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

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Version 2.0

Study Title	DARWIN EU®- Chondrosarcoma: patient demographics, treatments, and survival in the period 2010-2023
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Research question and objectives	The overall objective of this study was 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 classification system of malignant tumours (AJCC/UICC TNM) stage categories and histological grade in 2010-2023. The specific objectives of the study were: 1. To describe demographic characteristics (age and sex) of patients with chondrosarcoma at the time of diagnoses. 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 of the study were to describe treatment with medicines 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 or not surgery, radiotherapy, both or neither.
Country(-ies) of study	Finland, France, Spain, The Netherlands, United Kingdom
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TITLE

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

1. DESCRIPTION OF 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	CDWBordeaux
	Romain Griffier	CDWBordeaux
	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. Data analysts/programmers do not have an investigator role, and thus, a declaration of interest (DOI) for these people is not needed.

2. DATA SOURCES

This study used 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 (CDWBordeaux), 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

Country	Name of Database	Health Care setting	Type of Data	Number of active subjects	Calendar period covered by each data source
ES	BIFAP	primary care – GPs, community pharmacists, primary care specialists (e.g. paediatricians), hospital IP care	EHR hospital, claims	22.0 M	Till 2024-03-26
FR	CDWBordeaux	secondary care – specialists (ambulatory or hospital OP care), hospital IP care,	EHR hospital, claims, Biobank	2.2 M	Till 2024-01-17
GB	CPRD GOLD	primary care – GPs, primary care specialists (e.g. paediatricians)	EHR	17.3 M	Till 2024-03-22
FI	FinOMOP - HILMO	Secondary care – specialists (ambulatory or hospital OP care), hospital IP care	EHR, Registries	7.3 M	Till 2024-02-12
FI	FinOMOP - HUS	Secondary care – specialists (ambulatory or hospital OP care), hospital IP care	EHR	3.5 M	Till 2024-02-16
NL	NCR	Cancer registry, primary care, secondary care (ambulatory and hospital care)	Registries	2.5 M	Till 2024-01-01 (follow-up) Till 2022-12-31 (registration)

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.

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 aimed 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

The overall objective of this study was to describe demographics, treatments, and overall survival of patients with incident chondrosarcoma, stratified by age, sex, country/database, and, if available, by the American Joint Committee on Cancer/Union for International Cancer Control Tumour, Nodes, Metastases classification system of malignant tumours (AJCC/UICC TNM) stage categories and histological grade in 2010-2023.

The specific objectives of the study were:

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 of the study were to describe treatment with medicines 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 or not surgery, radiotherapy, both or neither.

Optional objectives were planned to be conducted if data on radiotherapy and/or surgeries was available and there was a sufficient number of patients in each cohort.

Research Methods

Study design

Population-based cohort study.

Population

The study population included all individuals with a first diagnosis of chondrosarcoma identified in each database between 01/01/2010 and 31/12/2022 (in order to allow for minimum one year of potential follow-up). Participants with a diagnosis of cancer (any, excluding non-melanoma skin cancer) before the diagnosis of chondrosarcoma were excluded.

Variables

Two main outcomes of interest were 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 was generated and when possible, patients were classified as having undergone surgery, radiotherapy, none or both. The outcomes were studied in all chondrosarcoma patients and in patients with different AJCC/UICC TNM categories 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 (CDWBordeaux), 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 was a descriptive Disease Epidemiology Study where we were interested in the characteristics of all newly diagnosed chondrosarcoma patients.

Data analyses

We described the age and sex of each patient at the time of chondrosarcoma diagnosis, as well as AJCC/UICC TNM categories 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 was described at index date, 0 to 90, 91 to 365, and >365 days post index date. When possible, this was done separately for patients who had undergone or not surgery, radiotherapy, or both. In addition, results from NCR were stratified by AJCC/UICC TNM categories, chondrosarcoma histological subtypes, tumor site and histological grades.

Overall crude survival (at years 1, 3, 5, and 10) was calculated using data on time at risk of death from any cause and the Kaplan-Meier method (KM). For all analyses, numbers and proportions were reported.

Results

The study described demographics, recorded treatments and overall survival of chondrosarcoma patients across six databases in five European countries. While we could identify chondrosarcoma patients in all of the data sources, the absolute number of patients was low. Overall, in the study period between 2010 and 2022 (14 years) we identified 2,498 patients with an initial diagnosis of chondrosarcoma. The majority of patients were identified in NCR (n=1,449) followed by BIFAP (n=379), FinOMOP-HILMO (n=382) and

FinOMOP-HUS (n=142). Less than 100 patients were identified in CDWBordeaux (n=92) and CPRD GOLD (n=54).

Despite the different nature of data sources, the demographics of chondrosarcoma patients were similar with the median age ranging between 53 and 55 years. Patients with chondrosarcoma were, on average, slightly older in FinOMOP-HILMO and slightly younger in NCR, but in general the distribution between age groups was similar. There was a similar proportion and men and women among chondrosarcoma patients across all databases.

Any specific drug treatment for chondrosarcoma was recorded in four out of six databases and overall, the proportion of patients with any drug treatment options reported did not exceed 5% in different time windows (0-90, 91-365 and more than 365 days after diagnosis). Conventional chemotherapy drugs were recorded more often than any other group. The following records were identified: Carboplatin, Cisplatin, Cyclophosphamide, Dasatinib, Docetaxel, Durvalumab, Etoposide, Gemcitabine, Ifosfamide, Irinotecan, Methotrexate, Nivolumab, Pazopanib, Regorafenib, Temozolomide, Vincristine.

Radiotherapy records were also rare, with a maximum of 6.4% patients in NCR. Surgical procedures were more common than any other treatment options and were identified variably in NCR (88.9% of records), FinOMOP-HILMO (65.2%), CPRD GOLD (57.4%), FinOMOP-HUS (53.5%), CDWBordeaux (15.2%) and BIFAP (6.6%).

Additional variables (Grade, AJCC/UICC Stage and TNM categories, anatomical site) were identified only in the NCR. The majority of cases (55%) were Stage 1, and Stage 4 was present only in 3.7% of patients. Nodal metastases within 180 days after diagnosis were recorded in 1.4% of patients and distant in 4.1%. Most patients had records of well-differentiated tumours -54.6%; moderately differentiated was present in 21.3%, and poorly differentiated only in 8.8%. The majority of patients in NCR had chondrosarcoma of extremities. There were 215 (14.8%) patients with non-conventional chondrosarcoma in NCR.

In terms of overall survival, more than 50% of patients were observed to be still alive in all databases by the end of the 10-year follow-up. Survival estimates were slightly lower in CDWBordeaux, and FinOMOP-HUS, 10-year survival probability was 58% (95%CI: 43, 78) and 61% (95%CI: 50, 75), respectively. 10-year survival probability was higher in NCR - 80% (95%CI: 78, 82) and BIFAP - 79% (95%CI: 74, 84). Overall survival estimates were lower in men compared to women in all databases.

In all subgroup analyses in NCR, survival was consistent with AJCC/UICC staging with patients with later stages having poorer survival. Patients with less differentiated tumours also had lower survival compared to patients with well differentiated tumours. Survival estimates were consistently lower for patients with axial skeleton tumours compared to tumours of extremities. In patients with non-conventional chondrosarcoma, survival was lower with dedifferentiated and myxoid morphology.

Discussion

Chondrosarcoma is a rare condition, and studies that describe the characteristics of patients in large representative databases are not common. Our study included 2,498 cases from six databases over the period between 2010 and 2022.

Our study identified less than 6% of patients with chondrosarcoma had records of any drug treatment, this is in line with previous studies. Similarly, in the National Cancer Database study from the US, drug treatment was identified in less than 7% of chondrosarcoma patients. Of those patients with tumour staging data available, the majority of patients with conventional chondrosarcoma had early-stage and low-grade disease, which is also in line with previous studies and may partially explain the lack of information on drug therapy. Most previous reports of new drug agents in chondrosarcoma are case reports or studies

with limited sample sizes. While this is a problem for most rare diseases, federated analysis across multiple data sources can help identify population and healthcare settings where conducting clinical trials is feasible.

Among the particular ingredients we could identify, most were conventional chemotherapy agents. Still, some records of immunotherapies and targeted agents were also identified. Those drug therapies are limited to off-label use in late-stage, high-grade, and metastatic disease cases.

Overall survival was in line with previous studies. Survival estimates were slightly lower in CDWBordeaux and FinOMOP-HUS and higher in NCR and BIFAP, partially explained by the differences in patient demographics (age and sex), population covered and referral patterns.

In conclusion, different real-world data sources can be successfully used to study chondrosarcoma patients' outcomes and characteristics, and while dedicated registries seem to have more complete and granular data, the combination of different sources allows a better understanding and interpretation of the obtained results.

4. 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
CDWBordeaux	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

5. 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

6. MILESTONES

Study deliverable	Timelines (planned)	Timelines (actual)
Draft Study Protocol	April 2024	April 2024
Final Study Protocol	June 2024	June 2024
Creation of Analytical code	June 2024	May-December 2024
Execution of Analytical Code on the data	July 2024	May-December 2024
Draft Study Report	August 2025	January 2025
Final Study Report	February 2025	12/02/2025

7. 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 presents 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 aimed 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.

8. RESEARCH QUESTION AND OBJECTIVES

The overall objective of this study was 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 classification system of malignant tumours (AJCC/UICC TNM) stage categories and histological grade in 2010-2023.

The specific objectives of the study were:

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 of the study were to describe treatment with medicines 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 or not surgery, radiotherapy, both or neither.

Optional objectives were planned to be conducted if data on radiotherapy and/or surgeries was available and there was a sufficient number of patients in each cohort.

Table 1. Primary and secondary research questions and objectives.

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 included 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 were excluded. We included patients newly diagnosed with cancer up to one year before the last date of data availability in each database. This was 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 were 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 was generated for the former.
Time (*when follow-up begins and ends*):	Study participants were 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 used 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 included all individuals with a first diagnosis of chondrosarcoma identified in the database between 01/01/2010 and 31/12/2022. We only included 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 was generated.
Time (*when follow-up begins and ends*):	Study participants were 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 used routinely collected health data from 6 databases in 5 European countries.
The main measure of effect:	Proportions.

9. RESEARCH METHODS

9.1 Study type and study design

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

Table 2. Description of study types and related study designs.

Study type	Study design	Study classification
Patient-level characterisation	Cohort analysis	Off the shelf

9.2 Study setting and data sources

This study used 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 (CDWBordeaux), 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 fulfilled 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 3. 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	CDWBordeaux	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 hospital, 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
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	Cancer registry, primary care, secondary care	Registries	2.5 M	2024-01-01 (follow-up) 2022-12-31	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
		chondrosarcoma diagnoses, mortality, and treatment.	(ambulatory and hospital care)			(registration)	

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 paediatricians, 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 (CDWBordeaux), 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 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.

9.3 Study period

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

9.4 Follow-up

Study participants were followed up from the date of the 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 was death and patients were censored at the time of loss to follow-up or administratively censored at the end date of data availability, whatever came first.

Table 4. 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

9.5 Study population with inclusion and exclusion criteria

The study population included 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 were excluded (**Table 5** and **Table 6**). We only included patients newly diagnosed with cancer one year before the last date of data availability in each database. This was done 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 was required to allow for the detection of prevalent cases.

This study identified 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) were used as the standard vocabulary for diagnosis codes. 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 5. Operational definitions of inclusion criteria.

Criterion	Details	Orderof 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 6. 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

9.6 Variables

9.6.1 Exposure /s

None.

9.6.2 Outcome/s

Two main outcomes of interest were 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 was 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 was also reported by class of drugs to reduce the number of strata in case several different classes are present.

Appendix I Table A3 presents a list of codes to identify these pharmacological treatments.

Overall survival in patients with incident chondrosarcoma was also calculated based on the registered date of death. Individuals contributed 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	IPand OP care	RxNorm	N/A	All study participants with incident chondrosarcoma	N/A	N/A
Overall survival	Time to event (death fromany cause)	Yes	Time	N/A	IPand 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

9.6.3 Other covariates, including confounders, effect modifiers and other variables

Age and sex at chondrosarcoma diagnosis were described. The following age groupings were used: 0-19; 20-39; 40-59; 60-79; 80 and over. The sex (male/female) of study participants was also be identified.

Additionally, AJCC/UICC TNM categories, chondrosarcoma histological subtypes, tumour site, histological grades were identified in NCR (see **Appendix I Table A2**), and were used in characterisation and survival analysis.

Following histological subtypes other than conventional chondrosarcoma were identified: periosteal/juxtacortical chondrosarcoma, dedifferentiated, mesenchymal, clear cell, myxoid. Anatomical sites were extremities that included 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 included: 1) rib, sternum, clavicle 2) skull and face 3) vertebral column and 4) pelvic bones, sacrum, coccyx (see **Appendix I Table A5**).

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

9.7 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.

9.8 Data transformation

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

The data partners locally executed the analytics against the OMOP CDM in R Studio and reviewed and approved the default aggregated results before returning them to the Coordination Centre. Multiple execution iterations were performed, and additional fine-tuning of the code base was needed in this study.

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

9.9 Statistical methods

9.9.1 Main summary measures

Absolute numbers, summary descriptive measures (median, mean, proportion), probability of survival.

9.9.2 Main statistical methods

We used the R packages “PatientProfiles” for the patient-level characterisation of demographics and description of treatments and ”CohortSurvival” for the estimation of overall survival.

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

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

The number and proportion of patients receiving each of a pre-specified list of chondrosarcoma treatments were described at index date, 0 to 90, 91 to 365, and >365 days post-index date.

Overall survival was calculated with the "survfit" function using data on time at risk of death from any cause. Results were reported as plots of the estimated survival curves and the estimated probability of survival at years 1, 3, 5 and 10, median survival (time until survival reached 50%), restricted mean survival time (the average event-free survival time over the whole follow-up period (10 years).

Individuals who were lost to follow-up were censored at the time of loss of follow-up. The Kaplan-Meier approach implicitly assumes censoring occurs at random. This analysis was conducted only for databases that systematically collect data on mortality. For all analyses, numbers and proportions were reported.

All analyses were 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 for NCR (see **Appendix I Table A2**)).

In objective 2 we also reported non-pharmacological treatment procedures (surgery and radiation).

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

9.9.3 Missing values

For characterisation, patients with missing values were reported as NAs, no imputations were conducted. In the survival analysis, individuals who were lost to follow-up were censored at the time of loss of follow-up. The KM approach implicitly assumes censoring occurs at random.

9.9.4 Sensitivity analysis

In data sources that could differentiate between conventional and non-conventional chondrosarcoma a sensitivity analysis was 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**).

10. DATA MANAGEMENT

10.1 Data management

All databases were mapped to the OMOP CDM. This enabled 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 was written in R. Each data partner executed the study code against their database containing patient-level data and returned the results set, which only contained aggregated data. The results from each contributing data site were combined in tables and figures for the study report.

10.2 Data Storage

For this study, participants from various European Union (EU) member states processed 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 were run, which generated non-identifiable aggregate summary results.

The output files were stored in the DARWIN EU DRE. These output files did not contain any data that allowed the 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.

11. QUALITY CONTROL

11.1 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.

11.2 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) was run to assess the use of different codes across the databases contributing to the study and identify any codes potentially omitted in error. This allowed for consideration of the validity of the study cohort of patients with chondrosarcoma in each of the databases and informed decisions around whether multiple definitions are required. The study code was 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 include numerous automated unit tests to ensure the validity of the codes, alongside software peer review and user testing. All these packages are available on GitHub (https://github.com/orgs/darwin-eu/).

12. RESULTS

All results are available in a web application ("Shiny app") at https://data-dev.darwin-eu.org/EUPAS1000000162/. This report includes the main results: descriptive data, treatment patterns and survival analysis. More detailed stratified analyses are also available in the Shiny app.

12.1 Participants

Overall, there were 2,498 patients with the initial diagnosis of chondrosarcoma identified in six databases between 2010 and 2022: BIFAP (n=379); CDWBordeaux (n=92); CPRD GOLD (n=54); FinOMOP – HILMO (n=382); FinOMOP – HUS (n=142), and NCR (n=1,449) (**Table 9**). The number of patients that were excluded because they had a prior history of cancer was 149 (32%) for BIFAP, 31 (25%) for CDWBordeaux, 20 (31%) for CPRD GOLD, 220 (37%) for FinOMOP – HILMO, 77 (35%) for FinOMOP – HUS, and 124 (8%) for NCR. There were 215 (14.8%) patients with non-conventional chondrosarcoma in NCR , which would allow additional analysis only in this database.

Table 9. Study attrition of individuals included in each cohort per database (all types of chondrosarcomas).

	BIFAP	CDW Bordeaux	CPRD GOLD	FinOMOP - HILMO **	FinOMOP - HUS	NCR
Database population	22.0M	2.2M	17.3M	7.3M	3.5M	2.5M
First occurrence of chondrosarcoma identified in the database between January 1, 2010, and December 31, 2022	528	123	74	602	219	1,573
365 days of prior observation*	459	Not applied	65	Not applied	Not applied	Not applied
No prior cancer diagnosis (any, excluding non-melanoma skin cancer and non-specific bone cancer 2 months prior) before the diagnosis of chondrosarcoma	379	92	54	382	142	1449
Conventional or NOS chondrosarcoma	379	92	54	382	142	1,234 (75.2%)
Non-conventional chondrosarcoma***	Not applied	Not applied	Not applied	Not applied	Not applied	215 (14.8%)

NOS = not other specified

* A minimum of 365 days of prior observation criteria was applied only to databases that primarily collect primary care data (BIFAP and CPRD GOLD) **Data from FinOMOP-HILMO were available only from 2011,

*** Patients with conventional and non-conventional chondrosarcoma could only be reliably distinguished in NCR.

12.2 Descriptive data

Median age of patients with chondrosarcoma ranged between 53 and 55 years in all databases. Patients with chondrosarcoma were, on average, slightly older in FinOMOP-HILMO. The proportion of patients older than 60 was between 44% in FinOMOP-HILMO and 35% in NCR. This proportion was 38% in BIFAP, 40% in CDWBordeaux, 40% in CPRD GOLD, and 37% in FinOMOP-HUS (**Table 10**). Overall, the proportion of men and women was similar across all databases, with slightly more women with a chondrosarcoma diagnosis in BIFAP (54%) and men in CDWBordeaux (55%) and FinOMOP-HILMO (53%).

Table 10. Demographic characteristics of patients with chondrosarcoma.

			BIFAP	CDW Bordeaux	CPRD GOLD	FinOMOP - HILMO	FinOMOP - HUS	NCR
N			379	92	54	382	142	1,449
Sex	Female	N (%)	204 (54%)	41 (45%)	28 (52%)	179 (47%)	70 (49%)	733 (51%)
	Male	N (%)	175 (46%)	51 (55%)	26 (48%)	203 (53%)	72 (51%)	716 (49%)
Age (years)	NA	Median [Q25-Q75]	53 [42 - 68]	54 [36 - 66]	53 [42 - 66]	55 [40 - 68]	52 [37 - 67]	53 [43 - 64]
		Mean (SD)	54.3 (16.9)	51.7 (19.4)	51.5 (17.6)	54.2 (18.6)	51.5 (19.2)	52.9 (15.5)
		Range	4 to 92	15 to 92	11 to 92	8 to 93	8 to 92	18 to 93
Age group (years)	0 to 19	N (%)	8 (2.1%)	<5	<5	13 (3.4%)	6 (4.2%)	12 (0.8%)
	20 to 39	N (%)	69 (18.2%)	25 (27.2%)	11 (20.4%)	81 (21.2%)	36 (25.4%)	281 (19.4%)
	40 to 59	N (%)	159 (42.0%)	30 (32.6%)	22 (40.7%)	120 (31.4%)	48 (33.8%)	656 (45.3%)
	60 to 79	N (%)	119 (31.4%)	27 (29.3%)	16 (29.6%)	142 (37.2%)	42 (29.6%)	439 (30.3%)
	80+	N (%)	24 (6.3%)	19 (10.9%)	5 (9.3%)	26 (6.8%)	10 (7.0%)	61 (4.2%)

A minimum of 365 days of prior observation criteria was applied only to databases that primarily collect primary care data (BIFAP and CPRD GOLD).

12.3 Treatment patterns

Any specific drug treatment for chondrosarcoma was analysed in four out of six databases (CPRD GOLD and BIFAP were excluded from this objective as they were not fit for purpose). In CDWBordeaux, no drug treatment was identified. Less than 5% of patients had a record of a prescription for any specific treatment across all databases with most records being for conventional chemotherapy (**Table 11**). For most drugs that were identified, the number of records was less than 5. The following records were identified: Carboplatin (NCR), Cisplatin (NCR, FinOMOP-HUS), Cyclophosphamide (NCR), Dasatinib (NCR), Docetaxel (NCR, FinOMOP-HUS), Durvalumab (NCR), Etoposide (NCR), Gemcitabine (NCR, FinOMOP-HUS), Irinotecan (NCR), Methotrexate (NCR, FinOMOP-HUS, FinOMOP-HILMO), Nivolumab (NCR), Pazopanib (NCR, FinOMOP-HUS), Regorafenib (FinOMOP-HILMO), Temozolomide (NCR, FinOMOP-HILMO), Vincristine (NCR). Periods (0 to 90 days, 91 to 365, and after 365) after diagnosis when those drugs were administrated/prescribed are available in **Table 12.**

Surgical procedures were recorded in all databases, from only 15.2% of CDWBordeaux, and up to 88.9% of NCR patients. The proportion of chondrosarcoma patients with surgical procedures recorded was 57.4% in CPRD GOLD, 65.2% in FinOMOP-HILMO and 53.5% in FinOMOP-HUS. In CPRD GOLD, FinOMOP – HILMO, FinOMOP – HUS and NCR radiotherapy records were also identified with a maximum 6.4% patients at NCR (**Table 13**).

Table 11. Treatment of patients with chondrosarcoma in different time windows after chondrosarcoma diagnosis.

		FinOMOP - HILMO	FinOMOP - HUS	NCR
		382	142	1,449
0 to 90 days	Conventional chemotherapy	<5	<5	6 (0.4%)
	LDH1 inhibitors*	0	0	0
	PD-L1 inhibitors**	0	0	0
	TK inhibitors***	0	0	<5
91 to 365 days	Conventional chemotherapy	5 (1.3%)	6 (4.2%)	12 (0.8%)
	LDH1 inhibitors*	0	0	0
	PD-L1 inhibitors**	0	0	0
	TK inhibitors***	0	0	<5
More than 365 days	Conventional chemotherapy	6 (1.6%)	5 (3.5%)	26 (1.8%)
	LDH1 inhibitors*	0	0	0

		FinOMOP - HILMO	FinOMOP - HUS	NCR
	PD-L1 inhibitors**	0	0	<5
	TK inhibitors***	<5	<5	<5

* - Lactate dehydrogenase- 1 inhibitors; ** - Programmed cell death protein-1 inhibitors; *** - Tyrosine kinase inhibitors

Table 12. Specific drugs mentioned in the records of patients with chondrosarcoma.

Time window	Ingredient	FinOMOP - HILMO	FinOMOP - HUS	NCR
0 to 90 days	Cisplatin	<5	<5	0
	Cyclophosphamide	0	<5	0
	Dasatinib	0	<5	0
	Methotrexate	<5	0	<5
	Vincristine	0	<5	0
91 to 365 days	Cisplatin	<5	<5	0
	Cyclophosphamide	0	7 (0.5%)	0
	Dasatinib	0	<5	0
	Docetaxel	<5	0	0
	Gemcitabine	<5	0	0
	Methotrexate	<5	0	5 (1.3%)
	Pazopanib	0	0	0
	Carboplatin	0	8 (0.6%)	0
91 to 365 days	Cisplatin	<5	<5	0
	Cyclophosphamide	0	9 (0.6%)	0
	Docetaxel	<5	<5	0
	Durvalumab	0	<5	0
	Etoposide	0	<5	0
	Gemcitabine	<5	<5	0
	Irinotecan	0	<5	0
	Methotrexate	<5	<5	5 (1.3%)
	Nivolumab	0	<5	0
	Pazopanib	<5	<5	<5
	Regorafenib	0	0	<5
	Temozolomide	0	<5	<5
	Vincristine	0	<5	0

Table 13. Procedures conducted 0-180 days after the initial diagnosis of chondrosarcoma.

	CDWBordeaux	FinOMOP - HILMO	FinOMOP - HUS	NCR
	92	**382**	**142**	**1449**
Radiotherapy	0	11 (2.9%)	<5	93 (6.4%)
Surgery	14 (15.2%)	249 (65.2%)	76 (53.5%)	1,288 (88.9%)

12.4 Subgroup analysis

Additional variables (Grade, AJCC/UICC Stage and TNM categories, anatomical site) were identified and analysed in the NCR database only. The majority of cases were Stage 1 (54.9%) and more specifically, Stage 1a (47.0%), while Stage 4 was present only in 3.7% of patients. Nodal metastases (N+) within 180 days after diagnosis were recorded in 1.4% of patients and distant (M1) in 4.1% of patients (**Table 14**).

Table 14. Distribution of newly diagnosed chondrosarcoma patients by AJCC/UICC TNM and Stage categories, and morphological grade in NCR.

		Non-conventional	Conventional	All chondrosarcoma cases
		215	1,234	1,449
AJCC/UICC stage	Stage 1	54 (25.1%)	741 (60.0%)	795 (54.9%)
	Stage 1a	20 (9.3%)	661 (53.6%)	681 (47.0%)
	Stage 1b	33 (15.3%)	75 (6.1%)	108 (7.5%)
	Stage 2	66 (30.7%)	269 (21.8%)	335 (23.1%)
	Stage 2a	32 (14.9%)	176 (14.3%)	208 (14.4%)
	Stage 2b	34 (15.8%)	93 (7.5%)	127 (8.8%)
	Stage 3	9 (4.2%)	13 (1.1%)	22 (1.5%)
	Stage 3a	<5	<5	<5
	Stage 3b	<5	0 (0.0%)	<5
	Stage 4	38 (17.7%)	15 (1.2%)	53 (3.7%)
	Stage 4a	16 (7.4%)	<5	20 (1.4%)
	Stage 4b	12 (5.6%)	8 (0.6%)	20 (1.4%)
	Not available	48 (22.3%)	196 (15.9%)	244 (16.8%)
T category	T1 category	78 (36.3%)	878 (71.2%)	956 (66.0%)
	T2 category	89 (41.4%)	188 (15.2%)	277 (19.1%)
	T3 category	13 (6.0%)	39 (3.2%)	52 (3.6%)
	T4 category	9 (4.2%)	14 (1.1%)	23 (1.6%)
	Not available	26 (12.1%)	115 (9.3%)	141 (9.7%)
N category	No nodal metastases (N0)	167 (77.7%)	1,020 (82.7%)	1,187 (81.9%)
	Nodal metastases (N+)	11 (5.1%)	9 (0.7%)	20 (1.4%)
	Not available	37 (17.2%)	205 (16.6%)	242 (16.7%)
M category	No distant metastases (M0)	168 (78.1%)	1,206 (97.7%)	1,374 (94.8%)
	Distant metastases (M1)	42 (19.5%)	18 (1.5%)	60 (4.1%)
	Not available	5 (2.3%)	10 (0.8%)	15 (1.0%)
Grade	Grade 1 well differentiated	14 (6.5%)	777 (63.0%)	791 (54.6%)
	Grade 2 moderately differentiated	14 (6.5%)	294 (23.8%)	308 (21.3%)
	Grade 3 poorly differentiated	43 (20.0%)	85 (6.9%)	128 (8.8%)
	Grade 4 undifferentiated	<5	0 (0.0%)	<5
	Not available	NR	78 (6.3%)	NR

American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) TNM classification system of malignant tumours, N and M categories refer to Tumour, Node and Metastasis; NR – not reported due to minimal cell count restriction

The majority of patients had records of Grade 1 (well differentiated) tumours (54.6%), Grade 2 (moderately differentiated) was present in 21.3%, Grade 3 (poorly differentiated) in 8.8%, Grade 4 undifferentiated tumours were recorded in less than five patients.

Most patients with chondrosarcoma had tumours of longer bones of the lower (n=510, 41.3%) and upper limbs (n=224, 18.2%) followed by Rib, sternum, and clavicle tumours (n=139, 11.3%) (**Table 15**). The majority of patients with non-conventional chondrosarcoma had dedifferentiated (n=94, 44.8%), myxoid

(n=71, 33.0%) or periosteal tumours (n=28, 13.0%) and about 5% had clear cell or mesenchymal chondrosarcoma (**Table 16**).

Table 15. Anatomical localisation of the tumour in patients with conventional chondrosarcoma (n=1,234) at the time of diagnosis in NCR.

		N(%)
Extremities	Long bones of upper limbs	224 (18.2%)
	Short bones of upper limbs	85 (6.9%)
	Long bones of lower limbs	510 (41.3%)
	Short bones of lower limbs	28 (2.3%)
Axial skeleton	Skull and face	97 (7.9%)
	Rib, sternum, clavicle	139 (11.3%)
	Vertebral column	29 (2.4%)
	Pelvic bones, sacrum, coccyx	98 (7.9%)

Table 16. Histological subtypes in patients with non-conventional chondrosarcoma in NCR (n=215).

	N(%)
Clear cell chondrosarcoma	11 (5.1%)
Mesenchymal chondrosarcoma	11 (5.1%)
Myxoid chondrosarcoma	71 (33.0%)
Periosteal chondrosarcoma	28 (13.0%)
Dedifferentiated chondrosarcoma	94 (44.8%)

12.4 Survival analysis

Median survival was not reached in all databases (meaning that more than 50% of patients were still alive by the end of the follow-up). Survival estimates (especially 10-year survival probability) were slightly lower in CDWBordeaux (58% (95%CI: 43, 78)), and FinOMOP-HUS (61% (50, 75)), and higher in NCR (80% (78, 82)) and BIFAP (79% (74, 84)). The 10-year survival probability were 73% (55, 95) and 68% (63, 74) in CPRD GOLD and FinOMOP – HILMO respectively (**Table 17 and Figure 1**). Overall survival probability was consistently lower in men compared to women in all databases (**Figure 2**).

Table 17. Overall 1,3,5,10-year survival of patients with chondrosarcoma by data source.

	BIFAP	CDWBordeaux	CPRD GOLD	FinOMOP - HILMO	FinOMOP - HUS	NCR
Records in the analysis	379	92	54	382	137	1,448
Number events	63	21	9	100	34	243
Median survival (95% CI)	NR	NR (9.2; NR)	NR	NR	NR	NR
Restricted mean survival (years) (SE)	8.5 (0.5)	7.4 (0.5)	8.1 (0.6)	8.0 (0.2)	7.5 (0.4)	8.7 (0.1)
1 year survival, % (95% CI)	94 (91, 96)	92 (87, 98)	90 (82, 99)	91 (88, 94)	89 (84, 95)	94 (93, 95)
3 year survival, % (95% CI)	88 (84, 91)	78 (68, 89)	85 (76, 96)	83 (79, 87)	80 (73, 88)	90 (88, 91)
5 year survival, % (95% CI)	84 (80, 88)	68 (57, 82)	82 (71, 95)	79 (75, 83)	76 (69, 85)	86 (84, 88)
10 year survival, % (95% CI)	79 (74, 84)	58 (43, 78)	73 (55, 95)	68 (63, 74)	61 (50, 75)	80 (78, 82)

NR - Median survival was not reached in the database (more than 50% of patients were still alive by the end of the follow-up).

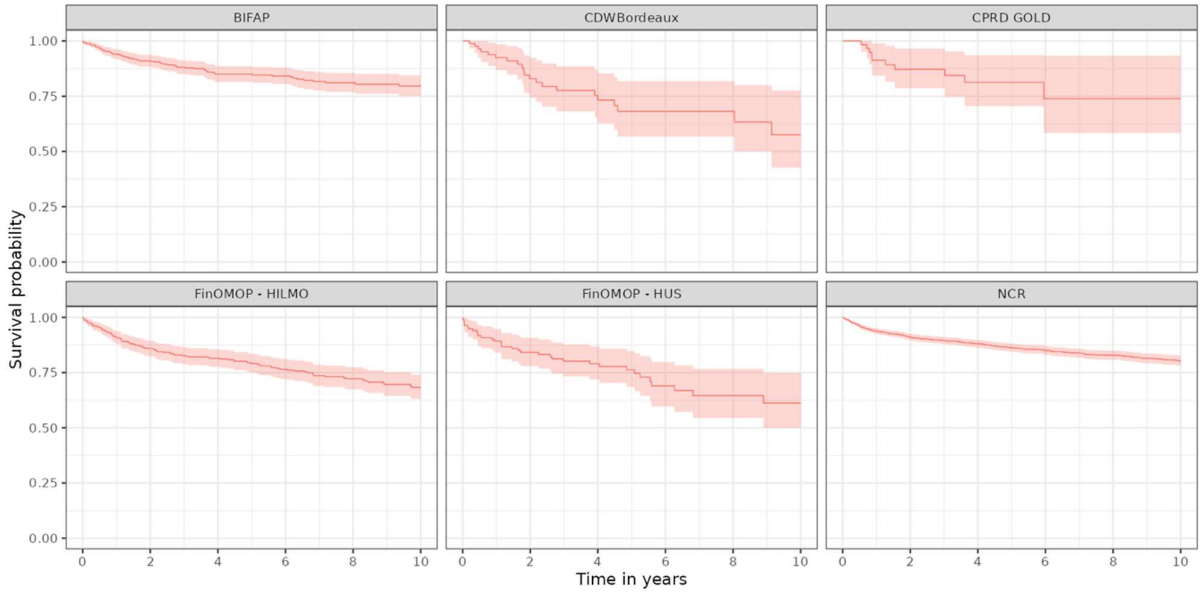

Figure 1. Overall survival of patients with chondrosarcoma by data source.

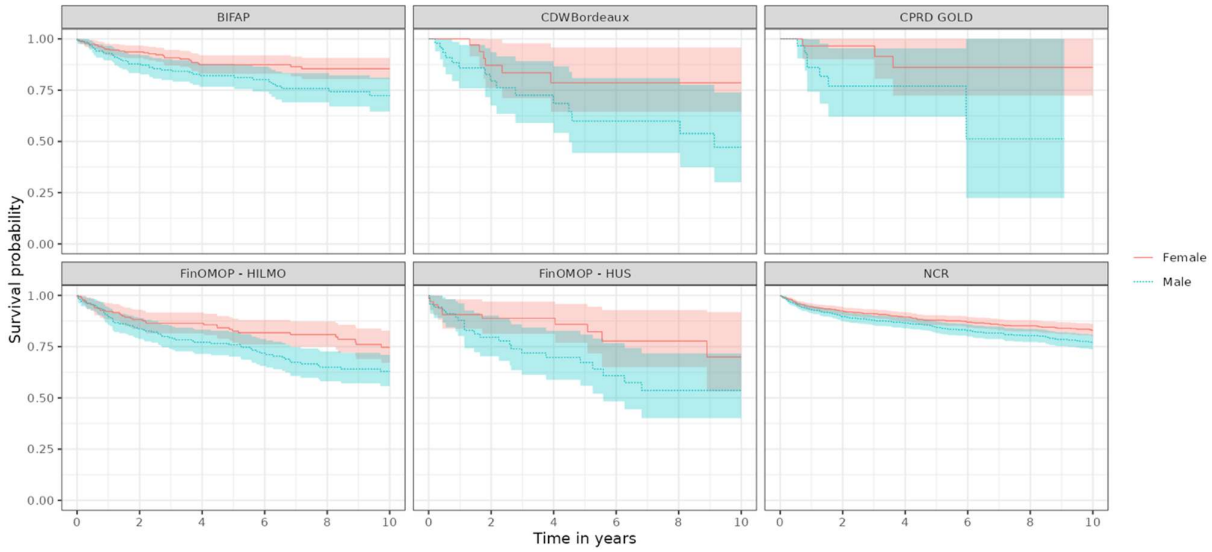

Figure 2. Overall survival of patients with chondrosarcoma by data source and sex.

12.5 Subgroup survival analysis

In a subgroup analysis in NCR, survival estimates were consistent with the AJCC/UICC stage categories (**Table 18**), with stage 1 patients having 95% (94, 97) 5-year survival, Stage 2 (77% (73, 83)), Stage 3 (36% (16, 81)) and Stage 4 only 15% (7, 32). Similarly, survival estimates aligned with TNM categories with the lowest survival estimates for patients with T4, N+ and M1 tumours (**Table 19**).

Table 18. Median survival, restricted mean survival time and overall, 1, 3, 5, 10-year survival probability of patients with chondrosarcoma in NCR by AJCC/UICC stage.

	N	Events	Median survival (95% CI)	Restricted mean survival (SE)	1 year survival, % (95% CI)	3 year survival, % (95% CI)	5 year survival, % (95% CI)	10 year survival, % (95% CI)
Stage 1	791	70	NR	9.5 (0.1)	99 (98, 100)	97 (96, 98)	95 (94, 97)	90 (88, 92)
Stage 1a	680	51	NR	9.6 (0.1)	99 (99, 100)	98 (97, 99)	96 (95, 98)	91 (89, 94)
Stage1b	108	19	NR	8.8 (0.3)	96 (93, 100)	93 (89, 98)	88 (82, 95)	80 (72, 89)
Stage 2	330	81	NR	7.9 (0.2)	91 (87, 94)	83 (79, 88)	77 (73, 83)	66 (59, 73)
Stage 2a	206	35	NR	8.7 (0.2)	96 (93, 99)	90 (86, 95)	86 (81, 92)	73 (65, 82)
Stage2b	127	47	NR (7.0, NR)	6.7 (0.4)	82 (76, 89)	72 (64, 81)	63 (54, 73)	53 (43, 65)
Stage 3	21	10	4.5 (2.0, NR)	4.8 (0.9)	89 (77, 100)	60 (41, 88)	36 (16, 81)	18 (4, 90)
Stage 4	53	44	0.5 (0.4, 1.3)	1.9 (0.4)	39 (28, 55)	22 (13, 38)	15 (7, 32)	NA
Stage information not available	248	37	NR	8.6 (0.2)	93 (90, 97)	88 (84, 92)	84 (79, 89)	80 (74, 87)

NR - Median survival was not reached in the database (more than 50% of patients were still alive by the end of the follow-up); NA – not available.
American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) TNM classification system of malignant tumours.

Table 19. Median survival, restricted mean survival time and overall, 1, 3, 5, 10-year survival probability of patients with chondrosarcoma in NCR by T, N and M AJCC/UICC categories.

	N	Events	Median survival (95% CI)	Restricted mean survival (SE)	1 year survival, % (95% CI)	3 year survival, % (95% CI)	5 year survival, % (95% CI)	10 year survival, % (95% CI)
T1	952	94	NR	9.4 (0.1)	98 (97, 99)	96 (94, 97)	94 (92, 95)	88 (85, 90)
T2	272	96	NR	7.0 (0.3)	84 (80, 88)	75 (70, 80)	68 (62, 74)	58 (52, 65)
T3	50	14	NR (4.8, NR)	7.0 (0.7)	86 (76, 96)	72 (59, 87)	63 (48, 82)	63 (48, 82)
T4	22	9	NR (1.3, NR)	5.5 (1.1)	72 (54, 94)	51 (32, 82)	51 (32, 82)	NA
T category information not available	146	30	NR	8.3 (0.3)	90 (85, 95)	85 (80, 91)	80 (74, 87)	77 (70, 85)
N0	1,185	196	NR	8.8 (0.1)	95 (93, 96)	90 (89, 92)	87 (85, 89)	79 (77, 82)

	N	Events	Median survival (95% CI)	Restricted mean survival (SE)	1 year survival, % (95% CI)	3 year survival, % (95% CI)	5 year survival, % (95% CI)	10 year survival, % (95% CI)
N+	19	10	1.8 (0.8, NR)	4.2 (1.1)	65 (45, 92)	45 (26, 78)	45 (26, 78)	NA
N category information not available	243	37	NR	8.7 (0.2)	92 (88, 95)	89 (85, 93)	85 (81, 90)	84 (80, 89)
M0	1,371	193	NR	9.0 (0.1)	96 (95, 97)	92 (91, 94)	89 (87, 91)	83 (81, 85)
M1	58	47	0.5 (0.4, 1.0)	1.8 (0.4)	35 (25, 51)	21 (12, 36)	14 (7, 30)	NA
M category information not available	17	<5	Not reached	9.1 (0.6)	100 (100, 100)	94 (84, 100)	88 (74, 100)	88 (74, 100)

American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) TNM classification system of malignant tumours, N and M categories refer to Tumour, Node and Metastasis

NR - Median survival was not reached in the databases (more than 50% of patients were still alive by the end of the follow-up); NA – not available.

Survival estimates were consistently lower for patients with axial skeleton tumours compared to tumours of extremities, with the highest survival estimates for short and long bones of upper and lower limbs and also face and skull tumours (**Table 20**). Higher histological Grades were associated with lower mortality estimates (**Table 21 and Figure 3**). The 10-year overall survival probability was 91% (89, 93) for Grade 1, 73% (67, 80) for Grade 2 and only 48% (37, 61) for Grade 3.

Table 20. Median survival, restricted mean survival time and overall, 1,3,5,10-year survival probability of patients with conventional chondrosarcoma in NCR by anatomical site.

	N	Events	Median survival (95% CI)	Restricted mean survival (SE)	1 year survival, % (95% CI)	3 year survival, % (95% CI)	5 year survival, % (95% CI)	10 year survival, % (95% CI)
Long bones of lower limbs	510	50	NR	9.6 (0.1)	99 (99, 100)	98 (97, 99)	95 (93, 97)	88 (85, 91)
Long bones of upper limbs	224	17	NR	9.6 (0.1)	99 (98, 100)	98 (96, 100)	95 (92, 98)	91 (87, 95)
Pelvic bones, sacrum, coccyx	98	20	NR	8.0 (0.4)	91 (86, 97)	82 (74, 90)	79 (71, 88)	75 (65, 86)
Rib, sternum, clavicle	139	24	NR	8.5 (0.3)	95 (92, 99)	87 (82, 94)	84 (78, 91)	74 (65, 85)
Short bones of lower limbs	28	<5	NR	9.8 (0.3)	100 (100, 100)	100 (100, 100)	96 (89, 100)	96 (89, 100)
Short bones of upper limbs	85	8	NR	9.2 (0.3)	96 (93, 100)	93 (87, 99)	93 (87, 99)	90 (83, 97)
Skull and face	97	7	NR	9.3 (0.2)	99 (97, 100)	97 (93, 100)	92 (86, 98)	90 (83, 98)
Vertebral column	29	9	NR (6.2, NR)	7.6 (0.7)	97 (90, 100)	89 (78, 100)	76 (60, 95)	57 (38, 85)

NR - Median survival was not reached in the databases (more than 50% of patients were still alive by the end of the follow-up).

Table 21. Median survival, restricted mean survival time over 10 years and overall, 1,3,5,10-year survival probability of patients with chondrosarcoma in NCR by histological grade.

	N	Events	Median survival (95% CI)	Restricted mean survival (SE)	1 year survival, % (95% CI)	3 year survival, % (95% CI)	5 year survival, % (95% CI)	10 year survival, % (95% CI)
Grade 1 (well differentiated)	783	62	NR	9.6 (0.1)	99 (99, 100)	98 (97, 99)	96 (95, 97)	91 (89, 93)
Grade 2 (moderately differentiated)	303	53	NR	8.5 (0.2)	96 (94, 98)	91 (88, 95)	84 (80, 89)	73 (67, 80)
Grade 3 (poorly differentiated)	125	51	7.2 (4.4, NR)	6.0 (0.4)	75 (68, 83)	62 (54, 72)	55 (46, 66)	48 (37, 61)
Grade information not available	228	74	NR	6.9 (0.3)	82 (77, 88)	70 (64, 77)	68 (62, 75)	61 (53, 69)

NR - Median survival was not reached in the database (more than 50% of patients were still alive by the end of the follow-up).

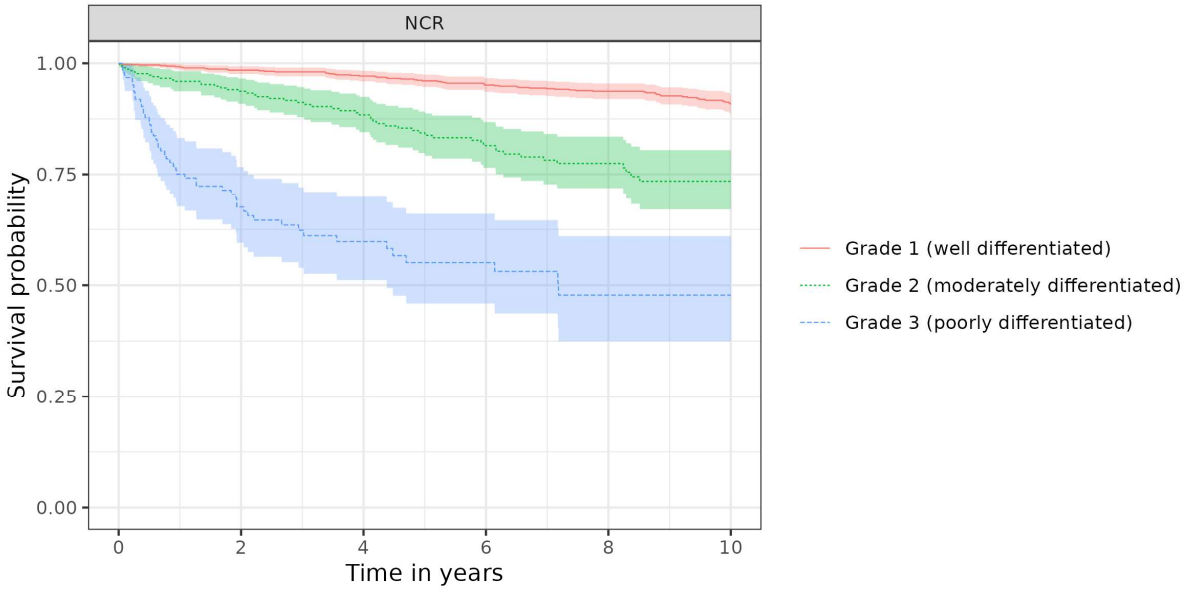

Figure 3. Overall survival of patients with chondrosarcoma by Grade in NCR.

12.5 Sensitivity analysis

We could obtain meaningful differentiation between conventional and non-conventional chondrosarcoma only in NCR database. We estimated survival by histological subtypes for non-conventional chondrosarcoma (**Table 22 and Figure 4**). Survival estimates were substantially lower for dedifferentiated (5-year survival (29% (20, 40)), mesenchymal (33% (13, 80)), but not for myxoid chondrosarcoma (76% (66, 88)). Periosteal and clear cell tumours had survival estimates similar to conventional chondrosarcoma but relatively low patient counts (n=28).

Table 22. Median survival, restricted mean survival time and overall, 1,3,5,10-year survival probability of patients with non-conventional chondrosarcoma in NCR by histological type.

	N	Events	Median survival (95% CI)	Restricted mean survival (SE)	1 year survival, % (95% CI)	3 year survival, % (95% CI)	5 year survival, % (95% CI)	10 year survival, % (95% CI)
Clear cell	11	0	NR	10.0 (0.0)	100 (100, 100)	100 (100, 100)	100 (100, 100)	100 (100, 100)
Dedifferentiated	94	64	0.9 (0.6, 1.8)	3.3 (0.4)	48 (39, 59)	32 (23, 43)	29 (20, 40)	21 (13, 37)
Mesenchymal	11	8	4.5 (1.8, NR)	4.6 (1.1)	91 (75, 100)	64 (41, 99)	33 (13, 80)	22 (7, 73)
Myxoid	71	22	NR (7.1, NR)	7.3 (0.5)	87 (80, 95)	81 (72, 91)	76 (66, 88)	58 (45, 75)
Periosteal	28	<5	NR	9.7 (0.3)	100 (100, 100)	100 (100, 100)	100 (100, 100)	94 (84, 100)

NR - Median survival was not reached in all databases (more than 50% of patients were still alive by the end of the follow-up).

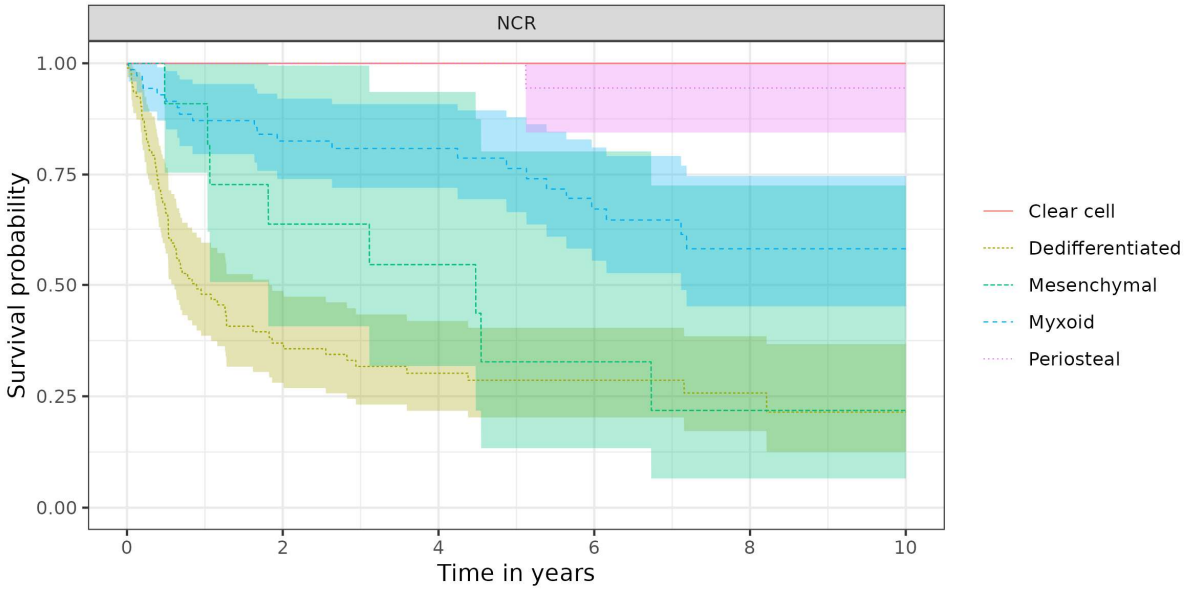

Figure 4. Overall survival probability of patients with non-conventional chondrosarcoma in NCR by histological type (n=215).

13. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

Adverse events/adverse reactions were not collected or analysed as part of this evaluation. The nature of this non-interventional evaluation, through the use of secondary data, does not fulfil the criteria for reporting adverse events, according to module VI, VI.C.1.2.1.2 of the Good Pharmacovigilance Practices (https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-good-pharmacovigilance-practices-gvp-module-vi-collection-management-submission-reports_en.pdf).

14. DISCUSSION

14.1 Key results

The study described demographics, recorded treatments and overall survival of chondrosarcoma patients across six databases in five European countries. This was the first study to describe chondrosarcoma patients in different data sources that represent primary healthcare (CPRD GOLD, BIFAP), secondary and tertiary care (CDWBordeaux, FinOMOP-HUS), national hospital registry (FinOMOP-HILMO) and national cancer registry (NCR). This study was intended to assess the granularity and breadth of data in the DARWIN EU network related to chondrosarcoma patients. While we could identify chondrosarcoma patients in all data sources, the absolute number of patients was low. Overall, in the study period between 2010 and 2023, we identified 2,498 patients with an initial diagnosis of chondrosarcoma. The majority of patients were identified in NCR (n=1,449) followed by BIFAP (n=379), FinOMOP-HILMO (n=379) and FinOMOP-HUS (n=142). Less than 100 patients were identified in CDWBordeaux (n=92) and CPRD GOLD (n=54).

Despite the different nature of data sources, the demographics of chondrosarcoma patients were similar, with the median age ranging between 53 and 55 years. Patients with chondrosarcoma were, on average, slightly older in FinOMOP-HILMO and slightly younger in NCR, but in general the distribution between age

groups was similar. There was also a similar proportion of men and women among chondrosarcoma patients across all databases.

The proportion of different drug treatment options did not exceed 5% in different time windows (0-90, 91-365 and more than 365 days after diagnosis). Conventional chemotherapy drugs were recorded more often than any other group. The following medicines were identified: Carboplatin, Cisplatin, Cyclophosphamide, Dasatinib, Docetaxel, Durvalumab, Etoposide, Gemcitabine, Ifosfamide, Irinotecan, Methotrexate, Nivolumab, Pazopanib, Regorafenib, Temozolomide, Vincristine. Radiotherapy records were also rare, with a maximum of 6.4% patients in NCR. Surgical procedures were more common than other treatment options and were identified in NCR (88.9% of records), FinOMOP-HILMO (65.2%), CPRD GOLD (57.4%), FinOMOP-HUS (53.5%), CDWBordeaux (15.2%).

Additional variables (Grade, AJCC/UICC Stage and TNM categories, anatomical site) were identified only in the NCR. Most cases were Stage 1 (54.9%), and Stage 4 was present only in 3.7% of patients. Nodal metastases within 180 days after diagnosis were recorded in 1.4% of patients and distant in 4.1% of patients. The majority of patients had records of well-differentiated tumours; 54.6%, moderately differentiated was present in 21.3%, and poorly differentiated only in 8.8%. The majority of patients in NCR had chondrosarcoma of the extremities. The non-conventional chondrosarcoma was identified only in NCR, where there were 215 (14.8%) patients with this type.

Overall survival was relatively high, with all the databases having more than 50% of patients still alive by the end of the 10-year follow-up. Survival estimates were slightly lower in CDWBordeaux and FinOMOP-HUS, 10-year survival probability was 58% (95%CI: 43, 78) and 61% (50, 75), respectively. It was higher in NCR (80% (78, 82)) and BIFAP (79% (74, 84)). Overall survival probability was slightly lower in men compared to women in all databases.

In all subgroup analyses in NCR, survival was consistent with AJCC/UICC staging with patients with later stages having poor survival outcomes. Patients with less differentiated tumours also had lower survival compared to well differentiated. Survival estimates were consistently lower for patients with axial skeleton tumours compared to tumours of extremities. In patients with non-conventional chondrosarcoma, survival was lower with dedifferentiated and myxoid morphology.

14.2 Limitations of the research methods

The study was informed by routinely collected healthcare data, so data quality issues must be considered. In particular, the identification of chondrosarcoma patients varied 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.

The number of patients that were excluded because they had a prior history of cancer was relatively high (25%-37%) for all databases except NCR (8%). While we always expect some proportion of patients with multiple primary tumours in all data sources, a relatively high proportion of patients with several cancer diagnoses can be explained by the fact that data sources collecting routine healthcare data do not systematically apply multiple primary tumours rules and conventions that are used for cancer registries (16). To be more specific, more general broad and less specific cancer diagnosis could be assigned before the more specific chondrosarcoma diagnosis in primary and secondary healthcare settings, making it difficult to distinguish true multiple primary tumours. In our study, that could lead to the exclusion of some patients with primary chondrosarcoma diagnosis, but while this is possible, it is not likely that with was differential and could affect study results.

We reported the proportion of patients with non-conventional chondrosarcoma only in NCR. While patients with concepts that reflect non-conventional chondrosarcoma diagnosis were also identified in

other databases, most patients had more broad concepts that describe chondrosarcoma diagnosis without mentioning the type, and proper distinction was not possible.

Finnish databases were analysed independently, but at least some of the 142 patients included in FinOMOP-HUS might also be among the patients contributing to FinOMOP-HILMO. Still information from FinOMOP-HUS mainly covers secondary and tertiary care at Helsinki University Hospital, while FinOMOP-HILMO is a national hospital discharge registry, so we expected to obtain a different sample of chondrosarcoma patients in those two databases.

Our study revealed very limited information about drug options available for chondrosarcoma patients, and while this could point to the lack of completeness in the database, it is more likely to reflect the true real-world data available for this rare tumour. The proportion of patients with any drug records was similarly low across all types of databases. Another possible explanation could be that patients are getting specific treatment in other specialized centres not captured by data sources. It is also important to mention that NCR is collecting only first-line treatments, so treatment after recurrence which is more likely to include drug therapies was not captured in our study for this data source.

Low drug counts were the main reason for not performing optional objectives: to describe treatment with medicines sequences and to describe chondrosarcoma treatment with medicines (chemotherapy and biologics) in patients that had undergone or not surgery, radiotherapy, both or neither.

Another limitation is related to detailed chondrosarcoma grading and histological subtypes, which were not present in all databases except one (NCR). Future studies might benefit from the inclusion of databases with this information available.

Surgical procedures were not common in CDWBordeaux. It is worth mentioning surgical procedures may be less formalised and less well mapped compared to drug treatments. While describing surgical procedures was not the primary objective of this study, future research using sources mapped OMOP-CDM could focus on the surgical treatment of cancer.

14.3 Interpretation

Chondrosarcoma is a rare condition, and studies that describe the characteristics of patients in large representative databases are not common. Our study included 2,498 cases from six databases over the period between 2010 and 2022. A previous population-based study from Norway included 311 cases over the period between 1990-2013 (7) , and in the Netherlands, 2,186 chondrosarcoma cases were treated between 1980-2013 (6). Several studies described patient and tumour characteristics, demographics, and survival of chondrosarcoma patients in the National Cancer Database (NCD) in the United States, with the latest covering 5,329 chondrosarcoma patients in 2004-2015 (8). While our study covered the most recent period, we were also focusing on various sources of data not limited to population-based registries.

The demographics of chondrosarcoma patients across all databases were similar, suggesting that hospital-based and primary care data sources may also provide evidence of chondrosarcoma. The median age range between 53 and 55 and an equal proportion of men and women was similar to other studies (7,8).

While our study identified less than 6% of patients with records of any drug treatment is it also in line with previous studies. In the NCD study drug treatment was identified in less than 7% of chondrosarcoma patients (8). The majority of patients with conventional chondrosarcoma had early-stage and low-grade disease, which is also in line with previous studies and may partially explain the lack of information on drug therapy.

Among the ingredients were prescribed, most were conventional chemotherapy agents, but still, some records of immunotherapies and targeted agents were also identified, e.g., durvalumab, nivolumab,

dasatinib, pazopanib and regorafenib. The use of pazopanib and dazatinib was previously reported to be used in phase 1 and 2 trials in chondrosarcoma patients (17–19). More recently, the use of regorafenib in patients with metastatic or locally advanced chondrosarcoma was tested in a phase 2 randomised trial (20). Finally, immunotherapy was also reported in chondrosarcoma patients (19) and some case reports mention the use of nivolumab in conventional chondrosarcoma (21). In one study, durvalumab and tremelimumab were also used in treatment of chondrosarcoma patient (22).

Those drug therapies remain limited to off-label use in cases with late-stage high-grade and metastatic disease. Our study showed that in NCR the proportion of patients with distant metastases is below 5%, but metastases are more common in non-conventional chondrosarcoma patients. The key problem for most reports of new drug agents in chondrosarcoma is that they are limited to case reports or trials with limited sample sizes (19). While this is a problem for most rare diseases, federated analysis across multiple data sources can also identify population and healthcare settings where the conduct of clinical trials is feasible.

Overall survival was relatively high in all the databases and in line with previous studies (6–8), however some variability between databases existed. Survival estimates were slightly lower in CDWBordeaux (10-year survival probability – 58% and FinOMOP-HUS 62% and higher in NCR - 80% and BIFAP - 79%. Differences in patients demographics (age and sex) might partially explain the differences in survival estimates, older age being one of the factors associated with a worse prognosis (6). While there are other factors and different unobserved patient characteristics, differences in demographics may still explain some differences in survival estimates across databases, suggesting that direct unadjusted comparison is not feasible. Patients with advanced might also be referred to hospitals or centres of excellence, such as CDWBordeaux and FinOMOP-HUS, while nationwide registries contain all cases. Subgroup analysis by stage, grade and anatomical site provided results similar to the previous study in NCR (6).

14.4 Generalisability

This study included data from six databases in five European countries (United Kingdom, France, Finland, Netherlands and Spain) over the period between 2010 and 2023. Different healthcare settings were represented, including hospital-based data sources (FinOMOP-HUS and CDWBordeaux), primary care data sources (BIFAP and CPRD GOLD), and national hospital (FinOMOP-HILMO) and cancer registries (NCR). Only one data source (NCR) provided information on several variables of interest – more specifically tumour characteristics.

At least one database (NCR) contained high-quality data on cancer diagnoses with the required degree of granularity. High-quality cancer registries remain the best and most detailed source of information about incident cases worldwide. Cancer registries collect data from several sources and perform additional consolidation and verification procedures to improve its quality. While not common for all cancer registries, the NCR also systematically collects information on first-line treatment. This enables a comprehensive analysis of treatment patterns on a national level.

It is also important to mention that Helsinki University Hospital, which is the source for FinOMOP-HUS is among several comprehensive cancer centres specialising in cancer care treatment.

All data sources could inform on the date of death, and survival estimates were similar across them. Hospital databases we included in this study also received information about patients from external sources, so this information is likely to be complete.

Also, in contrast to other conditions and more common cancer types, chondrosarcoma is less likely to be linked to environmental and lifestyle risk factors, meaning that differences across populations are less likely to be driven by different prevalence of these risk factors. Still, information on mutation status was not available in our study. Population-based analysis in the Netherlands highlighted the role of increased

medical imaging that can contribute to increasing chondrosarcoma rates (6), meaning that population differences may also be attributed to different access to medical diagnostics.

15. CONCLUSION

In our study, we described 2,498 chondrosarcoma patients from six databases in five countries between 2010 and 2023. The median age was between 53 and 55 across all databases, and we observed a relatively similar proportion of men and women in all data sources.

While surgical treatment was common in databases that reported management options, radiotherapy and, more specifically, drug treatments were rare. Drug use was recorded in less than 5% in different time windows after diagnosis, suggesting a marginal role of conventional chemotherapy and new antineoplastic agents in chondrosarcoma.

Overall survival was relatively high across all databases and can be explained by a substantial proportion of cases with early-stage and low-grade disease. However, explicit data about stage and grade was available only in one database. Non-conventional chondrosarcoma could be detected in only one database and was not frequent (14.8%) showing the difficulty of conducting studies in RWD in this population.

Different real-world data sources can be successfully used to study chondrosarcoma patients' outcomes and characteristics, while cancer registries offer the most granular information. The combination of different sources allows a better understanding and interpretation of the obtained results.

16. REFERENCES

1. Valery PC, Laversanne M, Bray F. Bone cancer incidence by morphological subtype: a global assessment. Cancer Causes Control. 2015 Aug;26(8):1127–39.
2. Thorkildsen J, Myklebust TÅ. The national incidence of chondrosarcoma of bone; a review. Acta Oncologica. 2023 Feb 1;62(2):110–7.
3. Gelderblom H, Hogendoorn PCW, Dijkstra SD, Van Rijswijk CS, Krol AD, Taminiau AHM, et al. The Clinical Approach Towards Chondrosarcoma. The Oncologist. 2008 Mar 1;13(3):320–9.
4. Suster D, Hung YP, Nielsen GP. Differential Diagnosis of Cartilaginous Lesions of Bone. Archives of Pathology & Laboratory Medicine. 2020 Jan 1;144(1):71–82.
5. Choi JH, Ro JY. The 2020 WHO Classification of Tumors of Bone: An Updated Review. Advances in Anatomic Pathology. 2021 May;28(3):119–38.
6. Van Praag (Veroniek) VM, Rueten-Budde AJ, Ho V, Dijkstra PDS, Fiocco M, Van De Sande MAJ, et al. Incidence, outcomes and prognostic factors during 25 years of treatment of chondrosarcomas. Surgical Oncology. 2018 Sep;27(3):402–8.
7. Thorkildsen J, Taksdal I, Bjerkehagen B, Haugland HK, Børge Johannesen T, Viset T, et al. Chondrosarcoma in Norway 1990–2013; an epidemiological and prognostic observational study of a complete national cohort. Acta Oncologica. 2019 Mar 4;58(3):273–82.
8. Ottesen TD, Shultz BN, Munger AM, Amick M, Toombs CS, Friedaender GE, et al. Chondrosarcoma patient characteristics, management, and outcomes based on over 5,000 cases from the National Cancer Database (NCDB). Nakamura T, editor. PLoS ONE. 2022 Jul 28;17(7):e0268215.
9. Maciá-Martínez M, Gil M, Huerta C, Martín-Merino E, Álvarez A, Bryant V, et al. *Base de Datos para la Investigación Farmacoepidemiológica en Atención Primaria* (BIFAP) : A data resource for pharmacoepidemiology in Spain. Pharmacoepidemiology and Drug. 2020 Oct;29(10):1236–45.

10. Ferté T, Jouhet V, Griffier R, Hejblum BP, Thiébaut R, Bordeaux University Hospital Covid-19 Crisis Task Force. The benefit of augmenting open data with clinical data-warehouse EHR for forecasting SARS-CoV-2 hospitalizations in Bordeaux area, France. JAMIA Open. 2022 Dec;5(4):ooac086.
11. Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, Van Staa T, et al. Data Resource Profile: Clinical Practice Research Datalink (CPRD). Int J Epidemiol. 2015 Jun;44(3):827–36.
12. Sund R. Quality of the Finnish Hospital Discharge Register: A systematic review. Scand J Public Health. 2012 Aug;40(6):505–15.
13. Leinonen MK, Anttila A, Malila N, Dillner J, Forslund O, Nieminen P. Type- and age-specific distribution of human papillomavirus in women attending cervical cancer screening in Finland. British Journal of Cancer. 2013;109(11):2941–50.
14. Vikkula J, Uusi-Rauva K, Ranki T, Toppila I, Aalto-Setälä M, Pousar K, et al. Real-world Evidence of Multiple Myeloma Treated from 2013 to 2019 in the Hospital District of Helsinki and Uusimaa, Finland. Future Oncol. 2023 Sep;19(30):2029–43.
15. Sanden GAC van D, Coebergh JWW, Schouten LJ, Visser O, Leeuwen FE van. Cancer incidence in the Netherlands in 1989 and 1990: First results of the nationwide Netherlands cancer registry. European Journal of Cancer. 1995 Oct;31(11):1822–9.
16. Bray F, Kohler B, Ferlay J. Chapter 5: Data comparability and quality. In: Forman D, Bray F, Brewster DH, Mbalawa CG, Kohler B, Piñeros M, editors. Cancer in Five Continents vol X. 2013.
17. Hurwitz HI, Dowlati A, Saini S, Savage S, Suttle AB, Gibson DM, et al. Phase I Trial of Pazopanib in Patients with Advanced Cancer. Clinical Cancer Research. 2009 Jun 15;15(12):4220–7.
18. Schuetze SM, Wathen JK, Lucas DR, Choy E, Samuels BL, Staddon AP, et al. SARC009: Phase 2 study of dasatinib in patients with previously treated, high-grade, advanced sarcoma. Cancer. 2016 Mar 15;122(6):868–74.
19. Rock A, Ali S, Chow WA. Systemic Therapy for Chondrosarcoma. Curr Treat Options in Oncol. 2022 Feb;23(2):199–209.
20. Duffaud F, Italiano A, Bompas E, Rios M, Penel N, Mir O, et al. Efficacy and safety of regorafenib in patients with metastatic or locally advanced chondrosarcoma: Results of a non-comparative, randomised, double-blind, placebo controlled, multicentre phase II study. European Journal of Cancer. 2021 Jun;150:108–18.
21. Wagner MJ, Ricciotti RW, Mantilla J, Loggers ET, Pollack SM, Cranmer LD. Response to PD1 inhibition in conventional chondrosarcoma. j immunotherapy cancer. 2018 Dec;6(1):94.
22. Somaiah N, Conley AP, Parra ER, Lin H, Amini B, Solis Soto L, et al. Durvalumab plus tremelimumab in advanced or metastatic soft tissue and bone sarcomas: a single-centre phase 2 trial. The Lancet Oncology. 2022 Sep;23(9):1156–66.

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)
Periosteal 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 of 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