Data Management Plan (DMP) for PAVE trial S66869

version 1.0 - 20-01-2023

GENERAL INFORMATION	
S-number & study acronym:	S66869
Protocol version & date	"Producing an Arthritis Value-Framework with Economic Evidence – Paving the Way for Rare Childhood Diseases"
Sponsor:	UZ/KU Leuven
Number of research sites:	12
Expected number of participants:	500
Coordinating/Principle Investigator:	Prof. Dr. Carine Wouters
DMP prepared/revised by:	CTC UZ Leuven
Study Statistician:	Ann Belmans (L-Biostat)
Study Safety Coordinator/Reviewer:	Not Applicable

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1. Purpose

This Data Management Plan serves to describe all study-specific clinical trial-related data management tasks and deliverables. This includes how the data are collected, how data quality and integrity is assured, how data is handled, transformed and processed, etc.

2. Scope

This DMP was developed for clinical trials for which KUL-UZ Leuven is Sponsor and/or for which data management tasks are contracted to KUL-UZL, and is governed by CTC DM-SOP-001

Out of scope:

Development and content of the Statistical Analysis Plan (SAP)

3. Scope of data management activities

A. DATA COLLECTION				
Data point	**Collect**	**Re-use**	**Recording**	**Comments**
Screening	☒	☐	Medical file (source data)	
Baseline data	☒	☐	Medical file (source data)	
Questionnaire (survey)	☒	☐	Data can be entered directly in the eCRF by the patient or legal representative or member of the study team with data entry rights. Template questionnaire (paper) can be used in case no tablet is available.	Tablets are provided by the study team
A.2 Was GDPR questionnaire completed?			☒ Yes Processing of personal data will be conducted under General Data Protection Regulation (GDPR), EU legislation 'Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)', Belgian legislation 'Belgian Law of 30 July 2018 on the protection of natural persons with regard to the processing of personal data'. ☐ No >>> *Please complete & submit to* ctc@uzleuven.be !	
A.3 Expected recruitment start date			Expected start date: May 2023 The study is expected to last 36 months.	
A.4 Name and version of (e)CRF platform or relational database used to capture study-specific data			REDCap™ Production version 13.1.9	
A.5 Party responsible for (e)CRF development			Hilde De Tollenaere – CTC Data Manager CTC.datamanagement@uzleuven.be Hilde.detollenaere@uzleuven.be	
B. DATA ACCESS AND SECURITY				
B.1 Physical location of CRF database			UZ Leuven REDCap is hosted on dedicated KU Leuven data servers at Campus Heverlee.	
B.2 System Administrator			For UZL REDCap the System Administrator is Gert Goos: gert.goos@kuleuven.be	
B.3 How will physical data access be restricted?			When using UZ Leuven REDCap, physical access to the data centers is logged and restricted to authorized KU Leuven Information Technology (IT) personnel, using badge identification. At the clinical database level only study team members, monitors and auditors/inspectors for whom the Coordinating or Principal Investigator (as	

	applicable) has requested project-specific eCRF access, are granted data access. Upon successful training completion, each user is centrally assigned a user role, associated with predefined system/data privileges, in accordance with CTC DM-WI-001. The gatekeeper for UZL REDCap user accounts is UZL CTC (ctc.datamanagement@uzleuven.be).
B.4 Will data be shared outside UZL during and/or following completion of the clinical research trial?	☒ Yes See protocol section 12 "Data transfer from the Leuven repository to other countries, including non-EU countries, will take into account national privacy legislations and privacy protection. Both ERN RITA and UCAN CANDU have mechanisms in place for sharing data and across borders." KU Leuven Research & Development was contacted to provide the necessary data sharing agreement. ☐ No*
*If "No": Please clarify why no data will/can be shared:NA	
B.5 Describe the use and format of required data exports	At the end of the study, the collected pseudonymised study data will be provided to the designated statistician in the format to be agreed between the Parties.
C. DATA STANDARDS & CODING	
C.1 Which medical coding dictionary/dictionaries will be used? *Note that safety event coding based on the MedDRA dictionary, is required for reporting study results in EudraCT.*	Not applicable
C.2 What measures will be taken to prevent collection and sharing of personal data from trial participants?	All participant data will be pseudonymized using a unique study-specific identifier for each trial participant, in compliance with applicable data protection regulations. No personal data will be collected in the eCRF. This will be verified as part of the eCRF testing and validation.
D. DATA CLEANING AND VALIDATION	
D.1 Describe the type, level and frequency of quality control (QC) activities.	Data quality will be checked through reviews of comprehensive data discrepancy reports, including information about missing and unreviewed / unvalidated data fields.
D.2 Will the study be monitored by a qualified, trained individual, who is independent from the study team?	☐ Yes ☒ No
If "Yes": Either describe the monitoring strategy and frequency, or refer to study-specific Monitoring Plan. *If "No": Provide justification (based on documented risk analysis!) for waiving monitoring responsibilities.* Not applicable as this is a non-interventional study	
D.3 Name of monitoring party	NA
D.4 Data cleaning strategy, i.e. query process	Several automated queries have been predefined or programmed for this study and data field validation is build-into the eCRF. Following periodic data reviews, the data will be cleaned using an interactive query workflow whereby the Data Manager will open a query when identifying missing and/or discrepant and/or unsubstantiated data, prompting the

	Investigator and/or designated study team members to address the issue.
D.5 Describe how protocol deviations and/or violations will be documented and/or reported. ***Note**: a description of protocol deviations/ violations will be handled as part of the statistical analysis, must described as part of the SAP.*	The Investigator and Trial team acknowledge and agree that prospective, planned deviations or waivers to the protocol are not permitted under applicable regulations on clinical studies. However, should there be an accidental protocol deviation, such deviation shall be adequately documented in the source documents and on the relevant forms and reported to the CI and Sponsor immediately. Deviations should also be reported to the EC as part of the EC's continued review of the Trial. Protocol deviations which are found to frequently recur, will require (immediate) action. Protocol violations will also be require a documented "Corrective Action Preventive Action (CAPA)" plan. Investigator acknowledges that such recurring protocol deviations could potentially be classified as a serious violation. It is understood that "a serious violation" is likely to affect to a significant degree: - the safety or physical or mental integrity of the Trial participants; or - the scientific validity of the Trial The Investigator is expected to take immediate action required to protect the safety of the trial participant(s), even if this action represents a deviation from the protocol. In such cases, the CI/Sponsor should be notified of this action and the EC at the Trial site should be informed according to local procedures and applicable regulations. The impact of the deviations/violations on the study results can only be assessed after their occurrence. Handling of such deviations cannot be foreseen in the SAP. If important deviations will be observed, corrective actions and possible biases will be discussed with the statistician.
E. RANDOMISATION / TREATMENT ALLOCATION	
E.1 Is the study randomized?	☐ Yes ☒ No
F. DATA INTEGRITY	
F.1 How will the integrity of the data be assured during data transfer and processing?	No data imports are foreseen. No patient identifying information is recorded in the eCRF. Exports will be used as described above for data verification/queries and statistical analysis. Data will be electronically saved and are accessible only to authorized personnel.
F.2 Which measures are taken to allow verification of data integrity throughout the entire data lifecycle?	A comprehensive audit trail is maintained within the eCRF allowing to demonstrate the validity of collected trial data. This includes historical records of original data entries, by whom the data was entered and when it was entered, as well as detailed records of who, when, which and why corrections to the original data entry were made. This also includes records pertaining to managing user access and data privileges.

F.3 What measures will be taken to assure the integrity of blinded treatment allocation/information?	Not Applicable
F.4 What measures will be taken to avoid bias of independent raters? (as applicable)	Not applicable
G. SAFETY REVIEW / REPORTING	
G.1 How will study participant safety be assured?	Not applicable
G.2 Party responsible for safety reviews	Not applicable
G.3 Party responsible for safety reporting, per applicable regulations, protocol and study-specific agreements	Not applicable
H. DATABASE LOCK	
H.1 Will an interim database lock be executed?	☐ Yes, expected date/timing for interim DB lock: ddMmmyyyy or Month/Year ☒ No
If "Yes", please describe timing, reason and conditions for interim database lock.	
H.2 When and under which conditions/at what point in time will the final database lock be executed?	After last visit of last patient and final data cleaning.
H.3 Expected data/timing for final DB lock	May 2026
H.4 Party responsible for final database lock	Hilde De Tollenaere Hilde.detollenaere@uzleuven.be Ctc.datamanagement@uzleuven.be
I. DATA RETENTION, CONTINGENCY & DISASTER RECOVERY	
I.1 Describe contingency procedures and data backup schedule	In the UZL REDCap database, data is backed up as follows: ▪ The web server backup regime is specified below: - An hourly backup, the last 6 versions of which are saved - A daily backup, the last 7 versions of which are saved - A weekly backup, the last 6 versions of which are saved ▪ The database backup regime is specified below: - A nightly cold backup of all databases - One month's storage of the nightly cold backups ▪ Data restore, upon request
I.2 Provide reference to relevant system disaster recovery procedures	For the UZL REDCap database, the following KU Leuven procedures for system recovery apply: ▪ Systems are proactively monitored 24 hours a day, 7 days a week. ▪ An emergency on-call service guarantees constant monitoring of the technical equipment, also outside office hours, but not at night. The on-call service is notified automatically in case of problems (between 7.00 - 23.00 hrs).

	▪ There are no fixed maintenance windows: a timely email is sent to inform the local IT Administrator of any planned maintenance or upgrades. ▪ Any service unavailability, scheduled or unscheduled, is announced on the ICTS status page. ▪ The web space is designed redundantly: in the event of system problems on one back-end server, all traffic is automatically diverted to another back-end server. The database platform is also designed redundantly.
J. END OF TRIAL DATA ARCHIVING	
J.1 Describe how (format and media) data will be archived at the end of the study	At KU Leuven, FAIR principles are applied. Pseudo anonymized survey data will be entered directly into the REDCAP secure web application for online survey and database management with backup on a university secure server. Data will be deposited with the UZ Leuven data repository at the end of the project. REDCap data will be backup on the server of UZ Leuven and stored for 25 years. Participants to the study will be informed on the possible re-use of the collected data. In addition, each site will be supplied with their site-specific final study data set for long-term archiving as part of the Investigator Site File (ISF)
J.2 How long will data be the study database be archived?	25 years or longer, as required per applicable regulations
J.3 Please provide archiving location following the end of the study	KU Leuven data repository
K. THIRD PARTY DATA HANDLERS	
K.1 Are any third parties involved with any aspects of data management?	☐ Yes ☒ No
If "Yes", please provide name and contact details of each party and indicate whether Confidentiality Agreements (CDAs) and/or Data Transfer Agreements have been established, as appropriate:	
L. INDEPENDENT DATA SAFETY MONITORING BOARD (DSMB)	
L.1 Will a DSMB be used?	☐ Yes ☒ No
If "Yes", please include DSMB project charter in DMP Appendix, or refer to the final, approved protocol if detailed information about the DSMB composition (members), organization (e.g. voting policy, requirements for meeting quorum, etc.), deliverables, scope, objectives and timing of DSMB activities is available in the protocol.	
L.2 Frequency of DSMB meetings?	Not applicable
L.3 Scope and objectives of DSMB activities?	Not applicable

4. Archiving

Final versions of this DMP will be filed in the appropriate section of the study-specific TMF.

5. Version history

Version	Reason for change
1.0 – 20-01-2023	New document

6. Approvals

Author	CTC Head
<Signature> Hilde De Tollenaere, CTC Data Manager Date: 14 Feb 2023	<Signature> Heidi Sterckx Date: 14Feb2023
Statistician	**Principal Investigator**
<Signature> Ann Belmans Date: 17 Febdel3	<Signature> Text Lien De Somer Lien De Somer 17 Feb 2023

Carine Wouters
18 Feb 2023