investigator Initiative
- NAF Travel Award



It is often challenging for junior researchers to get an overview in the field of a rare disease like ataxia. The Young Investigator Initiative (YII) was initiated by Helke Jacobi and Jennifer Faber and formed within the framework of SCA Global as a platform for scientific exchange amongst young researchers and for education and training purposes. The idea is to assure high quality of clinical assessments by trained clinicians and to attract and bring together young researchers within the field of ataxia research.



Jennifer Faber

The first Young Investigator Initiative Event was part of the SCA & ARCA Global online conference on October 29th 2020, including an introduction of the initiative, an ataxia scales training and an outline of our further steps. Here we also announced the awardees of the "Young Investigator – NAF Travel award", that we had organized together with the National Ataxia Foundation (NAF) to enable outstanding young researchers and clinicians without funding to attend the SCA Global conference 2020.



Helke Jacobi

The overarching Ataxia Global Young Investigator Initiative will be inclusive and wants to connect young researchers and clinicians devoted to Ataxia Research from all over the world. There is no fixed cut-off with regard to age, young is defined as "young in the field of ataxia" which means that investigator is not in a senior position in the field.

If you are interested in participating in the Ataxia Global Young Investigator Initiative, send your Expression of Interest for the YII ([click here to download the form](#)) to yii_ataxia-global@posteo.de.

Building a modular curriculum for multidisciplinary training on ataxias

Education and training


Offering resources for and providing approval of ataxia training and education programs

Instruction:

Proband is asked

(1) to walk at a safe distance parallel to a wall including a half-turn (turn around to face the opposite direction of gait) and

(2) to walk in tandem (heels to toes) without support.



0 Normal, no difficulties in walking, turning and walking tandem (up to one misstep allowed)

1 Slight difficulties, only visible when walking 10 consecutive steps in tandem

2 Clearly abnormal, tandem walking >10 steps not possible

3 Considerable staggering, difficulties in half-turn, but without support

4 Marked staggering, intermittent support of the wall required

5 Severe staggering, permanent support of one stick or light support by one arm required

6 Walking > 10 m only with strong support (two special sticks or stroller or accompanying person)

7 Walking < 10 m only with strong support (two special sticks or stroller or accompanying person)

8 Unable to walk, even supported

Please rate this video.

Score =

[Back to the Training Overview](#)

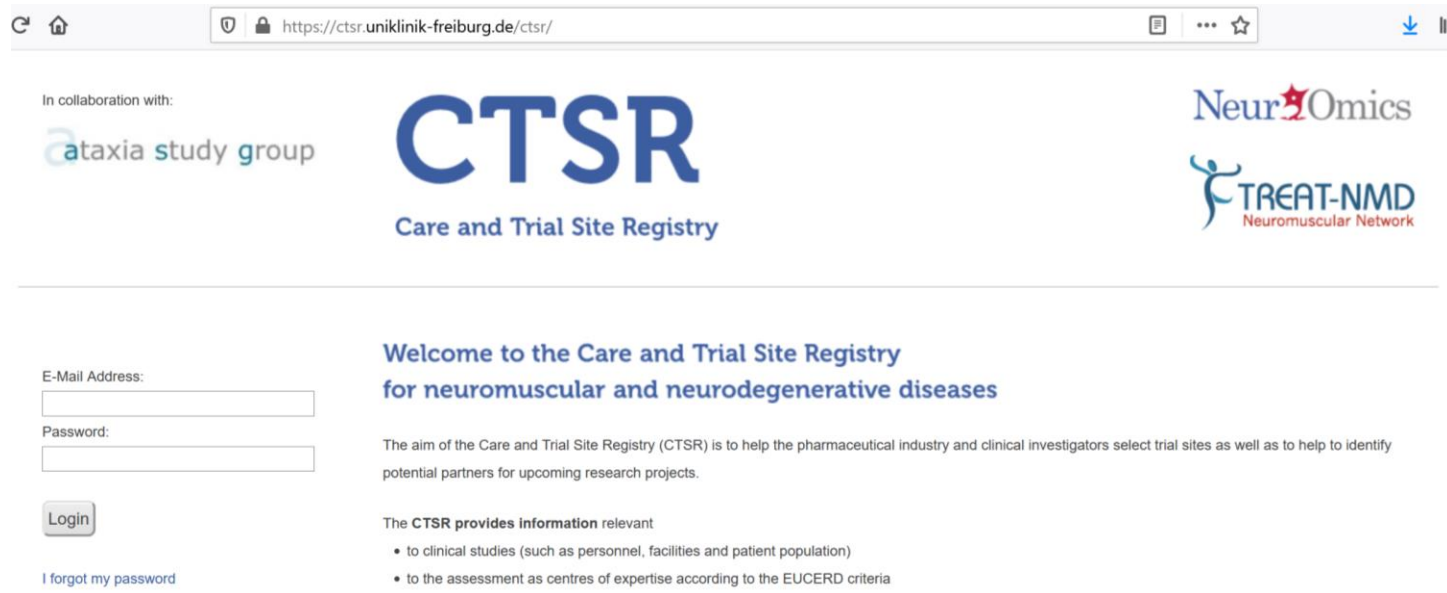
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Multicentre trial readiness services

Set-up of an **AGI Care and Trial Site Registry**

- Registry of care and trial sites worldwide
- infrastructure for clinical trial feasibility, recruitment, and other studies
 - Care and trial infrastructure
 - Numbers of ataxia patients
 - Staff



The screenshot shows a web browser window with the URL <https://ctsr.uniklinik-freiburg.de/ctsr/>. The page features logos for 'ataxia study group', 'CTSR Care and Trial Site Registry', 'NeurOmics', and 'TREAT-NMD Neuromuscular Network'. Below the logos, there is a login form with fields for 'E-Mail Address:' and 'Password:', a 'Login' button, and a link for 'I forgot my password'. The main content area contains a welcome message and a description of the CTSR's purpose.

In collaboration with:

ataxia study group

CTSR
Care and Trial Site Registry

NeurOmics

TREAT-NMD
Neuromuscular Network

E-Mail Address:

Password:

Login

[I forgot my password](#)

**Welcome to the Care and Trial Site Registry
for neuromuscular and neurodegenerative diseases**

The aim of the Care and Trial Site Registry (CTSR) is to help the pharmaceutical industry and clinical investigators select trial sites as well as to help to identify potential partners for upcoming research projects.

The CTSR provides information relevant

- to clinical studies (such as personnel, facilities and patient population)
- to the assessment as centres of expertise according to the EUCERD criteria

Multicentre trial readiness services

AGI Advisory Committee for Therapeutics

- Will be set up as multi-disciplinary international group of internationally recognized academic and industry drug development experts as well as representatives of patient foundations and regulatory experts
- review and provide guidance on the translation and development path of therapeutics programs in ataxias
- F2F review meeting will be used

- Uses example of



AGI - Membership and Partnership

Membership

- Individual membership
 - Ataxia researchers and clinical investigators
 - Ataxia clinicians
 - Representatives of patient organisations
 - Etc.
- No fee for membership

Partnership

- Organisations including pharmaceutical industry
- Partners are entitled to send representatives to AGI Working Groups
- No fee for partnership

AGI - Governance

Executive Committee

- 10-15 members
- AGI world regions will be represented
- Up to 3 patient organisation representatives
- Up to 2 member can be a non-academic investigator (of which 1 will be industry)

Office

- Provided by University Tübingen
- Supports the Executive Committee
- Tasks: communication, meeting planning, project management, administration, finance

TETSUO ASHIZAWA



ALEXANDRA DURR



LAURA JARDIM



THOMAS KLOCKGETHER



BIN-WENG SOONG



DAVID SZMULEWICZ



MATTHIS SYNOFZIK



HOLM GRAESSNER



BRENT FOGEL



BERNARD BRAIS



SUE HAGEN



JULIE GREENFIELD



JOSÉ LUIZ PEDROSO



OSAMU ONODERA



Q & A

ATAXIA  **GLOBAL**
INITIATIVE

worldwide platform for clinical research in ataxias