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MELCAYA

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

Grant Agreement: 101096667

D1.5 ExpoMel Initiation Package

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Document history

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0.1	10.02.2023	FCRB	First draft version
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0.3	18.07.2023	UT	Revised draft
0.4	20.09.2023	FCRB	Revised draft
0.5	31.10.2023	UT	Revised draft (after Ethical Committee review)
0.6	15.01.2024	UT	Revised draft
1.0	14.02.2024	FCRB	Final draft
2.0	01.10.2024	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 1 clinical study ExpoMel. It contains the final version of the study protocol and corresponding regulatory/ethics approval by the ethical committee of the study sponsor (University of Tuebingen). 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: Identification of risk factors, exposomics and genetic susceptibility of melanoma in children and young adults (ExpoMel)

Code or protocol identification number: NCT05773651 (*https://clinicaltrials.gov/*)

Version and date: v1 (31/10/2023)

1.2. Identification of the sponsor/principal investigator

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1.3. Identification of the principal investigators from participant centers

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Name: Tamara Schikowski

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2. Justification

Melanoma in childhood and adolescence is under-studied, lacking adequate preventive, diagnostic, and therapeutic strategies. Only a relatively small proportion of melanomas can be explained by what has been referred to as “exposome”, which indicates the entirety of environmental exposures of a person from conception onwards [1]. In general, the exposome consists of three overlapping domains: external factors, including the socio-economic environment as well as educational level and urban-rural environment, specific external factors, including lifestyles and pollutant exposures and, finally, the internal factors, which include biological effects such as inflammation and the microbiome. The internal environment does not

only reflect the biological effects, but also the responses to exposures [2]. Therefore, the inclusion of genetics provides additional insights into the internal environment [3]. This study pretends to clarify the role of polygenic risk scores in children and young adults (CAYA) with a high risk for melanoma at an early stage. MELCAYA will combine for the first-time information from European reference cohorts and registries that include information on genetic predisposition and epidemiology, with those that provide information in exposome in order to draw a complete picture of preventable risk.

3. Study hypothesis

As previously mentioned, only a relatively small proportion of melanomas can be explained by environmental factors alone, such as air pollution, climate factors, UV exposure, diet and socioeconomic status. On the other hand, the role of melanoma susceptibility genes, which has already been established in adult patients, is under debate in children and adolescent melanoma. A subset of CAYA melanoma cases occur in a familial context [4], however, less than 10 % have mutations in high-risk susceptibility genes. The variants in moderate melanoma risk genes play a more important role, such as the melanocortin-1 receptor gene (MC1R), which functions as a master regulator in human pigmentation [5,6]. Additional genetic polymorphisms were identified in adults, each associated with a small increase in melanoma risk, but which in combination to other factors may pose a relevant risk (polygenic risk scores) [7,8]. The question that arises is how to weigh the role of environmental and phenotypic risk factors and how they relate to genetic findings.

4. Objectives and purpose of the study

The primary objective of this study is the identification of environmental and genetic factors involved in the risk and progression of melanoma in CAYA. The secondary objectives are to generate a model integrating the genetic and environmental factors to estimate the risk of developing melanoma and improve the primary prevention of melanoma through evidence-based interpretation of environmental risk.

4.1. Principal and secondary variables

By retrieving data from several epidemiological and clinical registries across Europe we aim to integrate and maximize efforts in order to create a large dataset that serves for a comprehensive analysis of genetic and environmental factors influencing the etiology of melanoma in CAYA. The

data will be combined with exposome information about climate and pollution for the development of a weighted risk score. Furthermore, germline high risk mutations and germline low-medium risk variants will be analyzed. Genome and transcriptome sequencing of blood and in selected cases tumour will provide the most comprehensive data to create a polygenic risk score for CAYA melanoma. Transcriptome data will help to identify and characterize the effect of variants of unknown significance in coding, intronic as well as regulatory regions. Tumour sequencing can provide additional information on functional relevance of variants, e.g., secondary hits in tumour tissue or second hits in tumour suppressor genes. Such identification will be highly advantageous to design prevention strategies for melanoma development in CAYA.

5. Study design

ExpoMel is an international multicentric registry-based retrospective case-control study. It involves the review/analysis of the following type of data: age, sex, melanoma diagnosis, histopathological information, anatomical site, clinical and dermatoscopic images, stage and original genomic information, including (likely) pathogenic germline variants germline polymorphisms and in selected cases somatic mutations. Data collection period ranges from January 2000 to December 2022. For patients with available biospecimen, we will sequence the germline genome, transcriptome and in selected cases tumour normal exomes. Data will be stored and analyzed at the University of Tübingen and the Hospital Clínic de Barcelona and results will be made available to other study centers via a central database.

6. Participant selection

Due to its registry-based retrospective study, no formal recruitment of patients will occur in ExpoMel. Data and samples will be obtained from the following registries and associated biobanks:

- Catalonia Melanoma Network through Hospital Clinic Barcelona.
- The German Registry for Rare Pediatric Tumours (STEP) of the German Society for Pediatric Oncology and Hematology.
- Registry of the German Working Group of Dermatologic Oncology (ADOREG).
- German Childhood Cancer Registry (DKKR).
- Swedish Melanoma Registry (SweMR) through Karolinska Institute.

- Public Pathology Database of the Netherlands (PALGA) through Princess Maxima Center for Children Oncology.
- Central Registry of Malignant Melanoma of the German Dermatological Society (CMMR) and German Rare Pediatric Tumor Registry (STEP) through the University of Tübingen
- Polish Pediatric Rare Tumor Study group and selected Eastern/Southern Europe countries cooperating within the European Cooperative Study Group for Pediatric Rare Tumors (EXPERT) through the Medical University Gdansk.
- French Very Rare Tumors Committee (FRACTURE) database within the European Cooperative Study Group for Pediatric Rare Tumors (EXPERT).
- Italian Rare Tumors in Pediatric Age (TREP) Project within the European Cooperative Study Group for Pediatric Rare Tumors (EXPERT).
- Melanoma collection from the European Organization for Research and Treatment of Cancer (EORTC) through the University of Florence.
- Melanoma datasets from the Italian National Cancer Institute Foundation and University of Perugia.
- Second opinion portal from the Italian Melanoma Intergroup through the University of Florence and the University of Perugia.
- French collection of L/GCMN and collections from Necker and Timone hospital.
- Different population-based cancer registries as EUROCARE and Global Cancer Observatory (GLOBOCAN).

6.1. Subject inclusion criteria

To be eligible for inclusion in the study, an individual must meet the following criteria: (1) confirmed melanoma, (2) age until 30 years old. Justification for the targeted age range is based on the focus of the present project in CAYA patients.

6.2. Subject exclusion criteria

An individual will be excluded for the molecular studies if there is no available biological material or there is no signed informed consent.

7. Treatment and study calendar

Not applicable.

8. Statistics

8.1. Sample size

The Hospital Clínic de Barcelona through the Catalonia Melanoma Network has identified 675 germline samples from CAYA patients in the institutional biobank. Germline genome data is already available from some CAYA patients and large/giant congenital melanocytic nevi (L/GCMN) from different partners within the consortium. The University of Tübingen (UT) has extensive experience with next-generation-sequencing, bioinformatic data analysis and variant interpretation. Currently, data of more than 4000 genomes as well as more than 13.000 exomes and 600 transcriptomes are available at the UT providing an invaluable resource for detection and classification of candidate variants in broad sequencing studies. Moreover, data of more than 300 tumor normal panels and exomes of adult melanoma patients as well as 25 tumor-normal exomes of pediatric melanoma patients were sequenced at the UT. This institution also has a registry-based study of melanoma families, having access to 20 melanoma cases among patients aged 14 to 20 years old, of which 7 cases are from CDKN2A-mutated families and 13 from non-mutated families. In the field of childhood-onset melanoma, this is one of the largest patient cohorts in Europe.

8.2. Statistical analysis

Descriptive statistics will be used to assess demographic and clinical characteristics. Baseline data will be summarized and presented in tabular form. Normally distributed data will be presented as a mean with standard deviation (SD). Dichotomous and categorical data will be presented in proportions. Normality of the data will be assessed using histograms PP and linearity will be assessed using scatter plots. Differences between continuous variables will be assessed using Student's t-tests or Mann-Whitney-U test and categorical variables will be assessed using Chi squared test. We will use paired t-tests for normally distributed continuous repeated measures, the Wilcoxon signed-rank test and the McNemar test for dichotomous data. Pearson r correlation and Spearman correlation coefficient rho (r) will be used to evaluate the degree of relationship between variables. Crude and adjusted odds ratios and corresponding 95% confidence intervals (95% CI) will be calculated using linear regression for continuous outcomes and logistic regression for dichotomous outcomes.

In addition, for the assessment of the exposome by investigating the effects of all available influencing factors on the phenotypes, we will develop a weighted risk score for each environmental factor, which comprises the effects of several variables measuring the respective risk factor, for example, different air pollutants. Additionally, a weighted risk score for the epigenetic variables will be build. To estimate the relative contribution of environmental and epigenetic factors we will calculate the relative importance (proportion of explained variance) of the weighted risk scores in an ordinary linear regression model using the Lindeman-Merenda-Gold (LMG) method. We will further calculate confidence intervals for the relative contributions as well as for the respective regression coefficients using bootstrap samples. Our model can distinguish and quantify the contributions of various environmental and epigenetic risk factors of the exposome.

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

An exchange of biological samples including tumor tissues fixed in formalin within paraffin blocks (FFPE), frozen tumor tissues, genetic material (DNA/RNA) and blood may be performed within this study among participating institutions. This sample exchange will be carried out within the framework of an established scientific collaboration within the framework of a research project funded by Horizon Europe programme (HORIZON-MISS-2021-CANCER-02-03). 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

ExpoMel 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

[1] Wildt S. and Gerngross, T. U. Nature Reviews Microbiology vol. 3 119–128 (2005).

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[5] Pellegrini, C. et al. The Lancet Child and Adolescent Health 3, 332–342 (2019)

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36 167–168 (2022)

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[8] Bakshi, A. et al. J Natl Cancer Inst 113, 1379–1385 (2021)

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834/2023BO2	18.12.2023	31.01.2024
unsere Projekt-Nummer	eingegangen am	Datum

MELCAYA - Novel health care strategies for melanoma in children, adolescents and young adults.

Schreiben vom 31.10.2023, eingegangen am 18.12.2023.

Sehr geehrte Frau Dr. Brecht,

die wissenschaftlichen Teilprojekte im EU-Projekt „MELCAYA", an denen Sie beteiligt sind (WP1-WP5) haben der Ethik-Kommission an der Medizinischen Fakultät und am Universitätsklinikum Tübingen zur Beratung vorgelegen.

Danach bestehen gegen Ihre Teilnahme an den o.g. Studienteilen seitens der Kommission keine Bedenken.

Die Ethik-Kommission gibt folgende Hinweise zum WP4:
Die retrospektive Auswertung von Behandlungsformen mit Medikamenten, die möglicherweise für die in Frage stehenden Patientengruppen keine Zulassung durch EMA oder BfArM besitzen, wird von den zuständigen Aufsichtsbehörden (BfArM und PEI) sehr kritisch gesehen, weil dies als Umgehung der Arzneimittelgesetzgebung angesehen und ggf. verfolgt wird. Dies könnte möglicherweise für einen Teil der zu untersuchenden Teilnehmer dieser Patientengruppe (Abschn. 6.1) von Bedeutung sein.

Die Ethik-Kommission empfiehlt, vor Teilnahme an dieser Teilstudie Kontakt mit der zuständigen lokalen Landesaufsichtsbehörde (Regierungspräsidium Tübingen) aufzunehmen und ggf. juristische Probleme zu diskutieren.

Mit freundlichen Grüßen

Prof. Dr. med. Dieter Luft
Stellv. Vorsitzender der Ethik-Kommission
Seite 2: Mitgliederliste, allgemeine Hinweise, Auflistung der eingereichten Unterlagen

Vorsitz der Ethik-Kommission

N. N.	(Vorsitzender)	N. N.
Professor Dr. med. Dr. phil. Urban Wiesing	(1. stellv. Vorsitzender)	Medizinische Ethik
Professor Dr. med. Dieter Luft	(2. stellv. Vorsitzender)	Innere Medizin

Mitglieder der Ethik-Kommission

Sabine Braun-Trawally	Laie
Professor Dr. med. Berthold Drexler	Anästhesiologie
Professor Dr. iur. Michael Droege	Jurist
Professor Dr. med. Jürgen Honegger	Neurochirurgie
Professor Dr. med. dent. Bernd Koos	Zahnmedizin
Professor Dr. phil. Dipl. Psych. Stefan Klingberg	Psychologie, Psychotherapie
Professor Dr. med. Holger Lerche	Neurologie
Professor Dr. rer. nat. Peter Martus	Biometrie
Professor Dr. med. Christian F. Poets	Pädiatrie
Professor Dr. med. Matthias Schwab	Klinische Pharmakologie
Dipl.-Ing. Frank Stegmaier	Medizinproduktesicherheit

Die Ethik-Kommission an der Medizinischen Fakultät der Eberhard-Karls-Universität und am Universitätsklinikum Tübingen verfährt entsprechend den ICH-GCP-Richtlinien, der Deklaration von Helsinki in der jeweils gültigen Fassung sowie den gesetzlichen Bestimmungen. Die Ethik-Kommission ist bei den Bundesoberbehörden registriert.

Die Ethik-Kommission bestätigt, dass der Prüfplan mit den erforderlichen Unterlagen insbesondere nach ethischen und rechtlichen Gesichtspunkten beraten wurde. Die berufsethische und berufsrechtliche Beratung gemäß §15 Abs.1 Berufsordnung für Ärzte in Baden-Württemberg ist für 3 Jahre ab Ausstellungsdatum gültig.
Änderungen im Prüfplan und in der Phase der Umsetzung bitten wir der Kommission mitzuteilen; dabei wären wir Ihnen dankbar, wenn Sie geänderte Passagen deutlich kennzeichnen würden.
Unabhängig vom Beratungsergebnis macht die Ethik-Kommission darauf aufmerksam, dass die medizinische, ethische und rechtliche Verantwortung für die Durchführung des Forschungsvorhabens beim Projektleiter und allen an der Studie teilnehmenden Ärzten liegt.
Datenschutzrechtliche Aspekte des Forschungsvorhabens wurden nur kursorisch geprüft. Das Votum der Ethik-Kommission ersetzt nicht die Konsultation der/des zuständigen Datenschutzbeauftragten. Die Einhaltung der gesetzlichen Vorgaben sowie die Umsetzung des Datenschutzkonzepts liegen in der Verantwortung der Studienverantwortlichen.

Nach Abschluss der Studie bittet die Kommission um einen abschließenden Bericht.

Auflistung der eingereichten Unterlagen:
-Consortium Agreement (including agreement on data and material transfer)
-ExpoMel Study Protokoll (WP1-Tübingen)
-Ethikvotum Tübingen (786/2018BO2)
-Studienprotokoll und Ethikvotum WP2 NevustoMel Barcelona
-Ethikvotum vor „Molekulargenetisches wissenschaftliches Begleitprogramm zum Register für seltene Tumorerkrankungen in der Pädiatrie" (879/2020BO2)
-Ethikvotum „Molekularpathologische Untersuchung von proliferierenden Knoten auf kongenitalen Riesennävi" vom 19.07.2023
-Studienprotokoll und Ethikvotum WP3 (MolMel) Barcelona
-Ethikvotum „Therapie des fortgeschrittenen Melanoms im Kindes- und Jugendalter" (406/2023BO2)
-Studienprotokoll und Ethikvotum WP4 (ImmunoPED) aus Perugia
-Studienprotokoll WP5 (AI-MEL) und Ethikvotum Heidelberg vom 21.06.2023
-Amendment zum Projekt „Umfassende genetische Charakterisierung von pädiatrischen Patienten mit Melanom" (786/2018BO2) zur Teilnahme am WP5 vom 22.05.2023
-Ethikvotum Tübingen zur Teilnahme an WP5

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INDEPENDENT RESEARCH ETHICS COMMITTEE (IEC) APPROVAL FORM

DETAILS OF INVESTIGATOR/TRIAL

IEC-Project Number: **834/2023BO2**

Date of submission: 2023-12-18

Investigator (Name, Address):

PD Dr. med. Ines Brecht
Universitätsklinik f. Kinder- und Jugendmedizin
Abt. Kinderheilkunde I
Hoppe-Seyler-Str. 1
72076 Tübingend. Ines Brecht

Protocol title: **MELCAYA - Novel health care strategies for melanoma in chiidren, adolescents and young adults.**

The following documents were reviewed: letter dated 31 october 2023 (WP1-WP5)

Is the investigator a member of the IEC? ☒ no ☐ yes

IEC DECISION

☒ The study was approved

☐ Conditional approval was granted for the study. /Modifications are required prior to approval.

☐ The study was disapproved: documents may be resubmitted after changes have been made.

The IEC of the University of Tübingen is organized and operates according to ICH-GCP and applicable laws and regulations.

SIGNATURE:

I confirm that the details on this form are correct:

Signature of Chairman or Recording Secretary, IEC	Prof. Dr.med. Dieter Luft Stellv. Vorsitzender der Ethik-Kommission	2024-02-07
	Name	Date

valid only together with the approval letter (List of Committee members and their occupations s. approval letter)