A Personalised Integrated Care Platform

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D8.4 Annual Trial Progress and Ethical Report

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Trine F. Sørensen (IN-JET)	05-10-2017	Corrections and minor editing.

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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 the trials have not been started. In Italy ethical approval of the trial protocol has been achieved, patient recruitment started in September 2017.

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 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 *D8.3 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 the trial has not started. D8.2 has been delivered to the local ethics committee and other local administrative authorities. The process for the ethical approval is still ongoing.

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 will be presented in the forthcoming deliverable *D3.4 Ethical Analysis of Monitoring and Privacy Impact*. In addition, adherence to the Ethical Guidelines (in D3.3) will be assessed in the internal deliverables Annual Compliance Monitoring Reports in M28 and M38.

2.2 Intellectual Property (IP)

At UDUS new IP was identified: Some of the evaluation questionnaires that will be used in in PICASO (in a modified version) previously have been used by UDUS in a different project. In conformity with the contract project permission to use the questionnaires has been obtained. UDUS aims to include this IP into the project IPR Registry. The project management was informed.

No other new intellectual property was identified.

2.3 Content and structure of this deliverable

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

3 Trial Progress at UDUS

Trial 1 is carried by PICASO partner UDUS (Polyclinic of Rheumatology and Hiller Research Unit Rheumatology) and will involve patients above the age of 18 years with Rheumatoid Arthritis (RA) and any Cardiovascular Disease as co-morbidity. For UDUS this deliverable intends to give an overview of the status and implementation of the trials.

3.1 Preparatory work

A large amount of preparatory work for the trial conduction at UDUS has been performed. Among work that is reported in deliverables from other work packages (e.g. from WP 2, WP3, WP4, WP5 and WP10) the deliverable *D8.1 Trial Definition for Integrated Care Management* has been published. A detailed description of the trial exists in deliverable *D8.2 Trial Protocol for RA and Co-morbidities Trial in Germany*.

For elicitation of initial user requirements a user workshop was conducted involving all relevant stakeholders for development of PICASO. The first workshop was held in May at UDUS. A detailed description of the methodology as well as its outcomes is subject of *D2.1 Scenarios and Use Cases for Integrated Care*. As a result of the workshop, clinical workflows were described and visualized. The focus was on how current clinical workflows can be reproduced in PICASO and what requirements are needed for PICASO. Detailed descriptions of the user requirements relevant for the clinical and technical PICASO partners are provided in the deliverable *D2.2 Requirements report*.

The collaboration between the clinical and technical PICASO partners led to the description of the „TO-BE“ use cases described in deliverable *D2.1 Scenarios and Use Cases for Integrated Care*. They were used for the architecture description available in the deliverable *D2.3 The PICASO Architecture Specification*. In addition, the identification of relevant stakeholders from the clinical perspectives yielded profit for the description of the architecture as provided in the deliverable *D2.3 The PICASO Architecture Specification*.

In addition the preparatory work for the conduction of the UDUS trials included collaboration for the content of the due deliverable *D4.1 Sensor Network and WAN Access Point*, the deliverable *D4.2 First IoT Resource Management Subset* and the deliverable *D4.3 First version Patient Private Cloud*.

Furthermore, the collaboration of UDUS clinicians with the technical partners had impact on the results reports in the deliverable *D5.3 First Data Resource Browser* and in the deliverable *D5.1 Data Models & Shared Memory Objects*.

The UDUS PICASO team meets in person on a bi-weekly basis chaired by the Clinical PICASO Manager and the Head of the Polyclinic of Rheumatology and Hiller Research Unit Rheumatology at UDUS. In addition, meetings with IT UDUS and IT of the Polyclinic of Rheumatology and Hiller Research Unit Rheumatology at UDUS are scheduled as required. Phone calls with IT partners were performed as required. Participation in bi-weekly consortium telephone conference has been established.

Further clinical preparatory work is described in the deliverable *D8.1 Trial Definitions for Integrated Care Management*.

3.2 Trial

3.2.1 Protocol

The work done for deliverable *D8.1 Trial Definitions for Integrated Care Management* and the above mentioned collaboration with the technical partners resulted in the trial protocol that is available from the deliverable *D8.2 Trial Protocol for RA and Co-morbidities Trial in Germany*. In particular, patients' recruitment processes were defined including inclusion and exclusion criteria as well as the monitoring protocol. In addition, the trial execution time tables were developed and adjusted as required in collaboration with the technical PICASO partners.

Patient information and the informed consent forms were developed. A description of the devices for patients' home monitoring and the description of the installation/de-installation process are available in *D8.1 Trial*

Definitions for Integrated Care Management and in *D8.2 Trial Protocol for RA and Co-morbidities Trial in Germany* too.

Modified questionnaires (e.g. on IT knowledge) from a previous project will be used in a modified version in PICASO. In conformity to the contract with this project, written permission to use the questionnaires has been obtained by the UDUS team. UDUS aims to include this intellectual property into the project IPR Registry. The project management team has been informed.

One questionnaire covers the areas of IT and digital health knowledge, and patient's expectation of digital health in the context of PICASO. Usability and sustainability questionnaires for patients and physicians are under development. These will be applied at outpatients' visits after three, six and nine months from baseline at UDUS. A detailed evaluation framework is published in deliverable *D8.6 Evaluation Framework*.

3.2.2 Current recruitment status

Trial recruitment will begin as soon as ethical approval has been granted by the local ethics committee; the application is currently being assessed by the ethics committee and feedback is expected by mid of October 2017.

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 Polyclinic of Rheumatology and Hiller Research Unit Rheumatology was necessary and is still ongoing. This does not only apply to the local clinical and technical partners. Also the close interaction of the local IT partners and the PICASO technical partners was and is still necessary. The ODS solution has been developed in cooperation with the PICASO partners. The ODS will hold the data extracted from the clinical system that has been made available to the PICASO solution and will be fed by the HIS (hospital information system) at UDUS and the Rheumatology specific patient documentation system (DocuMed.rh) at UDUS. The ODS will interact with the other PICASO infrastructure. Also the Patient Dashboard information will be sent to the ODS via PICASO and will be stored there. The physician will be able to view the information stored in the ODS via the Clinician Dashboard. Transfer of detailed information out of the HIS and DocuMed.rh will only happen for PICASO patients. Thus, they will be marked in the HIS and/or DocuMed.rh.

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

To ensure maximum data safety, we have been in constant exchange with the data security officer at UDUS. Collaboration with the data security officer at UDUS was necessary to agree on the approach on how data from the medical devices can be transferred without breaching data security aspects as data from the activity tracker will be stored in a non-EU cloud. Our patients will be informed before their participation in Trial 1 on all relevant issues concerning their data and the processing of the data. This includes collection, access and storage aspects. In addition to local data security discussions, there will be another PICASO deliverable *D3.5 Privacy Compliance Laws Associated with Surveillance* which will highlight essential data protection issues that must be taken into account.

3.4 Ethical aspects

3.4.1 UDUS Ethical Board

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

However, when preparing the patient information and informed consent forms insurance coverage was identified to be of major importance. In interaction with the local ethics committee UDUS discussed whether UDUS will need to obtain insurance coverage and what this would need to cover. With the current knowledge,

apart from patients statutory health insurances it is not necessary to provide additional insurance for the PICASO participants and wording for the patient informed consent form was agreed upon.

Ethical approval is awaited.

No other local ethical aspects were yet identified.

3.4.2 PICASO Ethical Board

UDUS attended the PICASO ethical board meetings that included external board members in May 2016 (Bonn) and in January 2017 (Bonn). Detailed ethical guidelines have been published in the deliverable *D3.3 PICASO Ethical Guidelines*. For further progress notes see Chapter 5 of this deliverable.

3.5 Other trial relevant activities

During the above mentioned workshop we collaborated with a German statutory health insurance. The established contact is still networked for the dissemination of PICASO. Further collaboration was declared. In preparation of the upcoming patient recruitment (see above) we identified patients that are insured in that particular health insurance. However, patients from other statutory health insurance will be invited to participate in the trials as well.

Integration of the CHS (Centre of Health Society) at UDUS in the trials at UDUS is warranted. The Center for Health and Society (CHS) is an interdisciplinary organization of several institutions at the Medical Faculty of the Heinrich-Heine-University of Düsseldorf: The Institute of General Medicine, the Institute for Occupational, Social and Environmental Medicine, the Institute for Biometry and Epidemiology – DDZ, the environmental epidemiology group, the Institute of Medical Sociology and the Institute of Health Research and Health Economics belong to the CHS. Personal communications with the spokesman are ongoing. CHS collaborating physicians have been invited to participate in PICASO already, replies are still awaited. Relevant integration steps and prerequisites for participation need to be explored further and are planned for autumn 2017.

4 Trial Progress at UTV

Trial 2 will be carried out in the Department of Biomedicine and Prevention, University of Rome Tor Vergata (UTV, PICASO Partner) in conjunction with the Department of Neurology and Psychiatry of the Santa Lucia Hospital (SLUCIA) in Rome and will involve subjects affected by Parkinson disease (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. This chapter presented a progress report to date.

4.1 Preparatory work

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 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 UTV 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.

4.2 Trial protocol

The trial protocol is largely presented in deliverable *D8.3 Trial Protocol for PD and CVD trials in Italy*. In brief, case studies are subjected to a simple randomization that will lead to the creation of two arms: 1) 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). 20 patients will be 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. The simple randomization together with a detailed statistical comparison of data extrapolated from both standard and experimental arm will serve for an objective assessment of Trial 2 outcomes. To date, 30 subjects are recruited for the study.

4.3 Data security aspects

Establishing an appropriate Governance model for managing such a complex project is critical in order to comply with the requirements of the National and European Statement on Ethical Conduct in Human Research (LEGGE 6 aprile 2007, n. 46; LEGGE 6 agosto 2013, n. 96; LEGGE 6 agosto 2013, n. 97).

Moreover, the following Italian laws should be respected:

Decreto Legistativo n.196 del 30/06/2003; Linee guida per i trattamenti di dati personali nell'ambito delle sperimentazioni cliniche di medicinali adottate dal Garante per la Protezione dei dati personali in data 24/07/2008 (G.U. n.190 del 14/08/2008)

Autorizzazione n. 8/2014; Autorizzazione generale al trattamento dei dati genetici - 11 dicembre 2014

Autorizzazione n. 9/2014; Autorizzazione generale al trattamento dei dati personali effettuato per scopi di ricerca scientifica - 11 dicembre 2014.

The requirements listed above represent the background of several talks/discussions and meetings between information technologists (IT) of UTV and SLUCIA. Moreover, the main administrative representative of each hospital was informed of the decisions of each meeting both formally and informally. In collaboration and through workshops with IBM and INUIT, the Clinician Dashboard and clinical data requirements both for UTV and SLUCIA were defined. The requirements listed above represent the background of several discussions and meetings between information technologists (IT) of UTV and SLUCIA. Moreover, the main administrative representatives of each hospital were informed of the decisions of each meeting both formally and informally.

Finally, the intensive cooperation with PICASO partner INUIT led to the definition of the IT requirements mentioned above in conjunction with other technical requirements by other partners: certificates, static ips, ssh, http, https, outgoing connections to specific IPs and specified domains, incoming connections from a specific IP or from any IP.

4.4 Ethical aspects

Following the granting of funds in February 2016, ethics approval was sought and granted by the Local UTV Ethics Committee on July 2016 (registro sperimentazioni 158/16). After an internal meeting held in SLUCIA on September 2016, a representative of both UTV and SLUCIA in this project decided to perform a formal submission of Trial 2 to SLUCIA Ethics Committee. The Trial 2 was approved on November 2016.

UTV attended the PICASO ethical board meeting that included external board members in January 2017. Observations and comments were reported and then discussed internally between UTV and SLUCIA. Moreover an informal meeting between UTV partner representative Dr. Agostino Chiaravalloti and ethics committee representative Dott.ssa Alessandra Nistri was held in UTV on February 2017.

The UTV informed consent form is available in Appendix C.

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 "will act as an advisor" to project partners and patients involved in the trials.

This chapter reports on the Ethical Board activities in relation to the trial status and progress.

5.1 Ethical Board Meetings

The Ethical Board has met twice during the first year of the project: in May 2016 (M5) and in January 2017 (M12). On both occasions, the trials had not yet started and had no ethical concern to report. Thus, the meetings focused on discussing the ethical aspects of the trials as they involve patients, and the potential ethical issues and concerns that the trial owners and the project need to be aware of. The discussion therefore also focused mainly on how to handle these aspects and how to avoid or deal with potential issues.

The issues discussed included data protection and privacy, including the technical approach to anonymisation, data accuracy, patient informed consent, authorisation and access control to patient data, patient home monitoring, surveillance, the rationale, benefits and risks of the trials, and the responsibilities of the trial owners (clinicians).

The meetings have actually resulted in the elicitation of user requirements that are related to functionalities in the Patient Dashboard and the Clinical Dashboard:

Please refer to *D2.4 First Updated Requirements and Architectural Report* (to be submitted in September 2017) for full details on the updated user requirements.

Concurrently, the internal Annual Monitoring Compliance Reports (D3.7 in M28 and D3.8 in M38) will report in more detail on the input (comments, recommendations, etc.) from the PICASO Ethical Board.

The agendas for the two Ethical Board meetings are provided in Appendix A and B.

5.1.1 Trials reporting to the Ethical Board

The PICASO trial owners have not reported any ethical problems to the PICASO Ethical board to date. This is not unexpected as the trials have not yet started and only Trial 2 (UTV) has commenced the recruitment of patients. A written informed consent was obtained by 27 subjects until the 20th of March 2017.

The UDUS Trial is in the evaluation process the local ethics committee, Ethikkommission an der Medizinischen Fakultät der Heinrich-Heine Universität Düsseldorf, for approval.

The UTV Trial has applied for ethical approval from their local relevant ethics committee, Comitato Etico Indipendente – Policlinico Tor Vergata, which was granted on 22 July 2016. The letter of approval was received by the PICASO Ethical Manager on 11 November 2016.

Trial at UTV will be cooperating closely with the Department of Neurology and Psychiatry of the Santa Lucia Hospital in the trial and it was therefore decided that should also apply for ethical approval for their involvement in the PICASO trial. The letter of approval from the Comitato Etico Indipendente – Policlinico Tor Vergata was granted on 21 November 2016. The PICASO Ethical Manager received confirmation of the approval on 11 January 2017.

5.1.2 Right to personal data and informed consent

D3.3 PICASO Ethical Guideline obliges the project to give patients access to their personal data and to control who has access to their personal data. Discussions in WP2 lead to new user requirements, in particular PIC.208.

Key	Summary	Status	Component	Fit Criterion	Source	Rationale
PIC-208	Presentation as well as visualisation of results from home monitoring	Implemented	Narratives Manager (NM), Patient Dashboard UI (PD UI)	Presentation of values from home monitoring measurements and self-recordings to patients shall be configurable to patients' needs. As requested by the	E2E discussion with clinicians	During discussions about PICASO user trials it turned out that particularly for UTV trial, care needs to be taken that patients are not overburdened by being

Key	Summary	Status	Component	Fit Criterion	Source	Rationale
	measurements and self-recordings for patients should be adjustable to patients' needs.			trial owner patients participating in UTV trial shall not be presented results from blood pressure and heart rate variability measurements. Also, values out-of expected-range shall not be highlighted from any measurements. In t1 this will be achieved by according configuration of the Italian version of the Patient Dashboard. In t2 this shall be definable by clinicians when creating a patient's care plan.		confronted with unfavourable results from home monitoring measurements and self-recordings. Therefore, clinicians need to have the possibility to define whether or not results from home monitoring measurements and self-recordings should be presented retrospectively to patients. Presentation as well as visualisation of such results, e.g., in form of line graphs, has to be in accordance to patients' individual health situation, which can include a psychological disorder not allowing visualization of such information, because potentially too frightening. In case results of home monitoring like blood pressure measurements shall be visualized to a patient, clinicians also have to be able to define whether or not values out-of expected range (below or above defined threshold) shall be highlighted to a patient for the same reason explained above

In respect of the clinical rationale for not allowing patients to see their blood pressure and heart rate measurement this requirement was accepted *subject to compliance with legal requirements*, that patients can request access to this and other personal data at any time. Patients must be informed of this right and it must also be specified in the informed consent form. An item (no.11) referring to this has been added to the list presented in D3.3 PICASO Ethical Guidelines: "Access to all personal data collected during trial will be granted upon a request made to the trial representative."

As the informed consent form will be in the local languages, trial owners should either provide the PICASO Ethical Manager with a complete English version or a copy of the original form (in local language) together with a written statement confirming that the items below are included in the form prior to trial start. Trial owner must also submit a written statement prior to the trial start confirming that the informed consent process has been conducted in accordance with the recommendations in *D3.3 PICASO Ethical Guidelines*. These statements and/or translated copies of the informed consent forms will be documented in the Annual Compliance Reports. The statement forms are provided in Appendix D & E.

Appendix A: PICASO Ethical Board Meeting Agenda 25 May 2016

Meeting Subject:	PICASO Ethical Board Meeting
Venue:	Building C5, room 120 Fraunhofer Institute for Applied Information Technology (FIT), Schloss Birlinghoven, 53754 Sankt Augustin (close to Bonn)
Date:	25 May 2016
Chair:	Trine F. Sørensen (IN-JET)
Distribution:	The Ethical Board and PICASO Clinical Partners

Time	Subject	Topics to be covered	Time (mins)	Lead participant
8:45	**Welcome**	Arrival and coffee	15	ALL
9:00	**Introduction**	**The PICASO Project** • Desired outcomes of today • Brief overview of PICASO and the two trials	15	Trine F. Sørensen (IN-JET)
9:15	**Ethical Board Terms of Reference**	**Definition of PICASO Ethical Board Terms of Reference** • Comments and amendments to the proposed text	15	ALL
9:30	**Main Ethical Issues at Stake**	**Ethical Issues in the PICASO context** Comments and amendments to: • The predefined issues • Additional issues • The proposed Informed Consent Form • The proposed Ethical Check List	40	ALL
10:10	**The PICASO Ethical Principles**	**Definition of the PICASO Ethical Principles and Guidelines** Comments and amendments to: The proposed Ethical Principles and their Application	35	ALL
10:45	**Coffee break**		15	
11:00	**Ethical Board reporting to Consortium**	**Presenting the main issues & discussion**	45	ALL
11:45	**Close of meeting**			

Appendix B: PICASO Ethical Board Meeting Agenda 11 January 2017

Meeting Subject:	PICASO Ethical Board Meeting
Venue:	Fraunhofer Institute for Applied Information Technology (FIT), Schloss Birlinghoven, 53754 Sankt Augustin (close to Bonn)
Room:	C5-033
Date:	11 January 2017
Chair:	Trine F. Sørensen (IN-JET)
Distribution:	The PICASO Ethical Board. CC to consortium partners

Time	Subject	Topics to be covered	Time (mins)	Lead participant
13:00	**Welcome & Status update**	**Progress and current status** • Objectives of today • Overview of project status • Results from the review	15	Trine F. Sørensen (IN-JET)
13:15	**Trial 1: Cardio Vascular Disease (CVD) with Rheumatoid Arthritis (RA)**	**Trial 1 status update** • Trial definition and implementation plan • Recruitment & informed consent issues • Ethics committee approval status.	15	Jutta Richter (UDUS)
13:30	**Trial 2: Parkinson's Disease (PD) with Cardio Vascular Disease (CVD)**	**Trial 2 update** • Trial definition and implementation plan • Recruitment & informed consent issues • Ethics committee approval status.	15	Agostino Chiaravalloti (UTV)
13:45	**Discussion**	**Discussion** • Ethical issues to be investigated / resolved.	60	All
14:45	**Coffee break**		15	
15:00	**Discussion**	**Discussion** • Ethical issues to be investigated / resolved	45	All
15:45	**Concluding remarks**	**Next Steps** • Upcoming deliverable: D8.5 First Annual Trial Progress and Ethical Report (due 31 January 2017)	15	Trine F. Sørensen (IN-JET)
16:00	**Close of meeting**			

Appendix C: UTV informed consent

Disclaimer: the translation provided here below may not completely reflect the original italian legal language.

INFORMATION SHEET AND THE CONSENT CERTIFICATE (For a subject capable of giving informed consent)

INFORMATION SHEET

Dear Ms/Miss/Mrs/Mr/Dr,

In this structure is in progress a project entitled "**PICASO**: "A personalized integrated care platform". The project involves the Department of Biomedicine and Prevenction, University of Rome Tor Vergata and Department of Neuropsychiatry, IRCCS Santa Lucia, Rome. The trial will be completed in XX months.

For the realization of this study, we needed the collaboration and availability of people who meets the scientific requirements suitable for evaluation provided in this project. Before you make the decision to accept or decline participation at this trial, please read carefully the follow pages, taking all required time. For any clarification, you can ask more information to the staff involved in the experimentation. For more information, do not hesitate to contact your trusted doctor or who you think fit.

AIM OF THE STUDY

The study is direct to patients with diagnosis or suspected Parkinson's disease and cardiovascular or psychiatric co-morbidity. Specifically, the main aim of the study is to improve the multidisciplinary management of the complex patient. This goal will be achieved through two main ways: a) sharing information about your clinical conditions among the specialists who will take care of your health; b) monitoring your vital parameters during your daily activity by means of low invasive wearable systems.
All patients enrolled in this study will be randomized (included with a random criterion) in two groups: 1) Group standard: current clinical practice in patient management; 2) Experimental group: patient management based on sharing of electronic information and monitoring the vital parameters (see below) with electronic devices.

WHAT HAPPENS IF YOU PARTICIPATE AT THIS STUDY AND INVESTIGATIONS THAT WILL BE CARRIED OUT

If you decide to participate at this study, you will not be subject to any experimental protocols or pharmacological investigation. Indeed, the experimental design involves the execution of the following treatments that are part of the normal clinical routine:

- First outpatient medical examination with Anamnesis and objective examination;
- Collecting of both anamnestic and anthropometric data;
- Hematochemical Examinations;
- Neuropsychological evaluation;
- Magnetic Resonance (MR); Nuclear Medicine Investigations (PET / TC, SPECT) with 18F-Fluorodeoxyglucose, Dat Scan and 123I Metaiodobenzylguanidine.
- Testing of genetic risk factors for cardiovascular and neurodegenerative disease;
- Pharmacological treatment according to your clinical condition;
- Ambulatory medical examinations for clinical and laboratory follow-up.

However, your participation does not incur any additional expenses for you. All expenses will be charged to the departments above indicated. The study will take 36 months. The study does not include the application of experimental protocols.
If you are included in the experimental group, the experimental plan will also provide:

- Monitoring of your biological parameters (blood pressure, heart rate and mobility) by wearing worn medical devices;
- Installing a small size hardware system in your home, able to communicate with the above-mentioned monitoring systems.

BENEFITS THAT YOU WILL RECEIVE BY PARTICIPING IN THE STUDY

Patients enrolled in the study will receive an accurate diagnostic evaluation of the disease by matching of the data obtained from clinical practice with those derived from the home monitoring systems.

THE RISKS OF PARTICIPATING IN THE STUDY

It is important to note that to the participation at this study does not involve specific risks for the patients. Nevertheless, we want to clarify that, at present state of knowledge, you may not benefit from the above-mentioned procedures. However, for all patients that accept to participate at this trial, an insurance cover is provided. A copy of the Policy can be consulted at the Clinical Center. Also, if data emerged may influence your participation in the study, you will be promptly informed. The doctor who follows you in the experiment will provide all the clarifications and information you need.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

You are free to not participate in the study. Your participation is completely voluntary and you can suspend at any time your membership without obligation to motivate the decision and communicating it to doctors who will follow you within the project. In any case, you will receive all the therapies planned for your pathology. Likewise, experimentation may be interrupted if your doctor finds that side effects occur.

CONFIDENTIALITY AND PRIVACY OF PERSONAL DATA

All information related to your participation in this clinical trial will be strictly confidential. You will have the right to know both what information will be stored and to update or modify incorrect data. Specifically:

- Your personal data (initials of general information, clinical data, and other "sensitive" data) will be recorded, processed, managed and archived in both printed form and digital format - for the exclusive purposes linked to this clinical trial. Subsequently, personal data will be elaborated statistically and then processed in a totally anonymous form. In addition, your data (in anonymous form) may be used for publications and / or presented in congresses according to Personal Data Protection Act (D. Lgs. 196 del 30.06.2003).
- Consensus on the personal data processing is indispensable for your participation in the clinical trial. Your personal data will not be made accessible and/or available to third parties. Regulatory Authorities (Ministry of Health), medical staff, monitoring and auditing staff and the Ethics Committee will be allowed direct access to the original medical documentation for a review of clinical trial and / or data procedures, without violating the subject's privacy.

In addition, according to the Article 7 of Legislative Decree 196 of 30.06.2003, you have the right to obtain confirmation of the existence or not of your personal data, even if not yet registered, and their communication in an intelligible form. You have the right to obtain:

a) updating, correcting, and integrating of your data (when/if you are interested)
b) deletion, transformation into anonymous form or the blocking of data processed in violation of the law. Moreover, will be deleted data that is not necessary for storage in relation to the purposes of the study
c) the attestation that the operations referred to in points (a) and (b) have been communicated, also for their contents, to whom data will be transferred or diffused, except in cases where this is impossible or involves the use of means manifestly disproportionate respect to the protected patient privacy.

You have the right to object, in whole or in part, to the processing of your personal data, for: sending advertising material, direct sales or market research and commercial communication.

For further information and communications during the study, please contact the following medical staff:

- Dr. Clelia Pellicano. Dr. Francesca Assogna, Dr. Gianfranco Spalletta (Department of Neuropsychiatry, IRCCS “Santa Lucia”).
- Prof. Orazio Schillaci, Dr. Agostino Chiaravalloti (Department of Biomedicine and Prevention, University of Rome Tor Vegata)

The study’s protocol proposed was drafted in accordance with the European "Good Clinical Practice" and the current version of the Helsinki Declaration and approved by the Independent Ethics Committee at the University Hospital "Tor Vergata" and IRCCS “Santa Lucia”.

At the same Ethics Committee, you may report any relevant consideration related to this study.

DECLARATION OF CONSENT

I, Mr/Ms/Mrs/Miss. . . . . .

Born in. . . . . Province. . . . . .

date . . . . . and resident . . . . . .

in via/piazza . . . . . .

C.F. . . . . Health code (Health card) (USL/n°) . . . . . .

I **DECLARE** that I have received from the Doctor ……. comprehensive explanations concerning my participation at the study entitle **"PICASO:** A personalized integrated care platform**"**, as indicated in the attached information sheet, a copy of which has been delivered to me in satisfactory advance. I have been adequately informed about the purpose of the study and its methods. I am aware that at any time I will be able to suspend my participation of the study without obligation to motivate the decision. Also, I was informed about my free participation.

I therefore declare that my consensus is an expression of a free decision and that my participation is free, not affected by promises of money, other benefits, obligations of gratitude, friendship or kinship to doctors that they propose the study.

I consent the use of my data, in anonymous form, for scientific and administrative purposes related to the realization of the study and **I agree / do not agree** that the news data concerning the experiment, limited to those that may prove useful for my health, should be transmitted to my trusted doctor, Dr…….

I declare that I have been informed there is an insurance policy cover N°……. and, therefore, to accept freely to

participate in the study, having fully understood the meaning of my participation and the possible risks and benefits that may arise.

Date

Patient Signature

Date

Signatory of the Experimental Doctor

Signature of the Experimental Doctor (in block letters)

STANDARD INFORMATION SHEET AND DECLARATION OF CONSENT (If the patient can not read and / or sign)

I, Mr/Ms/Mrs/Miss.…… certify that the Dott……. has clearly explained to Mr/Ms/Mrs/Miss ……. the characteristics of the study entitle **"PICASO:** A personalized integrated care platform**"**, according to the attached information sheet, and after the opportunity to make any queries considered necessary, he/she agreed freely to participate in the study.

Date and Signature of Independent Witness

INFORMATIVE AND MANIFESTATION OF CONSENT TO TREATMENT OF PERSONAL DATA

OWNER OF THE TREATMENT AND RELATED PURPOSES

Testing Centres University Hospital "Tor Vergata" and IRCCS “Santa Lucia”, will treat your personal data, especially those relating to your health, according to the “Good Clinical Practice” (Legislative Decree 211/2003). and to the extent that they are indispensable in relation to the purpose of the study, other relevant data its origin, its lifestyles, and so on, exclusively in relation to the realization of the study. Other data about your origin, your lifestyles etc will be used if they are indispensable for the realization of the study.
The processing of your data related to pathology, therapy and personal data is indispensable for the study: the refusal to authorize the processing of its data will not allow you to take part in the study.

NATURE OF THE DATA

The doctor who will follow you in the study will identify you with a personal code: the data concerning you, with the exception of your name, will be recorded, processed and stored link to your personal code, at your date of birth, sex, weight and stature, and all variables related to the condition of your disease. Only your doctor and authorized persons involved in the study will be able to link this code to your name.

TREATMENT OF DATA

Data processed by electronic means will be published in strictly anonymous form. For example, these data will be used for scientific publications, statistics and scientific conferences. Your participation in the study implies that the Ethics Committee and the Italian and foreign health authorities will be able to know the data concerning you, contained in your original clinical documentation, ensuring the confidentiality of your identity.

EXERCISE OF RIGHTS

You may exercise your rights according to art. 7 of the Code (e.g. accessing your personal data, integrating them, updating them, correcting them, opposing their treatment for legitimate reasons, etc.) by addressing directly at the testing centre.
You may stop at any time and without giving any justification for your participation in the study: in that case, no further data will be collected about you. The data already collected will be used, without altering them, for the purposes of the study.

CONSENT

By subscribing to this form, I consent to the processing of my personal data for the purposes of the study within the limits and with the methods indicated in the information provided to me with this document.

Name and surname of the person concerned (in block letters) ……

Signature of the interested party …….

Date

Appendix D: Statement confirming informed consent process

Statement confirming that informed consent was obtained in accordance with guidelines

I hereby confirm that the recruitment of patients for [NAME OF TRIAL] has followed the guidelines laid out in D3.3 PICASO Ethical Guidelines for obtaining informed consent from participating patients.

Date: _____

Trial Owner: _____

Signature: _____

Appendix E: Statement confirming the content of the informed consent form

Statement confirming the content of the informed consent form

I hereby confirm that the informed consent form presented to patients for [NAME OF TRIAL] contains the obligatory items as identified in D3.3 PICASO Ethical Guidelines.

Date:_____

Trial Owner:_____

Signature:_____