Fondazione Regionale per la Ricerca Biomedica

DECRETO NR. 53 del 08 luglio 2024

OGGETTO: BANDO ERAPERMED JOINT TRANSNATIONAL CALL FOR PROPOSALS 2019 — EROGAZIONE IN FAVORE DELLA FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI PARTNER NR. 3 DEL PROGETTO ACRONIMO SuPerTreat (ERAPERMED2019-281) - RESPONSABILE SCIENTIFICO LORIS DE CECCO - DI UNA RATA PARI A **€ 144.692,30** (CUP B42F19000080002)

L'atto si compone di 38 pagine
di cui 34 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 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 nr. XI/1016 del 17.12.2018 con la quale è stato approvato lo schema di Accordo di collaborazione tra FRRB e la Direzione Generale Welfare di Regione Lombardia;
- la DGR n. XI/5786 del 21.12.2021 con la quale è stato approvato il nuovo Statuto di FRRB;
- la DGR nr. XI/1106 del 19.12.2018 con la quale è stato approvato il Piano di Azione 2018 che prevede, al suo interno, l'allocazione fino ad un massimo di € 1.500.000,00 per la partecipazione di FRRB al bando ERA PerMed JTC 2019;

VISTI:

- il Regolamento (UE) nr. 1291/2013 del Parlamento Europeo e del Consiglio dell'11.12.2013 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 tra la Commissione Europea ed un partenariato internazionale coordinato dall'Instituto de Salud Carlos III e composto da un totale di 32 enti, tra cui FRRB, provenienti da 23 paesi con il quale è stato approvato il progetto "ERA-Net Cofund in Personalised Medicine — ERA PerMed";

CONSIDERATO CHE:

- la Fondazione IRCCS Istituto Nazionale dei Tumori (di seguito "*Beneficiario*"), Partner nr. 3 del progetto transnazionale dal titolo "*Supporting Personalized Treatment*

Decisions in Head and Neck Cancer through Big Data", Acronimo SuPerTreat (ERAPERMED2019-281), Responsabile scientifico Dr. Loris De Cecco, è risultato tra i progetti ammessi a finanziamento in risposta al programma europeo ERA Permed, Bando JTC 2019 per un importo complessivo assegnato pari a **€ 345.000,00**;

- il Beneficiario ha inviato, a FRRB, a mezzo PEC, in data 17.12.2019 (Prot. nr. 20190436E) 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*";

CONSIDERATO CHE:

- il progetto SuPerTreat (ERAPERMED2019-281) ha avuto avvio in data **01.09.2020** per una durata di 36 mesi, come comunicato dal Responsabile Scientifico in data 09.04.2020 (PEC Prot. nr. 20200128E) e riportato nella Convenzione stipulata tra FRRB ed il Beneficiario;
- in data 13.06.2023 (PEC Prot. 20230197E) il Beneficiario ha richiesto e ottenuto un'estensione di nr. 6 mesi, come previsto dalla Convenzione sopracitata, e che pertanto il progetto avrà una durata totale di **42 mesi** con nuova data di termine il **29.02.2024;**
- ai sensi dell'Art. 8.1 (Erogazione del contributo) della Convenzione sopracitata, l'erogazione al Beneficiario sarà effettuata da FRRB secondo le seguenti modalità:
  - "*due tranche successive entro 60 giorni dalla presentazione della prima e della seconda rendicontazione annuale, previa accettazione della documentazione ricevuta da parte di FRRB. L'importo del contributo sarà calcolato in base ai costi eleggibili effettivamente rendicontati da ciascun Beneficiario.*";

DATO ATTO CHE:

- in data 29/05/2024 è pervenuta dal Beneficiario la documentazione relativa agli ultimi sei mesi di attività – periodo 01.09.2023 - 29.02.2024 – del progetto SuPerTreat;
- in seguito alla verifica della documentazione pervenuta e dei successivi chiarimenti trasmessi, in data 25.06.2024 (Protocollo 20240218U) il Direttore Generale ha comunicato l'esito positivo dell'istruttoria di verifica della rendicontazione

economica richiedendo, al contempo, l'invio della richiesta di erogazione;

VISTI:

- la scheda di rendicontazione economica (*Financial report*) contenente il dettaglio dei costi sostenuti dal Beneficiario nel corso del terzo anno di attività pari a **€ 144.692,30** *(Reporting period 01/09/2023 – 29/02/2024,* **Allegato 1**);
- la richiesta di erogazione pervenuta in data 04.07.2024 per un importo complessivo pari a **€ 144.692,30** (**Allegato 2**), corrispondente a quanto rendicontato negli ultimi sei mesi di progetto;
- il Codice Unico di Progetto (CUP) B42F19000080002, generato dal Beneficiario in fase di avvio del progetto;
- il report scientifico annuale inviato dal PI, Prof. Loris De Cecco (**Allegato 3**);

VISTA E VERIFICATA:

- la regolarità contributiva dell'ente assegnatario del contributo – Fondazione IRCCS Istituto Nazionale dei Tumori – tramite acquisizione d'ufficio del DURC da parte di FRRB (**Allegato 4**);

DECRETA

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

di autorizzare l'erogazione in favore della Fondazione IRCCS Istituto Nazionale dei Tumori, con sede legale in Milano, via Venezian nr. 1, di una rata finale pari a **€ 144.692,30,** corrispondente ai costi ritenuti eleggibili nel corso degli ultimi sei mesi di progetto.

IL DIRETTORE GENERALE
Veronica Comi
f.to digitalmente

Veronica
Comi
08.07.2024
16:36:20
GMT+01:00

COST STATEMENT

NAME OF LOMBARDY BENEFICIARY	FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI MILANO
NAME OF PRINCIPAL INVESTIGATOR	DOTT. LORIS DE CECCO
PROJECT ID	ERAPERMED2019-281
CUP NUMBER	B42F19000080002
REPORTING PERIOD (FROM-TO)	LAST 6 MONTHS: 01/09/2023 - 29/02/2024
IS VAT RECOVERABLE? (YES/NO)	NO

COST CATEGORIES	TOTAL BUDGET	REPORTING PERIOD 1	REPORTING PERIOD 2	*REPORTING PERIOD 2 adjusted*	REPORTING PERIOD 3	REPORTING PERIOD LAST 6 MONTHS	TOTAL COST STATEMENT	DEVIATION FROM ORIGINAL BUDGET
TOTAL PERSONNEL COSTS	120.000,00							120.000,00
-Scientist								
-PhD Student	85.000,00	15.206,10	24.078,17		42.735,41		82.019,68	2.980,32
-Technician	5.000,00					5.000,00	5.000,00	0,00
-Other (*Oncologist)*	30.000,00		15.000,00			15.000,00	30.000,00	0,00
CONSUMABLES								
EQUIPMENT (LEASING OR ON HIRE)	6.000,00		6.000,06				6.000,06	-0,06
STUDY/CLINICAL TRIAL								
TRAVEL & ACCOMODATION	4.000,00		2.771,95	-50,00			2.721,95	1.278,05
OTHER DIRECT COSTS	120.000,00		365,00		20.498,44	97.984,42	118.847,86	1.152,14
SUBTOTALE	**250.000,00**	**15.206,10**	**48.215,18**	**-50,00**	**63.233,85**	**117.984,42**	**244.589,55**	**5.410,45**
OVERHEADS	50.000,00	3.041,22	9.643,04	-10,00	12.646,77	23.596,88	48.917,91	1.082,09
SUBCONTRACTING COSTS	45.000,00		37.999,34			3.111,00	41.110,34	3.889,66
TOTAL REQUESTED BUDGET	**345.000,00**	**18.247,32**	**95.857,56**	**-60,00**	**75.880,62**	**144.692,30**	**334.617,80**	**10.382,20**

PERSONNEL COSTS

(In case of public IRCCS and ASST ONLY temporary contracts will be considered eligible)

Max 50% of direct costs

NAME	POSITION	CONTRACT TYPE	PERIOD (FROM - TO)	EURO AMOUNT
IMPERIA NUZZOLESE prot.4989031/22 DCE	ONCOLOGIST	Natural Persons working under Direct Contract (Collaborazione Professionale)	15/05/23-05/10/2023	15.000,00
FICORILLI MARICA PROT.5270945/23 DOS	TECHNICIAN	Natural Persons working under Direct Contract (Collaborazione Occasionale)	01/07/23-31/08/23	5.000,00
			TOTAL € AMOUNT	**20.000,00**

CONSUMABLES

(Under this cost categories animal costs can be listed)

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

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
							0,00

TRAVEL AND ACCOMODATION

Max 10% of direct costs

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

SUBCONTRACTING

Max 20% of direct costs

NAME	PROCEDURE APPLIED	DESCRIPTION (provide details on service duration)	INVOICE NR.	INVOICE DATE	EURO AMOUNT
RIA GRANT THORNTON S.P.A.	Service assignment	Project audit	PA24-000100	18/04/2024	3.111,00
				TOTAL € AMOUNT	**3.111,00**

OTHER DIRECT COSTS

Publication costs can be listed here up to a maximum of 5% of direct costs

NAME	DESCRIPTION	INVOICE NR.	INVOICE DATE	EURO AMOUNT
IDEA-Z	Agency activities in support to WP6: reimbusement of travel and accomodation expences to Experts participating to 07/07/2023 Plenary Meeting	Ft 3PA	16/10/2023	1.734,50

IDEA-Z	Agency activities in support to project (last tranche): mailing with Experts participating to WP6 surveys and 07/07/2023 Plenary Meeting setting (IT/communication coordination, translation, catering, virtual/printed material)	Ft 8PA	31/12/2023	18.384,84
MIRABILE AURORA-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	13	12/07/2023	1.000,00
FARINA DAVIDE-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
DE FELICE FRANCESCA-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
MATTAVELLI DAVIDE-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
CAMARDA ANNA MARIA-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
BONOMO PIERLUIGI-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
ORLANDI ESTER-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
SCHINDLER ANTONIO-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
PREDA LORENZO-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
VISCHIONI BARBARA-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00
LOCATI LAURA DEBORAH-fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	nota 1	23/02/2024	1.000,00

PAOLO BOSSI -fee	Expert fee for participating to WP6 activities and 07/07/2023 Plenary Meeting	12/001	26/02/2024	1.020,00
COCKTAIL SERIVCE SRL	Catering 26/01/2024: breakfast and lunch	4/4	31/01/2024	1.359,63
IOCCA ORESTE-reimbursement	Reimbursement of travel and accomodation expences to Expert participating to Final Clinical Meeting 26/01/2024	nota	12/02/2024	70,80
SAINTIGNY PIERRE-reimbursement	Reimbursement of travel and accomodation expences to Expert participating to Final Clinical Meeting 26/01/2024	nota	12/02/2024	787,94
MEHANNA HISHAM-reimbursement	Reimbursement of travel and accomodation expences to Expert participating to Final Clinical Meeting 26/01/2024	159	29/02/2024	409,97
SIMON CHIRISTIAN-reimbursement	Reimbursement of travel and accomodation expences to Expert participating to Final Clinical Meeting 26/01/2024	157	29/02/2024	232,93
FERRAROTTO RENATA-reimbursement	Reimbursement of travel and accomodation expences to Expert participating to Final Clinical Meeting 26/01/2024	163	29/02/2024	10.197,53
SPESE BANCARIE PROV.163	Reimbursement of travel and accomodation expences to Expert participating to Final Clinical Meeting 26/01/2024	153	29/02/2024	12,13
HADDAD ROBERT-reimbursement	Reimbursement of travel and accomodation expences to Expert participating to Final Clinical Meeting 26/01/2024	161	29/02/2024	3.525,38
SPESE BANCARIE PROV.161	Reimbursement of travel and accomodation expences to Expert participating to Final Clinical Meeting 26/01/2024	156	29/02/2024	12,13
REGENT	25/01/2024 Dinner "Piero e Pia" + Hotel Dieci + Transfer for Experts	38/PA	31/01/2024	2.629,00
REGENT - fee agenzia		43/PA	31/01/2024	42,09

EASYB S.R.L. - medical writer 2 meeting	26/01/2024 Final Clinical Meeting: medical writer support for meeting report and scientific paper redaction; 07/07/2023 Plenary Meeting: medical writer support for transcription of the videorecording and scientific paper redaction	46/2024/FT	06/02/2024	25.498,00
CACTUS COMMUNICATIONS SERVICE PTE. LTD. (scientific editing+rapid statistical review)	Scientific editing for scientific paper	ABISD_3	31/01/2024	1.729,15
CACTUS COMMUNICATIONS SERVICE PTE. LTD. (scientific editing+rapid statistical review)	Scientific editing for scientific paper	ABISD_4	31/01/2024	1.414,00
commissione su banca estera -CACTUS COMMUNICATIONS SERVICE PTE. LTD.		PROVV.96	09/02/2024	12,18
CACTUS COMMUNICATIONS SERVICE PTE. LTD. ABISD_3 (platinum pack)	Scientific editing for scientific paper	ABISD_5	13/02/2024	1.308,12
commissione su banca estera-CACTUS COMMUNICATIONS SERVICE PTE. LTD.		PROVV.151	28/02/2024	12,10
EASYB S.R.L. - medical writer 2 pubblicazioni	Medical writer support on the redaction of 2 scientific paper within the project	60	16/02/2024	16.592,00
			TOTAL € AMOUNT	**97.984,42**

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

Dott. Giovanni Apolone

Signature of the Beneficiary Legal Representative

Firmato da:
GIOVANNI APOLONE
Codice fiscale: PLNGNN56E10B664E
Valido da: 17-08-2023 15:14:34 a: 17-08-2026 02:00:00
Certificato emesso da: InfoCert Qualified Electronic Signature CA 3, InfoCert S.p.A., IT
Riferimento temporale 'SigningTime': 24-05-2024 16:13:12
Motivo: Approvo il documento

Date, Place and Stamp:

21st May 2024, Milan

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 rata a saldo relativa al progetto ERAPERMED2019-281 (acronimo "SuPerTreat")

TITOLO PROGETTO: Supporting Personalized Treatment Decisions in Head and Neck Cancer through Big Data

RESPONSABILE SCIENTIFICO: dottor Loris De Cecco

CODICE CUP: B42F19000080002

Il sottoscritto Giovanni Apolone

Nato a [redacted]

Residente a [redacted]

[redacted]

In qualità di Direttore Scientifico e delegato del Legale Rappresentante dell'Ente Fondazione IRCCS Istituto Nazionale dei Tumori, Partner nr. 3 del progetto ID 281,

con sede legale in comune di Milano

CAP 20133, Via G. Venezian n. 1, prov. MI,

CODICE FISCALE 80018230153 PARTITA IVA 04376350155

INDIRIZZO E-MAIL (direzione.scientifica@pec.istitutotumori.mi.it , direzione.scientifica@istitutotumori.mi.it)

CHIEDE

l'erogazione della rata a saldo pari a € 144.629,30

Le coordinate per il versamento sono le seguenti:

Banca Popolare di Sondrio
Agenzia 21 Politecnico – Via Edoardo Bonardi 4, 20133, Milano
IBAN: IT15 C056 9601 6200 0000 2001 X82

Cordiali saluti,

Milano, 2 luglio 2024

F.to DIGITALMENTE
DAL LEGALE RAPPRESENTANTE
(*o suo delegato, ai sensi dell'Art. 24 del DLgs n. 82/2005*)

Firmato da:
GIOVANNI APOLONE
Codice fiscale: PLNGNN56E10B664E
Valido da: 17-08-2023 15:14:34 a: 17-08-2026 02:00:00
Certificato emesso da: InfoCert Qualified Electronic Signature CA 3, InfoCert S.p.A., IT
Riferimento temporale 'SigningTime': 03-07-2024 12:32:28
Motivo: Approvo il documento

Joint Transnational Call for Proposals (2019) for

"PERSONALISED MEDICINE: MULTIDISCIPLINARY RESEARCH TOWARDS IMPLEMENTATION"

Final Report

1. General information

Project title	Supporting Personalized Treatment Decisions in Head and Neck Cancer through Big Data
Project acronym	SuPerTreat
Project duration (months)	**42 (36 + 6 months of extension)**
Starting date of the project	**01/09/2020**
Period covered by the report*	01/09/2020-29/02/2024
Project website	not applicable

** Third year of the project plus potential extensions. Main results, including impact, publications or patents, should be indicated for the whole project duration.*

Please indicate the main disease area that your project consortium addresses:
Oncology, Cardiovascular Diseases, Psychiatric Disorders, Neurological Disorders, Nephrology, Immunological Disorders, Other (please specify):

Oncology

2. Project Consortium

Coordinator (Partner 1):

Affiliation, Address:	Università degli Studi di Milano
Country:	Italy
Name of Principal Investigator:	Lisa Licitra
E-Mail:	lisa.licitra@unimi.it
Phone:	+39 02 2390 2182
Gender:	Female
Funding Organisation:	FRRB

Project Partners:

Partner no.	Affiliation	Country	Gender	Name of Principal Investigator
2	Charité – Universitaetsmediz in Berlin	Germany	Female	Ingeborg Tinhofer- Keilholz
3	Fondazione IRCCS Istituto Nazionale dei Tumori Milano	Italy	Male	Loris De Cecco
4	University of Oslo	Norway	Male	Arnoldo Frigessi

5	Institut Curie - Paris & Saint-Cloud	France	Male	Christophe Le Tourneau
6	Athens Technology Center	Greece	Female	Maritini Kalogerini

Please indicate any changes in the project team: None

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. 2,000 characters including spaces). **This abstract may be published (e.g. ERA PerMed website).***

SuPerTreat integrates clinical, pathology and genomic data from large cohorts (over 1800 cases from 4 reference centres in Italy, Germany and France) of patients diagnosed with head and neck cancer (HNC), to identify risk profiles – risk signatures – and predict treatment outcome. Mathematical models using Artificial Intelligence inform a Clinical Decision Support tool that provides to the multidisciplinary team of physicians data and information useful to tailor a personalized and optimum treatment, and is designed to inform patients through understandable presentation of data and predictions, facilitating treatment co-decisions. The project addressed the ethical and scientific challenges on the use of big data and artificial intelligence in clinical practice for "data driven" decision making based on algorithms. A dedicated study using Delphi approach has involved 75 physicians and 75 patients and caregivers, as well as experts in ethics and legal aspects, who experienced and evaluated to which extent and under which conditions these new technologies might be applied in clinical practice, and identified the critical aspects that need to be overcome. Data collected in dedicated focus groups and surveys conducted by specialised onco-psychologists are being analysed and will be published in the next months.

The results of the data analysis (models, predictive and prognostic signatures, risk profiles) are being consolidated in scientific publications. The project has produced a large dataset with harmonised clinical and genomic data for HNC patients, available at University of Oslo TSD secure data infrastructure. In addition, a confirmatory biological study was conducted on preclinical models. In particular, patient-derived organoids (PDO) were used to validate the mathematical models developed in the project, by expanding the number of available PDO models, and in-depth characterizing these models at molecular level (genomics, transcriptomics, proteomics).

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

Objectives/Deliverables			
No.	***Title***	***Partner in charge***	***Short Description***
1	Clinical dataset harmonization	INT	The clinical datasets of the SuPerTreat project have been harmonized following a common semantic developed in another previously concluded European project, the BD2Decide.
2	Biological dataset harmonization	INT	The biological datasets of the SuPerTreat project have been harmonized following a common ontology described in WP1.
3	Data transfer agreement and ethical approval in place	UMIL, Charité, Curie, INT, UiO	After ethical approvals, as per local regulations, the legal offices of the clinical partners providing data and those of the data recipients have signed a specific data transfer agreement.

4	Consortium Agreement	UMIL, Charité, Curie, INT, UiO, ATC	The Consortium Agreement has been signed by all partners
5	Data management plan	UMIL	The DMP was delivered describing data management during the project and prospects for making data available for research after the end of the project
6	Data coherence rules and data semantics enrichment	INT, UMIL, Charité, Curie	The semantics annotation and the data coherence and data consistency rules were upgraded to include recurrent-metastatic HNC data
7	**WP1. Multi-omic and multi-platform bioinformatic analysis and semantic harmonization**	**Partner 3 INT** Collaborating partners: Charité, Curie, UMIL, UiO	All available datasets have been annotated, harmonized, integrated for data analysis and have been made available at the UiO Elixir node. Data include omics and clinical information. Status: completed
8	**WP2. Data annotation and integration platform**	**Partner 3 INT** Collaborating partners: Charité, Curie, UMIL, UiO	The data annotation and quality rules are defined, the ontology is completed and the semi-automatic annotation tools are available. Status: completed
9	**WP2. Data transfer and data access established at UiO**	**Partner 4 UiO**	The sensitive data server at the UiO (called the TSD) is established and access granted to authorised partners for data upload and processing. Status: completed
10	**WP3. Mathematical models and data integration of multilayer -omics and clinical data**	**Partner 4 UiO** Collaborating partners: Charité, and clinical partners INT, Curie	Performed descriptive analysis and advanced time-to-event models for the prediction of patient's overall survival (and diseases-free survival) and effects of tumor heterogeneity (gene signatures) on treatment. Collaborating with external partner (H&N5000, UK) to obtain data for sensitivity analyses as part of a manuscript being written about the validation of gene signatures. A data transfer agreement between UiO and H&N5000 has been agreed on. Status: completed
11	**WP5. T5.1 Data visualization tools**	**Partner 6 ATC**	Personalized decision support and visualization environment, enabling a formal prediction representation and analysis of factors on which the prediction is built.

		Collaborating partners: Charité, Curie, UMIL, UiO	Semantics to allow Knowledge Assisted Visualization will be also integrated. The objective is to create role-based data visualization dashboards, enabling collaboration between patients' management team within an integrated-care framework. Status: completed
12	**WP7. Coordination. Data processing agreement**	**Coordinator UMIL** Collaborating partners: ALL	The agreement between all partners for data access and data sharing and the relevant rules. Status: DPA signed
13	**WP7. Coordination. Consortium and partners' meetings (in person and virtual)**	**Coordinator UMIL** Collaborating partners: ALL	Perform periodic meetings and dedicated meetings to monitor the project progress and to orient the next activities and address issues and risks. Status: completed
14	**WP7. Coordination. Periodic reporting**	**Coordinator UMIL** Collaborating partners: ALL	Submit the periodic reports and the costs declaration to the Funding Authorities. Submit deliverables as requested by national funding Authorities (e.g. for partner 6) Status: Reports accepted by Funding Authorities
15	**WP1. Multi-omic and multi-platform bioinformatic analysis and semantic harmonization**	**Partner 3 INT** Collaborating partners: Charité, Curie, UMIL, UiO	All available datasets annotated, integrated for data analysis and available at UiO Elixir node. Data include omics and clinical information. Status: completed
16	**WP2. Data annotation and integration (including-omics)**	**Partner 3 INT** Collaborating partners: Charité, Curie, UMIL, UiO	The data annotation rules are defined, the ontology is completed and the semi-automatic annotation tools are available. -Omics data from different studies and -omic platforms and datasets (including public data repositories) have been annotated and integrated. The head and neck cancer ontology will be uploaded in BioMed portal by end of October 2023. Status: completed
17	**WP2. Data annotation and integration platform established and operational**	**Partner 4 UiO** **Partner 3 INT + INT subcontractor**	The sensitive data server at the UiO (called the TSD) is established and access granted to authorised partners for data upload and processing. A data quality check using REDCap has been implemented in the server to ensure coherence and define pre-processing tasks for high-quality data analysis

			Status: completed
18	**WP3. Mathematical models and data integration of multilayer -omics and clinical data**	**Partner 4 UiO**	Model have been developed and risk profiles considering different combinations of markers (clinical, biological, pathological) have been produced and internally validated. Data analysis on patient-derived organoids produced by Charité has been performed to validate the mathematical models developed in the project, by in-depth characterizing the developed models at molecular level (genomics, transcriptomics, proteomics). Status: completed
19	**WP4. Models validation and data interpretation for patients' stratification.**	**Partner 4 UiO**	Uncertainty estimates for WP3 model outputs and corresponding predictions are calculated and presented. Status: completed
20	**WP4. Functional validation of the prognostic/predictive models (contribution Charite, WP4)**	**Partner 2 Charité and Partner 4 UiO**	Charité have selected datasets from HNSCC patients treated with definitive or adjuvant chemotherapy that include transcriptome data and functional data on treatment response established in patient-derived organoids (PDOs) available at Charité and newly produced ones. The study protocol has been produced and approved. Charité has provided UiO with gene expression data from PDOs and UiO has processed these data and calculated gene signature scores. Charité is currently collecting data on treatment sensitivity from the PDOs, and UiO will then analyse and correlate these with the gene signatures. Status: ongoing, results expected by June 2024
21	**WP5. Personalised clinical decision support system deployment**	**Partner 6 ATC** Collaborating partners: Charité, Curie, UMIL, UiO	Personalised decision support and visualisation environment, enabling a formal prediction representation and analysis of factors on which the prediction is built, and models according to six use scenarios (use cases) defined by oncologists have been integrated into the CDSS. Semantics to allow Knowledge Assisted Visualisation is also integrated. Role-based data visualisation dashboards, enabling collaboration between patients' management team within an integrated-care framework have been created for physicians. Visualisation dashboards for patients have been agreed

			and are under development and integration in the CDSS. Initial validation and acceptability testing started in focus groups and will be completed in the next period. Status: First release completed and presented for evaluation at the users' workshop held on July 7th 2023. Final version of the CDSS, including visual representation for patients foreseen by the end of the project, taking into consideration the patients' feedbacks collected in WP6 pilot study, was released in January 2024.
22	**WP6. Pilot study setup and execution**	**Coordinator UMIL** Collaborating partners: INT	T6.1 Pilot study protocol drafted and submitted for ethics approval. Focus Groups with Italian patients, health care professionals and ethics experts have been performed and qualitative analysis of the collected feedbacks is being finalised. Workshop with stakeholders performed on July 7th 2023 in Milano. Quantitative analysis definition and the preparation of the quantitative evaluation questionnaires are completed. The study protocol was approved by INT Ethical Committee in February 2024. Patient (n=90) and clinician (n=75) recruitment completed in March 2024. Status: quantitative study was delayed but participant recruitment has been concluded by the end of the project. Analyses are ongoing and will be published soon.
23	**WP7. Coordination. Data sharing**	**Coordinator UMIL** Collaborating partners: ALL	The agreement between all partners for data access and data sharing and the relevant rules. Status: DPA signed
24	**WP7. Coordination. Consortium and partners' meetings (in person and virtual)**	**Coordinator UMIL** Collaborating partners: ALL	Perform periodic meetings and dedicated meetings to monitor the project progress and to orient the next activities and address issues and risks. Duration of the project extended for 6 months due to impacts of COVID-19 pandemic. Extension granted by Funding Authorities. Status: Completed
25	**WP7. Coordination. Periodic reporting**	**Coordinator UMIL** Collaborating partners: ALL	Submit the periodic reports and the costs declaration to the Funding Authorities. Submit deliverables as requested by national funding Authorities (e.g., for partner 6) Status: Reports ongoing

26	**WP7. Dissemination**	**Coordinator UMIL** Collaborating partners: ALL	Dissemination ongoing also jointly with other ongoing project H2020 BD4QoL and the cluster CS_AIW (Cancer Survivorship AI for Wellbeing), and the Make Sense Campaign. An article is being prepared by UiO and the Consortium partners, presenting the results of data analysis.

Add lines as relevant.

5. Work performed during the reporting period and main results achieved during the whole project duration

Please describe the work performed per work package (WP). Please add WPs as relevant. M = Month.

WP 1	**Multi-omics and multi-platform bioinformatic analysis and semantic harmonization**
Leading Partner: 3 - Loris De Cecco (INT)	
Additional involved Partners: Charité, Curie, UMIL, INT subcontractor (UPM)	
Planned timeline (according to GANTT chart): (from M1 to M12)	**Actual timeline:** (from M1 to M24)
Work performed, Challenges, Achievements T1.1) Complete information was obtained from 11 proprietary datasets (832 cases with >16,000 genes present in all platforms) that profiled primary tumor specimens. Raw transcriptomic data were re-annotated to the most recent GeneBank version including GeneSymbol and EntrezID to avoid redundancy in gene nomenclature. The clinical data were curated in close collaboration with clinicians from INT, Charité, Curie, and subcontractors. The updated dataset was uploaded to the UiO STD server for secure data analysis T1.2) We evaluated the performance of LncRNAs to define a new biological-oriented prognostic model. LncRNA were extracted from the normalised gene expression matrix of the BD2D training cohort, for a total of 8078 probesets corresponding to non-coding transcripts . Univariable Cox proportional hazards regression analysis revealed 5 lncRNAs with a p-value < 0.0005, that were also present in the TCGA data matrix used a test dataset. Multivariable Cox proportional hazards regression and a stepwise algorithm were then applied in order to choose the model with the best Akaike's Information Criterion (AIC). In this way, 4 out of 5 lncRNAs were selected from the original list (LINC01322, LCAL1, INTS6-AS1, ANKRD44-IT1). T1.3) Following the survey on public repositories, 16 datasets including 1998 cases were retrieved. We follow the harmonisation, batch correction and re-annotation procedures as in T1.1. These data were instrumental to test a selected number of signatures (RSI, 172-gene signature, chemo-sensitive models, ect). All the activities foreseen in this WP have been completed.	
Has there been a deviation from the original work plan or from the original timeline? This WP was completed with delays due to COVID-19 as reported in the previous period. New RNAseq data have been produced for an additional study proposed by Charité, aiming to validate the mathematical models of treatment response in head and neck cancer patients' organoids.	

WP 2	**Data annotation and data integration platform**
Leading Partner: 3 - Loris De Cecco (INT)	

Additional involved Partners: INT subcontractor (UPM), Charité, Curie, UiO	
Planned timeline (according to GANTT chart): (from M1 to M12)	**Actual timeline:** (from M1 to M24)

Work performed, Challenges, Achievements

T2.1 The ontology extension for data mapping and interoperability was based on the previous BD2Decide ontology (https://bioportal.bioontology.org/ontologies/HENECON). This was enriched with newly harmonised data from the SuPerTreat datasets, including new clinical variables, updated information in pre-existing fields, and 17.000 genes. Within the following months, subcontractors and WP2 involved partners will start working on a journal publication detailing the methodologies and frameworks utilised to achieve the resulting SuPerTreat ontology. The ontology will be uploaded to BioPortal when journal publication is ready. This will ensure FAIRSHARING principles within SuPerTreat data.

T2.2 Data quality rules were extended based on the harmonisation results and validated with clinical experts. A study of automatic data quality tools was performed to ensure the most appropriate option for the project and the best possible outcomes. Based on this study, the implementation of 343 quality rules was performed using the REDCap tool within the UiO server. The reports generated were delivered for data analysis coherence and consistency checks.

Has there been a deviation from the original work plan or from the original timeline?

The final implementation was slightly delayed due to some technical constraints at Oslo for the installation of the data management tool (REDCap). The foreseen adoption of HL7 FHIR standard will be studied based on the data policies applied in each participating centre and reported in the next period. The secure data storage in Oslo already complies with current data standards (set in their ELIXIR environment).

WP 3	Mathematical models and data integration of multilayer -omics and clinical data
Leading Partner: 4 Arnoldo Frigessi (UiO)	
Additional involved Partners: Charité, Curie, INT, UMIL, INT subcontractor (UPM)	
Planned timeline (according to GANTT chart): (from M7 to M18)	**Actual timeline:** (from M17 to M28)

Work performed, Challenges, Achievements

WP3 comprises the development of statistical models for prognosis and prediction for HNC clinical outcomes and response to treatment. Using data from WP1 and WP2, we build advanced time-to-event models to predict patients' overall survival and disease-free survival, by modelling the effects of clinical variables and the interactive effects of tumor heterogeneity (gene signatures) and treatments. Gene expression data was batch corrected to remove technical effects caused by the studies using different expression platforms and providers. We identified that data on patients' treatment was limited by only including the treatment received, but not including the timing of treatment or treatment intent. We therefore performed sensitivity analyses to ensure that patients' received treatment could be used as a good proxy for the intended treatment. These sensitivity analyses involved obtaining new data from an external partner (H&N5000) and making a new data transfer agreement between UiO and H&N5000. Predictions of survival for hypothetical patients were performed and exported for visualisation in the CDSS (WP5). A manuscript is drafted and circulating between coauthors for comments.

Has there been a deviation from the original work plan or from the original timeline?

This WP was completed with delays due to COVID-19 as reported in the previous periods. A new collaboration with an external partner (H&N5000, UK) was established to obtain data for use in sensitivity analyses.

WP 4	Model validation and data interpretation for patients' stratification
Leading Partner: 1 - Lisa Licitra (UMIL)	
Additional involved Partners: INT, UiO, Curie, Charité	
Planned timeline (according to GANTT chart): (from M19 to M34)	**Actual timeline:** (from M19 to M34)

Work performed, Challenges, Achievements

In WP4, the mathematical models developed in WP3 have been validated from a clinical perspective and strategies for data interpretation were derived.

T4.1 Preclinical models, e.g. patient-derived organoid (PDO) models, have been used to validate the mathematical models developed in WP3. Charité has further expanded the number of available PDO models, and the in-depth characterisation of models at molecular level (genomics, transcriptomics, proteomics) has been completed. Establishment of functional ex vivo assays for inherent tumor sensitivity testing of standard treatment of HNSCC (radiation, cisplatin, and cetuximab) has been completed. Transcriptome data from 22 PDO models were used by the partner UiO to derive radiosensitivity scores and predictive gene expression signatures for sensitivity to cisplatin and EGFR. Upon completion of experimental series assessing sensitivity to irradiation, cisplatin and EGFR blockade, UiO will correlate gene signatures to treatment sensitivity measures in PDO. Analyses are expected to be completed by the end of April, and a manuscript prepared by June 2024.

T4.2 This task comprises equipping the models and predictions from WP3 with uncertainty estimates. We used state-of-the-art methods to calculate p-values and confidence intervals around hazard ratios and restricted mean survival times presented in WP3. We also calculated 95% confidence intervals for the predicted survival curve for each hypothetical patient.

T4.3 Clinical interpretation of models and predictions. The work is ongoing with clinicians and will also be part of the evaluation foreseen in WP6 (T6.3).

Has there been a deviation from the original work plan or from the original timeline?

Due to the delayed completion of the consortium agreement and data transfer agreement in the first year of the project (due to COVID 19 induced burden on all institutions), there was a delay in data integration and the development of mathematical models. As a result, the first validation of new biomarkers / signatures in clinical cohorts and organoid models (T4.1) could not start as planned in month 19 and is now being completed. The clinical interpretation of results is therefore still ongoing.

WP 5	Personalized Clinical Decision Support System
Leading Partner: 6 Maritini Kalogerini (ATC)	
Additional involved Partners: all partners (as soon as the results of WP3 and WP4 are integrated) to finalise the visualisation tools	
Planned timeline (according to GANTT chart): (from M7 to M31)	**Actual timeline:** (from M7 to M31)

Work performed, Challenges, Achievements

During the reporting period ATC has completed the development of the CDSS and the user I/F comprising of four main logical units:

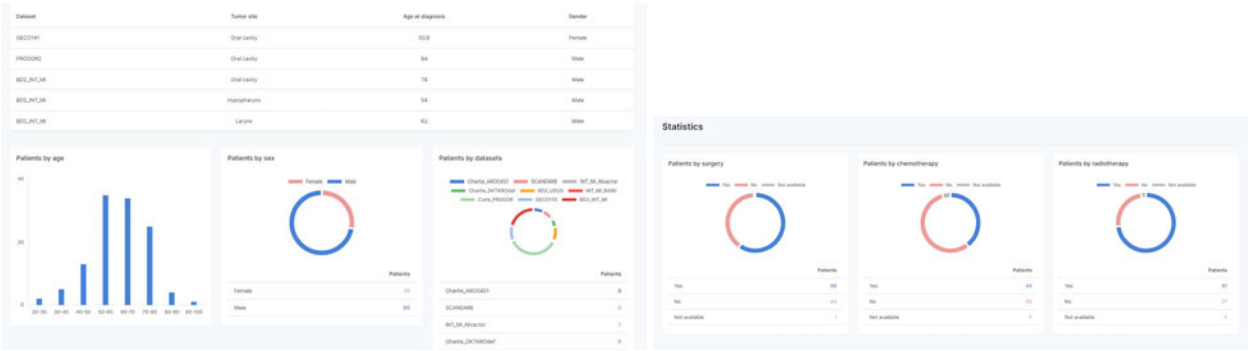
- the Patient Data Dashboard (PDD), which is meant to provide all the patient information to the clinicians as well as some general statistics of the enrolled patients.

● the Advanced Statistics Dashboard (ASD), which gives the clinicians the opportunity to look for statistics on the patient population,

● the Patient Predictions Dashboard (PPD), which provides a prediction based on the clinical profile of a patient and

● the User Management Dashboard (UMD), which allows the platform administrators to manage the SuPerTreat users.

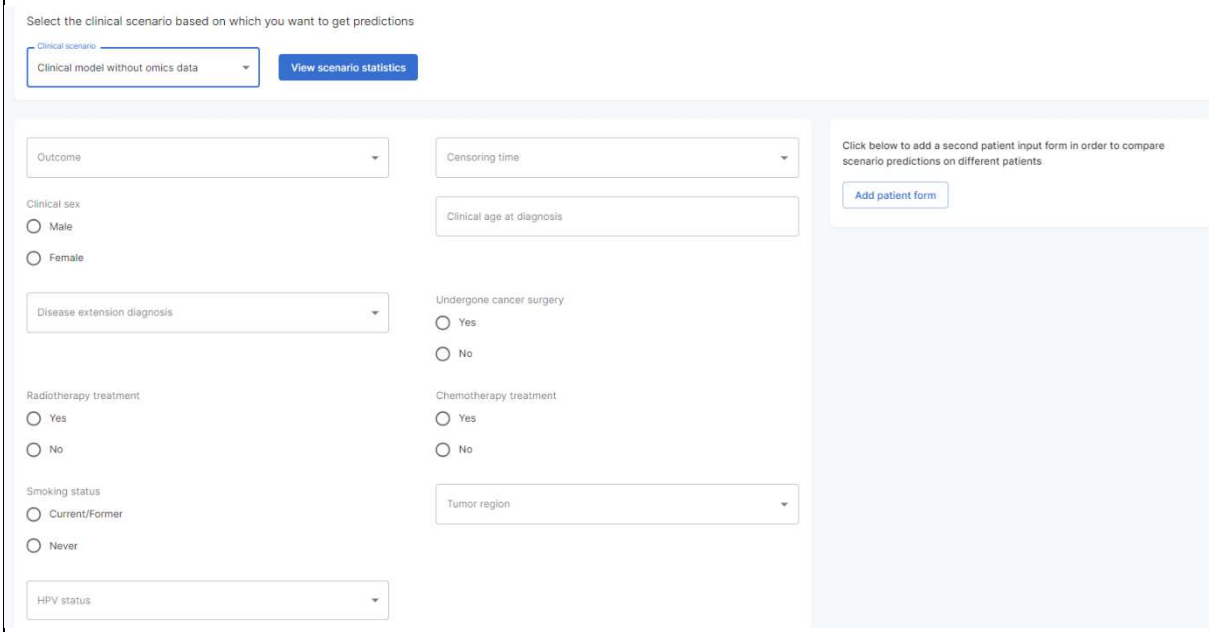
In the previous reporting period, ATC created a set of mock-ups for the CDSS tool. These mock-ups drove further the discussion with the users and was the basis for the implementation of the CDSS tool. In the following figures the final CDSS is depicted.



The models developed for six scenarios requested by physicians have been successfully integrated into the CDSS.

In the Predictions page (the one which includes the core information for the developed CDSS), clinicians can get clinical predictions based on existing models. First of all, a clinical scenario should be selected from a drop-down field. There are 6 available scenarios such as "Base model" or "HPV negative". The form displayed adapts to the selected scenario, with specific input

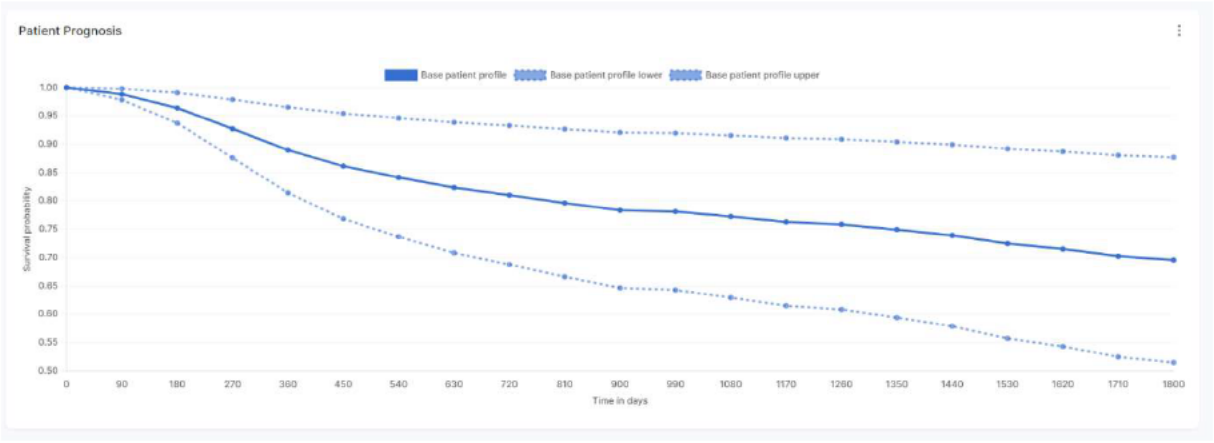
fields.



After filling in the form, including prediction model details and patient information, clinicians can get a diagram displaying the predicted survival probability over time, along with upper and lower bounds.

If clinicians want to compare scenario predictions for different patients, they can use an additional button next to the patient form. In this case, a 2 line charts with upper and lower bounds are depicted,

representing the predicted survival probability for each patient profile. The CDSS acceptability tests have been performed also as part of the task T6.1



Has there been a deviation from the original work plan or from the original timeline?

The works planned in T5.2 and T5.3 were delayed due to the delays accumulated due to the burden and restrictions imposed by COVID-19 during 2020-2021 which affected the collaborations required to complete not only the required technical and scientific works (e.g., data collection/annotation/transfer to UiO) and the relevant administrative duties (e.g. sign the Data Sharing Agreements, fulfil all the ethical approvals at the originally scheduled times). The restrictions regarding physical meetings also contributed to communications and mock-ups presentation and validation efficiency and timing.

WP 6	**Pilot study for consensus measurement on big data-driven PM approaches**
Leading Partner: 1 Lisa Licitra (UMIL)	
Additional involved Partners. ALL PARTNERS	
Planned timeline (according to GANTT chart): (from M23 to M36)	**Actual timeline:** (from M18 to M36)

Work performed, Challenges, Achievements

WP6 activities aim to investigate potential obstacles to the implementation, acceptability, and adoption of an AI CDSS in the medical decision process.

T6.1. The qualitative part of the study foreseen in the WP6 has been completed and feedbacks collected and elaborated by the psychologists. A presentation of the results and a discussion and feedbacks collection was performed as part of the Delphi study preparation's workshop held in Milan, on July 7th 2023, to which all stakeholders involved were invited and participated (patients, caregivers, health care professionals, ethics experts). The Focus Groups with Italian patients, health care professionals and ethics experts have been performed. Results have been analysed. The proposed visualisation and presentation of the models' predictions using the CDSS have been re-designed accordingly (see implementation in WP5).

A preliminary quantitative analysis involving attendees at plenary workshop in Milan is being organised, including a training session in which the CDSS was presented to attendees and evaluation questionnaires were collected using the Qualtrics^{XM} tool (https://www.qualtrics.com/). A specialised agency has been contracted to help organise and manage the Focus Groups scheduling and the plenary workshop held on July 7th 2023.

T6.2 Impacts assessment activities has been conducted by INT. The clinical impacts of SuPerTreat were evaluated by simulating the potential effects of personalised treatment decisions based on the developed models on patients' survival and on treatment optimization. This assessment was performed by means of simulations using the MAFEIP tool (https://tool.mafeip.eu/overview/). The results of this activity provided new insights informing healthcare policies. The results of our analyses showed that we can compute the total cost reductions and the total incremental utility to obtain an overall ICER for SuPerTreat of -1,302 €/QALY. This ICER is below zero, confirming that the application of the SuPerTreat CDSS to the current clinical workflow would be viable and highly cost-effective, even when accounting for the economic unviability of the escalation approaches.

T6.3. The study protocol of the quantitative study was approved by INT Ethical Committee in February 2024. Patients (n=90) and clinicians (n=75) recruitment completed in March 2024. The quantitative study conduction was delayed but participant recruitment has been concluded by the end of the project (March 2024). Analyses are ongoing and will be published soon.

Has there been a deviation from the original work plan or from the original timeline?

The execution of the Focus Groups (qualitative study) experienced delays due to difficulties faced in recruiting groups of patients and health care professionals (at least 6-8 participants for each Focus Group) at the specified dates. Involvement of regulatory and legal experts, to discuss the implications of an AI-based Big Data-driven CDSS in the medical decision process, met the same difficulties and is still ongoing. Some constraints concerning privacy of participants to the online questionnaires collection for the quantitative study were raised by German partners. These are being addressed. Consequently the quantitative study and the Delphi consensus in T6.3 have been delayed and has been completed by the end of the project (February 2024). Analyses are ongoing and the results will be submitted for publication in a scientific journal soon.

WP 7	**Coordination**
Leading Partner: 1 Lisa Licitra (UMIL)	
Additional involved Partners: all	
Planned timeline (according to GANTT chart): (from M1 to M36)	**Actual timeline:** (from M1 to M36)

Work performed, Challenges, Achievements

T7.1. Project management activities (conference calls, continuous monitoring of project progress and issues) have been regularly performed during the second year. One meeting was held jointly with the workshop held in Milano on July 7th, 2023. Specific meetings to check status of interconnected tasks were held on a periodic basis and ad hoc online meetings were organized to coordinate and check the activities performed in particular to integrate the models into the CDSS, to finalize the models based on the use scenarios defined by the physicians, to follow the execution of the pilot study (WP6) and to check status and risks. A weekly coordination meeting (online) is also performed. The dissemination foreseen in the period (presentation at ESMO 2022) has been performed.

T7.2. The scientific coordination during the third year has overviewed the work performed so far in terms of technical deployment of the CDSS, the consolidation of the models based on user-defined scenarios and on the interpretation of the results from the models. In parallel scientific work has been conducted to complete the data quality tasks and the pilot study.

T7.3. Ethical and legal constraints on data reuse were continuously monitored throughout the execution of WP1, WP2 and WP3 and the data presentation in WP5. Privacy and legal aspects relevant to the execution of the pilot study (WP6) have been addressed. Ethical concerns and scientific concerns regarding the use of the predictions and the data proposed by the CDSS have been discussed in the first

phase of T6.1 and are continuing as part of the quantitative study and the Delphi consensus foreseen in the next months

T7.4. IPRs regarding data provided and generated during the project have been addressed in the DTA and DSA signed in the first year of the project. Data publication and data management agreements are being discussed, in order to adhere to FAIR principles. Data relevant to published results will be made available for scientific research.

Has there been a deviation from the original work plan or from the original timeline?

Given the hurdles encountered during the project conduction, so far the Consortium partners have published only two out of the several articles which will derive from the analysis and the interpretation of the data produced within the SuPerTreat project. However, by the end of the project (February 2024) the Consortium managed to finalize the main project tasks. The only currently undergoing activities deal with result interpretation and scientific manuscript drafting.

An article describing the predictive and prognostic models developed in WP3 and WP4, already drafted and under revision by the Consortium partners, will be submitted in the next months. Articles interpreting models' results and reporting the qualitative and quantitative studies are under preparation and will be submitted by the end of 2024.

6. Transnational Collaboration, Meetings and Mobility

Please describe consortium meetings (physical and virtual) including more than 2 partners (date, location, purpose, results):

Participants	*Date*	*Location*	*Purpose*	*Results*
All Consortium partners	*07/10/2020 09/10/2021*	*Virtual*	*Kickoff meeting*	*Start of the Project activities and coordination on the tasks due by M12*
INT, Curie, UiO, ATC, Charité	*12/02/2021*	*Virtual*	*Discussion about the expected work*	*Intermediate Consortium update about the pending activities*
INT, Curie, UiO, UMIL	*26/02/2021*	*Virtual*	*Discussion about the harmonization of clinical data*	*Maud Kamal (Curie) presented an overview of the clinical data and Stefano Cavalieri (INT) delineated a plan for translating and harmonising the data.*
INT, Charité, Curie, UiO, UMIL	*30/04/2021*	*Virtual*	*Discussion about the -harmonization of genomic data*	*Partners discussed the different data platforms from which the -omics data are provided*
INT, UiO, ATC, UPM, UMIL	*28/06/2021*	*Virtual*	*Discussion about data harmonisation and integration*	*Loris De Cecco and Stefano Cavalieri shared the main strategies and achievements with regards to the data harmonisation (-omics and clinical data).*

All Consortium partners involved persons and subcontractors	*20 December 2021*	*Virtual*	*2nd consortium meeting: Project monitoring*	*Assessed project status and addressed issues and delays due to COVID 19. Revised deadlines for some tasks affected by the pandemic.*
Partners 1, 2, 3, 4, 5 involved persons and subcontractors	*11 February 2022*	*Virtual*	*WP1,2,3 meeting*	*Discuss open points regarding data integration, annotation and harmonization, address missing data and take decisions to progress the status of the WPs delayed by COVID 19 pandemic in year 1*
Partners 1, 2, 4, 5, 6 involved persons and subcontractors	*14 February 2022*	*Virtual*	*WP5-6 meeting*	*Discussion about WP5 and WP6 tasks (e.g., data visualization)*
Partners 1, 2, 3, 4, 5 involved persons and subcontractors	*1 March 2022*	*Virtual*	*WP1,2,3 meeting*	*Followed up from previous WP1,2,3 meeting to clarify harmonization doubts*
Partners 3, 4, 6 involved persons and subcontractors	*23 March 2022*	*Virtual*	*Call for CDSS*	*Discussion regarding CDSS visualization tool and possible endpoints of analyses*
Partners 1, 3, 4, 6 involved persons and subcontractors	*28 March 2022*	*Virtual*	*Call for CDSS*	*Discussion regarding CDSS characteristics*

Partners 1, 2, 3, 4, 5 involved persons and subcontractors	*24 May 2022*	*Virtual*	*Harmonization, codebook, quality rules*	*Discuss quality rules and semantic validation in regard to the final codebook*
All consortium partners involved persons and subcontractors	*30 May 2022*	*Mixed (Partner 6 ATC virtual and other partners in-person in Milano)*	*3rd Consortium meeting*	*Assessed project status and results, addressed delays in data collection and issues in data integration. Prepare the periodic report.*
Partners 3 and 5	*13 June 2022*	*Virtual*	*Clinical data harmonization*	*Discussion and agreements on the harmonization of clinical datasets of partner 5*
Partners 3, 4 and 5	*20 June 2022*	*Virtual*	*Clinical data harmonization*	*Finalization and final agreements on the harmonization of clinical datasets of partner 5*
All Consortium partners	*25-26 October 2022*	*Virtual*	*JTC Midterm seminar*	
All Consortium partners involved persons and subcontractors	*8th November 2022*	*Mixed – Madrid (in person partners 1,3,5 and subcontractor of Partner 3; partner 2, 4 and 6 virtual)*	*Updates on the status of activities and agreement on next actions*	*Agreed works on models finalization and use scenarios initial discussion. Discussion possible extension of the project duration.*
Partner 1, Partner 3	*Weekly*	*Virtual*	*Coordination meeting*	*Risks assessment, status of tasks*
All Consortium partners involved	*7 July 2023*	*Milano and virtual (partners 1,2,3,4,5*	*3nd consortium meeting and*	*Presented results to*

persons and subcontractors		*and subcontractors in person – partner 6 virtual)*	*WP6 workshop in Milano (Italy)*	*Consortium partners and external stakeholders (during the workshop). Launched new activities for the next months and agreed deadlines.*
Partner 1, Partner 3	*WP6 Meetings Monthly from March 2023 onwards*	*Virtual*	*Monthly coordination meetings to organize the activities in T6.2 and T6.3 and the July workshop*	*Definition of the questions and discussions to be proposed in Focus Groups, organization of Focus Groups, revision of feedbacks and of the results from the workshop, plans for the quantitative study*
Partner 1, Partner 3, Partner 4, Partner 6	*24 May 2023*	*Virtual*	*WP5 – use scenarios and models integration*	*Defined use scenarios and model integrations, discussed final user I/F*
Partner 1, Partner 3	*1 June 2023*	*Virtual*	*WP6 activities coordination*	*Next actions to organize the July workshop*
All partners	*6 July 2023*	*Mixed (partner 1, 3 in person)*	*Rehearsal and preparation of the meeting of July 7th*	*Prepared the meeting and discussed what to present and to be decided*
Partner 1, 3 and 6	*31st October 2022* *28th November 2022* *24th May 2023* *25th September 2023*	*Virtual*	*Definition of scenarios to be integrated into the CDSS and the relevant user I/F*	

	29th September 2023			
Partner 4, Partner 6	*23 March 2023* *27 March 2023* *09 May 2023* *23 May 2023*	*Virtual*	*Integration of models in the CDSS*	*Definition of integration modalities and access through the TSD platform in Oslo*
Partner 1, Partner 3, and Partner 3 subcontractor, Partner 4	*18 November 2022* *25 November 2022* *11 January 2023* *18 January 2023*	*Virtual*	*Consolidation of data quality check rules and implementation in the TSD*	*Defined the rules*
Partner 3 subcontractor, Partner 4	*UPM and UiO pls insert dates*	*Virtual*	*Consolidation of data quality checks and access to the data stored in the TSD in Oslo*	*Agreed on modalities for*
Partner 2, Partner 4	*18 September 2023* *20 February 2024*	*Virtual*	*WP4 organoid data and analyses*	*Coordinate roles and plans for WP4, agreement on next steps for analyses*
Partner 1, Partner 3, Partner 4	*25 September 2023*	*Virtual*	*Inclusion of H&N5000 data*	*Agreement about steps needed to include H&N5000 data in WP3*
All partners	*26 February 2024*	*Virtual*	*Final meeting*	*Agreed activities for final reporting*

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 collaborations established by this project have allowed cross-country recruitment (e.g., in the Frigessi team), generation of training opportunities for new staff and recruitment of young researchers (e.g., at UiO, INT and UMIL) and new technical staff (e.g., at ATC). Collaboration is also established with ongoing H2020 Project DTH01-2019-GA 875192 (BD4QoL) and previous H2020-PHC-2015 GA 689715 BD2Decide partners. The work performed on data semantics for HNC and data integration from different biomolecular platforms has promoted new knowledge generation and exchange between medical oncologists and bio-informaticians from the participating hospitals and

experts in ontology systems from Universidad Politecnica de Madrid. The data annotation, quality check rules and integration processes and know-how are also being reused in the newly funded IDEA4RC Horizon Europe project. The generated data have also fostered further analyses of the produced models on completely independent datasets (e.g., from the Head and Neck 5000 study in UK) as well as a new research with a group in the US, to study radiosensitivity index and to reuse the data as a basis for a novel experiment on the generation and use of synthetic cohorts for in-silico studies. The Project has established collaborations with partners of previous BD2Decide Project and with ongoing H2020 BD4QoL project and the Head and Neck 5000 study in UK. The Project Coordinator is also actively involved in complementary initiatives in the frame of the European Organization for Research and Treatment of Cancer (EORTC), and in the Make Sense Campaign promoted at European level. In this perspective a dedicated meeting will be held at the level of the Italian Ministry of Health in September 2023. The Project Coordinator collaborates with the Italian Government in new initiatives on head and neck cancer. The Consortium partners have constantly kept in touch by means of the above-mentioned virtual meetings and physical meetings (November 2022 Madrid, July 2023 Milan). Collaboration with a newly funded Horizon Europe aimed at building a European Health Data Space for Rare cancers (specifically Sarcomas and Head and Neck Cancer) is also ongoing which involves 11 reference hospitals of the URACAN ERN. Further interdisciplinary collaboration is ongoing with partners of the Cluster CS_AIW (Cancer Survivorship AI for Wellbeing) that involves 11 EU funded projects. In this framework SuPerTreat partners are contributing to a white paper and recommendations to be presented to the European Commission regarding the implementation of best practices to promote the use of innovative technologies for personalised medicine for cancer and survivorship involvement.

7. 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 modifications vs. the delivered Data Management Plan.

8. Patient and Public Involvement

a. Does your project involve a patient representative/organization? yes/no

No representative/organization were involved. However, patients were directly and actively involved in the qualitative and quantitative studies conducted within WP6.

b. How valuable is/was the involvement/participation/engagement of a patient organization to the success of the consortium? Please rate on a scale of 1-7 (1=not valuable, 7=extremely valuable)

7

c. 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)
X Commenting and developing patient information leaflets or other research materials
X 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
X 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):

X 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
X Raising awareness of the project through media such as television programmes, newspapers and social media
X Dissemination to patient organizations and the patient community on the findings of a study
☐ Other (please specify)

9. 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."*

As specified in the paragraph dedicated to WP7 in Section 5, given the hurdles encountered during the project conduction, so far the Consortium partners have published only two out of the several articles which will derive from the analysis and the interpretation of the data produced within the SuPerTreat project. However, by the end of the project (February 2024) the Consortium managed to finalize the main project tasks. The only currently undergoing activities deal with result interpretation and drafting of several scientific manuscripts. All the articles cited in the following table will be submitted to impacted scientific journals, will be published in Open Access form, and will include the clear acknowledgment of ERAPerMed funding.

Type of Publication*	Partner No	Publication (authors, title, journal, year, issue, pp.)	DOI	Open access (yes/no)	Confir-mation **
Article in journal	1 (UMIL) and 3 (INT)	Serafini MS, Cavalieri S, Licitra L, Pistore F, Lenoci D, Canevari S, Airoldi M, Cossu Rocca M, Strojan P, Kuhar CG, Merlano M, Perrone F, Vingiani A, Denaro N, Perri F, Argiris A, Gurizzan C, Ghi MG, Cassano A, Allegrini G, Bossi P, De Cecco L. Association of a gene-expression subtype to outcome and treatment response in patients with recurrent/metastatic head and neck squamous cell carcinoma treated with nivolumab. J Immunother Cancer. 2024 Jan 30;12(1):e007823.	10.1136/jitc-2023-007823	Yes	X

Article in journal	1 (UMIL) and 3 (INT)	Cavalieri S, Serafini MS, Carenzo A, Canevari S, Lenoci D, Pistore F, Miceli R, Vecchio S, Ferrari D, Moro C, Sponghini A, Caldara A, Rocca MC, Secondino S, Moretti G, Denaro N, Caponigro F, Vaccher E, Rinaldi G, Ferraù F, Bossi P, Licitra L, De Cecco L. An Inflammatory Signature to Predict the Clinical Benefit of First-Line Cetuximab Plus Platinum-Based Chemotherapy in Recurrent/Metastatic Head and Neck Cancer. Cells. 2022 Oct 10;11(19):3176.	10.3390/cells11193176	Yes	X

** 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.*

Articles in preparation (submission foreseen in 2024)

Type of Publication*	Partner No	Publication (authors, title, journal, year, issue, pp.)	DOI	Open access (yes/no)	Confir-mation **
Article in journal	All partners	Results of WP3 and WP4 models using data developed in WP1 and annotated/integrated in WP2	Not assigned yet	Yes	X
Article in journal	All partners	Usability and acceptability (assessed in WP6) of an AI-based CDSS (developed in WP5)	Not assigned yet	Yes	X
Article in journal	3 (INT)	In-depth analysis of prognostic models for HPV-negative HNSCC patients treated with curative radiotherapy	Not assigned yet	Yes	X
Article in journal	3 (INT)	Results of translational research to develop prognostic models for epithelial non-glandular paranasal carcinoma patients treated with induction chemotherapy and loco-regional treatments	Not assigned yet	Yes	X

Moreover, the following pre-print (i.e., no peer review has been performed so far) has been delivered acknowledging the ERAPerMed funding: Ho E, De Cecco L, Cavalieri S, Sedor G, Hoebers F, Brakenhoff RH, Scheckenbach K, Poli T, Yang K, Scarborough JA, Campbell S, Koyfman S, Eschrich SA, Caudell JJ, Kattan MW, Licitra L, Torres-Roca JF, Scott JG. A clinicogenomic model including GARD predicts outcome for radiation treated patients with HPV+ oropharyngeal squamous cell carcinoma. medRxiv [Preprint]. 2023 Sep 14:2023.09.14.23295538 (doi: 10.1101/2023.09.14.23295538). The manuscript is under finalization and will be submitted by the end of 2024. The accepted article will be published as Open Access paper and will acknowledge the ERAPerMed funding.

10. 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 scientific conference	4	Submitted an abstract to the 28th Norwegian Epidemiological Association conference. Title: "Establishment of a multi-source cohort of head and neck cancer patients with biomarkers and clinical outcomes - challenges, solutions and perspectives"	http://nofe.no/nofe-conference-2022/	Scientific community
Communication in scientific conference	2	The SuPerTreat research project was presented at ESMO 2022 Congress during the session "Application of novel technologies in head & neck cancer"	https://www.esmo.org/meetings/esmo-congress-2022	Scientific community
Dissemination in Italian Newspaper	1 and 3	Article published in the Italian newspaper "Il Sole 24 Ore " on July 11th, 2023	N/A (see below)	Citizens at large and scientific communities
Communication in scientific conference	4	Oral presentation at the 29th Norwegian Epidemiological Association conference. Title: "External validation of prognostic and predictive gene signatures in head and neck cancer patients"	http://nofe.no/nofe-conference-2023/	Scientific community
Communication in scientific conference	2	Oral presentation at the 8th Trends in Head Neck Oncology Meeting in Amsterdam (Nov 2021)	https://www.thno2021.org	Head Neck Cancer specialists across Europe
Communication in scientific conference	2	Presentation at ESMO congress 2022 in Paris	https://cslide.ctimeetingtech.com/play/9L2404R037C. (The webcast is only accessible for ESMO members)	ESMO community
Communication via social media	1 and 3	Presentation of the project	Linkedin / Facebook homepage of INT	General public

Add lines as relevant.

** Type 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*

11. Impact

Detailed description of the impact
The SuPerTreat validated in-silico new, powerful Big Data driven Artificial Intelligence (AI) methods to build an actionable personalised treatment decisions support system (CDSS) for cancer, to inform design of confirmatory clinical trials and new treatment guidelines. The project integrated ethical dimensions for novel approaches in personalised medicine. The focus was on Head and Neck Cancer (HNC), which poses many therapeutic challenges due to its heterogeneity and aggressiveness, for which the Consortium has internationally recognized wide expertise. With this project we aimed at demonstrating how the use of Big Data and AI technologies contribute to increased understanding of HNC heterogeneity across different individuals, and its impact on disease outcome treated by curative standard of care approaches. The project let us model personalised disease prediction of recurrence to

orient therapeutic decisions at diagnosis by predicting outcomes, and by assessing the role of individual and combined biomolecular and clinical factors as related to different treatment options. The developed in-silico predictions were validated on the whole HNC study cohort. The project combined clinical research with advanced mathematical modeling and bio-informatics to exploit available and combined results from high-quality multisource and multidimensional datasets built by converging efforts of partners of this consortium to accelerate their clinical use for personalised treatment decisions.

The clinical impacts of SuPerTreat were evaluated by simulating the potential effects of personalised treatment decisions based on the developed models on patients' survival and on treatment optimization. The results of our HTA provided new insights informing healthcare policies. In particular, we found that we can compute the total cost reductions and the total incremental utility to obtain an overall Incremental Cost-Effectiveness Ratio (ICER) for SuPerTreat of -1,302 €/QALY. This finding confirms that the application of the SuPerTreat CDSS to the current clinical workflow would be viable and highly cost-effective, even when accounting for the economic unviability of the escalation approaches.

12. Patents and Licences

Please indicate the patents, licences and other outcomes that resulted from the funded project.	
Patents	*None*
Licences	*None*
Others	*None*

13. Collaborations

Did the partners of this project collaborate before applying to the ERA PerMed joint transnational call? If YES, please specify which partners were collaborating before and list the funding received (if applicable).

INT, INT subcontractor (UPM), and Charité subcontractor (UDUS) previously collaborated in the BD2Decide project, an international research project funded by the European Union Horizon 2020 Framework Programme (Grant/Award Number: 689715). The project website is https://www.bd2decide.eu/ and the overall study report was published by Cavalieri S et al. Head and Neck 2020 (PMID: 33107152).

Were there any collaborations with groups outside the consortium during the lifetime of the project? If YES, please specify (name of researcher, organisation, country)

UMIL, INT, UiO, and INT subcontractor (UPM) are actively collaborating in the BD4QoL project, an international research project funded by the European Union Horizon 2020 Framework Programme (Grant/Award Number: 875192). The project website is https://www.bd4qol.eu and the overall study report was published by Cavalieri S et al. Front Oncol 2023 (PMID: 36798825).

14. Consortium Sustainability

Did the collaboration and results obtained in this project lead to new initiatives/applications to national and/or international funding programmes (e.g. grants, grant applications)? ***Yes/No***

If YES, please specify if the initiatives were undertaken as single group or with partners (of the current consortium and others), and specify the partners who applied and the corresponding call (e.g. H2020, Horizon Europe, etc.).

No

Are future collaborations planned/in progress (e.g. grants, grant applications)? ***Yes/No***

If YES, please specify if the initiatives will be undertaken as single group or with partners (of the current consortium and others), and specify the partners participating and the corresponding call (e.g. H2020, Horizon Europe, etc.).

No

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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.