Fondazione Regionale per la Ricerca Biomedica

DECRETO NR. 65 del 29.07.2024

OGGETTO: BANDO ERAPERMED JOINT TRANSNATIONAL CALL FOR PROPOSALS 2021 -EROGAZIONE DELLA RATA CORRISPONDENTE ALLA SECONDA ANNNUALITA' PARI A EURO 12.809,65 ASSEGNATA AL PARTNER UNIVERSITA' DEGLI STUDI DI MILANO BICOCCA DEL PROGETTO ERAPERMED2021-383 DAL TITOLO: "*RAMAN ANALYSIS OF SALIVA FROM COPD PATIENTS AS NEW BIOMARKER: AI-BASED POINT-OF-CARE FOR THE DISEASE MONITORING AND MANAGEMENT* (ACRONIMO CORSAI)" - CUP H45E22000030006

L'atto si compone di 22 pagine
di cui 18 pagine di allegati

Fondazione Regionale per la Ricerca Biomedica

IL DIRETTORE GENERALE DELLA FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA

RICHIAMATI:

- la DGR nr. IX/2401 del 26.10.2011 con la quale la Regione Lombardia ha costituito la "Fondazione Regionale per la Ricerca Biomedica" (di seguito "FRRB"), il cui scopo statutario è quello di promuovere la ricerca scientifica e sanitaria nel settore delle Scienze della Vita;
- la DGR n. X/5221 del 31.05.2016 con la quale è stato approvato lo Statuto di FRRB, successivamente modificato con DGR n. XI/5786 del 21.12.2021;
- la DGR n. XI/1016 del 17.12.2018 con la quale è stato approvato il nuovo schema di Accordo di collaborazione tra FRRB e la Direzione Generale Welfare di Regione Lombardia;
- la DGR n. XI/3476 del 05.08.2020 con la quale è stato approvato il Piano d'Azione 2020 che prevede, al suo interno, l'allocazione fino ad un massimo di euro 1.500.000,00 per la partecipazione di FRRB al bando internazionale ERA PerMed JTC 2021;

CONSIDERATO CHE:

- l'Università degli Studi di Milano Bicocca (di seguito "Beneficiario"), Partner Nr. 1 del progetto dal titolo "*Raman analysis of saliva from COPD patients as new biomarker: AI-based point-of-care for the disease monitoring and management*", Acronimo CORSAI, ID 383, Responsabile Scientifico Prof.ssa Vincenzina Messina, è risultato ammesso a finanziamento nell'ambito del programma europeo ERA PerMed JTC 2021;

VISTI:

- il Regolamento (UE) nr. 1291/2013 del Parlamento Europeo e del Consiglio dell'11 Dicembre 2013 che istituisce il Programma Quadro di Ricerca e Innovazione (2014-2020) "*Horizon 2020*" quale strumento di finanziamento della ricerca scientifica e dell'innovazione per progetti di ricerca o azioni volte all'innovazione scientifica e tecnologica che portino un significativo impatto sulla vita dei cittadini europei;
- il Grant Agreement nr. 779282 firmato il 21.11.2017 dalla Commissione Europea ed un partenariato internazionale coordinato dall'Instituto de Salud Carlos III e composto da un totale di 32 enti provenienti da 23 paesi con il quale è stato approvato il progetto "*ERA-Net Cofund in Personalised Medicine — ERA PerMed*";
- la "*Dichiarazione di svolgimento di attività non economica ai sensi delle norme in materia di*

aiuti di Stato" e la "*Dichiarazione di accettazione del contributo* inviate a FRRB, a mezzo PEC, in data 22.12.2021 (Prot. nr. 20210340E);

- la Convenzione stipulata tra FRRB e l'Università degli Studi di Milano Bicocca, inviata da FRRB al Beneficiario via PEC (Prot. nr. 20220079U) in data 22.02.2022, firmata digitalmente dalla Dott.ssa Giovanna Iannantuoni, Rettrice dell'Università degli Studi Milano Bicocca e controfirmata digitalmente dall'allora Direttore Generale di FRRB, Dott. Luigi Cajazzo;

DATO ATTO CHE:

- in data 22.12.2021 il Beneficiario ha comunicato sulla Dichiarazione di accettazione contributo a firma del Legale Rappresentante inviata via PEC (Prot. 20210340E), la data di inizio del Progetto, concordata con il Partenariato transnazionale, fissata al **1° febbraio 2022**;
- In data 09.03.2022 è pervenuta a FRRB la richiesta di erogazione del contributo a mezzo PEC (Prot. nr. 20220057E) per un importo complessivo pari a euro 24.000,00, corrispondente al 30% del contributo totale assegnato al Partner nr. 1 del progetto Acronimo CORSAI, Responsabile Scientifico Prof.ssa Vincenzina Messina;
- in data 18.03.2024 è pervenuta da parte del Beneficiario (PEC Prot. Nr.20240104E), la documentazione economica relativa al secondo anno di attività – periodo 1° febbraio 2023 – 31 gennaio 2024 – in relazione al progetto CORSAI;
- tra la documentazione sopracitata è pervenuta la scheda di rendicontazione economica (*Financial report*) contenente il dettaglio dei costi sostenuti dal Beneficiario nel corso del secondo anno per complessivi **€ 30.322,16** (**Allegato 1**);
- in data 20.05.2024 il Direttore Generale di FRRB ha comunicato al Beneficiario (PEC Prot. Nr. 20240182U) l'approvazione dei costi dichiarati a conclusione del secondo anno di attività richiedendo, al contempo, l'invio della richiesta di erogazione;

VISTI:

- la richiesta di erogazione del contributo relativo alla seconda annualità, a mezzo PEC, in data 25.05.2024 (Prot. nr. 20240194E) per un importo pari a **€ 12.809,65** nell'ambito del progetto CORSAI (**Allegato 2**);
- il Codice Unico di Progetto (CUP) E23C23000070002, generato dal Beneficiario in fase di avvio del progetto;
- il report scientifico annuale trasmesso da *Università degli Studi di Milano-Bicocca,* via e-mail,

Fondazione Regionale per la Ricerca Biomedica

in data 28.03.2024 e che riporta lo stato di avanzamento scientifico del progetto transnazionale (**Allegato 3**);

VISTA E VERIFICATA:

- la regolarità contributiva dell'ente assegnatario del contributo – Università degli Studi di Milano Bicocca – tramite trasmissione del DURC da parte di Università degli Studi di Milano Bicocca (**Allegato 4**);

DECRETA

per i motivi espressi in premessa, parte integrante del presente provvedimento:

di autorizzare l'erogazione in favore dell'Università degli Studi di Milano Bicocca con sede legale in Milano, Piazza dell'Ateneo Nuovo, 1, di un importo pari a **euro 12.809,65**, come rata pari alla differenza tra le spese rendicontate nei primi due anni di progetto e l'anticipo di 24.000€ assegnato al Partner nr. 1 del progetto Acronimo CORSAI, Responsabile Scientifico Prof.ssa Vincenzina Messina (CUP H45E22000030006);

IL DIRETTORE GENERALE
Veronica Comi
f.to digitalmente

Veronica
Comi
29.07.2024
15:45:39
GMT+01:00

Fondazione Regionale per la Ricerca Biomedica

COST STATEMENT

Rev.0 del 31/10/2022

EU PROJECT (please select)	ERAPERMED		
JTC	2021		
PROJECT ID	383		
PROJECT TITLE AND ACRONYM	Raman analysis of saliva from COPD patients as new biomarker: AI-based point-of-care for the disease monitoring and management - "CORSAI"		
LOMBARDY BENEFICIARY	Università degli Studi di Milano-Bicocca		
NAME OF PRINCIPAL INVESTIGATOR	Vincenzina Messina		
CUP NUMBER	H45E22000030006		
REPORTING PERIOD (FROM-TO)	01/02/2023 - 31/1/2024	YEAR (please select)	2
IS VAT RECOVERABLE? (YES/NO)	NO		

COST CATEGORIES	TOTAL BUDGET	REPORTING PERIOD 1	REPORTING PERIOD 2	REPORTING PERIOD 3	TOTAL COST STATEMENT	DEVIATION FROM ORIGINAL BUDGET
TOTAL PERSONNEL COSTS	*€ 30.000,00*	*€ 4.003,65*	*€ 17.005,05*		€ 21.008,70	€ 8.991,30
CONSUMABLES	*€ 12.000,00*		*€ 4.880,00*		€ 4.880,00	€ 7.120,00
EQUIPMENT (LEASING OR ON HIRE)	*€ 8.000,00*	*€ 1.476,76*	*€ 3.309,25*		€ 4.786,01	€ 3.213,99
TRAVEL & ACCOMODATION	*€ 6.000,00*				€ 0,00	€ 6.000,00
PUBLICATIONS	*€ 3.000,00*				€ 0,00	€ 3.000,00
OTHER DIRECT COSTS	*€ 1.000,00*				€ 0,00	€ 1.000,00
SUBTOTAL	**€ 60.000,00**	**€ 5.480,41**	**€ 25.194,30**	**€ 0,00**	**€ 30.674,71**	€ 29.325,29
OVERHEADS	*€ 12.000,00*	*€ 1.096,08*	*€ 5.038,86*	*€ 0,00*	*€ 6.134,94*	€ 5.865,06
SUBCONTRACTING COSTS	*€ 8.000,00*	*€ 0,00*	*€ 0,00*	*€ 0,00*	*€ 0,00*	€ 8.000,00
TOTAL REQUESTED BUDGET	**€ 80.000,00**	**€ 6.576,49**	**€ 30.233,16**	**€ 0,00**	**€ 36.809,65**	**€ 43.190,35**

PERSONNEL COSTS

Please refer to the JTC guidelines for the eligibility of personnel costs

NAME	POSITION	CONTRACT TYPE	PERIOD (FROM - TO)	EURO AMOUNT
Marco Piazza	fellowship	fellowship	01/02/2023 - 15/10/2023	17.005,05
			TOTAL € AMOUNT	**17.005,05**

CONSUMABLES

Please refer to the JTC guidelines for the eligibility of costs

NAME	ITEM DESCRIPTION	INVOICE NR.	INVOICE DATE	PAYMENT DATE	EURO AMOUNT
ROLOS by Constructor	Rolos license (research & education edition) for 12 months	IN7000005	23/2/2023	7/3/2023	4.880,00
				TOTAL € AMOUNT	**4.880,00**

EQUIPMENT (LEASING OR ON HIRE)

NAME	ITEM DESCRIPTION	INVOICE NR.	INVOICE DATE	EURO AMOUNT	% OF USE OF THE EQUIPMENT FOR PROJECT'S PURPOSES	AMORTISATION MONTHS	EURO AMOUNT
1 SERVER HPE Proliant DL560 Gen10	server	22303802	31/07/22	9.786,84	100%	48,00	2.446,71
HPE NVIDIA Tesla T4 16GB Module	scheda GPU per server	22303803	31/07/22	3.101,24	100%	48,00	775,31
PowerMe UPS RPMM/9 3K	UPS	23300360	21/02/23	380,64	100%	48,00	87,23
						TOTAL € AMOUNT	**3.309,25**

TRAVEL AND ACCOMODATION

Max 10% of direct costs

NAME	REASON FOR TRAVELING	DESTINATION	PERIOD (FROM - TO)	EURO AMOUNT
			TOTAL € AMOUNT	**0,00**

PUBLICATIONS

max 5% of direct costs

NAME	DESCRIPTION	INVOICE NR.	INVOICE DATE	EURO AMOUNT
			TOTAL € AMOUNT	**0,00**

OTHER DIRECT COSTS

Please refer to the JTC guidelines for the eligibility of costs

NAME	ITEM DESCRIPTION	INVOICE NR.	INVOICE DATE	PAYMENT DATE	EURO AMOUNT
				TOTAL € AMOUNT	**0,00**

SUBCONTRACTING

Max 20% of direct costs

NAME	PROCEDURE APPLIED	DESCRIPTION	INVOICE NR.	INVOICE DATE	EURO AMOUNT
				TOTAL € AMOUNT	0,00

I declare that all the documentation listed in this table is archived at the Beneficiary premises and available in case of financial audits.

Name of the Beneficiary Legal Representative
Giovanna Iannantuoni

Name of the Principal Investigator
Vincenzina Messina

UNIVERSITA' DEGLI STUDI DI MILANO BICOCCA
Firmato digitalmente da Vincenzina Messina
Data: 27.02.2024 18:14:01 CET
Organizzazione: BICOCCAMILANO/12621570154

Firmato digitalmente da: Giovanna Iannantuoni
Organizzazione: UNIVERSITA' DEGLI STUDI MILANO BICOCCA/12621570154
Data: 08/03/2024 09:14:57

Milano

UNIVERSITA' DEGLI STUDI DI MILANO - BICOCCA

UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

RICHIESTA EROGAZIONE CONTRIBUTO

DICHIARAZIONE SOSTITUTIVA DI ATTO NOTORIO

(D.P.R. 445/2000)

Spett.
le Fondazione Regionale
per la Ricerca Biomedica
P.za Città di Lombardia 1
20124 Milano

PEC: fondazioneregionalericercabiomedica@pec.it

OGGETTO: richiesta di erogazione della prima rata relativa al progetto ERAPERMED2021-383 (acronimo "CORSAI")

TITOLO PROGETTO: Raman analysis of saliva from COPD patients as new biomarker: AI-based point-of-care for the disease monitoring and management - "CORSAI" - ERAPERMED2021-383

RESPONSABILE SCIENTIFICO: Prof.ssa Vincenzina Messina

CODICE CUP: H45E22000030006

La sottoscritta Giovanna Iannantuoni, nata a [redacted], domiciliata per la carica a Milano in Piazza dell'Ateneo Nuovo, 1, C.F. [redacted], in qualità di Legale Rappresentante dell'Università degli Studi di Milano-Bicocca partecipante al progetto in oggetto, con sede legale in Piazza dell'Ateneo Nuovo 1, 20126 Milano, C.F./P.IVA 12621570154

UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

ateneo.bicocca@pec.unimib.it

segreteria.scienze2@unimib.it

CHIEDE

l'erogazione della prima rata pari a € 12.809,65

Il pagamento dovrà essere effettuato tramite Nota di debito/avviso pagoPA.

Cordiali saluti,

Milano

Il Legale Rappresentante
Prof.ssa Giovanna Iannantuoni

(Firmato digitalmente ai sensi dell'art.24 del D.Lgs.82/05)

Firmato digitalmente da: Giovanna Iannantuoni
Organizzazione: UNIVERSITA' STUDI MILANO-BICOCCA/12621570154
Data: 23/05/2024 08:27:27

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ENTE CREDITORE Cod. Fiscale 12621570154

Universita' degli Studi di Milano - Bicocca

Piazza dell'Ateneo Nuovo 1
20126 Milano (MI)

DESTINATARIO AVVISO Cod. Fiscale 97608860157

FONDAZIONE REGIONALE PER LA RICERCA BIOMEDICA (FRRB)

Piazza Città di Lombardia 1
20124 MILANO (MI)

QUANTO E QUANDO PAGARE

12.809,65 Euro entro il **25/08/2024**

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EROGAZIONE PRIMA RATA - PROGETTO CORSAI

BANCHE ALTRI CANALI **entro il** **25/08/2024**

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Destinatario **FONDAZIONE REGIONALE PER LA** Euro **12.809,65**
Ente Creditore **Universita' degli Studi di Milano - Bicocca**
Oggetto del pagamento **EROGAZIONE PRIMA RATA - PROGETTO CORSAI**

Codice CBILL	Codice Avviso	Cod. Fiscale Ente Creditore
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INFORMAZIONI

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CAUSALE DEL BOLLETTINO

EROGAZIONE PRIMA RATA - PROGETTO CORSAI

Servizio di incasso in collaborazione con il partner tecnologico **Banca Popolare di Sondrio**

Joint Transnational Call for Proposals (2021) for

"Multidisciplinary Research Projects on Personalised Medicine – DEVELOPMENT OF CLINICAL SUPPORT TOOLS FOR PERSONALISED MEDICINE IMPLEMENTATION"

2nd Annual Report

1. General information

Project title	Raman analysis of saliva from COPD patients as new biomarker: AI-based point-of-care for the disease monitoring and management
Project acronym	**CORSAI**
Project duration (months)	**36**
Starting date	01/02/2022
Period covered by the report:	01/02/2023 – 31/01/2024
Periodic report:	[2nd]
Project website and social media accounts	Project webpage: https://www.labion.eu/erapermed-granted_corsai-project/ Twitter: @CORSAI_project Instagram: labion_

2. Project Consortium

Coordinator (Partner 1):

Affiliation, Address:	IRCCS Fondazione Don Carlo Gnocchi ONLUS (FDG), Via Capecelatro 66, Milano
Country:	Italy
Name of Principal Investigator:	Paolo Innocente Banfi
E-Mail:	pabanfi@dongnocchi.it
Phone:	+39 0240308832
Type of institution (academic, clinical, industrial)	Clinical
Funding Organisation:	Fondazione Regionale per la Ricerca Biomedica

Project Partners:

Partner no.	Affiliation	Country	Name of Principal Investigator	Type of partner (academic, clinical, industrial)
2	Università di Milano Bicocca (UNIMIB)	Italy	Vincenzina Messina	Academia
3	Geratherm Respiratory GmbH (GERA)	Germany	Manuel Heinz	For-profit private partner

4	Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS)	Spain	Nestor Soler	Clinical
5	Riga Stradins University (RSU)	Latvia	Madara Tirzīte	Academia

Please indicate any changes in the project team.

There are no changes in the project team.

3. Publishable summary of the context and overall objectives of the project

*Please summarize the project **objectives and major achievements** using language accessible to the public (max. 2000 characters including spaces). **This abstract may be published (e.g. ERA PerMed website).***

The main goal of the project is to create and validate a new method based on the Raman spectroscopy (RS) analysis of saliva for the optimised and personalised management of patients with Chronic Obstructive Pulmonary disease (COPD). The combination of the clinical instrumental data with the RS-approach will increase the quality of the clinical practice through appropriate stratification of patients, i.e., early identification of COPD phenotypes and attribution of precise therapies, assessment of potential exacerbation risk and adherence to therapy. By the integration of instrumental and RS measures with Artificial Intelligence (AI), patients' COPD phenotype will be predicted to guide, in a measurable and objective way, the COPD patients' management with a particular focus on: patients' stratification, prediction of exacerbation risk and adherence to therapy. The feasibility of the work is supported by the use of a sensitive and portable Raman Spectroscope, used by non-specialized personnel for the creation of a point-of care (POC). During the first year of CORSAI project most of expected deliverables have been achieved. First of all, partners involved in the recruitment of subjects obtained the approval documentation from the Ethics Committees and started the saliva samples collection. The consortium collected a total of 211 samples and pre-screened 336 eligible COPD patients. Spirostick Blue was installed in all the clinical locations and experts have been chosen to be included in the list for the establishment of the EAB. Social pages have been created for the dissemination of activities, achievements and updates related to CORSAI project. In parallel, the Consortium is involved in the planned dissemination activities.

4. General overview of the objectives and deliverables for the period covered

Objectives/Deliverables			
No.	***Title***	***Partner in charge***	***Short Description***
D5	**Report about Raman spectra of drugs (month 12)**	**FDG**	All the drugs selected and procured during the first year of project, were acquired and analyzed by Raman spectroscopy. Despite the initial delay due to problems with laser source, the Raman spectra of drugs were successfully obtained, and the classical least square (CLS) fitting analysis was performed to investigate the drugs contribution in the saliva of COPD patients.
D6	**Report on first year EAB annual activities (month 12)**	**FDG**	The EAB activities were delayed due to a change in the initial composition of the EAB board. They will meet in April and then they will deliver a report.
D7	**List of patients and control subjects recruited (month 22)**	**FDG, IDIBAPS, RSU, GERA**	At month 24, the list of patients and controls is completed for the 62% of the scheduled population. All the partners involved have multiplied their efforts to achieve the goal, by accelerating the enrolment of new subjects.
D8	**Completed saliva sample collection and clinical database (REDCap) (month 22)**	**FDG, IDIBAPS, RSU, GERA**	At month 24, saliva samples were obtained from 62% of the scheduled population. All the partners involved have multiplied their efforts to achieve the goal, by accelerating the enrollment of new subjects.
D9	**Completed Raman spectra collection with benchtop Raman (month 24)**	**FDG**	Delays in the recruitment have resulted in delays in the acquisition of Raman spectra with benchtop Raman. However, FDG has completed the acquisition of all delivered samples and with the delivery of new saliva samples, the acquisition will be completed within a few months.

D10	**Completed Raman spectra collection with portable Raman (month 24)**	**FDG**	D10 is delayed due to the delayed collection of saliva samples and due to the delayed installation of the portable Raman (February 2024).
D11	**Complete data sets of diagnostic information of all patients and control subjects (month 24)**	**FDG, GERA, IDIBAPS, RSU**	At month 24, the dataset about patients and controls is completed for the 62% of the scheduled population
D12	**Creation of high-performance computing for data analysis (month 24)**	**UNIMIB, GERA**	The infrastructure to send the data acquired at the POC for analysis to a central server running the AI algorithm is implemented.
D13	**Report on second year EAB annual activities (month 24)**	**FDG, IDIBAPS, RSU, UNIMIB, GERA**	The EAB activities were delayed due to a change in the initial composition of the EAB board. They will meet on April and then they will deliver a report.

5. Work performed during the reporting period and main results achieved so far

Please describe the work performed per WP.

WP 1	**Patients recruitment and saliva samples collection**
Leading Partner: FDG	
Additional involved Partners: IDIBAPS, RSU, GERA	
Planned timeline (according to GANTT chart): from M1 to M22	**Actual timeline:** from M13 to M24

Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*)

During the second year of CORSAI project, FDG, RSU and IDIBAPS continued the recruitment of patients for saliva sample collection and created a list of patients and control subjects recruited, as foreseen by D7 of WP1. The collaboration between the clinical partners allowed the enrolment of 340 subjects: 173 from COPD patients, 106 from asthmatic subjects and 50 healthy controls. COPD phenotypes are distributed as follow: 8 aCOPD, 59 neCOPD, 51 eeCOPD and 25 ebCOPD.

IDIBAPS contributed by recluting a total of 43 samples, divided into: 22 COPD patients, 2 asthmatic subjects and 19 healthy controls.

RSU collected a total of 75 samples: 25 COPD, 22 asthmatic subjects and 27 healthy controls.

Subjects involved in the project are aged between 40-90 years old for COPD patients, 19-90 years old for asthmatics and 20-70 years old for Healthy controls. The FEV1/FVC ratio measurements, for each recruited subject, were performed using the Spirostik Blue in combination with Blue Cherry software provided by GERA.

Personal and clinical data of the subjects collected were entered in REDCap.

The consortium reached the 62% of the stated recruitment aim.

Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.*

The main deviation from the timeline is related to subjects' recruitment. The reasons are to be ascribed to home treatment that postpones recruitment, eg. LABA/LAMA longitudinal group, or to patients' passing away. Considering COPD subjects, the limited number of recruited aCOPD and ebCOPD phenotypes and the difficulties in their enrolment could be related to their limited incidence in the COPD population compared to other phenotypes (neCOPD, eeCOPD) whose goals were successfully

achieved. All partners are involved in the enlistment of new subjects, especially the underrepresented COPD phenotypes.

WP 2	**Raman analysis**
Leading Partner: FDG	
Additional involved Partners: /	
Planned timeline (according to GANTT chart): from M3 to M24	**Actual timeline:** from M13 to M24

Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*)

In the 2nd year, the collection of Raman spectra with benchtop Raman (Task 2.1) continued concurrently with the new sample recruitment, as described in the 1st Annual Report.

Regarding Task 2.2, the acquisition of Raman spectra with the portable Raman was delayed due to a deferral of the instrument arrival at LABION.

Task 2.3 was accomplished as planned, the drugs procured and stored previously at FDG were acquired on aluminium coated slides, using the new 785 nm laser source, a 50x objective, an acquisition time of 30s, accumulation of 2 and 100% laser power. Drugs were analyzed both in powder form and dissolved in physiological solution, 10 spectra for each drug were obtained. The average spectrum for every drug dissolved in the physiological solution was used for the analysis. Drugs in physiological solution seemed to reproduce better the natural condition of consumption.

A report about the Raman spectra of drugs was made (D5) and a Classical Least Square (CLS) fitting analysis was performed in order to determine the spectral contributions of singles molecules within the complex saliva fingerprint.

Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.*

D9 and D10 of WP2 were not completed at month 24 as planned in the GANTT chart. The reasons for the delay are: 1) the delay on the sample recruitment (see WP1), 2) delayed installation of the selected portable Raman. FDG will complete sample acquisitions with both benchtop and portable Raman as soon as new samples will be delivered.

WP 3	**Collection and integration of instrumental and clinical data**
Leading Partner: GERA	
Additional involved Partners: FDG, IDIBAPS, RSU	
Planned timeline (according to GANTT chart): (from M3 to M24 and from M27 to M36)	**Actual timeline:** (from M13 to M24)

Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*)

The supplied spirometry devices (Spirostik Blue) and the modified version of BLUE CHERRY, which is able to store all identified clinical relevant data in the database for later statistical analysis, are used at the clinical sites to assess spirometry and other relevant clinical data. In parallel GERA is standby for support of the clinical sites during data acquisition.

During the 2nd year there was a problem with the data entry on RedCap and part of the clinical data were initially lost. It has generated further delays. However, the consortium was able to successfully reconstitute and re-enter data correctly on RedCap database.

Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.* As the recruitment of patients has been delayed (WP1), also the collection of instrumental and clinical data is delayed in parallel.

WP 4	**Data analysis and classification model development**
Leading Partner: FDG	
Additional involved Partners: UNIMIB	
Planned timeline (according to GANTT chart): from M7 to M26	**Actual timeline:** from M13 to M24
Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*) Raman data processing (Task 4.1) has been updated with the same pipeline explained in the previous report. Briefly, raw data from benchtop Raman underwent baseline correction and normalization to obtain the average fingerprint for each experimental group. Regarding Task 4.2, the classification model has been updated and Origin 2023b was used to perform Principal Component Analysis and Linear Discriminant Analysis, and to calculate the accuracy of the classification model. The accuracy of the updated classification model, trained with an increased number of spectra from the benchtop Raman, was about 74%. The other statistical analyses are ongoing. UNIMIB and FDG had monthly meetings to continue the development of the classification model.	
Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.* Due to the delayed installation of the portable Raman, FDG sample acquisitions and data analysis with portable Raman are still ongoing. Nonetheless, the preliminary acquisition and optimization of the procedure performed in Year1, when the portable Raman was selected, guarantee that the acquisition will be completed soon on all collected samples.	

WP 5	**Correlation Between Raman Database and Instrumental/Clinical Data**
Leading Partner: FDG	
Additional involved Partners: FDG, UNIMIB, GERA	
Planned timeline (according to GANTT chart): from M12 to M26	**Actual timeline:** from M13 to M24
Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*) Task5.1 related to the statistical analysis of the clinical data repository and Task5.2, correlation analysis are still ongoing and will be completed as soon as the dataset will be fulfilled. Similarly, the evaluation of the adherence to therapy will be accomplished by the end of the WP5, when the longitudinal collection will be completed.	
Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.*	

The correlation analysis is delayed due to delay in WP1 and WP2. Nonetheless, preliminary data guarantee the completion of the analysis as soon as a complete dataset will be obtained. The delay of WP1 and WP2 also delays the statistical analysis of the clinical data repository.

WP 6	**Deep Learning Model Development and Interpretability**
Leading Partner UNIMIB	
Additional involved Partners GERA	
Planned timeline (according to GANTT chart): from M7 to M30	**Actual timeline:** from M13 to M24
Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*) Classification models (CM) using DL models was conducted employing ResNet and CNN models. Using 78 COPD and 61 Asthma, a CNN obtained accuracy of 78% at patient level and 74% at spectra level. These results are preliminary, but all the computational modules of the classification pipeline have been implemented. The integration of the CM into the blue cherry platform will be implemented when the final model will be available. The modules developed and integrated on a ML development platform to minimize human intervention are: pre-processing for spectra filtering and data cleaning aimed at removing the therapy contribution from Raman spectra to enhance CM's performance, data augmentation (Gaussian noise injection and a Deep generative model), Model selection, Automatic Hyperparameter Optimization based on Bayesian Optimization. Explainability techniques, based on CAM, grad-CAM, and Game Theory, were developed addressing the specific challenges of Raman data. UNIMIB will proceed with validation. GERA developed a possible POC device to connect to the portable Raman spectroscope, to send data to a central server for analysis using the AI algorithm. An upload service on the POC device sends the clinical data stored in the POC database to a webserver, which stores the data into a central database for evaluation. This central database is accessed by the AI algorithm to evaluate the incoming data.	
Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces* The final Deep Learning model is not yet available due to delay in data collection as explained in WP1 and WP2. Nonetheless, preliminary analysis and experiments are encouraging and the analysis will be completed as soon as the full set of data is collected. For this reason, the integration of the classification model into the Blue Cherry platform has also been delayed.	

WP 8	**Impact analysis in terms of ethical, legal and social aspects**
Leading Partner FDG	
Additional involved Partners IDIBAPS, GERA, UNIMIB, RSU	
Planned timeline (according to GANTT chart): (from M1 to M36)	**Planned timeline (according to GANTT chart):** (from M1 to M36)
Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*) During the 2nd year FDG organized a RedCap trainig addressed to the consortium's clinicians in order to guarantee the correct data entry. LABION activities, regarding samples acquisition and analysis were showed and explained to doctoral students of the Respiratory Rehabilitation Department. The co-PI, Professor Marzia Bedoni, held lectures on CORSAI project to Computational Chemistry PhD students at University of Milan (UNIMI) and to FDG scientific clinical community. For the next year an AI education webinar will be scheduled by FDG in collaboration with UNIMIB, as forseen by Task 8.1. Task 8.2 The recruitment of experts from different stakeholders for EAB constitution was completed The EAB is now composed by: the Italian patient's association of pulmonary disease, Walgreens Boots Alliance	

Healthcare Pharmacy and Director, Legal, Compliance and Governance from Roche. An online meeting is planned for next April.
Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including space*

WP 9	**Management, exploitation and dissemination**
Leading Partner FDG	
Additional involved Partners IDIBAPS, GERA, UNIMIB, RSU	
Planned timeline (according to GANTT chart): from M1 to M36	**Actual timeline**: from M13 to M24
Work performed, Challenges, Achievements (*Max. 1,200 characters including spaces*) On 3rd March 2023 a virtual Consortium Meeting was organized to discuss achievements and pitfalls of the first year of the CORSI meeting, During the meeting all partners presented their achievements. Then, one in person Consortium Meeting was hosted by FDG on 8th September 2023. Preliminary data by FDG were presented to the Consortium, difficulties in the patient recruitment, sample shipment and database completion were discussed. Monthly meetings were organized by FDG and UNIMIB to work on the classification model and data analysis. Dissemination activity included presentation of preliminary results to scientific meeting and conferences: ERS 2023, VISPEC2023 and Science Together (online meetings organized by FDG aimed at researchers and scientific community)	
Has there been a deviation from the original work plan or from the original timeline? *If so, explain the reasons for deviation, the consequences and the proposed corrective actions. Max. 600 characters including spaces.* Considering unexpected errors and delays were encountered in the data entry of clinical parameters in Redcap registry (WP1), FDG created a new Redcap registry and organized an extra-training with the RSU colleagues on 20th December to avoid further slowdown in data acquisition.	

Transnational Collaboration, Meetings and Mobility

Describe consortium meetings (physical and virtual) including more than 2 partners (date, location, purpose, results).

Participants	*Date*	*Location*	*Purpose*	*Results*
FDG, IDIBAPS, RSU, UNIMIB, GERA	*03/03/2023*	Virtual (Microsoft Teams)	Timetable of WPs and deliverables. Discussion of operative procedures for sample shipment and data entry.	*Update about ongoing Raman acquisition; Agreement on desirable recruitment timeline and shipment schedule.*
FDG, IDIBAPS, RSU, UNIMIB, GERA	*08/09/2023*	Milan (in presence meeting)	Timetable of WPs and deliverables.	*Identification of main obstacles in patients recruitment and data entry.*

Please describe the benefits and the synergies of the collaboration including: any joint project or initiative, any staff exchange or cross-country recruitment, training opportunities for new staff, any obstacles to the transnational collaboration and the proposed solution (max 2,000 characters including spaces).

The synergy among the Consortium Partners and the periodical discussion allowed for the identification of similarities and differences in the treatment of COPD patients and alignment of therapeutic strategies. Besides, the project was the opportunity for young RSU staff member to have a training on Redcap registry and the use of digital databases for clinical data storage.

6. Data Management Plan

Please describe all changes (if any) from the strategy described in the Data Management Plan (DMP) sent to the ERA PerMed Joint Call Secretariat. (Max. 2,000 characters including spaces).

No changes occur in Data Management Plan. Data will be acquired using a dedicated software (REDCap) from all Partners.

7. Patients Involvement

Does your project involve a patient representative/organization? yes

What is the role(s) of the patient representative(s)/organization(s) in your project (please select all that apply)?

INVOLVEMENT (where patient representative/organization are actively involved in the research project):

☐ Involvement in identifying research priorities within the project
☒ Serving as members of the project advisory or steering committee(s)
☐ Commenting and developing patient information leaflets or other research materials
☒ Undertaking interviews with research participants
☐ Carrying out specific aspects of the research projects
☐ Other (please specify)

PARTICIPATION (where patients take part in the research study):
☐ People being recruited to a clinical trial
☐ Completing a questionnaire or participating in a focus group as part of a research study
☐ Other (please specify)

ENGAGEMENT (where information and knowledge about research is provided and disseminated):
☒ Scientific conferences/open day with debates and discussions on research where patient representative(s)/organization(s) are invited to find out about the research projects
☒ Raising awareness of the project through media such as television programmes, newspapers and social media
☒ Dissemination to patient organizations and the patient community on the findings of a study
☐ Other (please specify)

8. Peer Reviewed Articles

Only include publications after the start date of the project, ***with clear acknowledgement of ERA PerMed funding:*** *"This project was supported by [name of funding organization, or an acknowledgment as requested by your national funding organization], under the frame of ERA PerMed."*

Type of Publication*	Partner No	Publication (authors, title, journal, year, issue, pp.)	DOI	Open access (yes/no)	Confir-mation **
					☐
					☐
					☐

Add lines as relevant.

** Type of publication: Article in journal, Publication in conference proceedings, Books-Monographs.*

*** I, the coordinator, confirm that this publication includes content generated within our ERA PerMed project and that ERA PerMed was acknowledged as indicated above.*

9. Further Dissemination Activities

Only include publications and activities after the start date of the project.

Type of dissemination activity*	Partner No	Description	Link	Target audience**
Communication in a scientific conference	1	Oral presentation "Raman Spectroscopy on salivary samples: a new approach for diseases diagnosis", VISPEC 2023, Perugia (IT), June 2023		Scientific community

Communication in a scientific conference	1	ERS 2023, Milan (IT), September 2023 BANFI		Scientific community and biomedical enterprise
Webinar	1	Analisi salivare con spettroscopio RAMAN, Science Together, 18/05/2023		Clinicians and researchers of FDG network

Add lines as relevant.

** Type of publication or dissemination activity: Master/PhD/MD thesis; Communication in scientific conferences or workshops; dissemination to the general public; e.g. Organisation of a Conference/Workshop, Press Release, Exhibition, Flyers, Social media, Web-site, Communication campaign; Other (please specify).*

*** Target audience: scientific community, general public, policymakers, industry, etc.*

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Con il presente Documento si dichiara che il soggetto sopra identificato RISULTA REGOLARE nei confronti di

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Il Documento ha validità di 120 giorni dalla data della richiesta e si riferisce alla risultanza, alla stessa data, dell'interrogazione degli archivi dell'INPS, dell'INAIL e della CNCE per le imprese che svolgono attività dell'edilizia.