Study Protocol

P3-C1-003

DARWIN EU®- Chondrosarcoma: patient demographics, treatments, and survival in the period 2010-2023

19/11/2024

Version 6.0

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Study Title	DARWIN EU®- Chondrosarcoma: patient demographics, treatments, and survival in the period 2010-2023
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Research question and objectives	To describe demographics, treatments, and overall survival of patients with incident chondrosarcoma, stratified by age, sex, country/database, and, if available, by AJCC/UICC TNM categories, chondrosarcoma histological subtypes, tumour site and histological grades in 2010-2023. The specific objectives of this study are: 1. To describe demographic characteristics (age and sex) of patients with chondrosarcoma at the time of diagnosis. 2. To describe chondrosarcoma treatment with medicines (chemotherapy and biologics). 3. To estimate the overall survival of newly diagnosed chondrosarcoma patients during the study period (2010-2023). Optional objectives To describe treatment sequences and treatments other than medicines, e.g. surgery, radiotherapy. To describe chondrosarcoma treatment with medicines (chemotherapy and biologics) in patients that had undergone surgery, radiotherapy, both or neither.
Country(ies) of study	Finland, France, Spain, The Netherlands, United Kingdom
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LIST OF ABBREVIATIONS

Acronyms/terms	Description
AJCC/UICC TNM	The AJCC/UICC TNM (Tumour, Nodes, Metastases) classification system of malignant tumors
AJCC	American Joint Committee on Cancer
BIFAP	Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público, Spain
CDM	Common Data Model
CDW Bordeaux	Clinical Data Warehouse of Bordeaux University Hospital, France
CPRD GOLD	Clinical Practice Research Datalink GOLD (Oxford), UK
DARWIN EU®	Data Analysis and Real-World Interrogation Network
DOI	Declaration Of Interests
DRE	Digital Research Environment
DUS	Drug utilization study
EHR	Electronic Health Record
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
FinOMOP - HILMO	Finnish Care Register for Health Care, Finland
FinOMOP - HUS	Hospital District of Helsinki and Uusimaa (HUS), Finland
GP	General practitioner
GDPR	General Data Protection Regulation
ICD-O-3	The WHO International Classification of Diseases for Oncology
IP	Inpatient
IRB	Institutional Review Board
KM	Kaplan-Meier method
NCR	Netherlands Cancer Registry, the Netherlands
OHDSI	Observational Health Data Sciences and Informatics
OMOP	Observational Medical Outcomes Partnership
OP	Outpatient
SNOMED	Systematized Nomenclature of Medicine
UICC	Union for International Cancer Control
UK	United Kingdom

1. TITLE

DARWIN EU®- Chondrosarcoma: patient demographics, treatments, and survival in the period 2010-2023

2. RESPONSIBLE PARTIES – STUDY TEAM

Study team role	Names	Organisation
Study Project Manager/ Principal Investigator	Talita Duarte-Salles Anton Barchuk	Erasmus MC
Epidemiologist	Talita Duarte-Salles	
	Anton Barchuk	
	Berta Raventós Roca	
Clinical Domain Expert	Anton Barchuk	
Data Analysts/Programmers	Maarten van Kessel	
	Ger Inberg	
	Cesar Barboza	
	Ross William	
	Adam Black	
Data Partner*	**Names**	**Organisation – Database**
Local Study Coordinator/Data Analyst	Peter Prinsen	NCR
	Jelle Evers	NCR
	Michiel AJ van de Sande	NCR
	Vincent KY Ho	NCR
	Anna Hammais	FinOMOP - HUS
	Kimmo Porkka	FinOMOP - HUS
	Antonella Delmestri	CPRD GOLD
	Guillaume Verdy	CDW Bordeaux
	Romain Griffier	CDW Bordeaux
	Tiina Wahlfors	FinOMOP - HILMO
	Tuomo Nieminen	FinOMOP - HILMO
	Airam de Burgos-González	BIFAP
	Ana Llorente-Garcia	BIFAP
	Cristina Justo-Astorgano	BIFAP
	Miguel-Angel Macia-Martinez	BIFAP

*Data partners' role is only to execute code at their data source, review and approve their results. These people do not have an investigator role.

3. ABSTRACT

Title

DARWIN EU®- Chondrosarcoma: patient demographics, treatments, and survival in the period 2010-2023

Rationale

Chondrosarcoma is a relatively rare bone cancer characterised by cartilage matrix production. Chondrosarcoma, along with myeloma and osteosarcoma, represent the majority of primary bone malignancies. The estimated incidence of chondrosarcoma is around 1-5 per million per year. There are several morphological subtypes of chondrosarcoma, with conventional chondrosarcoma representing around 75% of all cases. Surgery is the primary treatment for chondrosarcoma with curative intent, while most chondrosarcomas are resistant to standard anticancer therapies. Treatment options are, therefore, limited in patients with metastatic or unresectable tumours, and novel treatment strategies are needed.

Chondrosarcoma's relative rarity and limited number of studies in the area make it challenging to have a clear picture across Europe of the characteristics of these patients at the time of diagnosis, the therapy they receive, and their overall survival. This study aims to inform these aspects, which are important from a regulatory point of view, to provide context and help understand how new medicines may add value for patients.

Research Objectives

To describe demographics, treatments, and overall survival of patients with incident chondrosarcoma, stratified by age, sex, country/database, and, if available, by the AJCC/UICC TNM (Tumour, Nodes, Metastases) classification system of malignant tumors (AJCC/UICC TNM) stage categories, chondrosarcoma histological subtypes, tumour site and histological grade in 2010-2023.

The specific objectives of this study are:

1. To describe demographic characteristics (age and sex) of patients with chondrosarcoma at the time of diagnosis.
2. To describe chondrosarcoma treatment with medicines (chemotherapy and biologics).
3. To estimate the overall survival of newly diagnosed chondrosarcoma patients during the study period (2010-2023).

Optional objectives

To describe treatment sequences and treatments other than medicines, e.g. surgery, radiotherapy.

To describe chondrosarcoma treatment with medicines (chemotherapy and biologics) in patients that had undergone surgery, radiotherapy, both or neither. Optional objectives will only be conducted if data on radiotherapy and/or surgeries is available as well as sufficient number of patients in each cohort.

Research Methods

Study design

Population-based cohort study.

Population

The study population will include all individuals with a first diagnosis of chondrosarcoma identified in each database between 01/01/2010 and 31/12/2022. Participants with a diagnosis of cancer (any, excluding non-melanoma skin cancer) before the diagnosis of chondrosarcoma will be excluded. We will only include

patients newly diagnosed with cancer one year before last date of data availability in each database. This will be done in order to allow for a minimum year of potential follow-up of patients.

Variables

Two main outcomes of interest will be studied: treatment/s initiated within 0 to 90, 91 to 365, and >365 days after diagnosis and death from any cause. A pre-specified list of chondrosarcoma drug treatments will be generated and when possible patients will also be classified as having undergone surgery, radiotherapy, none or both. The outcomes will be studied in all chondrosarcoma patients and in patients with different AJCC/UICC TNM categories, chondrosarcoma histological subtypes, tumour site and histological grades, depending on data availability.

Data sources

1. Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP), Spain
2. Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux), France
3. Clinical Practice Research Datalink GOLD (CPRD GOLD), UK
4. Finnish Care Register for Health Care (FinOMOP - HILMO), Finland
5. Hospital District of Helsinki and Uusimaa (FinOMOP - HUS), Finland
6. Netherlands Cancer Registry (NCR), the Netherlands

Sample size

No sample size has been calculated as this is a descriptive Disease Epidemiology Study where we are interested in the characteristics of all newly diagnosed chondrosarcoma patients.

Data analyses

We will describe the age and sex of each patient at the time of chondrosarcoma diagnosis, as well as AJCC/UICC TNM categories, chondrosarcoma histological subtypes, tumour site and histological grades if available with the index date being the date of the diagnosis.

The number and proportion of patients receiving each of a pre-specified list of chondrosarcoma drug treatments will be described at index date, 0 to 90, 91 to 365, and >365 days post index date. This will be done separately for patients that had undergone or not surgery, radiotherapy or both. If possible, results will also be stratified by AJCC/UICC TNM categories, chondrosarcoma histological subtypes, tumour site and histological grades.

When available, treatment sequences over time will also be described using sunburst plots and Sankey diagrams. This will be done for cohorts larger than 100.

Overall survival will be calculated using data on time at risk of death from any cause and the Kaplan-Meier method (KM). Results will be reported as plots of the estimated survival curves and the estimated probability of overall survival, as well as at years 1, 3, 5, and 10. Individuals who are lost to follow-up will be censored at the time of loss of follow-up. The KM approach implicitly assumes censoring occurs at random. This analysis will be conducted only for databases that systematically collect data on mortality (see Table 3 for more details). For all analyses, numbers and proportions will be reported. If possible, results will be stratified by AJCC/UICC TNM categories, chondrosarcoma histological subtypes, tumour site and histological grades.

1. AMENDMENTS AND UPDATES

Number	Date	Section of study protocol	Amendment or update	Reason
Version 2.0	24/05/2024	Overall	Adding optional objectives Clarifying inclusion criteria, maintaining 365 days potential follow up for all objectives Phenotypes added for surgery and radiotherapy.	
Version 4.0	30/10/2024	Overall	Additional subgroup analysis was introduced to all objectives Some concepts were excluded from concept sets	Amendment required for NCR IRB approval
Version 5.0	05/11/2024	Responsible parties – study team	List of collaborators from NCR was updated	Amendment required for NCR IRB approval
Version 6.0	19/11/2024	Supplementary	Some concepts were excluded from concept sets	Refining concept sets for NCR amendment

2. MILESTONES

Study-specific deliverable	Timeline
Draft Study Protocol	24th April 2024
Final Study Protocol	June 2024 (depending on number of reviews)
Creation of Analytical code	30th June 2024
Execution of Analytical Code on the data	July 2024
Interim Study Report (if applicable)	Not applicable
Draft Study Report	August 2024
Final Study Report	October 2024

3. RATIONALE AND BACKGROUND

Chondrosarcoma is a relatively rare bone cancer characterised by cartilage matrix production. Chondrosarcoma, along with myeloma and osteosarcoma, represent the majority of primary bone malignancies. The estimated incidence of chondrosarcoma is around 1-5 per million per year. There are several morphological subtypes of chondrosarcoma, with conventional chondrosarcoma representing around 75% of all cases. Surgery is the primary treatment for chondrosarcoma with curative intent, while most chondrosarcomas are resistant to standard anticancer therapies. Treatment options are, therefore, limited in patients with metastatic or unresectable tumours, and novel treatment strategies are needed. An international study incorporating data from 43 countries showed that chondrosarcoma age-standardized incidence rates (Segi-Doll World population standard) were 1–3 per million per year [1]. Only several national epidemiological studies specifically examined the population-based incidence of chondrosarcoma, with the range between 0.27 (Saudi Arabia) and 5.4 (The Netherlands) per million per year [2]. Most recent reports showed an incidence between 3.4 and 4.1 per million per year.

In general, chondrosarcoma is characterised by the cartilage matrix production by the tumour cells, but several morphological subtypes should be distinguished. Conventional chondrosarcoma is presented with the most common histological appearance, while dedifferentiated and mesenchymal chondrosarcoma represents rare, high-grade and highly malignant variants; clear-cell chondrosarcoma is also distinguished from conventional sarcoma, but it is a low-grade tumour [3]. Conventional chondrosarcoma can also be characterised by grade (Grades 1 to 3) but should be distinguished from non-malignant enchondroma, osteochondroma and atypical cartilaginous tumours. This term “atypical cartilaginous tumours” appeared in 2013 [4] and has been considered an intermediate tumour with chondrosarcoma grade 1; however, in the 2020 classification, it was separated from chondrosarcoma grade 1, which is now considered a malignant disease [5].

Chondrosarcomas can be characterised by clinical stage and histological grade. The increase in grade I chondrosarcoma cases was partially attributed to increased diagnostic imaging [6]. The optimal type of curative surgical procedure for chondrosarcoma is debated, varying from wide excision to curettage. Distant metastases are more common in high-grade chondrosarcoma, and they can be detected more than ten years after initial treatment [7]. Some studies show little progress in chondrosarcoma survival in more recent periods [8]. Chondrosarcoma’s relative rarity and limited number of studies make it challenging to have a clear picture across Europe of the characteristics of these patients at the time of diagnosis, the therapy they receive, and their overall survival. This study aims to inform these aspects, which are important from a regulatory point of view, to provide context and help understand how new medicines may add value for patients.

4. RESEARCH QUESTION AND OBJECTIVES

The overall objective is to describe demographics, treatments, and overall survival of patients with incident chondrosarcoma, stratified by age, sex, country/database, and, if available, by AJCC/UICC TNM stage categories, histological grade in 2010-2023 (**Table 1A**).

The specific objectives of this study are:

1. To describe demographic characteristics (age and sex) of patients with chondrosarcoma at the time of diagnosis.

2. To describe chondrosarcoma treatment with medicines (chemotherapy and biologics).
3. To estimate the overall survival of newly diagnosed chondrosarcoma patients during the study period (2010-2023).

Optional objectives

To describe treatment sequences and treatments other than medicines, e.g. surgery, radiotherapy.

To describe chondrosarcoma treatment with medicines (chemotherapy and biologics) in patients that had undergone surgery, radiotherapy, both or neither.
Optional objectives will only be conducted if data on radiotherapy and/or surgeries is available as well as sufficient number of patients in each cohort (**Table 1B**).

Table 1: Primary and secondary research questions and objective**.**

A. Primary research question and objectives.

Objective:	To describe demographics, treatments, and overall survival of patients with incident chondrosarcoma, stratified by age, sex, country/database, and, if available, by AJCC/UICC TNM stage categories and histological grade in 2010-2023
Hypothesis:	N/A
Population (*mention key inclusion-exclusion criteria*):	The study population will include all individuals with a first diagnosis of chondrosarcoma identified in the database between 01/01/2010 and 31/12/2022. Participants with a diagnosis of cancer (any, excluding non-melanoma skin cancer) before the diagnosis of chondrosarcoma will be excluded. We will only include patients newly diagnosed with cancer one year before last date of data availability in each database. This will be done in order to allow for a minimum year of potential follow-up of patients.
Exposure:	N/A
Comparator:	N/A
Outcome:	Two main outcomes of interest will be studied: treatment/s initiated within 0 to 90, 91 to 365, and >365 days after diagnosis and death from any cause. A pre-specified list of chondrosarcoma treatments will be generated for the former.
Time (*when follow-up begins and ends*):	Study participants will be followed up from the date of first chondrosarcoma diagnosis (index date) until the following events: loss to follow-up, end of data availability, or date of death.
Setting:	This study will use routinely collected health data from 6 databases in 5 European countries.

The main measure of effect:	Proportions and probability of survival

B. Optional objectives.

Objective:	To describe treatment sequences and treatments other than medicines, e.g. surgery, radiotherapy and to describe chondrosarcoma treatment with medicines (chemotherapy and biologics) in patients that had undergone surgery, radiotherapy, both or neither.
Hypothesis:	N/A
Population (*mention key inclusion-exclusion criteria*):	The study population will include all individuals with a first diagnosis of chondrosarcoma identified in the database between 01/01/2010 and 31/12/2022. We will only include patients newly diagnosed with cancer one year before last date of data availability in each database.
Exposure:	N/A
Comparator:	N/A
Outcome:	A pre-specified list of chondrosarcoma treatments will be generated.
Time (*when follow-up begins and ends*):	Study participants will be followed up from the date of first chondrosarcoma diagnosis (index date) until the following events: loss to follow-up, end of data availability, or date of death.
Setting:	This study will use routinely collected health data from 6 databases in 5 European countries.
The main measure of effect:	Proportions

5. RESEARCH METHODS

8.1 Study type and study design

This will be a patient-level characterisation study classified as "off-the-shelf" (C1) and as described in the DARWIN EU® Complete Catalogue of Standard Data Analyses (**Table 2**). A cohort study of all newly diagnosed chondrosarcoma cases will be conducted.

Table 1. Description of Potential Study Types and Related Study Designs.

STUDY TYPE	STUDY DESIGN	STUDY CLASSIFICATION
Patient-level characterisation	Cohort analysis	Off the shelf (C1)

8.2 Study setting and data sources

This study will use routinely collected health data from 6 nationwide and region-wide databases in 5 European countries.

All databases were previously mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM).

1. Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP), Spain
2. Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux), France
3. Clinical Practice Research Datalink GOLD (CPRD GOLD), UK
4. Finnish Care Register for Health Care (FinOMOP - HILMO), Finland
5. Hospital District of Helsinki and Uusimaa (FinOMOP - HUS), Finland
6. Netherlands Cancer Registry (NCR), the Netherlands

Databases were selected among those onboarded in Data Analysis and Real World Interrogation Network (DARWIN EU®) in 2024 (**Table 3**). The selection of databases for this study was performed based on data reliability and relevance to the proposed research question. The selected databases fulfil the criteria required for a patient-level characterisation study of chondrosarcoma, allowing for large-scale characterisation while covering different settings and regions of Europe.

Table 2. Description of the selected Data Sources.

Country	Name of Database	Justification for Inclusion	Health Care setting	Type of Data	Number of active subjects	Data lock for the last update	Ability to answer study objectives
ES	BIFAP	Information on chondrosarcoma patient characteristics at the time of diagnosis and hospital registry data with high-quality information on chondrosarcoma diagnoses, mortality.	primary care – GPs, community pharmacists, primary care specialists (e.g. paediatricians), hospital IP care	EHR hospital, claims	22.0 M	2024-03-26	1 and 3
FR	CDW Bordeaux	Hospital registry data with high-quality information on chondrosarcoma diagnoses, mortality, and treatment.	secondary care – specialists (ambulatory or hospital OP care), hospital IP care,	EHR, claims Biobank	2.2 M	2024-01-17	1, 2, and 3
GB	CPRD GOLD	Information on chondrosarcoma patient characteristics at the time of diagnosis and information on mortality.	primary care – GPs, primary care specialists (e.g. paediatricians)	EHR	17.3 M	2024-03-22	1 and 3
FI	FinOMOP - HILMO	Nation-wide hospital registry data with high-quality information on chondrosarcoma diagnoses and mortality	Secondary care – specialists (ambulatory or hospital OP care), hospital IP care	EHR, Registries	7.3 M	2024-02-12	1, 2, and 3

Country	Name of Database	Justification for Inclusion	Health Care setting	Type of Data	Number of active subjects	Data lock for the last update	Ability to answer study objectives
FI	FinOMOP - HUS	Hospital registry data with high-quality information on chondrosarcoma diagnoses, mortality, and treatment.	Secondary care – specialists (ambulatory or hospital OP care), hospital IP care	EHR	3.5 M	2024-02-16	1, 2, and 3
NL	NCR	Nationwide cancer registry data with high-quality information on chondrosarcoma diagnoses, mortality, and treatment.	Cancer registry, primary care, secondary care (ambulatory and hospital care)	Registries	2.5 M	2024-01-01 (follow-up) 2022-12-31 (registration)	1, 2, and 3

IP = inpatient, OP = outpatient, EHR = electronic health records, OT = other, NA = not applicable, GP = general practitioner

ES = Spain, FR = France, GB = the United Kingdom of Great Britain and Northern Ireland, FI = Finland, NL = the Netherlands.

Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP), Spain

BIFAP is a longitudinal population-based data source of medical patient records of the Spanish National Health Service from several participating Regions throughout Spain [9]. The population currently included represents 36% of the total Spanish population. The Spanish National Health Service provides universal access to health services through the Regional Healthcare Services. Primary care physicians, both General practitioners (GPs) and pediatricians, have a central role. They act as gatekeepers of the system and exchange information with other levels of care to ensure continuity. Most (98.9%) of the population is registered with a primary care physician and, in addition, most drug prescriptions are written at the primary care level. BIFAP includes a collection of databases linked at individual patient levels. The main one is the Primary care Database, given the central role of primary care physicians in the Spanish National Health Service. There are additional important structural databases like the medicines dispensed at community pharmacies and the patients' hospital diagnosis at discharge linked to BIFAP. Linkage to SARS-CoV-2 diagnostics test and COVID-19 vaccination registries are also included. Additional databases are also linked for a subset of patients (hospital pharmacy, cause of death registry). BIFAP program is a non-profit program financed by the Spanish Agency of Medicines and Medical Devices, a government agency belonging to the Ministry of Health in collaboration with the regional health authorities. The main use of BIFAP is for research purposes to evaluate the adverse and beneficial effects of drugs and drug utilisation patterns in the general population under real conditions of use.

Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux), France

The clinical data warehouse of the Bordeaux University Hospital comprises Electronic Health Records (EHR) on more than 2 million patients, with data collection starting in 2005 [10]. The hospital complex is made up of three main sites and comprises a total of 3,041 beds (2021 figures). The database currently holds information about patient characteristics (demographics), visits (inpatient and outpatient), conditions and procedures (billing codes), drugs (outpatient prescriptions and inpatient orders and administrations), measurements (laboratory tests and vital signs) and dates of death (in or out-hospital death). The hospital production information system data are loaded daily into a CDW in i2b2 format. A specific Extract, Transform & Load process from i2b2 to OMOP has been set up to standardise the data in OMOP-CDM format. Currently,

this mapping process is launched manually when needed. The data is integrated into the OMOP CDM version and is stored in Oracle version 19c.

Clinical Practice Research Datalink GOLD (CPRD GOLD), UK

The Clinical Practice Research Datalink (CPRD) GOLD is a database of anonymised EHRs from GP clinics in the UK that use the Vision® software system for their management [11]. 98% of the population in the United Kingdom (UK) is registered with a GP primarily responsible for non-emergency care and referrals to secondary care as needed. Participating GPs provide CPRD EHR for all registered patients who did not specifically request to opt out of data sharing. GOLD currently contains data from 985 up-to-standard GP practices and for nearly 21 million patients whose data quality is routinely assessed by CPRD as acceptable for clinical research. More than 3 million of these patients are alive and registered in 401 contributing practices. Based on the latest UK population estimates from the UK Office of National Statistics, GOLD covers 4.6% of the current UK population and includes 4.9% of currently contributing GP practices. GOLD contains data from all four UK constituent countries, and the current regional distribution of its GP practices is 5.7% in England, 55.6% in Scotland, 28.4% in Wales, and 10.2% in Northern Ireland (May 2022). GOLD data include the patient's demographic, biological measurements, clinical symptoms and diagnoses, referrals to specialists/hospital and their outcomes, laboratory tests/results, and prescribed medications. GOLD has been assessed and found broadly representative of the UK general population regarding age, gender, and ethnicity. GOLD has been widely used internationally for observational research to produce nearly 3,000 peer-reviewed publications, making GOLD the most influential UK clinical database so far.

Finnish Care Register for Health Care (FinOMOP - HILMO), Finland

The Finnish Care Register for Health Care (fi: Hoitoilmoitusrekisteri) continues the former Hospital Discharge Register, which originally gathered data on patients discharged from hospitals [12]. The Care Register has comprehensive data on the use of services and service users from Finnish public inpatient and outpatient primary and specialised care nationwide. Since 1998, the register has covered public outpatient and inpatient specialised care and private inpatient care (TerveysHilmo). Since 2011, the register has covered public primary care (AvoHilmo). Since 2020, the register has covered private outpatient care and occupational care. The CDM is currently produced from the data collection on inpatient and outpatient specialised care (TerveysHilmo) and is limited to observation periods commencing after 01/01/2015. The Register of Primary Health Care Visits (AvoHilmo) is currently outside the scope of the CDM and will be added to CDM during the remainder of 2023. The inclusion of data collected before 2015 is also being planned. The National Population Registry is also used as a source for the CDM database. The National Population Registry data forms the basis for forming the patient population. This ensures up-to-date location (municipality of residence) of patients and complete death occurrences (although not the cause of death). Using the complete population as a basis for the person table also facilitates calculations on a population level, e.g. incidence rates. HILMO database is used to assess the quality of cancer registry data in Finland [13].

Hospital District of Helsinki and Uusimaa (FinOMOP - HUS), Finland

The HUS data lake is a comprehensive, integrated data source derived in real-time from all patients who visit the HUS hospitals and receive treatment [14]. HUS is responsible for specialised healthcare in Finland's Uusimaa region and the treatment of many rare and severe diseases nationally centralised to HUS. HUS's catchment area covers about 2.2 million people. In 2023, there were 2.43 million booked appointments and 255,896 emergency department visits for specialist medical care. A total of 691,702 patients received any treatment in HUS specialist medical care and at emergency departments and 86,849 surgical procedures were performed. All visits, examinations, laboratory tests, procedures, and treatments are recorded in the HUS IT systems and integrated into the data lake. The data lake stores decades of clinical information in digital format, and data from both past and current source systems are available.

Netherlands Cancer Registry (NCR), the Netherlands

The NCR compiles clinical data of all individuals newly diagnosed with cancer in the Netherlands [15]. Cancer registration clerks have registered newly diagnosed cancer patients since 1989 on a national basis, with 3 million patients included. Data since 1992 is available in the OMOP-CDM. Over the past 35 years, this registry has provided clinicians and researchers with a wealth of clinical data (e.g., patient and tumour characteristics, primary treatment, survival) on cancer patients of all ages. Specifically, it also comprises information on tumour staging (according to the AJCC/UICC TNM classification), tumour site (topography) and morphology (histology) (according to the WHO International Classification of Diseases for Oncology (ICD-O-3)), co-morbidity at diagnosis and treatment received directly after diagnosis (within the first 9 months after diagnosis). Overall, patients are followed up for less than one year, except for death, collected any time after diagnosis. See https://iknl.nl/en for more information.

8.3 Study Period

The study period will be from 01/01/2010 to 31/12/2023 or the end of available data in each source (see **Table 3** for more details).

8.4 Follow-up

Study participants will be followed up from the date of first chondrosarcoma diagnosis (index date, **Table 4**) until the following events: loss to follow-up, end of data availability, or date of death.

In the survival analysis, the event is death and patients will be censored at the time of loss to follow-up or administratively censored at the end date of data availability, whatever comes first.

Table 3. Operational Definition of Time 0 (index date) and other primary time anchors.

Study population name(s)	Time Anchor Description (e.g. time 0)	Number of entries	Type of entry	Washout window	Care Setting[1]	Code Type[2]	Diagnosis position	Incident with respect to…	Measurement characteristics/ validation	Source of algorithm
All patients with incident chondrosarcoma eligible for the study	Date of Incident diagnosis	Single entry	Incident	Anytime prior to diagnosis	IP, OP, OT	SNOMED	Any	Any cancer diagnosis except nonmelanoma skin cancer	N/A	N/A

[1] IP = inpatient, OP = outpatient, OT = other, n/a = not applicable

[2] SNOMED = Systematized Nomenclature of Medicine

8.5 Study population with inclusion and exclusion criteria

The study population will include all individuals with a first diagnosis of chondrosarcoma identified in the database between 01/01/2010 and 31/12/2022. Participants with a diagnosis of cancer (any, excluding non-melanoma skin cancer) before the diagnosis of chondrosarcoma will be excluded (**Table 5** and **Table 6**). We will only include patients newly diagnosed with cancer one year before last date of data availability in each database. This will be done in order to allow for a minimum year of potential follow-up of patients. For primary care databases, a minimum observation period of one year prior to cancer diagnosis will be required in order to allow for detection of prevalent cases.

This study will identify cases based on a record indicating a diagnosis or observation of the disease. Conditions in the OMOP CDM and the Systematized Nomenclature of Medicine (SNOMED) are used as the standard vocabulary for diagnosis codes. Preliminary concept codes are provided **Table A1** in **Appendix I**. Concepts that explicitly identify non-conventional and other chondrosarcoma are listed in **Table A2 in Appendix I**.

Table 4. Operational Definitions of Inclusion Criteria.

Criterion	Details	Order of application	Assessment window	Care Set-tings*	Code Type	Diagnosis position	Applied to study populations:	Measurement characteristics and validation	Source for algorithm
Patients with incident chondrosarcoma between 01/01/2010 – 31/12/2022	Primary chondrosarcoma diagnosis	-	-	IP, OP, OT	N/A	N/A	All study participants with incident chondrosarcoma	N/A	N/A
Minimum prior observation period of 365 days	Only participants with a minimum observation period of 365 days prior to diagnosis of chondrosarcoma (index date) s	Before	365 days	OP, OT	N/A	N/A	All study participants from databases that represent primary care	N/A	N/A

* IP = inpatient, OP = outpatient, OT = other, n/a = not applicable

Table 5. Operational Definitions of Exclusion Criteria.

Criterion	Details	Order of application	Assessment window	Care Settings*	Code Type	Diagnosis position	Applied to study populations:	Measurement characteristics and validation	Source for algorithm
History of cancer diagnosis	Participants with a diagnosis of cancer (any, excluding non-melanoma skin cancer) any time prior to the diagnosis of chondrosarcoma or prior to the start of the study period	After	Anytime prior to chondrosarcoma diagnosis	IP, OP, OT	SNOMED	Any	All study participants with incident chondrosarcoma	N/A	N/A

* IP = inpatient, OP = outpatient, OT = other, n/a = not applicable

8.6 Variables

8.6.1. Exposure/s

Non.e

8.6.2. Outcome/s

Two main outcomes of interest will be studied: treatment/s initiated within 0 to 90, 91 to 365, and >365 days after diagnosis and death from any cause. A pre-specified list of chondrosarcoma treatments will be generated for the former. Outcomes are described in **Table 7**.

Chondrosarcoma drug treatment options are highly limited, with quite a few specific options or drugs recommended. Drugs that can be potentially used in chondrosarcoma treatment are carboplatin, afatinib,

atezolizumab, avelumab, cabozantinib, cemiplimab, cisplatin, cyclophosphamide, dactinomycin, dasatinib, decitabine, docetaxel, dostarlimab, doxorubicin, durvalumab, enasidenib, etoposide, everolimus, gemcitabine, ifosfamide, irinotecan, ivosidenib, lapatinib, lurbinectedin, methotrexate, nivolumab, pazopanib, pembrolizumab, regorafenib, retifanlimab, sorafenib, temozolomide, topotecan, toripalimab, vincristine.

Chondrosarcoma drug treatment will be also reported by class of drugs to reduce the number of strata in case several different classes are clearly present.

Please check **Appendix I Table A3** for a preliminary list of codes to identify these pharmacological treatments.

Overall survival in patients with incident chondrosarcoma will also be calculated based on the registered date of death. Individuals will contribute to survival time per the follow-up.

Table 7. Operational Definitions of Outcome.

Outcome name	Details	Primary outcome?	Type of outcome	Washout window	Care Setting*	Code Type	Diagnosis position	Applied to study populations	Measurement characteristics and validation	Source of algorithm
Initiation of chondrosarcoma pharmacological treatments	Preliminary code lists provided in Appendix 1 Table A3	Yes	Counts	N/A	IP and OP care	RxNorm	N/A	All study participants with incident chondrosarcoma	N/A	N/A
Overall survival	Time to event (death from any cause)	Yes	Time	N/A	IP and OP care	Date of death	N/A	All study participants with incident chondrosarcoma	N/A	N/A

* IP = inpatient, OP = outpatient, OT = other, n/a = not applicable

8.6.3. Other covariates, including confounders, effect modifiers and other variables

Age and sex at chondrosarcoma diagnosis will be described. The following age groupings will be used: 0-19; 20-39; 40-59; 60-79; 80 and over. The sex (male/female) of study participants will also be identified. If available, AJCC/UICC TNM categories, chondrosarcoma histological subtypes, tumour site, histological grades (see **Appendix I Table A2**), and grade information will be used in characterisation and survival analysis. Following histological subtypes other than conventional chondrosarcoma would be identified: periosteal/ juxtacortical chondrosarcoma, dedifferentiated, mesenchymal, clear cell, myxoid. Anatomical sites would be: extremities that include 1) long bones of upper limb and scapula; 2) short bones of upper limb, 3) long bones of the lower limbs and 4) short bones of lower limb; and axial skeleton that includes: 1) rib, sternum, clavicle 2) skull and face 3) vertebral column and 4) pelvic bones, sacrum, coccyx (see **Appendix I** Table A**5**).

Surgery and radiation will be identified based on procedures recorded during the first 6 months after the cancer diagnosis. A preliminary list of Concepts IDs is available in **Appendix I Table A4.**

8.7 Study size

No sample size has been calculated as this is a descriptive Disease Epidemiology Study where we are interested in the characteristics of all newly diagnosed chondrosarcoma patients.

8.8 Analysis

8.8.1 Federated network analyses

Analyses will be conducted separately for each database. Before the study initiation, the analytics are tested on a subset of the data sources or a simulated set of patients, and quality control checks are performed. Once all the tests are passed, the final package is released in the version-controlled study repository for execution against all the participating data sources.

The data partners locally execute the analytics against the OMOP CDM in R Studio and review and approve the default aggregated results before returning them to the Coordination Centre. Sometimes, multiple execution iterations are performed, and additional fine-tuning of the code base is needed. A service desk will be available for support during the study execution.

The study results of all data sources are checked, after which they are made available to the team in the Digital Research Environment (DRE), and the Study Dissemination Phase can start. All results are locked and timestamped for reproducibility and transparency.

R-packages

We will use the R packages “PatientProfiles” for the patient-level characterisation of demographics and description of treatments, ”TreatmentPatterns” for the description of treatment sequences when possible, and ”CohortSurvival” for the estimation of overall survival.

8.8.2 Patient privacy protection

Cell count suppression will be applied as required by databases to protect people’s privacy. Cell counts of less than five will be masked.

8.8.3 Primary, secondary, and subgroup analysis

Descriptive analysis

Age and sex will be described at the index date for each generated study cohort. The index date will be the date of the chondrosarcoma diagnosis for each patient.

Treatment characterization

The number and proportion of patients receiving each of a pre-specified list of chondrosarcoma treatments will be described at index date, 0 to 90, 91 to 365, and >365 days post index date. When available, treatment sequences will also be described. When possible, sunburst plots and Sankey diagrams will describe treatment sequences over time. Sankey diagrams will be limited with three layers of treatment. Sunbursts diagrams will be censored at the third line of treatment, as described in Section 8.5.

Overall survival

Overall survival will be calculated using data on time at risk of death from any cause and the KM. Results will be reported as plots of the estimated survival curves and the estimated probability of survival at years 1, 3, 5 and 10. Individuals who are lost to follow-up will be censored at the time of loss of follow-up. The KM approach implicitly assumes censoring occurs at random. This analysis will be conducted only for databases that systematically collect data on mortality. For all analyses, numbers and proportions will be reported.

Subgrouping

All analyses will be reported by country/database, overall and stratified by age and sex when possible (minimum cell count reached) and (AJCC\UICC TNM stage groups, chondrosarcoma histological subtypes, tumour site and histological grades (see **Appendix I Table A2**), as mentioned in Section 8.6.3).

Treatment characterization in objective 2 will also be stratified by non-pharmacological treatment options (surgery and radiation) when possible.

The type of analysis can be observed from **Table 8**.

Table 8. Description of Study Types and Type of Analysis.

STUDY TYPE	STUDY CLASSIFICATION	TYPE OF ANALYSIS
Patient-level characterisation	Off-the-shelf	- Patient-level characteristics - Prognosis / progression to a pre-specified outcome - Standard care description

8.8.4 Sensitivity analysis

In data sources that can differentiate between conventional and non-conventional chondrosarcoma a sensitivity analysis will be performed by running all study objectives in a cohort of patients with conventional chondrosarcoma only (i.e. excluding patients with a chondrosarcoma code listed in Table A2 in Appendix I).

8.9 Evidence synthesis

Results from analyses described in section 8.8 will be presented separately for each database, and no meta-analysis of results will be conducted.

9. DATA MANAGEMENT

9.1 Data management

All databases are mapped to the OMOP CDM. This enables the use of standardised analytics and tools across the network since the structure of the data and the terminology system are harmonised. The OMOP CDM is developed and maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative and is described in detail on the wiki page of the Common Data Model (CDM): https://ohdsi.github.io/CommonDataModel and in The Book of OHDSI: https://book.ohdsi.org

The analytic code for this study will be written in R. Each data partner will execute the study code against their database containing patient-level data and return the results set, which will only contain aggregated data. The results from each contributing data site will be combined in tables and figures for the study report.

9.2 Data storage and protection

For this study, participants from various European Union (EU) member states will process personal data from individuals, which is collected in national/regional electronic health record databases. Due to the sensitive nature of this personal medical data, it is important to be fully aware of ethical and regulatory aspects and to strive to take all reasonable measures to ensure compliance with ethical and regulatory issues on privacy.

All databases used in this study are already used for pharmaco-epidemiological research and have a well-developed mechanism to ensure that European and local regulations dealing with ethical use of the data and adequate privacy control are adhered to. In agreement with these regulations, rather than combining person-level data and performing only a central analysis, local analyses will be run, which generate non-identifiable aggregate summary results.

The output files are stored in the DARWIN EU DRE. These output files do not contain any data that allows identification of subjects included in the study. The DRE implements further security measures to ensure a high level of stored data protection to comply with the local implementation of the General Data Protection Regulation (GPRD) (EU) 679/20161 in the various member states.

10. QUALITY CONTROL

10.1 General database quality control

Several open-source quality control mechanisms for the OMOP CDM have been developed (see Chapter 15 of The Book of OHDSI (https://book.ohdsi.org/DataQuality.html). In particular, data partners are expected to run the OHDSI Data Quality Dashboard tool (https://github.com/OHDSI/DataQualityDashboard). This tool checks the mapped data's conformance, completeness and plausibility. Conformance focuses on checks that describe the compliance of data representation against internal or external formatting, relational, or computational definitions; completeness assessment is solely focused on quantifying missingness or the absence of data, while plausibility seeks to determine the believability or truthfulness of data values. Each category has one or more subcategories and is evaluated in two contexts - validation and verification. Validation relates to how well data align with external benchmarks with expectations derived from known true standards, while verification relates to how well data conform to local knowledge, metadata descriptions, and system assumptions.

10.2 Study specific quality control

When defining chondrosarcoma, a systematic search of possible codes for inclusion was previously identified using CodelistGenerator R package (https://github.com/darwin-eu/CodelistGenerator).

This software allows the user to define a search strategy and then query the vocabulary tables of the OMOP CDM to find potentially relevant codes. Two clinical epidemiologists then reviewed the codes returned to consider their relevance.

In addition, the CohortDiagnostics R package (https://github.com/OHDSI/CohortDiagnostics) will be run to assess the use of different codes across the databases contributing to the study and identify any codes potentially omitted in error. This will allow for a consideration of the validity of the study cohort of patients with multiple myeloma in each of the databases and inform decisions around whether multiple definitions are required. The study code will be based on three R packages currently being developed to (1) characterise demographics and characteristics ("PatientProfiles"), (2) characterise treatment patterns ("TreatmentPatterns"), and (3) estimate overall survival using the OMOP CDM ("CohortSurvival"). These packages will include numerous automated unit tests to ensure the validity of the codes, alongside software peer review and user testing. All these packages are available in GitHub (https://github.com/orgs/darwin-eu/).

11. LIMITATIONS OF THE RESEARCH METHODS

The study will be informed by routinely collected healthcare data, so data quality issues must be considered. In particular, the identification of chondrosarcoma patients may vary across databases. While relatively few false positives would be expected, false negatives may be more likely, especially for databases that do not have patient-level linkage to secondary care data. Nevertheless, at least one database contains high-quality data on cancer diagnoses. Previously published studies on chondrosarcoma used NCR) Dutch data from the NCR [3]. Data from Helsinki University Hospital were also previously used for chondrosarcoma studies [9]. Helsinki University Hospital is among several comprehensive cancer centres specialising in cancer care treatment.

In addition, in databases with information on cancer treatment, the recording of treatment use may be incomplete. This may occur particularly for newly available treatments, which might not have been mapped to the OMOP CDM. However, most databases have updated their mapping in the last 6 months.

Another limitation is related to chondrosarcoma grading, which may not be present in some databases or might not have been mapped to the OMOP CDM. Histological subtypes (conventional, undifferentiated, mesenchymal and clear cell; see sections 8.5 and 8.6.3.) might also not be present or mapped. In that case, the abovementioned subgroups will be analysed only in databases with these data.

12. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

In agreement with the guideline on good pharmacovigilance practice (EMA/873138/2011), there will be no requirement for expedited reporting of adverse drug reactions as only secondary data will be used in this study.

13. GOVERNANCE BOARD ASPECTS

All data sources require their respective Institutional Review Board (IRB)s approvals.

14. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

14.1 Study report

A PDF report, including an executive summary and the specified tables and/or figures, will be submitted to the European Medicines Agency (EMA) by the DARWIN EU® coordination centre upon completion of the study. An interactive dashboard incorporating all the results (tables and figures) will be provided alongside the PDF report. The full set of underlying aggregated data used in the dashboard will also be made available if requested.

15. OTHER ASPECTS

None.

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17. ANNEXES

Appendix I: Definitions

Table A1. Conventional Chondrosarcoma Concept IDs

37151900	Chondrosarcoma
40481938	Chondrosarcoma
40486574	Chondrosarcoma of bone
607436	Chondrosarcoma of bone of pelvic wall
607437	Chondrosarcoma of clavicle
37162938	Chondrosarcoma of gingiva
607434	Chondrosarcoma of mandible
607435	Chondrosarcoma of rib
607438	Chondrosarcoma of skull
607433	Chondrosarcoma of sternum
607439	Chondrosarcoma of vertebral column
45773107	Chondrosarcoma, grade 2
45766523	Chondrosarcoma, grade 3
36534641	Chondrosarcoma, NOS, of accessory sinus, NOS
36523756	Chondrosarcoma, NOS, of acoustic nerve
42511630	Chondrosarcoma, NOS, of anterior wall of nasopharynx
42512935	Chondrosarcoma, NOS, of body of penis
36524031	Chondrosarcoma, NOS, of bones of skull and face and associated joints
36551284	Chondrosarcoma, NOS, of brain stem
44499912	Chondrosarcoma, NOS, of brain, NOS
36533603	Chondrosarcoma, NOS, of cauda equina
36550660	Chondrosarcoma, NOS, of cerebellum, NOS
36535191	Chondrosarcoma, NOS, of cerebral meninges
36551471	Chondrosarcoma, NOS, of cerebrum
42512383	Chondrosarcoma, NOS, of connective, Subcutaneous and other soft tissues of head, face, and neck
36529266	Chondrosarcoma, NOS, of connective, Subcutaneous and other soft tissues of lower limb and hip
36537890	Chondrosarcoma, NOS, of connective, Subcutaneous and other soft tissues of pelvis
42511882	Chondrosarcoma, NOS, of connective, Subcutaneous and other soft tissues of thorax
36518305	Chondrosarcoma, NOS, of connective, Subcutaneous and other soft tissues of trunk, NOS
36538559	Chondrosarcoma, NOS, of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36527602	Chondrosarcoma, NOS, of cranial nerve, NOS
44501747	Chondrosarcoma, NOS, of dome of bladder
36545965	Chondrosarcoma, NOS, of ethmoid sinus
44499586	Chondrosarcoma, NOS, of frontal lobe
36540261	Chondrosarcoma, NOS, of frontal sinus
36526411	Chondrosarcoma, NOS, of glottis
36520352	Chondrosarcoma, NOS, of hypopharyngeal aspect of aryepiglottic fold
36547692	Chondrosarcoma, NOS, of hypopharynx, NOS
36563462	Chondrosarcoma, NOS, of laryngeal cartilage
44502056	Chondrosarcoma, NOS, of larynx, NOS
36548029	Chondrosarcoma, NOS, of long bones of lower limb and associated joints
36518039	Chondrosarcoma, NOS, of long bones of upper limb, scapula and associated joints
44499598	Chondrosarcoma, NOS, of mandible
36549873	Chondrosarcoma, NOS, of maxillary sinus
36527279	Chondrosarcoma, NOS, of meninges, NOS
36544650	Chondrosarcoma, NOS, of nasal cavity
42512891	Chondrosarcoma, NOS, of nasopharynx, NOS
36541137	Chondrosarcoma, NOS, of nervous system, NOS
36529737	Chondrosarcoma, NOS, of occipital lobe
36532862	Chondrosarcoma, NOS, of olfactory nerve
36565610	Chondrosarcoma, NOS, of optic nerve
42512428	Chondrosarcoma, NOS, of ovary
36535535	Chondrosarcoma, NOS, of overlapping lesion of accessory sinuses

36532068	Chondrosarcoma, NOS, of overlapping lesion of bladder
36529826	Chondrosarcoma, NOS, of overlapping lesion of bones, joints and articular cartilage
36534535	Chondrosarcoma, NOS, of overlapping lesion of bones, joints and articular cartilage of limbs
36546085	Chondrosarcoma, NOS, of overlapping lesion of brain
36533147	Chondrosarcoma, NOS, of overlapping lesion of brain and central nervous system
36531275	Chondrosarcoma, NOS, of overlapping lesion of hypopharynx
36522901	Chondrosarcoma, NOS, of overlapping lesion of larynx
36554271	Chondrosarcoma, NOS, of parietal lobe
36529504	Chondrosarcoma, NOS, of pelvic bones, sacrum, coccyx and associated joints
36546977	Chondrosarcoma, NOS, of postcricoid region
36564901	Chondrosarcoma, NOS, of posterior wall of hypopharynx
36559448	Chondrosarcoma, NOS, of prostate gland
36538017	Chondrosarcoma, NOS, of pyriform sinus
44503177	Chondrosarcoma, NOS, of retroperitoneum
36526470	Chondrosarcoma, NOS, of rib, sternum, clavicle and associated joints
36557249	Chondrosarcoma, NOS, of short bones of lower limb and associated joints
36538913	Chondrosarcoma, NOS, of short bones of upper limb and associated joints
36535268	Chondrosarcoma, NOS, of sphenoid sinus
36551347	Chondrosarcoma, NOS, of spinal cord
36556860	Chondrosarcoma, NOS, of spinal meninges
36535371	Chondrosarcoma, NOS, of subglottis
36518500	Chondrosarcoma, NOS, of supraglottis
36563136	Chondrosarcoma, NOS, of temporal lobe
44502133	Chondrosarcoma, NOS, of trachea
36519748	Chondrosarcoma, NOS, of ventricle, NOS
44501863	Chondrosarcoma, NOS, of vertebral column
4028692	Clear cell chondrosarcoma
36534545	Clear cell chondrosarcoma of autonomic nervous system, NOS
36535201	Clear cell chondrosarcoma of bone of limb, NOS
36564258	Clear cell chondrosarcoma of bone, NOS
36526737	Clear cell chondrosarcoma of bones of skull and face and associated joints
36564132	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of abdomen
36556686	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of head, face, and neck
36526745	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of lower limb and hip
36522616	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of pelvis
36533886	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of thorax
36527978	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of trunk, NOS
36526660	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36539180	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues, NOS
42511684	Clear cell chondrosarcoma of laryngeal cartilage
36535683	Clear cell chondrosarcoma of long bones of lower limb and associated joints
36564835	Clear cell chondrosarcoma of long bones of upper limb, scapula and associated joints
36537788	Clear cell chondrosarcoma of mandible
36537195	Clear cell chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36564498	Clear cell chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36538216	Clear cell chondrosarcoma of overlapping lesion of connective, subcutaneous and other soft tissues
36518295	Clear cell chondrosarcoma of overlapping lesion of peripheral nerves and autonomic nervous system
36530851	Clear cell chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
36552197	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of abdomen
36556938	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of head, face, and neck
36559564	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of lower limb and hip
36541972	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of pelvis
36520663	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of thorax
36550393	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of trunk, NOS
36527454	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of upper limb and shoulder
36525914	Clear cell chondrosarcoma of rib, sternum, clavicle and associated joints
36541718	Clear cell chondrosarcoma of short bones of lower limb and associated joints
36535736	Clear cell chondrosarcoma of short bones of upper limb and associated joints
36523751	Clear cell chondrosarcoma of vertebral column

37207682	Conventional central chondrosarcoma tumour and germline WGS (whole genome sequencing)
4029031	Dedifferentiated chondrosarcoma
36541913	Dedifferentiated chondrosarcoma of autonomic nervous system, NOS
36547961	Dedifferentiated chondrosarcoma of bone of limb, NOS
36527824	Dedifferentiated chondrosarcoma of bone, NOS
36562329	Dedifferentiated chondrosarcoma of bones of skull and face and associated joints
36551597	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of abdomen
36534710	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of head, face, and neck
36558682	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of lower limb and hip
36519746	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of pelvis
36547274	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of thorax
36556041	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of trunk, NOS
36545734	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36544020	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues, NOS
36530319	Dedifferentiated chondrosarcoma of long bones of lower limb and associated joints
36521865	Dedifferentiated chondrosarcoma of long bones of upper limb, scapula and associated joints
36539340	Dedifferentiated chondrosarcoma of mandible
36549870	Dedifferentiated chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36553941	Dedifferentiated chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36562669	Dedifferentiated chondrosarcoma of overlapping lesion of connective, subcutaneous and other soft tissues
36534973	Dedifferentiated chondrosarcoma of overlapping lesion of peripheral nerves and autonomic nervous system
36549134	Dedifferentiated chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
36545787	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of abdomen
36563241	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of head, face, and neck
36559047	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of lower limb and hip
36529873	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of pelvis
36530294	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of thorax
36526712	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of trunk, NOS
36534410	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of upper limb and shoulder
36563608	Dedifferentiated chondrosarcoma of rib, sternum, clavicle and associated joints
36541869	Dedifferentiated chondrosarcoma of short bones of lower limb and associated joints
36524419	Dedifferentiated chondrosarcoma of short bones of upper limb and associated joints
36561917	Dedifferentiated chondrosarcoma of vertebral column
4094509	Juxtacortical chondrosarcoma
4209580	Mesenchymal chondrosarcoma
36567464	Mesenchymal chondrosarcoma of accessory sinus, NOS
36537160	Mesenchymal chondrosarcoma of autonomic nervous system, NOS
36526302	Mesenchymal chondrosarcoma of bone of limb, NOS
36558815	Mesenchymal chondrosarcoma of bone, NOS
36522746	Mesenchymal chondrosarcoma of bones of skull and face and associated joints
36529880	Mesenchymal chondrosarcoma of cerebral meninges
36532686	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of abdomen
36547128	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of head, face, and neck
36541806	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of lower limb and hip
36526673	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of pelvis
36553616	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of thorax
36538170	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of trunk, NOS
36530577	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36561252	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues, NOS
36523867	Mesenchymal chondrosarcoma of ethmoid sinus
36555967	Mesenchymal chondrosarcoma of frontal sinus
36554653	Mesenchymal chondrosarcoma of long bones of lower limb and associated joints
36561410	Mesenchymal chondrosarcoma of long bones of upper limb, scapula and associated joints
36520760	Mesenchymal chondrosarcoma of mandible
44501291	Mesenchymal chondrosarcoma of maxillary sinus
36558448	Mesenchymal chondrosarcoma of meninges, NOS
36535126	Mesenchymal chondrosarcoma of nasal cavity

730576	Mesenchymal chondrosarcoma of nervous system, NOS
36559413	Mesenchymal chondrosarcoma of overlapping lesion of accessory sinuses
36554862	Mesenchymal chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36521506	Mesenchymal chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36558095	Mesenchymal chondrosarcoma of overlapping lesion of connective, subcutaneous and other soft tissues
36549191	Mesenchymal chondrosarcoma of overlapping lesion of peripheral nerves and autonomic nervous system
44501105	Mesenchymal chondrosarcoma of parietal lobe
36549848	Mesenchymal chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
36558215	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of abdomen
36556153	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of head, face, and neck
36535054	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of lower limb and hip
36553329	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of pelvis
36552040	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of thorax
36556462	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of trunk, NOS
36523227	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of upper limb and shoulder
42512942	Mesenchymal chondrosarcoma of retroperitoneum
36565209	Mesenchymal chondrosarcoma of rib, sternum, clavicle and associated joints
36526023	Mesenchymal chondrosarcoma of short bones of lower limb and associated joints
36562445	Mesenchymal chondrosarcoma of short bones of upper limb and associated joints
36531428	Mesenchymal chondrosarcoma of sphenoid sinus
36548053	Mesenchymal chondrosarcoma of spinal meninges
36557713	Mesenchymal chondrosarcoma of vertebral column
37207540	Mesenchymal chondrosarcoma tumour and germline WGS (whole genome sequencing)
4328092	Myxoid chondrosarcoma
36557238	Myxoid chondrosarcoma of bone of limb, NOS
36544751	Myxoid chondrosarcoma of bone, NOS
36549378	Myxoid chondrosarcoma of bones of skull and face and associated joints
44502584	Myxoid chondrosarcoma of brain, NOS
36531230	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of abdomen
36567516	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of head, face, and neck
36529383	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of lower limb and hip
36563461	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of pelvis
36529095	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of thorax
36561941	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of trunk, NOS
36533470	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36535870	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues, NOS
42512852	Myxoid chondrosarcoma of laryngeal cartilage
36540963	Myxoid chondrosarcoma of long bones of lower limb and associated joints
36542064	Myxoid chondrosarcoma of long bones of upper limb, scapula and associated joints
42512923	Myxoid chondrosarcoma of lung, NOS
36556500	Myxoid chondrosarcoma of mandible
36547671	Myxoid chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36557726	Myxoid chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36531067	Myxoid chondrosarcoma of overlapping lesion of brain
36540285	Myxoid chondrosarcoma of overlapping lesion of connective, subcutaneous and other soft tissues
36561481	Myxoid chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
42511997	Myxoid chondrosarcoma of posterior mediastinum
44500820	Myxoid chondrosarcoma of retroperitoneum
36533058	Myxoid chondrosarcoma of rib, sternum, clavicle and associated joints
36534364	Myxoid chondrosarcoma of short bones of lower limb and associated joints
36548525	Myxoid chondrosarcoma of short bones of upper limb and associated joints
44502736	Myxoid chondrosarcoma of ventricle, NOS
44503049	Myxoid chondrosarcoma of vertebral column
42513751	Neoplasm defined only by histology: Clear cell chondrosarcoma
42513752	Neoplasm defined only by histology: Dedifferentiated chondrosarcoma
42513749	Neoplasm defined only by histology: Mesenchymal chondrosarcoma
42513748	Neoplasm defined only by histology: Myxoid chondrosarcoma
42513744	Neoplasm defined only by histology: Periosteal chondrosarcoma
2102793	NR4A3, RBF56, or TCF12 (myxoid chondrosarcoma) (Deprecated)

36558653	Periosteal chondrosarcoma of bone of limb, NOS
36541445	Periosteal chondrosarcoma of bone, NOS
36544561	Periosteal chondrosarcoma of bones of skull and face and associated joints
36520008	Periosteal chondrosarcoma of glottis
36538806	Periosteal chondrosarcoma of laryngeal cartilage
36544844	Periosteal chondrosarcoma of larynx, NOS
36540974	Periosteal chondrosarcoma of long bones of lower limb and associated joints
36533938	Periosteal chondrosarcoma of long bones of upper limb, scapula and associated joints
36534232	Periosteal chondrosarcoma of mandible
36547380	Periosteal chondrosarcoma of nasal cavity
36539588	Periosteal chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36563361	Periosteal chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36547009	Periosteal chondrosarcoma of overlapping lesion of larynx
36553907	Periosteal chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
36530596	Periosteal chondrosarcoma of rib, sternum, clavicle and associated joints
36519044	Periosteal chondrosarcoma of short bones of lower limb and associated joints
36562042	Periosteal chondrosarcoma of short bones of upper limb and associated joints
36561619	Periosteal chondrosarcoma of subglottis
36565377	Periosteal chondrosarcoma of supraglottis
36545603	Periosteal chondrosarcoma of trachea
36544240	Periosteal chondrosarcoma of vertebral column
42539037	Primary chondrosarcoma of articular cartilage
37109898	Primary chondrosarcoma of articular cartilage of limb
37109899	Primary chondrosarcoma of articular cartilage of pelvis
37109900	Primary chondrosarcoma of articular cartilage of rib
42539556	Primary chondrosarcoma of bone
602670	Primary chondrosarcoma of bone of left foot
602671	Primary chondrosarcoma of bone of left hand
602672	Primary chondrosarcoma of bone of left lower limb
602669	Primary chondrosarcoma of bone of left upper limb
37109897	Primary chondrosarcoma of bone of limb
37018647	Primary chondrosarcoma of bone of lower limb
37018646	Primary chondrosarcoma of bone of pelvis
37119229	Primary chondrosarcoma of bone of rib
602153	Primary chondrosarcoma of bone of right foot
602154	Primary chondrosarcoma of bone of right hand
602155	Primary chondrosarcoma of bone of right lower limb
602152	Primary chondrosarcoma of bone of right upper limb
37018644	Primary chondrosarcoma of bone of upper limb
602673	Primary chondrosarcoma of left scapula
602036	Primary chondrosarcoma of mandible
602674	Primary chondrosarcoma of right scapula
609187	Primary chondrosarcoma of sternum
602037	Primary chondrosarcoma of vertebral column

Table A2. Non-conventional chondrosarcoma Concept IDs

Concept ID	Concept name
Mesenchymal chondrosarcoma	
42513749	Neoplasm defined only by histology: Mesenchymal chondrosarcoma
37207540	Mesenchymal chondrosarcoma tumour and germline WGS (whole genome sequencing)
36557713	Mesenchymal chondrosarcoma of vertebral column
36548053	Mesenchymal chondrosarcoma of spinal meninges
36531428	Mesenchymal chondrosarcoma of sphenoid sinus
36562445	Mesenchymal chondrosarcoma of short bones of upper limb and associated joints
36526023	Mesenchymal chondrosarcoma of short bones of lower limb and associated joints
36565209	Mesenchymal chondrosarcoma of rib, sternum, clavicle and associated joints

42512942	Mesenchymal chondrosarcoma of retroperitoneum
36523227	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of upper limb and shoulder
36556462	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of trunk, NOS
36552040	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of thorax
36553329	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of pelvis
36535054	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of lower limb and hip
36556153	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of head, face, and neck
36558215	Mesenchymal chondrosarcoma of peripheral nerves and autonomic nervous system of abdomen
36549848	Mesenchymal chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
44501105	Mesenchymal chondrosarcoma of parietal lobe
36549191	Mesenchymal chondrosarcoma of overlapping lesion of peripheral nerves and autonomic nervous system
36558095	Mesenchymal chondrosarcoma of overlapping lesion of connective, subcutaneous and other soft tissues
36521506	Mesenchymal chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36554862	Mesenchymal chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36559413	Mesenchymal chondrosarcoma of overlapping lesion of accessory sinuses
730576	Mesenchymal chondrosarcoma of nervous system, NOS
36535126	Mesenchymal chondrosarcoma of nasal cavity
36558448	Mesenchymal chondrosarcoma of meninges, NOS
44501291	Mesenchymal chondrosarcoma of maxillary sinus
36520760	Mesenchymal chondrosarcoma of mandible
36561410	Mesenchymal chondrosarcoma of long bones of upper limb, scapula and associated joints
36554653	Mesenchymal chondrosarcoma of long bones of lower limb and associated joints
36555967	Mesenchymal chondrosarcoma of frontal sinus
36523867	Mesenchymal chondrosarcoma of ethmoid sinus
36561252	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues, NOS
36530577	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36538170	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of trunk, NOS
36553616	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of thorax
36526673	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of pelvis
36541806	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of lower limb and hip
36547128	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of head, face, and neck
36532686	Mesenchymal chondrosarcoma of connective, Subcutaneous and other soft tissues of abdomen
36529880	Mesenchymal chondrosarcoma of cerebral meninges
36522746	Mesenchymal chondrosarcoma of bones of skull and face and associated joints
36558815	Mesenchymal chondrosarcoma of bone, NOS
36526302	Mesenchymal chondrosarcoma of bone of limb, NOS
36537160	Mesenchymal chondrosarcoma of autonomic nervous system, NOS
36567464	Mesenchymal chondrosarcoma of accessory sinus, NOS
4209580	Mesenchymal chondrosarcoma
Dedifferentiated chondrosarcoma	
42513752	Neoplasm defined only by histology: Dedifferentiated chondrosarcoma
36561917	Dedifferentiated chondrosarcoma of vertebral column
36524419	Dedifferentiated chondrosarcoma of short bones of upper limb and associated joints
36541869	Dedifferentiated chondrosarcoma of short bones of lower limb and associated joints
36563608	Dedifferentiated chondrosarcoma of rib, sternum, clavicle and associated joints
36534410	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of upper limb and shoulder
36526712	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of trunk, NOS
36530294	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of thorax
36529873	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of pelvis
36559047	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of lower limb and hip
36563241	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of head, face, and neck

36545787	Dedifferentiated chondrosarcoma of peripheral nerves and autonomic nervous system of abdomen
36549134	Dedifferentiated chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
36534973	Dedifferentiated chondrosarcoma of overlapping lesion of peripheral nerves and autonomic nervous system
36562669	Dedifferentiated chondrosarcoma of overlapping lesion of connective, subcutaneous and other soft tissues
36553941	Dedifferentiated chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36549870	Dedifferentiated chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36539340	Dedifferentiated chondrosarcoma of mandible
36521865	Dedifferentiated chondrosarcoma of long bones of upper limb, scapula and associated joints
36530319	Dedifferentiated chondrosarcoma of long bones of lower limb and associated joints
36544020	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues, NOS
36545734	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36556041	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of trunk, NOS
36547274	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of thorax
36519746	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of pelvis
36558682	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of lower limb and hip
36534710	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of head, face, and neck
36551597	Dedifferentiated chondrosarcoma of connective, Subcutaneous and other soft tissues of abdomen
36562329	Dedifferentiated chondrosarcoma of bones of skull and face and associated joints
36527824	Dedifferentiated chondrosarcoma of bone, NOS
36547961	Dedifferentiated chondrosarcoma of bone of limb, NOS
36541913	Dedifferentiated chondrosarcoma of autonomic nervous system, NOS
4029031	Dedifferentiated chondrosarcoma
Clear cell chondrosarcoma	
42513751	Neoplasm defined only by histology: Clear cell chondrosarcoma
36523751	Clear cell chondrosarcoma of vertebral column
36535736	Clear cell chondrosarcoma of short bones of upper limb and associated joints
36541718	Clear cell chondrosarcoma of short bones of lower limb and associated joints
36525914	Clear cell chondrosarcoma of rib, sternum, clavicle and associated joints
36527454	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of upper limb and shoulder
36550393	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of trunk, NOS
36520663	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of thorax
36541972	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of pelvis
36559564	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of lower limb and hip
36556938	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of head, face, and neck
36552197	Clear cell chondrosarcoma of peripheral nerves and autonomic nervous system of abdomen
36530851	Clear cell chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
36518295	Clear cell chondrosarcoma of overlapping lesion of peripheral nerves and autonomic nervous system
36538216	Clear cell chondrosarcoma of overlapping lesion of connective, subcutaneous and other soft tissues
36564498	Clear cell chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36537195	Clear cell chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36537788	Clear cell chondrosarcoma of mandible
36564835	Clear cell chondrosarcoma of long bones of upper limb, scapula and associated joints
36535683	Clear cell chondrosarcoma of long bones of lower limb and associated joints
42511684	Clear cell chondrosarcoma of laryngeal cartilage
36539180	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues, NOS
36526660	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36527978	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of trunk, NOS
36533886	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of thorax
36522616	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of pelvis
36526745	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of lower limb and hip
36556686	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of head, face, and neck

36564132	Clear cell chondrosarcoma of connective, Subcutaneous and other soft tissues of abdomen
36526737	Clear cell chondrosarcoma of bones of skull and face and associated joints
36564258	Clear cell chondrosarcoma of bone, NOS
36535201	Clear cell chondrosarcoma of bone of limb, NOS
36534545	Clear cell chondrosarcoma of autonomic nervous system, NOS
4028692	Clear cell chondrosarcoma
Myxoid chondrosarcoma	
4328092	Myxoid chondrosarcoma
36557238	Myxoid chondrosarcoma of bone of limb, NOS
36544751	Myxoid chondrosarcoma of bone, NOS
36549378	Myxoid chondrosarcoma of bones of skull and face and associated joints
44502584	Myxoid chondrosarcoma of brain, NOS
36531230	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of abdomen
36567516	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of head, face, and neck
36529383	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of lower limb and hip
36563461	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of pelvis
36529095	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of thorax
36561941	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of trunk, NOS
36533470	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues of upper limb and shoulder
36535870	Myxoid chondrosarcoma of connective, Subcutaneous and other soft tissues, NOS
42512852	Myxoid chondrosarcoma of laryngeal cartilage
36540963	Myxoid chondrosarcoma of long bones of lower limb and associated joints
36542064	Myxoid chondrosarcoma of long bones of upper limb, scapula and associated joints
42512923	Myxoid chondrosarcoma of lung, NOS
36556500	Myxoid chondrosarcoma of mandible
36547671	Myxoid chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36557726	Myxoid chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36531067	Myxoid chondrosarcoma of overlapping lesion of brain
36540285	Myxoid chondrosarcoma of overlapping lesion of connective, subcutaneous and other soft tissues
36561481	Myxoid chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
42511997	Myxoid chondrosarcoma of posterior mediastinum
44500820	Myxoid chondrosarcoma of retroperitoneum
36533058	Myxoid chondrosarcoma of rib, sternum, clavicle and associated joints
36534364	Myxoid chondrosarcoma of short bones of lower limb and associated joints
36548525	Myxoid chondrosarcoma of short bones of upper limb and associated joints
44502736	Myxoid chondrosarcoma of ventricle, NOS
44503049	Myxoid chondrosarcoma of vertebral column
42513748	Neoplasm defined only by histology: Myxoid chondrosarcoma
2102793	NR4A3, RBF56, or TCF12 (myxoid chondrosarcoma) (Deprecated)
Periostal chondrosarcoma	
42513744	Neoplasm defined only by histology: Periosteal chondrosarcoma
36541445	Periosteal chondrosarcoma of bone, NOS
36544561	Periosteal chondrosarcoma of bones of skull and face and associated joints
36520008	Periosteal chondrosarcoma of glottis
36538806	Periosteal chondrosarcoma of laryngeal cartilage
36544844	Periosteal chondrosarcoma of larynx, NOS
36540974	Periosteal chondrosarcoma of long bones of lower limb and associated joints
36533938	Periosteal chondrosarcoma of long bones of upper limb, scapula and associated joints
36534232	Periosteal chondrosarcoma of mandible
36547380	Periosteal chondrosarcoma of nasal cavity

36539588	Periosteal chondrosarcoma of overlapping lesion of bones, joints and articular cartilage
36563361	Periosteal chondrosarcoma of overlapping lesion of bones, joints and articular cartilage of limbs
36547009	Periosteal chondrosarcoma of overlapping lesion of larynx
36553907	Periosteal chondrosarcoma of pelvic bones, sacrum, coccyx and associated joints
36530596	Periosteal chondrosarcoma of rib, sternum, clavicle and associated joints
36519044	Periosteal chondrosarcoma of short bones of lower limb and associated joints
36562042	Periosteal chondrosarcoma of short bones of upper limb and associated joints
36561619	Periosteal chondrosarcoma of subglottis
36565377	Periosteal chondrosarcoma of supraglottis
36545603	Periosteal chondrosarcoma of trachea
36544240	Periosteal chondrosarcoma of vertebral column
36558653	Periosteal chondrosarcoma of bone of limb, NOS
4094509	Juxtacortical chondrosarcoma

Table A3. Preliminary Code list for chondrosarcoma pharmacological management options

Drug	Class	Concept ID	RxNorm
carboplatin	Chemotherapy	1344905	40048
cisplatin	Chemotherapy	1397599	2555
cyclophosphamide	Chemotherapy	1310317	3002
dactinomycin	Chemotherapy	1311443	3100
decitabine	Chemotherapy	19024728	15657
docetaxel	Chemotherapy	1315942	72962
doxorubicin	Chemotherapy	1338512	3639
etoposide	Chemotherapy	1350504	4179
gemcitabine	Chemotherapy	1314924	12574
ifosfamide	Chemotherapy	19078187	5657
irinotecan	Chemotherapy	1367268	51499
methotrexate	Chemotherapy	1305058	6851
temozolomide	Chemotherapy	1341149	37776
topotecan	Chemotherapy	1378509	57308
vincristine	Chemotherapy	1308290	11202
ivosidenib	IDH1 inhibitor	1560123	2049873
enasidenib	IDH2 inhibitor	1940332	793797
everolimus	mTOR kinase inhibitor	19011440	141704
toripalimab	PD-1 inhibitor	747052	2669406
retifanlimab	PD-1 inhibitor	1302024	2632981
dostarlimab	PD-1 inhibitor	1536789	2539967
cemiplimab	PD-1 inhibitor	35200783	2058826
pembrolizumab	PD-1 inhibitor	45775965	1547545
nivolumab	PD-1 inhibitor	45892628	1597876
avelumab	PD-L1 inhibitor	1593273	1875534
durvalumab	PD-L1 inhibitor	1594034	1919503
atezolizumab	PD-L1 inhibitor	42629079	1792776
afatinib	TK inhibitor	43533090	1430438
cabozantinib	TK inhibitor	43012292	1363268
dasatinib	TK inhibitor	1358436	475342
lapatinib	TK inhibitor	1359548	480167
lurbinectedin	TK inhibitor	1146139	2374729
pazopanib	TK inhibitor	40167554	714438

regorafenib	TK inhibitor	42903460	1312397
sorafenib	TK inhibitor	1363387	495881

Table A4. Preliminary list oa concept IDS for surgical and radiotherapy procedures

Concept ID	Concept name
3662206	Dissection of lymph node
4001562	Chest wall excision
4003076	Nose excision
4024005	External beam radiation therapy protons
4040441	Iodine 131 meta-iodobenzylguanidine therapy
4045162	Reconstruction procedure
4046732	Embolization procedure
4059385	Radiotherapy - intraoperative control
4059831	Internal radiotherapy - unsealed source
4061550	External beam with internal radiotherapy
4084585	Maxillectomy
4101626	Craniotomy
4107982	Autogenous vascularized bone graft
4118281	Excision of base of skull
4120425	Excision of group of lymph nodes
4120657	Interventional debulking surgery
4120958	Lateral lymph nodes neck dissection
4120961	Excision of axillary lymph node
4131910	Excision of lesion of pelvic wall
4134732	Orbitectomy
4136166	Tumor destruction
4141448	Teleradiotherapy procedure
4144920	Electrocautery operation
4146273	Cryosurgery
4157779	Excision of malignant neoplasm
4161415	Radionuclide therapy
4165515	Total body irradiation
4167550	Mohs surgery
4193369	Complete excision
4217482	Amputation
4219032	Amputation of lower limb
4236996	Scraping
4238646	Excision of lymph node
4250344	Electrocoagulation
4251481	Pedicle graft
4261829	Laser surgery
4273761	Excision of mandible
4279903	Excision
4280798	Reexcision
4285420	Excision of lesion of bone
4301351	Surgical procedure
4304452	Partial excision
4323226	Operative procedure on lumbosacral spinal structure
4338944	Radical excision with lymph node dissection
4346411	Excision of bone
36684841	Microwave ablation
37109332	Intravenous radionuclide therapy
40317890	Brachytherapy
40480519	Intensity modulated radiation therapy
40481912	Excision of sentinel lymph node
40489482	Megavoltage radiation therapy using photons
42872600	Excision of lesion of anterior abdominal wall
44790293	Radiotherapy delivery
44790448	Anterolateral lymph nodes neck dissection
44803149	Partial excision of organ NOC

44803160	Excision of organ NOC
44813718	Laser excision of lesion of organ NOC
45763838	Radium 223 brachytherapy
46272913	Robotic assisted surgery

Table A5. Preliminary list for concept IDS for tumor site

Extremities	
Long bones of upper limb and scapula	
36518039	Chondrosarcoma, NOS, of long bones of upper limb, scapula and associated joints
602152	Primary chondrosarcoma of bone of right upper limb
602669	Primary chondrosarcoma of bone of left upper limb
37018644	Primary chondrosarcoma of bone of upper limb
602673	Primary chondrosarcoma of left scapula
602674	Primary chondrosarcoma of right scapula
Short bones of upper limb	
36538913	Chondrosarcoma, NOS, of short bones of upper limb and associated joints
602671	Primary chondrosarcoma of bone of left hand
602154	Primary chondrosarcoma of bone of right hand
Long bones of the lower limbs	
37018647	Primary chondrosarcoma of bone of lower limb
602155	Primary chondrosarcoma of bone of right lower limb
602672	Primary chondrosarcoma of bone of left lower limb
36548029	Chondrosarcoma, NOS, of long bones of lower limb and associated joints
Short bones of lower limb	
36557249	Chondrosarcoma, NOS, of short bones of lower limb and associated joints
602670	Primary chondrosarcoma of bone of left foot
602153	Primary chondrosarcoma of bone of right foot
Axial skeleton	
Rib, sternum, clavicle	
37119229	Primary chondrosarcoma of bone of rib
36526470	Chondrosarcoma, NOS, of rib, sternum, clavicle and associated joints
37109900	Primary chondrosarcoma of articular cartilage of rib
609187	Primary chondrosarcoma of sternum
607433	Chondrosarcoma of sternum
607435	Chondrosarcoma of rib
607437	Chondrosarcoma of clavicle
Skull and face	
602036	Primary chondrosarcoma of mandible
36546977	Chondrosarcoma, NOS, of postcricoid region
36564901	Chondrosarcoma, NOS, of posterior wall of hypopharynx
36538017	Chondrosarcoma, NOS, of pyriform sinus
36535268	Chondrosarcoma, NOS, of sphenoid sinus
36535371	Chondrosarcoma, NOS, of subglottis
36518500	Chondrosarcoma, NOS, of supraglottis
36535535	Chondrosarcoma, NOS, of overlapping lesion of accessory sinuses
36531275	Chondrosarcoma, NOS, of overlapping lesion of hypopharynx
36522901	Chondrosarcoma, NOS, of overlapping lesion of larynx
44499598	Chondrosarcoma, NOS, of mandible
36549873	Chondrosarcoma, NOS, of maxillary sinus
36544650	Chondrosarcoma, NOS, of nasal cavity
42512891	Chondrosarcoma, NOS, of nasopharynx, NOS
36545965	Chondrosarcoma, NOS, of ethmoid sinus
36540261	Chondrosarcoma, NOS, of frontal sinus
36526411	Chondrosarcoma, NOS, of glottis
36520352	Chondrosarcoma, NOS, of hypopharyngeal aspect of aryepiglottic fold
36547692	Chondrosarcoma, NOS, of hypopharynx, NOS
36563462	Chondrosarcoma, NOS, of laryngeal cartilage
44502056	Chondrosarcoma, NOS, of larynx, NOS
36524031	Chondrosarcoma, NOS, of bones of skull and face and associated joints
42511630	Chondrosarcoma, NOS, of anterior wall of nasopharynx

607438	Chondrosarcoma of skull
37162938	Chondrosarcoma of gingiva
607434	Chondrosarcoma of mandible
Vertebral column	
44501863	Chondrosarcoma, NOS, of vertebral column
602037	Primary chondrosarcoma of vertebral column
607439	Chondrosarcoma of vertebral column
Pelvic bones, sacrum, coccyx	
37018646	Primary chondrosarcoma of bone of pelvis
36529504	Chondrosarcoma, NOS, of pelvic bones, sacrum, coccyx and associated joints
37109899	Primary chondrosarcoma of articular cartilage of pelvis
607436	Chondrosarcoma of bone of pelvic wall

Appendix II: ENCePP checklist for study protocols

ENCePP Checklist for Study Protocols (Revision 4)

Study title: DARWIN EU®- Chondrosarcoma: patient demographics, treatments and survival in the period 2010-2023

EU PAS Register® number: N/A

Study reference number (if applicable): N/A

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1. Does the protocol specify timelines for 1.1.1 Start of data collection[1] 1.1.2 End of data collection[2] 1.1.3 Progress report(s) 1.1.4 Interim report(s) 1.1.5 Registration in the EU PAS Register® 1.1.6 Final report of study results.	X			5. Milestones, 8.2 Data Sources

Comments:

Section 2: Research question	**Yes**	**No**	**N/A**	**Section Number**
2.1 Does the formulation of the research question and objectives clearly explain: 2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue) 2.1.2 The objective(s) of the study? 2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised) 2.1.4 Which hypothesis(-es) is (are) to be tested? 2.1.5 If applicable, that there is no *a priori* hypothesis?	X			7. Research question and objectives 8. Research methods

Comments:

Section 3: Study design	**Yes**	**No**	**N/A**	**Section Number**
3.1 Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	X			8.1 Study type and Study Design
3.2 Does the protocol specify whether the study is based on primary, secondary or combined data collection?	X			8.2 Study Setting and Data Sources
3.3 Does the protocol specify measures of occurrence? (e.g., rate, risk, prevalence)	X			8.8 Analysis

3.4	Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))	X			8.8 Analysis
3.5	Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)			X	

Comments:

Section 4: Source and study populations		**Yes**	**No**	**N/A**	**Section Number**
4.1	Is the source population described?	X			8.5 Study Population
4.2	Is the planned study population defined in terms of:				
	4.2.1 Study time period				8.3 Study Period
	4.2.2 Age and sex	X			8.6.3. Other covariates
	4.2.3 Country of origin				8.2 Study Setting and Data Sources
	4.2.4 Disease/indication				8.6.1. Exposures
	4.2.5 Duration of follow-up				8.4 Follow-up
4.3	Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	X			8.5 Study Population with inclusion and exclusion criteria

Comments:

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.1 Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	X			8.6.1. Exposures
5.2 Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)			X	
5.3 Is exposure categorised according to time windows?	X			8.6.1. Exposures
5.4 Is intensity of exposure addressed? (e.g. dose, duration)	X			8.6.1. Exposures
5.5 Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?			X	
5.6 Is (are) (an) appropriate comparator(s) identified?	X			8.8 Analysis

Comments:

Section 6: Outcome definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	X			8.6.2. Outcomes
6.2 Does the protocol describe how the outcomes are defined and measured?	X			8.6.2. Appendix I

6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)			X	
6.4 Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease or treatment, compliance, disease management)			X	

Comments:

Section 7: Bias	**Yes**	**No**	**N/A**	**Section Number**
7.1 Does the protocol address ways to measure confounding? (e.g. confounding by indication)	X			8.8 Analysis
7.2 Does the protocol address selection bias? (e.g. healthy user/adherer bias)			X	
7.3 Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)	X			8.8 Analysis

Comments:

Section 8: Effect measure modification	**Yes**	**No**	**N/A**	**Section Number**
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	X			8.8 Analysis

Comments:

Section 9: Data sources	**Yes**	**No**	**N/A**	**Section Number**
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	X			8.6.1. Exposures
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	X			8.6.2. Outcomes
9.1.3 Covariates and other characteristics?	X			8.6.3. Other covariates
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	X			8.2 Study Setting and Data Sources
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	X			8.2 Study Setting and Data Sources
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	X			8.2 Study Setting and Data Sources
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	X			8.6.1. Exposures
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	X			8.6.2. Outcomes

9.3.3 Covariates and other characteristics?	X			8.6.3. Other covariates
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)			X	

Comments:

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.1 Are the statistical methods and the reason for their choice described?	X			8.8 Analysis
10.2 Is study size and/or statistical precision estimated?			X	
10.3 Are descriptive analyses included?	X			8.8.2 Descriptive statistics
10.4 Are stratified analyses included?	X			8.8 Analysis
10.5 Does the plan describe methods for analytic control of confounding?	X			8.8 Analysis
10.6 Does the plan describe methods for analytic control of outcome misclassification?	X			8.8 Analysis
10.7 Does the plan describe methods for handling missing data?			X	
10.8 Are relevant sensitivity analyses described?	X			8.8 Analysis

Comments:

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	X			9. Data management
11.2 Are methods of quality assurance described?	X			10. Quality Control
11.3 Is there a system in place for independent review of study results?			X	

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of: 12.1.1 Selection bias? 12.1.2 Information bias? 12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods).	X			11. Limitations of the research methods
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	X			Table 8.2. Description of the selected Data Sources.

Comments:

Section 13: Ethical/data protection issues	**Yes**	**No**	**N/A**	**Section Number**

13.1 Have requirements of Ethics Committee/ Institutional Review Board been described?	X			13. Governance board aspects
13.2 Has any outcome of an ethical review procedure been addressed?			X	
13.3 Have data protection requirements been described?	X			9.2 Data storage and protection

Comments:

Section 14: Amendments and deviations	**Yes**	**No**	**N/A**	**Section Number**
14.1 Does the protocol include a section to document amendments and deviations?	X			4. Amendments and updates

Comments:

Section 15: Plans for communication of study results	**Yes**	**No**	**N/A**	**Section Number**
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	X			14. Plans for disseminating and communicating study results
15.2 Are plans described for disseminating study results externally, including publication?	X			14. Plans for disseminating and communicating study results

Comments:

Name of the main author of the protocol: Talita Duarte-Salles and Anton Barchuk

Date: 24/04/2024

Signature: _____