A Personalised Integrated Care Platform

(Grant Agreement No. 689209)

D8.9 Third Annual Trial Progress and Ethical Report

Date: 04-07-2019

Version 1.0

Published by the PICASO Consortium

Dissemination Level: Confidential

Co-funded by the European Union's Horizon 2020 Framework Programme for Research and Innovation under Grant Agreement No 689209

Document control page

Document file: D8.9 Third Annual Trial Progress and Ethical Report.docx
Document version: 1.0
Document owner: UDUS

Work package: WP8 – Trials preparation, Migration and Evaluation
Task: T8.2 Trial 1 Implementation and T8.3 Trial 2 Implementation
Deliverable type: R

Document status: ☒ approved by the document owner for internal review
☒ approved for submission to the EC

Document history:

Version	Author(s)	Date	Summary of changes made
0.1	Richter, Jutta (UDUS)	16-04-2019	First draft
0.2	Richter, Jutta (UDUS) & Chiaravalloti, Agostino (UNITOV), Trine F. Sørensen (IN-JET)	11-06-2019	Added content
0.3	Chiaravalloti, Agostino (UNITOV)	12-06-2019	Review of comments from partners
0.8	Richter, Jutta (UDUS)	12-06-2019	Added content
1.0	Richter, Jutta (UDUS)	04-07-2019	Final version submitted to the European Commission

Internal review history:

Reviewed by	Date	Summary of comments
Paul Quinn (VUB)	27-06-2019	Minor corrections
Armanas Povilionis (BOSARC)	27-06-2019	Minor corrections

Index:

1 Executive Summary

This deliverable presents the annual progress of the PICASO trials in Germany (UDUS) and Italy (UTV). The trial protocols are available from D8.2 Trial Protocol for RA and Co-morbidities Trial in Germany and D8.2 Trial Protocol for PD and CVD trials in Italy. In Germany recruitment for the trials started in February 2018. In Italy patient recruitment started in September 2016. Trials have been finalised in Germany in June 2019 and in Italy in March 2019.

Furthermore, the deliverable gives a brief report of the PICASO Ethical Board's activities in relation to the trials.

2 Introduction

2.1 Purpose, Context and Scope of this Deliverable

This deliverable presents the third annual progress of the PICASO trials in Germany (UDUS) and Italy (UTV). It covers the period from M33 to M41. The trial protocols are available from *D8.2 Trial Protocol for RA and Co-morbidities Trial in Germany* and *D8.3 Trial Protocol for PD and CVD trials in Italy*. In Italy ethical approval of the trial protocol has been achieved and patient recruitment started in September 2016. In Germany ethical approval of the trial protocol has also been achieved and the trial started in February 2018. In Germany an amendment was submitted because the protocol was updated in March 2019 and April 2019 regarding hand-out of FitBits at the end of the trial.

Furthermore, the deliverable gives a status report on local ethical issues, i.e. in relation to the trials' progress and current status. A deeper analysis of the ethical issues relevant to the trials and the project as a whole was presented in deliverables *D3.3 The PICASO Ethical Guidelines* and *D3.4 Ethical Analysis of Monitoring and Privacy Impact*. In addition, adherence to the Ethical Guidelines were assessed in the deliverables Annual Compliance Monitoring Reports.

2.2 Intellectual Property (IP)

Intellectual property was identified in regard to the technical component developments and have been added to an IPR list of the consortium.

No other new intellectual property was identified since the preceding deliverable on this topic.

2.3 Content and Structure of this Deliverable

Chapters 3 and 4 present a progress report of the UDUS and UTV trial respectively. These chapters provide an insight into all the work involved in setting up and deploying the trials.

3 Trial Progress at UDUS

Trial 1 was carried out by PICASO partner UDUS (Policlinic of Rheumatology and Hiller Research Unit Rheumatology) and involved patients above the age of 18 years with Rheumatoid Arthritis (RA) and any Cardiovascular Disease or risk factor as co-morbidity. For UDUS this deliverable intends to give an overview of the status and the conduction of the trials.

UDUS met in person on a bi-weekly basis and are co-chaired by the Head of the Department and the PICAOS Clinical Manager. During the meetings the research team discussed upcoming topics and determined the further procedures. Additionally, the team monitored the progress against project milestones and budget. Contact to UDUS IT was performed as necessary and within the above mentioned meetings.

3.1 Current Status

The Trial at UDUS was performed with n=30 patients according to the protocol presented in D8.2 Trial Protocol for RA and Co-morbidities Trial in Germany.

3.2 Trial

3.2.1 Protocol

The trial protocol that is available from the deliverable *D8.2 Trial Protocol for RA and Co-morbidities Trial in Germany* reached ethical approval on 13th December 2017. Patients' recruitment was performed until January 2019.

Evaluation questionnaires were developed according to the evaluation framework available from deliverable *D8.6. Evaluation framework*. They considered the work performed in the related tasks T3.5 Patient Empowerment and evaluation aspects *T8.5 Trials Evaluation UDUS trial evaluation processes* were aligned as much as possible to UTV trial. Developed questionnaires were shared among each other's.

In Germany an amendment to the protocol was submitted in March 2019 and April 2019 regarding hand-out of FitBits at the end of the trial. Handing out the FitBits was in line with the ethics committee. The ethics committee at UDUS requested that data collection with the FitBits was stopped when the individual finished (and left) the trial.

3.3 Technical Issues and Data Security Aspects

For setting up the IT infrastructure and thus for trial implementation a close adjustment process with the UDUS IT and the IT personal of the Policlinic of Rheumatology and Hiller Research Unit Rheumatology was necessary. Also the interaction of the local IT partners and the PICASO technical partners was performed. The ODS solution was developed in cooperation with the PICASO partners. The ODS held the data extracted from the clinical system that has been made available to the PICASO solution and an interaction with the Rheumatology specific patient documentation system (DocuMed.rh) at UDUS was aimed for. The ODS interacted with the other PICASO infrastructure.

The ODS design was developed in close collaboration between UDUS IT and IT personal of the Policlinic of Rheumatology and Hiller Research Unit Rheumatology and the technical partners predominantly CNET and INUIT.

3.4 Ethical Aspects

3.4.1 UDUS Ethical Board

Informed consent was an important component of PICASO project and especially of UDUS. Most of the patients that were recruited have been treated by the UDUS over several years. This intimate care process formed a good basis for achieving informed consent.

An incident was discovered which was immediately solved in accordance with the applicable regulations. This action took into account the relevant requirements of the GDPR. The incident confirmed that the protocols and ethical guidelines implemented in the project worked as intended and no serious harm was done.

No other local ethical aspects were identified.

3.4.2 PICASO Ethical Board

UDUS attended the PICASO ethical board meeting that was performed as a telephone conference on 20 February 2019. For further progress notes see Chapter 5 of this deliverable and the internal deliverable *D3.7 Annual Compliance Monitoring Report.*

3.5 Other Trial Relevant Activities

We collaborated with a German statutory health insurance. The established contact was networked for the dissemination of PICASO.

Integration of the CHS (Centre of Health Society) at UDUS in the trials at UDUS was warranted. Personal communications with The Institute of General Medicine were performed for recruitment of collaboration CHS physicians. CHS was part of the workshop at UDUS in February 2019.

In addition, an information letter was developed for the general practitioners of the participating PICASO patients. It informed them on the project and was sent with the physician information and informed consent that was developed as well.

PICASO was presented at the Annual Meeting of the German Society for internal Medicine as a poster presentation (6th May 2019). An abstract has been submitted to the Annual Meeting of the German Society for Rheumatology in Dresden (Germany) (5th-7th September 2019) in collaboration with FIT, it was accepted for poster presentation 3rd June 2019. An abstract has been submitted to the Annual Meeting of the “Deutsches Netzwerk Versorgungsforschung e.V.” that will take place 9th-11th October 2019. It was accepted as an oral presentation.

4 Trial Progress at UTV

Trial 2 has been carried out in the Department of Biomedicine and Prevention, University of Rome Tor Vergata (UNITOV, PICASO Partner) in conjunction with the Department of Neurology and Psychiatry of the Santa Lucia Hospital (SLUCIA) in Rome. The trial was based on the recruitment of subjects affected by PD and at least one of the following pathologies as comorbidities: cardiovascular disease (i.e. hypertensive diseases, congestive heart failure) and/or psychiatric condition as depression or anxiety. Twenty subjects have been enrolled in the “standard arm” while 10 have been enrolled in the “experimental arm”. For additional details please check *D8.3 Trial Protocol for PD and CVD trials in Italy*. This chapter presented a report of progress to date.

Preparatory work for trial 2 required the conjunction of data derived from the experience of several professional figures involved in the management of patients with the Parkinson disease (PD) and co-morbidities. In particular, since the number of patients that may show the clinical characteristics mentioned in the previous paragraph is relatively high, the efforts of the clinical, medical and paramedical personnel involved in the trial was aimed to a) identify in detail the prototype of the patients to be enrolled in the study; and b) identify the main operational and technical aspects and scenarios where trial implementation could introduce the most significant benefits.

A retrospective analysis of clinical records was performed in order to identify those crucial points that may represent a good substrate for clinical implementation of Trial 2 for both patients and physicians. For example, the lack of seamless communication between physicians represents one of the major problems when the coordination of the activities between two hospitals is required, leading to inefficient and time consuming procedures for physicians and frustration for the patients who await agreements between doctors. Patients with PD and autonomic dysfunction or mood disorder represent the optimal prototype, grouping the main limitations of clinical management/aspects mentioned above.

SLUCIA and UNITOV meet in person or via teleconference on a bi-weekly basis and are chaired by the Project Manager or the Clinical Trial Coordinator. During the meetings, the two research teams also monitor progress against project milestones. An internal review for the evaluation of the progress of the trial is scheduled monthly until the end of the project.

4.1 Current Status

At the time of writing, 20 subjects have been enrolled in the “standard arm” while 10 have been enrolled in the “experimental arm”. For additional details please check *D8.3 Trial Protocol for PD and CVD trials in Italy*.

Clinical data including blood tests, imaging data, clinical history, medications and other relevant medical parameters have been collected for both patients included in the experimental arm. As for standard arm, clinical data have been collected and served only for patient’s selection during the recruitment phase.

During the whole trial, data derived from home monitoring have been carefully evaluated by physicians at UNITOV and SLUCIA. Data derived from UNITOV trial are under evaluation for correlation analysis of health parameters with data from diagnostic imaging modalities (as MRI or DaTscan).

During the trial ongoing, experts at UNITOV performed a series of testing in order to evaluate the empowerment of patients during the trial. Moreover, separate focus groups have been organized at SLUCIA for testing the empowerment of caregivers (for details see *D3.6 Practical Implementation of Patient Empowerment and Joint Care).*

The trial ended in March 2019.

4.2 Trial Protocol

The trial protocol is presented in detail in deliverable *D8.3 Trial Protocol for PD and CVD trials in Italy*. In brief, case studies are divided in two arms: 1) the standard arm (the patient will be followed as in current clinical practice) and 2) the experimental arm (the patient management based on electronic information sharing and monitoring vital signs with electronic devices). At the end of the recruitment 20 patients was enrolled in the standard arm, and 10 patients in the experimental arm. Informal carers with their crucial role in supporting the patient in managing and living with their condition(s) and in caring for the patient at home are involved in the trial as well. A detailed statistical comparison of data extrapolated from both standard and experimental arm will serve for an objective assessment of Trial 2 outcomes.

The performance of PICASO on Trial 2 has been assessed a) by means of detailed questionnaires administered for both patients and their caregivers (see Deliverable 3.6) and b) a statistical analysis of differences between number of re-visits or access to hospital. Lastly, a detailed questionnaire was administered to physicians in order to evaluate the impact of PICASO on workflow. These data are currently under evaluation.

4.3 Data Security Aspects

There were no further data security aspects to report than those already reported in *D8.7 Second Annual Trial Progress and Ethical Report.*

4.4 Ethical Aspects

Due to the extension of the UNITOV trial, two amendments were submitted to SLUCIA and UNITOV ethics committee. Patients were informed on trial extension and confirmed their participation in the study.

4.5 Other Trial Relevant Activities

The project has been successfully presented in several medical conferences. In particular, PICASO project was presented on 24-25 January 2019 at Karolinska Institutet, Stockholm, Sweden “International Research Workshop on user adapted knowledge bases and real-world data in medicine and pharmacology: data acquisition, design, implementation and effects” and on 12-15 April 2018 in Pacific Yokohama, Japan

JRC 2018 Japan Radiology Congress, Innovative Science and Humanism in Radiology by Prof. Orazio Schillaci.

5 Ethical Status and Progress

The PICASO Ethical Board has a special interest in the status and progress of the two trials in the project. As defined in the Ethical Board's Term of Reference (please see *D3.3 The PICASO Ethical Guidelines*), the board "acts as an advisor" to project partners and patients involved in the trials.

5.1 Ethical Board Meeting (IN-JET)

The PICASO Ethical Board had had its last board meeting in January 2018 (see D8.7), however, it was decided to conduct a telephone conference with the board. This meeting was held on 20th February 2019. The board members were updated on the trial status and progress. The results of the first software usability testing with patients and clinicians were discussed; the suggested changes have since been implemented and has improved the dashboard. Clinicians find the clinical dashboard very useful. No patients have reported any problems with using the home-monitoring devices (notably the blood pressure device) which was positive.

No ethical issues had been raised at the time of the board meeting. The preparation of the deliverable *ID3.8 Annual Compliance Monitoring Report* 2 was also discussed with the Ethical Board. This report was later submitted to and approved by the Ethical Board. The report showed that both trials were in compliance with the project's ethical guidelines.