REPOTRIAL

An in silico-based approach to improve the efficacy and precision of drug REPurpOsing TRIALs for a mechanism-based patient cohort with predominant cerebro-cardiovascular phenotypes

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 777111.

Deliverable
D3.9 "Publication on results of pilot study 1: STROKE"

Work Package
WP3 "Clinical validation of in-silico trial prediction"

Disclaimer

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 777111. Any dissemination of results reflects only the author's view and the European Commission is not responsible for any use that may be made of the information it contains.

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Document information

Grant Agreement Number: 777111				**Acronym: REPO-TRIAL**
Full title	An in silico-based approach to improve the efficacy and precision of drug REPurpOsing TRIALs for a mechanism-based patient cohort with predominant cerebro-cardiovascular phenotypes			
Topic	In-silico trials for developing and assessing biomedical products			
Funding scheme	RIA - Research and Innovation action			
Start Date	1 February 2018	**Duration**	72 months	
Project URL	https://repo-trial.eu/			
EU Project Officer	Dusan Sandor, Programme Officer, European Commission			
Project Coordinator	Prof. Dr. Harald H.H.W. Schmidt, Universiteit Maastricht (UM)			
Deliverable	D3.9			
Work Package	WP3			
Date of Delivery	**Contractual**	31.01.2024	**Actual**	27.03.2024
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Lead Beneficiary	4 - UKE			
Responsible Author(s)	PD Dr. med. Benedikt Frank (UKE)			
Keywords	Publication on results of pilot study			

History of changes

Version	Date	Contributions	Contributors (name and institution)
V0.1	21/03/2024	First draft	Benedikt Frank (UKE), Vanessa Köhler (concentris)
V1	21/03/2024	Final version	Benedikt Frank (UKE)
V1	27/03/2024	Approval	Harald Schmidt (UM)
V1	27/03/2024	Submission	Vanessa Köhler (concentris)

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Table of Content

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 777111.

1 Objectives of the deliverable based on the Description of Action (DoA)

This deliverable provides the results of the REPO-STROKE II study (Full title: Networked Drug REpurposing for Mechanism-based neuroPrOtection in Acute Ischaemic STROKE). The report contains the results preview that has been published on ClinicalTrials.gov.

2 Attachment

Results preview - “Networked Drug REpurposing for Mechanism-based neuroPrOtection in Acute Ischaemic STROKE (REPO-STROKE II)”

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ID: REPO-STROKE II Networked Drug REpurposing for Mechanism-based neuroPrOtection in Acute Ischaemic STROKE NCT05762146

Results Preview

Hide All

Participant Flow

Recruitment Details	
Pre-assignment Details	

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care	Total (Not public)
Arm/Group Description	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors	Control group: each patient in this group will receive only standard of care	

	Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.		
Period Title: **Overall Study**			
Started	16	5	21
Completed	16	5	21
Not Completed	0	0	0

Baseline Characteristics

Information is required

Outcome Measures

1. Primary Outcome

Title:	SICH as Per ECASS III
Description:	Frequency of symptomatic intracranial hemorrhages as per ECASS III
Time Frame:	30 days

Outcome Measure Data ✓

Analysis Population Description
[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care

▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	Control group: each patient in this group will receive only standard of care
Overall Number of Participants Analyzed	16	5
Measure Type: Count of Participants Unit of Measure: participants	0 0%	0 0%

2. Secondary Outcome

Title:	SICH as Per Heidelberg Bleeding Classification
▼ Description:	Frequency of symptomatic intracranial hemorrhages as per Heidelberg Bleeding Classification
Time Frame:	30 days

▼ Outcome Measure Data 

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	Control group: each patient in this group will receive only standard of care
Overall Number of Participants Analyzed	16	5
Measure Type: Count of Participants Unit of Measure: participants	0 0%	0 0%

3. Secondary Outcome

Title:	SICH as Per SITSMOST
▼ Description:	Frequency of symptomatic intracranial hemorrhages as per SITSMOST
Time Frame:	30 days

▼ Outcome Measure Data ✓

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	Control group: each patient in this group will receive only standard of care
Overall Number of Participants Analyzed	16	5
Measure Type: Count of Participants Unit of Measure: participants	0 0%	0 0%

4. Secondary Outcome

Title:	SICH as Per NINDS
▼ Description:	Frequency of symptomatic intracranial hemorrhages as per NINDS
Time Frame:	30 days

▼ Outcome Measure Data ✓

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	Control group: each patient in this group will receive only standard of care
Overall Number of Participants Analyzed	16	5
Measure Type: Count of Participants Unit of Measure: participants	0 0%	0 0%

5. Secondary Outcome

Title:	Mortality
▼ Description:	Frequency of all cause mortality
Time Frame:	30 days

▼ Outcome Measure Data ✓

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	Control group: each patient in this group will receive only standard of care
Overall Number of Participants Analyzed	16	5
Measure Type: Count of Participants Unit of Measure: participants	0 0%	0 0%

6. Secondary Outcome

Title:	SAE
▼ Description:	All (S)AEs considered related to the triple combination therapy
Time Frame:	30 days

▼ Outcome Measure Data ✓

▼ Analysis Population Description
[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	Control group: each patient in this group will receive only standard of care
Overall Number of Participants Analyzed	16	5
Measure Type: Count of Participants Unit of Measure: participants	0 0%	0 0%

7. Secondary Outcome

Title:	Duration of Hospital Stay
▼ Description:	Time from randomization to discharge
Time Frame:	30 days

Outcome Measure Data Not Reported

8. Secondary Outcome

Title:	Duration of Intensive Care Unit (ICU) Stay
▼ Description:	Period during which the patient stayed at a ward with capacity for mechanical ventilation
Time Frame:	30 days

▼ Outcome Measure Data 

▼ Analysis Population Description
[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	Control group: each patient in this group will receive only standard of care
Overall Number of Participants Analyzed	16	5

Measure Type: Number Unit of Measure: days	0	0

9. Secondary Outcome

Title:	Duration of Invasive Mechanical Ventilation
▼ Description:	in hours NOTE : Outcome Measure Description is shorter than the Outcome Measure Title.
Time Frame:	30 days

▼ Outcome Measure Data ✓

▼ Analysis Population Description
[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	Control group: each patient in this group will receive only standard of care

Overall Number of Participants Analyzed	16	5
Measure Type: Number Unit of Measure: hours	0	0

10. Secondary Outcome

Title:	Duration of Non-invasive Mechanical Ventilation
▼ Description:	in hours NOTE : Outcome Measure Description is shorter than the Outcome Measure Title.
Time Frame:	30 days

▼ Outcome Measure Data ✓

▼ Analysis Population Description
[Not specified]

Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description:	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory	Control group: each patient in this group will receive only standard of care

	characteristics compared to other compounds of the same drug class.	
Overall Number of Participants Analyzed	16	5
Measure Type: Number Unit of Measure: hours	0	0

11. Secondary Outcome

Title:	Change of Initial ‘Volume of Hypoperfusion’
▼ Description:	Change in "ml" of volume of hypoperfusion in initial Computed Tomography Perfusion (CTP) to final 'volume of infarct core' as assessed through follow-up Magnetic Resonance Imaging (MRI).
Time Frame:	5 days

Outcome Measure Data Not Reported

12. Secondary Outcome

Title:	Change of Initial ‘Volume of Infarct Core’
▼ Description:	Change in "ml" of infarct core of initial Computed Tomography Perfusion (CTP) to final 'volume of infarct core' as assessed through follow-up Magnetic Resonance Imaging (MRI).
Time Frame:	5 days

Outcome Measure Data Not Reported

13. Secondary Outcome

Title:	mRS
▼ Description:	Shift analysis of mRS
Time Frame:	30 days

Outcome Measure Data Not Reported

14. Secondary Outcome

Title:	NIHSS Change
▼ Description:	Change from baseline in National Institute of Health Stroke Scale (NIHSS) score If reporting a score on a scale, please include the unabbreviated scale title, the minimum and maximum values, and whether higher scores mean a better or worse outcome.
Time Frame:	5 days

Outcome Measure Data Not Reported

Adverse Events

Information is required		
Time Frame		
Adverse Event Reporting Description		
Source Vocabulary Name for Table Default	[Not specified]	
Collection Approach for Table Default	[Not specified]	
Arm/Group Title	Riociguat +Propylthiouracil +Perphenazine	Standard of Care
▼ Arm/Group Description	Triple combination therapy group: ○ each patient in this group will receive two doses (8 +/- 2 hours between doses) of orally administered combination therapy of riociguat, propylthiouracil, and perphenazine, in addition to standard of care. Riociguat: Riociguat is an sGC stimulator currently approved and marketed for pulmonary arterial hypertension. Propylthiouracil: Propylthiouracil, already marketed for the treatment of various subtypes of hyperthyroidism, has been identified as a new member of the class of	Control group: each patient in this group will receive only standard of care

	potent and effective neuronal nitric oxide synthase (NOS1) inhibitors Perphenazine: Perphenazine, already marketed as an antiemetic and antipsychotic drug, presents the best NADPH oxidase (NOX) inhibitory characteristics compared to other compounds of the same drug class.	

All-Cause Mortality
Information is required

	Riociguat +Propylthiouracil +Perphenazine	**Standard of Care**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	--- /---	--- /---

▼ **Serious Adverse Events**
Information is required

	Riociguat +Propylthiouracil +Perphenazine	**Standard of Care**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	--- /---	--- /---

▼ **Other (Not Including Serious) Adverse Events**
Information is required

Frequency Threshold for Reporting Other Adverse Events	%

	Riociguat +Propylthiouracil +Perphenazine	**Standard of Care**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	--- /---	--- /---

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact

Name/Official Title:	---
Organization:	---
Phone:	---
Email:	---

Information is required