MELCAYA

NOVEL HEALTH CARE STRATEGIES FOR MELANOMA IN CHILDREN, ADOLESCENETS AND YOUNG ADULTS

Grant Agreement: 101096667

D3.5 Mol-Mel initiation package

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Document history

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0.2	09.05.2023	UNIFI	Revised draft
0.3	30.05.2023	FCRB	Revised draft
0.4	21.09.2023	UNIFI	Revised draft
0.5	27.11.2023	UNIFI	Revised draft (after Ethical Committee review)
0.6	28.12.2023	UNIFI	Revised draft
1.0	05.01.2024	FCRB	Final draft
2.0	30.09.2024	FCRB	Revised final draft

Executive Summary

The purpose of this deliverable is to present all the documentation necessary for the initiation of the MELCAYA work package 3 clinical study Mol-Mel. It contains the final version of the study protocol and corresponding regulatory/ethics approval by the ethical committee of the study sponsor (Hospital Clínic de Barcelona). The protocol includes an introduction in which a review on relevant literature, the objectives of the study, the design and study procedures are presented. Details on data collection and management are also discussed, as well as ethical considerations such as how incidental or secondary findings will be communicated or how personal data will be processed. The documents presented in this deliverable will be subsequently used by the other clinical sites for approval in their respective ethical committees.

1. General information

1.1. Identification of the study

Title: Histological, computational, and molecular pathology for improved diagnosis (Mol-Mel)

Code or protocol identification number: NCT06602648 (*https://clinicaltrials.gov/*)

Version and date: v3 (03/06/2024)

1.2. Identification of the sponsor/principal investigator

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1.3. Identification of site investigators

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1.4. Identification of the principal investigators from participant centers

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Additional organizations:

This study will utilize data from existing datasets, cohorts, registries, and databases, including the European Organization for Research and Treatment of Cancer (EORTC) Melanoma Group, the Italian Intergroup Melanoma (https://www.melanomaimi.it), a melanoma dataset from the University of Perugia (IT), the Catalan Melanoma Network and Registry and the Melanomas and Melanocytomas Registry (Clinic Health Corporation).

2. Justification

Melanoma is the deadliest form of skin cancer and the second leading cause of cancer in children, adolescents, and young adults (CAYA) patients [1,2]. The incidence of melanoma is reported to be about 1.3-1.6 per million in children under 15 years of age and 15 per million in 15-19 years old, with increasing incidence in adolescents by 4.1% annually since 1997 [3,4].

Melanocytic tumors in CAYAs represent a heterogeneous group of biologically distinct subtypes of disease that differ in their genetic signature, clinical and histopathological features, age of onset, cell of origin and prognosis. Additionally, the lower sensitivity observed in CAYAs, particularly in children, compared to adults leads to delayed diagnosis, resulting in poorer outcomes. However, if diagnosed early, CAYA patients, especially children, have the potential to exhibit a 90% 10-year survival rate even for stage I/II disease [5].

In real-life, obtaining complete agreement in diagnosis based solely on morphology can be difficult, especially for ambiguous lesions. It has been observed that when evaluating melanocytic tumors in CAYAs, pathologists may use different diagnostic terms based on individual or local practices, which can further complicate the diagnostic process.

The reproducibility of diagnoses between pathologists is poor, especially for low-grade and intermediate lesions for which diagnostic inconsistency is frequent [6, 7]. Based on conventional histopathological and molecular genomic alterations, the current World Health Organization (WHO) classification (4th edition) identifies three major categories of melanomas in childhood and adolescence: 1) conventional adult-type melanoma, 2) Spitz melanomas and 3) melanomas arising in congenital nevi [8]. Nevoid melanomas, which are notoriously difficult to diagnose clinically and histologically, are less likely to develop in late adolescence. Regarding intermediate melanocytic proliferations, the so-called melanocytomas, atypical Spitz tumors, and proliferative nodules arising in congenital nevi are more frequent in the pediatric population.

Therefore, the integration of molecular pathology with conventional morphology is now considered essential for accurate melanoma classification in CAYAs patients. However, due to the rarity of melanoma in childhood, adolescence, and young age, there is currently limited information available on the molecular alterations underlying the diverse subtypes of melanoma in this population. Additionally, there is a lack of accurate prognostic and predictive biomarkers.

3. Study hypothesis

Mol-Mel study will focus on combined phenotypic-genotypic diagnostics. Artificial intelligence (AI)-based technologies will allow to optimize current classification by an updated and integrated taxonomic structure in multiple ethnicities populations, including Northern European and Southern European ancestries. The refinement of melanocytic tumor subclassification can led to an improvement in the tailoring of patient therapy, more accurate prognosis, follow-up and prediction of treatment response, better patient stratification for clinical trials, and more precise categorization for epidemiological purposes.

Mol-Mel study is structured in 4 main tasks:

1. **Standardization and tissue quality control:** standardized protocols and proper handling of formalin-fixed and paraffin-embedded (FFPE) tumor tissues and frozen tumor tissue samples from retrospective and prospective data collections will be shared between collaborating institutions. This part includes the evaluation of harmonized protocols for tissue processing and homogenous collection of samples for pathology transported from clinical centers. Tissue quality control of hematoxylin & eosin (HE)-stained samples will be performed and feedback to clinical centers regarding any quality issues on incoming prospective samples will be provided.
2. **Histopathology & computational pathology:** melanoma samples will undergo a detailed central pathology review and analysis of conventional prognostic staging parameters. Intermediate and diagnostically challenging melanocytic undetermined neoplasms will be included and inter-observer agreement by multiple pathologists will be assessed. To overcome the lack of systematic analysis of phenotype defining immunohistochemistry (IHC) expression markers in melanoma of CAYA across subtypes, we will apply an extensive immunophenotypic characterization by single and multi-plex IHC in whole sections and/or tissue microarrays (TMA), and an automated digital quantification. Spatial proteomics by automated ultra-high content imaging/MACSima Imaging Cyclic Staining (MICS) technology

enables simultaneous analysis of hundreds of marker antigens on a single sample. MICS will be performed on the novel automated ultra-high content imaging platform MACSimaTM (Miltenyi Biotec).

3. **Comprehensive somatic, transcriptional and DNA methylation landscape and data integration:** melanoma in CAYA is a complex disease influenced by genetic and epigenetic alterations in both the tumor and its microenvironment consisting of immune cells and surrounding epithelial or stromal cells. We will extract DNA and RNA from FFPE melanoma tissue sections collected by the clinical partners and characterize the tumor samples using whole-exome sequencing (WES) and single nucleotide polymorphisms (SNP) arrays for matched tumor/normal pairs, as well as RNA sequencing (RNAseq) of tumors. Next, we will characterize recurrent somatic aberrations, define major expression-based and DNA methylation-based subclasses, and characterize patterns of tumor evolution.

4. **Pan-European digital second opinion platform**: this task will focus on enhancing the digital tools available to pathologists, including a pan-European second opinion platform for collaboration between pathologists that facilitates European standardization for melanoma reporting and knowledge sharing of clinically validated biomarkers and algorithms for updated and strengthened subtype classification.

4. Objectives and purpose of the study

Primary objectives:

- To assess the histopathological and molecular features of pediatric melanomas.
- To integrate histopathology and molecular analyses to provide a novel hybrid taxonomy of melanoma in CAYA.

Secondary objectives:

- To identify driver mutations, transcriptomes, and DNA methylation subclasses with morphological, immunophenotypic analyses and clinical data to provide a novel hybrid taxonomy and identify tissue prognostic and predictive biomarkers.
- To create a pan-European digital pathology platform to assess diagnostic inter-observer reproducibility, enhance international collaboration and achieve diagnosis standardization.
- To identify prognostic biomarkers in the context of immunotherapy and targeted therapy.

5. Study design

Mol-Mel is a multicenter retrospective registry-based cohort study with histopathological and molecular analysis. This study will utilize tumor tissue samples from patients diagnosed in the consortium cancer registry with a first registration from 2005 to 2021. Therefore, no formal recruitment of patients will occur. Individuals will be selected from hospital discharge records, cancer registries and pathology archives of the consortium. Individuals who meet the inclusion criteria will be included in the study. Adolescent and childhood patients (< 20 years) as well as young adults (< 30 years) with histologically confirmed melanoma will be considered.

6. Participant selection

6.1. Subject inclusion criteria

In order to be eligible for participation in the Mol-Mel study, an individual must meet the following criteria: adolescent and childhood patients (<20 years) as well as young adults (<30 years) with histologically confirmed melanoma or intermediate/ambiguous melanocytic neoplasm (*i.e.*, melanocytomas, SAMPUS, IAMPUS and MELTUMP according to WHO classification).

6.2. Subject exclusion criteria

An individual will be excluded as follows: adult patients (> 30 years of age); adolescent and childhood patients (< 20 years) as well as young adults (20-30 years) with histologically confirmed melanoma or intermediate/ambiguous melanocytic tumor lacking adequate formalin-fixed and paraffin-embedded (FFPE) and/or frozen tumor tissue lacking follow-up information on the patient's outcome.

7. Treatment and study calendar

Not applicable.

8. Statistics

8.1. Sample size

Collaborative approach between centers involved in Mol-Mel will be used to identify tumor samples and slides from CAYA (N=100).

8.2. Statistical analysis

Bioinformatics and biostatistics with relevant expertise will contribute to data analysis. For patient's demographic and baseline clinical characteristics will be summarized descriptively, namely mean ± standard deviation (SD) or median interquartile range (IQR) for continuous variables and number (percentage) for categorical data. Normality assumption will be assessed using the Shapiro-Wilk or Kolmogorov-Smirnov tests. Data will be assessed for missing data and outliers. For comparisons, if assumption of normality is met, parametric test as the analysis of variance (ANOVA) followed by post-hoc test for multiple comparisons if appropriate or Student's t-test for two group will be used. For repeated measures, the two-way mixed model ANOVA followed by the post-hoc Bonferroni's test (or other as appropriate) will be used. If the data failed the test of normality, the respective non-parametric tests will be used. Effect sizes will be reported for all comparisons. For survival analysis disease free survival (DFS) is defined as the time between diagnosis and disease relapse or death from any cause (*i.e.*, DFS events are the events of relapse or/and death) and overall survival (OS) as the time between diagnosis and death from any cause. Patients who have not relapsed/died or died will be censored at the date of the last follow-up visit. Crude or adjusted Kaplan-Meier log-rank or Breslow analyses will be performed. Univariate and multivariate Cox proportional hazard regression models will be performed. The multivariate Cox model will be adjusted for significative predictor variables in univariate with a forward stepwise selection. Alternative models will be considered as necessary, adding or modifying predictor variables. The goodness-of-fit of the model will be measured using log-likelihood. Results will be reported as hazard ratio (HR), adjusted HR (aHR) and 95% confidence interval. A p-value < 0.05 will be considered significant for all variables if not otherwise stated. Corrections will be applied for multiple comparisons. All data will be analyzed using SPSS software version 26.0 (IBM Corp. SPSS Statistics, Armonk, NY, USA), Jamovi v.2.2.5.0 and graphs designed using GraphPad Prism version 9.00 (La Jolla, USA).

9. Ethical and legal aspects

9.1. Legal and ethical basis

The partners have a lawful basis for the re-use of health data for scientific purposes under specified conditions and with adequate safeguards i.e., legitimate interests (article 6.1 (f) GDPR), combined with 'scientific research' article 9.2 (j) GDPR. In the cases that the subjects could be re-identified, the guidelines on registry-based studies (EMA/426390) will be followed to ensure that access and use of the proposed data poses minimum to no risk to the study subjects or their

fundamental rights and freedoms. In the cases where pre-existing ethics approvals are currently not in place, an authorization (or an amendment in the case of existing approval) to access and use this data will be requested from each partner's respective local ethics committee or national competent body prior to study start-up.

All study materials, including clinical and laboratory protocols, will be submitted to pertinent Institutional Review Boards (IRBs) for review and approval. Approval of the study protocol will be obtained prior to participant/case selection. Any changes to the study protocol, materials, etc. will be subjected to ethics review and approval before the changes are implemented into the study. All participating institutions will comply with international ethical standards regarding principles for medical research involving human subjects and data (Declaration of Helsinki, 2013). In the particular case of Hospital Clínic de Barcelona, compliance at the Spanish level with the Ley 14/2007 de 3 de julio, de Investigación biomédica will be ensured. On top of that, the guidelines set out in the International Conference on Harmonisation of Good Clinical Practice (ICH GCP) and the EMA/426390/2021 (Guideline on registry-based studies) will be followed.

9.2. Communication of incidental/secondary findings

In the event that incidental/secondary finding occur during the study, the researcher is expected to inform an officer from his or her local Ethics Committee and coordinate a consultation with the medical professionals involved in the study from their participating institution to review and evaluate if the finding is relevant and how it should be communicated to the participant. In case of doubt, consultation can be made with other medical experts within the consortium. Contact with the patient would be done through the practitioner that generally attends the patient, using the available data recorded in the clinical history (if any). For minors, the general practitioner would contact with the parents or legal representatives (signatory of the informed consent). Ideally, a medical appointment would be scheduled when sharing this information to reassure the patient and avoid unnecessary stress.

The general conditions that must be always met to communicate an incidental/secondary finding are the following:

- It may affect a participant's health and welfare.
- It is scientifically and clinically valid.
- Ethical approvals have been obtained and the participant or their legal representative has

opted in to receiving such results through their clinician(s) in the informed consent form.

Incidental and secondary findings will not be communicated:

- When the clinical information is anonymized, as it will be justifiably impractical or impossible to contact the research participant.
- When the participant has indicated that he/she does not want to be informed about such findings.

9.3. Supervision of legal-ethical issues

The institutions involved in this study will establish an Ethical Monitoring Board (EMB) that will act as liaison between them and local competent IRBs. This will be done to ensure that data collection methods and clinical aspects of the study protocol are efficacious and in agreement with competent IRBs policies and procedures, as well as to oversee the process of obtaining scientific advice and regulatory guidance from the appropriate regulatory agencies. In addition, access to regulatory expertise will be ensured through each institution ethics committee. Communication between the partners and competent IRBs will be continuous in order to verify that the study is in compliance with European and national regulatory guidelines.

10. Data management

10.1. Data storage

All data will be stored in a secured electronic database known as Xarxa Melanoma approved by the Ethical Committee of the Hospital Clínic de Barcelona on the 14/04/2015 (Reg. HCB/2015/0298). This database is routinely used by dermatology medical professionals of our hospital and complies with international standards on data protection and offers a consistent, auditable and integrated electronic database environment. Each institution involved in the clinical studies will count with a local data protection officer (DPO) to advice on highly complex, sensitive or large-scale data processing. Upon completion of the study, data will be preserved for a minimum of 10 years to guarantee continued accessibility and data discovery. Personal data information will only be kept for updating follow-up by the local center investigator. The sponsors will only use the data collected for other scientific purposes if participants have given prior consent and if the legal basis for processing is still in place (see section 9.1). After that, paper and electronic records will be destroyed or erased per institutional/University policy.

10.2. Data codification

Before uploading the collected patient data to the database, a codification procedure will be implemented at each local data source center. The procedure will be carried out in the following way: a researcher from our center will assign a code to the clinical information of each patient, which will be kept in a separated database to which only the Principal Investigator or authorized personnel in his research team will have access to. In that way, without knowledge of the respective assignment of code and patient, no re-identification of individual persons is possible. Data processing will be carried out exclusively by persons who had no direct patient contact during data collection.

10.3. FAIR data

All publishable data resulting from this study will be identified by a digital object identifier (DOI) to ensure that it is findable and made available through scientific publications and publicly accessible data repositories such as Zenodo. Priority will be given to open access high impact journals. The Directory of Open Access Journals or a similar index will be used to determine the most appropriate one for submission of the study data and results to ensure immediate and unrestricted access to new knowledge. Open data formats (such as XML, PNG, HTML) will be used to increase data interoperability. The data will be released under an open access license, for instance, Creative Commons Attribution International Public Licence (CC BY) or similar. This will facilitate the reuse of data and ultimately maximize the overall impact.

11. Treatment of data, record keeping and data confidentiality

The processing, communication and transfer of personal data of all participants shall comply with Regulation EU 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of data and the Organic Law 3/2018 of December 5 on the Protection of Personal Data and guarantee of digital rights. The legal basis that justifies the processing of your data is the consent you give in this act, in accordance with the provisions of article 9 of EU Regulation 2016/679. The data collected for these studies will be only identified by a code, so no information will be included that would allow to identify the participants. Only the study physician and his collaborators with the right to access the source data (medical history) could relate the collected data with the patient's medical history. The identity of the participants will not be available to any other person except for a medical emergency or legal requirement.

Health authorities, Research Ethics Committee and personnel authorized by the study sponsor may have access to the identified personal information when necessary to verify data and procedures of the study, but always maintaining confidentiality in accordance with current legislation.

Only the encrypted data will be transferred to third parties and other countries, which in no case will contain information that can directly identify the participant (such as name and surname, initials, address, social security number, etc.). In the event that this transfer was to occur, it would be for the same purpose of the study described and guaranteeing confidentiality. If encrypted data is transferred outside the EU, whether to entities related to the hospital where the patient participates, to service providers or collaborating researchers, the data of the participants will be protected by safeguards such as contracts or other mechanisms established by the data protection authorities.

Data processing will be done in accordance with EU Regulation 2016/679. As a result, a record of all the processing activities will be kept and a risk assessment of those activities will be performed to know what measures will be needed and how to implement them. In addition to the rights already provided for in the previous legislation (access, modification, opposition and cancellation of data, deletion in the new Regulation), participants can now also limit the processing of data collected for the project that is incorrect, request a copy or transfer them to a third party (portability). To exercise these rights, they should contact the principal investigator of the study or the Data Protection Officer of the Hospital Clínic de Barcelona through protecciodades@clinic.cat. Likewise, they have the right to contact the Data Protection Agency if they are not satisfied. Data cannot be deleted, even if a patient leaves the study, to ensure the validity of the research and comply with legal duties and drug authorization requirements. The Investigator and the Sponsor are obliged to keep the data collected for the study for at least 25 years after its completion. Subsequently, personal information will only be retained by the health care facility and by the sponsor for other scientific research purposes if the patient has consented to do so, and if permitted by applicable law and ethical requirements.

12. Management of biological samples

FFPE (formalin-fixed paraffin-embedded) blocks and slides, require careful management to ensure that they are prepared, processed, and shipped between research centers correctly. FFPE samples will be centralized at University of Florence (Department of Health Sciences). This

sample exchange will be carried out within the framework of an established scientific collaboration between Prof Susana Puig from Hospital Clínic de Barcelona and Prof Daniela Massi from the University of Florence. Particularly, this study belongs to a research project funded by Horizon Europe programme (HORIZON-MISS-2021-CANCER-02-03) in which the University of Florence is the institution in charge of developing all the molecular pathology studies of melanoma in CAYA. The fulfillment of the objectives of these studies (detailed in sections 3 and 4) requires the samples to be centralized at the aforementioned institution. The samples will undergo a quality control analysis and subsequent preparation for immunohistochemical and molecular analysis. Where necessary, the Parties shall cooperate in order to enable one another to fulfil legal obligations arising under applicable data protection laws (the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data and relevant national data protection law applicable to said Partner). When a Partner (the "Provider") sends biological material to another Partner (the "Recipient") in respect of the study, a bilateral material transfer agreement (MTA), shall be concluded between such Parties to specify the conditions applying to such transfer of material. The material shall only be used for the purpose of the study and only for as long as is necessary for that purpose. The Recipient will be entirely responsible for the use of the biological material and the Provider shall have no obligation or liability for the material, except for gross negligence or willful misconduct. Material provided in the performance of the study shall remain the property of the Provider. The Recipient shall not be entitled to transfer the material to any third partner (including another consortium partner) without the Provider's prior written consent. Finally, in the event that there are leftover biological samples after the completion of the relevant analyses, they will be returned to their original center.

13. Financing

Mol-Mel study was conceived independently of any commercial organization and will be coordinated, managed and analyzed in an independent form. The costs related to the analyses envisaged on the samples, for research purposes only, will be supported by research fundings of MELCAYA project (HORIZON-MISS-2021-CANCER-02, proposal number: 101096667).

14. Publication policy

The transmission or dissemination of the data, through scientific publications and/or

presentation in congresses, conventions, and seminars, may be carried out only after each Principal Investigator's written authorization. Accordingly, the Principal Investigator of the study undertakes to produce a report on the study, publish all data collected as described in the protocol and ensure that the data are reported responsibly and coherently. In particular, the publication of the data deriving from this study will be independent of the results obtained. The transmission or dissemination of data, through scientific publications and/or presentation in congresses, conventions and seminars, participation in Multicentric studies, will take place only following a purely statistical elaboration of the same, or otherwise in anonymous form.

15. References

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Comitato Etico Regione Toscana
AREA VASTA CENTRO
Segreteria Tecnico Scientifica ubicata c/o: Nuovo Ingresso Careggi (NIC) - Largo Brambilla, 3 - 50134 Firenze
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Firenze, il 27/12/2023

Al promotore Dipartimento di Scienze della Salute, Università di Firenze

Allo sperimentatore Principale locale Massi Daniela

e p.c. al Direttore Generale della struttura di afferenza dello Sperimentatore Principale locale
Oggetto: Comunicazione del parere relativo alla richiesta di approvazione alla conduzione dello studio clinico

"Novel health care strategies for melanoma in children, adolescents, and young adults. Histological, computational, and molecular pathology for improved diagnosis (Mol-Mel) "

Codice Protocollo: (Mol-Mel)

In riferimento alla richiesta di cui all'oggetto, si trasmette il parere del Comitato Etico Regionale per la Sperimentazione Clinica della Toscana - sezione AREA VASTA CENTRO riunitosi in data **19/12/2023.**

Si ricorda che l'avvio della sperimentazione da parte del Promotore è subordinato a:

- stipula della convenzione economica (se applicabile)
- rilascio della disposizione autorizzativa della Direzione Generale dell'Azienda sanitaria.

Il Comitato si riserva la facoltà di monitorare nel corso del suo svolgimento, in accordo alle disposizioni normative vigenti, lo studio clinico approvato.

Il Responsabile della Segreteria Tecnico Scientifica

Dr. Michele Vietri

Il Comitato Etico
in osservanza alle legislazioni vigenti in materia di
studi osservazionali / studi con interventi sanitari diversi da farmaci e dispositivi medici
ha esaminato la richiesta di parere relativa allo studio

"Novel health care strategies for melanoma in children, adolescents, and young adults. Histological, computational, and molecular pathology for improved diagnosis (Mol-Mel) "

Codice Protocollo: (Mol-Mel)

Avendo valutato la seguente documentazione nella seduta del 19/12/2023

DOCUMENTAZIONE GENERALE

- **Dichiarazione sulla natura osservazionale dello studio**
- **Dichiarazione per l'accertamento della natura indipendente dello studio (se no-profit)**
- **Elenco dei Centri partecipanti (se multicentrico)**
- **Scheda di raccolta dati**
- **Scheda di raccolta dati** (versione *track change*)
- **Scheda di raccolta dati** (versione *2 TC*)
- **Protocollo di studio** (versione *2* del *27/11/2023*)
- **Protocollo di studio** (versione *2 Track change* del *27/11/2023*)
- **Sintesi del protocollo in lingua italiana** (versione *2 Track change* del *27/11/2023*)
- **Sintesi del protocollo in lingua italiana** (versione *2* del *27/11/2023*)
- **Grant Agreement 101096667 MELCAYA**
- **Consortium Agreement MELCAYA**

DOCUMENTAZIONE CENTRO-SPECIFICA

- **Foglio informativo e consenso** (versione *1 - ADULTO* del *15/05/2023*)
- **Modulo di consenso informato/assenso per la partecipazione allo studio** (versione *7-13 ANNI*)
- **Modulo di consenso informato/assenso per la partecipazione allo studio** (versione *14-18 ANNI*)
- **Modulo informativo per il paziente/genitore/tutore legale** (versione *Tutori legali*)
- **Dichiarazione pubblica sul conflitto di interessi (Appendice 15 al DM 21/12/2007)** (versione del *16/05/2023*)
- **Lettera di intenti del promotore per il CE**
- **Richiesta di parere studio**
- **Analisi d'impatto aziendale per la fattibilità locale** (versione *1* del *06/09/2023*)
- **Lettera di intenti del promotore per il CE - in risposta a Parere Sospensivo** (versione *Track change*)
- **Lettera di intenti del promotore per il CE - in risposta a Parere Sospensivo**
- **Dichiarazione sostitutiva al consenso informato**
- **Lettera di intenti del promotore per il CE** (versione *2* del *27/11/2023*)

Data di arrivo della documentazione completa: 30/11/2023

Ha espresso il seguente parere:
FAVOREVOLE

Numero registro pareri del Comitato Etico: 24680_bio

Elenco componenti del CE presenti alla discussione e votanti che hanno dichiarato assenza di conflitti di interessi di tipo diretto o indiretto:
Dr.ssa Manuela ANGILERI, *Farmacista Servizio Sanitario Regionale*

Dr.ssa Silvia ASARO, *Esperto in Dispositivi Medici*
Dr. Alessandro BUSSOTTI, *Medico di Medicina Generale*
Avv. Giulia CARRAVETTA, *Esperta in materia assicurativa*
Dr.ssa Antonina CHICCOLI, *Pediatra*
Prof. Renato CORRADETTI, *Farmacologo*
Dr. Matteo GALLETTI, *Esperto di bioetica*
Dr. Donato Antonio GENZANO, *Medico legale*
Dr. Pietro GRIECO, *Ematologo*
Avv. Leonardo LASCIALFARI, *Esperto in materia giuridica*
Dr. Luca LIVRAGHI, *Oncologo*
Dr. Giuseppe PEPE, *Internista*
Ing. Francesca SATTA, *Ingegnere clinico*
Dr. Francesco SOFI, *Esperto in Nutrizione*

Elenco componenti del CE presenti non votanti:
i sottoindicati componenti del Comitato dichiarano di astenersi dal pronunciarsi sullo studio, poiché sussiste un conflitto di interessi di tipo diretto e/o indiretto.

Sussistenza numero legale (n. 14 su 20)

Si ricorda che è obbligo notificare al Comitato Etico:

- data di arruolamento del primo paziente;
- stato di avanzamento dello studio, con cadenza semestrale e/o annuale, corredato da una relazione scritta;
- fine del periodo di arruolamento;
- data di conclusione dello studio a livello locale ed a livello globale;
- risultati dello studio, entro un anno dalla conclusione della stessa.

Il Proponente deve ottemperare alle disposizioni legislative vigenti e riferire immediatamente al Comitato relativamente a:

- deviazioni dal protocollo, anche quando queste si rendano necessarie per eliminare i rischi immediati per i partecipanti
- modifiche al protocollo, che non potranno essere messe in atto senza che il Comitato abbia rilasciato parere favorevole ad uno specifico emendamento, eccetto quando ciò sia necessario per eliminare i rischi immediati per i partecipanti o quando le modifiche riguardino esclusivamente aspetti logistici o amministrativi dello studio.

Firenze, il 19/12/2023

Il Presidente

Prof Matteo Galletti