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Nationwide incidence of sarcomas and connective tissue tumors of intermediate malignancy over four years using an expert pathology review network

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Abstract (N=228 words)

Background:
Since 2010, NETSARC and RREPS collected and reviewed prospectively all cases of sarcomas and tumors of intermediate malignancy (TIM) nationwide.

Methods:
The nationwide incidence of sarcoma or TIM (2013-2016), confirmed by expert pathologists using WHO classification are presented. Yearly variations and correlation with published clinical trials was analyzed.

Results:
139 histological subtypes are reported among the 25172 patients with sarcomas (n=18710, 64%) or TIM (n=6460, 36%), respectively n=5838, n=6153, n=6654, and n=6527 yearly from 2013 to 2016. Over these 4 years, the yearly incidence of sarcomas and TIM was therefore 79.7, 24.9 and 95.1/10^6/year, above that previously reported. GIST, liposarcoma, leiomyosarcomas, undifferentiated sarcomas represented 13%, 13%, 11% and 11% of tumors. Only GIST, as a single entity had a yearly incidence above 10/million/year. There were respectively 30, 63 and 66 different histological subtypes of sarcomas or TIM with an incidence ranging from 10 to 1/10^6, 1-0.1/10^6, or < 0.1/10^6/year respectively. The 2 later "incidence groups" included 21% of the patients. The incidence of 8 histotypes varied significantly over this 4 years. Patients with tumors with an incidence above 1/10^6per year have significantly higher numbers of dedicated published phase III and phase II clinical trials ($p<10^{-6}$).

Conclusions:
This nationwide registry of sarcoma patients with histology reviewed by sarcoma experts shows that the incidence of sarcoma and TIM is higher than reported, and that tumors with an incidence<10^6/year have a much lower access to clinical trials.

Introduction

Sarcomas is an heterogeneous group of rare connective tissue cancers, with variable clinical presentations, and a reported incidence thought to be close to $2/10^5$/year 15 years ago, which has more recently been reported to range from 3 to 7 $/10^5$/year (1-16).

The reported incidence of sarcoma varies considerably across countries and according to the date of analysis (2-16). The overall incidence of sarcoma is therefore not precisely known, and even less so that of individual histological subtypes, which are not unfrequently misdiagnosed. Indeed, because of their rarity, sarcoma are initially misclassified in up to 30% of cases (1,5,6,11,17). As a consequence patients with sarcomas may not treated according to clinical practice guidelines (1-21). In all clinical practice guidelines, it is recommended that the diagnosis of sarcoma should be confirmed by an expert pathologist. In general, management of sarcoma patients should be performed by a dedicated multidisciplinary team, including expert pathologists and surgeons, treating a large number of patients (5-7). It was recently reported that central pathology review of sarcoma cases is cost effective, reducing both morbidity, mortality and cost of management (22,23).

Since 2010, the French National Cancer Institute (INCa) funded pathology and clinical networks for sarcoma called RREPS and NETSARC, subsequently joined by RESOS focused on bone sarcomas, to improve the quality of management of sarcoma patients. Initially, the network of 23 expert reference centers for pathology (RRePS) was in charge of the mandatory histological review for each suspected case of sarcoma nationwide. These networks have merged since 2019 in a single NETSARC+ network. The common database (netsarc.org) gathering all cases of sarcoma presented to MDTB was created and implemented, collected data on the diagnostic, therapeutic management, and the clinical outcome in terms of relapse and survival. From Jan 1st 2010, this database prospectively included over 59000 patients with sarcoma or tumor of intermediate malignancy. Since 2013, the overall accrual in the database reached a plateau, suggesting that the closest to exhaustive collection of cases in this country was obtained.

The incidence of sarcoma and TIM has seldom been reported in exhaustive nationwide series with organized reference center pathology review. We report here on the incidence of the different histological subtypes of sarcomas and TIM reported in the NETSARC+ database from 2013 to 2016.

Patient, material and methods

The NETSARC+ network and the referral of the pathology sample to the network of experts.

The RREPS (pathology, NETSARC (clinical management), and RESOS (bone sarcoma) networks which gathered experts from the same centers were merged into the NETSARC+ network in 2019. The organization of these networks has been reported previously (24,25): each RREPS and NETSARC center organizes a multidisciplinary tumor board (MDTB) gathering sarcoma specialized pathologist(s), radiologist(s), surgeon(s), radiation oncologist(s), medical oncologist(s), and often molecular biologist(s), orthopedist(s), pediatrician(s).

Since 2010, it is mandatory for the primary pathologist to refer all suspected cases of sarcomas or TIM to one of the reference centers. In addition, if this has not been done previously, pathology review is will be requested for any clinical case referred to one of the 26 multidisciplinary tumor board of NETSARC without initial prior central pathology review, thus ensuring a double check. These two modes of entry improve the rate of review of the sarcoma/TIM samples nationwide. All sarcoma/TIM or suspected sarcoma/TIM patient cases presented to the MDTB of all 26 centers were recorded in the electronic online database, by a dedicated team of Clinical research assistant (CRAs), supervised by the Coordinating centers (Centre Leon Bérard, Gustave Roussy, Institut Bergonié, CHU Tours, CHU Nantes). Patient files may be presented before any diagnostic procedure, before initial biopsy, before primary surgery, after primary surgery, at relapse, and/or in case of a possible inclusion in a clinical trial as previously described (24,25). Patients and treatment data were prospectively included and regularly updated by the dedicated study coordinators.

The RREPS/NETSARC Database

The RREPS/NETSARC database may therefore enable to describe as exhaustively as possible the incident and prevalent population of sarcoma patients in France. Of note, the database includes a limited set of data, on purpose, describing patients and tumor characteristics, surgery, relapse and survival (24, 25), centers performing the first resection, as well as potential secondary surgery types and sites, the final quality of resection, etc...

Of note, about 24% of patients in the database discussed in a NETSARC MDTB had a diagnosis which was not that of a sarcoma/TIM (e.G. lipoma, carcinoma, lymphoma…). Again, it is important to note that in NETSARC, patients with suspected sarcoma/TIM can enter the process of MDTB either through the pathology network, or directly by the physician, leading both to a final MDTB review after central pathology confirmation.

All data presented here were extracted from the NETSARC.org database accessible online for a period of 4 years between 2013 and 2016. These 4 years were selected since: 1) the yearly incidence of sarcoma and TIM started to plateau since 2013, and 2) data monitoring and implementation is still ongoing for year 2017 and later.

Presentation of the data

The WHO classification is used to describe the histological subtypes in the database (1). The number of patients for each individual histological subtype of sarcoma or TIM per year, from 2013 to 2016, is therefore presented in these tables. To facilitate the comparison with other databases using previous classifications, the incidence for groups of tumors are also presented in the Tables, when they are clinically relevant (e.g. uterine sarcoma), or used as entities for clinical trials (e.g. liposarcomas, leiomyosarcoma, solitary fibrous tumors, giant cell tumors of the bone…). To estimate the incidence of these tumors, we used the official number of French citizens in the years 2013 to 2016, which were respectively 65.56, 66.13, 66.42 and 66.60 millions inhabitants.

Matching histotypes with published clinical trials

Each individual histotype was screened to identify a dedicated clinical trial within the Pubmed database. The name of the entity (e.g. angiosarcoma, pleomorphic liposarcoma…) was used in the interrogation, together with a filter on clinical trial, adding « phase III », « randomized phase II », or « phase II ». Pubmed was interrogated between Jan 15 and Jan 30 2020.

Statistical analyses

The number of patient per year with the different histotypes is presented in tables. To analyze the variation of incidence over the 4 years, an ANOVA procedure was used for the whole dataset. Histotypes with a significant variation in the period of observation are detailed. The comparison of the frequency of published clinical trials per histological subtypes or groups of subtypes was performed using the chi square or Fisher's exact test. All statistical tests were two-sided. All statistical analyses were performed using SPSS (v 23.0) (IBM, Paris France).

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Results

Incidence of sarcoma and TIM in NETSARC

Table 1 to 3 present the incidence of the individual histological subtypes of soft tissue, visceral, bone sarcomas or connective tissue tumors included in the NETSARC+ databases from 2013 to 2016, the first 4 years for which it was considered close to exhaustive.
From 2013 to 2016, a total of 25172 incident patients were included in the database (Table 1 and 2), with n=5838, n=6153, n=6654, and n=6527 new patients for each year.
The NETSARC database includes 156 individual tumors or groups of sarcoma/TIM, 31 groups of sarcomas/TIM (e.g. « liposarcoma ») and 125 distinct individual histological subtypes of sarcomas or TIM (Table 1-3). Twelve additional histological subtypes of bone sarcomas (leiomyosarcomas, synovial etc) were also distinguished in this work (Table 3).
Finally, Table 3 also presents the incidence of sarcomas diagnosed in patients with reported genetic predispositions.
With an official number of the French population of 65.56, 66.13, 66.42 and 66.60 millions inhabitants in these 4 years, the estimated incidence of sarcomas and tumors of intermediate malignancy from 2013 to 2016 was 89.05, 93.04, 100.18, and 98.00 per million inhabitants respectively. Over these 4 years, the estimated yearly incidence of sarcomas and TIM was therefore 95,10/10^6/year.
There were 18710 (64%) patients with sarcomas (incidence 70.87/10^e/year) and 6460 (36%, 24.47/10^6/year) patients with TIM.
The observed overall incidence of sarcoma and TIMs is therefore above that previously reported (1-15).

Over 100-fold difference in incidence in different sarcoma histotypes

Figure 1 presents the individual histotypes and relevant groups of histotypes (eg liposarcoma, leiomyosarcoma, unterine sarcomas) ordered by incidence. GIST, liposarcoma, leiomyosarcomas, undifferentiated sarcomas represented 13%, 13%, 11% and 11% of all sarcomas (47% all 4 together). Only gastrointestinal stromal tumors, if considered as single entities, exceeded a yearly incidence above 10/10^6/ year (Figure 1). The other histological types of sarcomas with a yearly incidence above 10/10^6/year are histotypes groups 1) all liposarcomas, 2) all smooth muscle tumors, 3) all undifferentiated sarcomas, and 4) all fibroblastic or myofibroblastic tumors lumped together. This later group a group is not clinically homogenous and usually not considered as a specific entity in clinical trials or retrospective studies.
There were respectively 35, 63 and 66 different histological subtypes or groups (e.g. MPNST, or vascular sarcomas…) of sarcomas or TIM with an incidence ranging from 10 to 1/10^6/year, 1-0.1/10^6 per year, or <0.1/10^6/year respectively.
These 3 groups gathered respectively 18542 (74%), 4766 (19%) and 568 (2%) of patients.
The total number of patients in the different incidence groups exceeds the total number of patients of the series since some histological subtypes are listed as a group : for instance all liposarcoma as well as individual subtypes of liposarcomas (eg myxoid liposarcoma) are both listed.
A simple description of mean age, sex ratio, and site of the tumori s presented in table 4. It also shows the large clinical heterogeneity of these tumors with a mean age ranging from 5 years (infantile fibrosarcoma) to 78 (atypical fibroxanthoma), and a sex ratio from 0 (for sexual organs) to 153 for adenosarcoma.

Variable incidence of sarcoma histotypes over the 2013-2016 period

We investigated then the variability of the yearly incidence of these different tumors in the database. The analysis of variance of the observed incidence indicated a significant interaction between time and histology ($p<0.001$). Supplementary figure presents the eight histological subtypes whose yearly incidence was found to vary significantly between 2013 and 2016. Adenosarcoma, central chondrosarcoma, solitary fibrous tumour, endometrial stromal sarcoma - high-grade increaseover the4 years, while intimal sarcoma, Kaposi sarcoma, Liposarcoma - round cell, myoepithelioma apprear to decrease. Most have an incidence <1/10^6 year. While for Kaposi sarcoma, this maybe related to the evolving

epidemiology of an associated condition (HIV infection), the significance of these variations remain unclear and will deserve to be explored in other registries with a central review.

Incidence of individual histotypes and published clinical trials

Figure 1 presents graphically, and in ranking order (decreasing), the incidence of the different histotypes and groups of histotypes. These were matched with the presence of a published clinical trial on Pubmed focused specifically on this histological group (eg liposarcoma) or specific histotype (e.g. pleomorphic liposarcoma). Phase III studies, randomized phase II studies, and non randomized phase II studies are indicated in green, dark blue and light blue respectively. An histological subtype is considered covered by a trial only if the trial includes a specific arm (phase II) or a specific strata (phase III) in this given histotype.

As expected, phase III trials are available mostly in histotypes or groups of histotypes with an incidence $>1/10^6$ per year (Figure 1).

14 of 35 (40%) histotypes with an incidence $>1/10^6$ had a dedicated phase III study vs 6 of 129 (4.6%) histotypes for sarcomas with a incidence $<1/10^6$ ($p<10^{-6}$). 20100 (79,7%) patients of the database had a specific histotype for which no phase III trial had been reported.

21 of 35 (60%) histotypes with an incidence $>1/10^6$ had a dedicated randomized phase II study vs 10 of 129 (7.7%) histotypes for sarcomas with a incidence $<1/10^6$ ($p<10^{-10}$)). 13154 (52.1%) patients of the database had a specific histotype for which no randomized phase II trial had been reported.

Twenty-eight of 35 (80%) histotypes with an incidence $>1/10^6$ had a dedicated phase III study vs 36 of 129 (27.9%) histotypes for sarcomas with a incidence $<1/10^6$ ($p<10^{-8}$). 6516 (25.8%) patients of the database had a specific histotype for which no phase II trial had been reported.

Discussion

The objective of this work was to describe the incidence of individual histological subtypes of sarcomas and TIM according to the most recent WHO classification. These cases were collected from the single NETSARC+ database, gathering the previous RREPS, RESOS and NETSARC databases (netsarc.org).

This work supported by the French NCI allowed therefore to measure the incidence of sarcomas and TIM in a nationwide database, close to exhaustivity given the stringent criteria of central pathology review in place since 2010. Since 2013, the number of patients included in the database per year is relatively stable suggesting that this is close to exhaustivity. We stopped the description on year 2016, since years 2017 to 2019 are still being monitored by the NETSARC+ now.

The first important observation is that the incidence of these tumors is larger than previously reported in each of these 4 years (1-15). Recently published data from countries in 4 continents reported an overall incidence ranging from 3 to $7.7/10^6$/year. The results of these studies are also heterogenous in terms of respective proportion of the groups of histotypes, ranging from 4 to 20% for undifferentiated sarcomas for instance. Taken together these observations suggest that mandatory central pathology review, results in a higher than reported incidence of almost all subtypes.

The present work also confirm that sarcoma histotype is a highly fragmented group of diseases, whose individual incidences may range from $10/10^6$ to less than $0.01/10^6$, ie a >1000-fold difference in incidence for tumors altogether considered as rare according to the international classification.

This is also a highly heterogenous group of tumors in terms of clinical presentations as shown by the diversity of sex ratio and mean age for diagnosis. Each of these entities should therefore benefit from a specific research programs to describe their natural history as well as the impact of current treatment on their disease course. This require a coordinated effort, worldwide, to achieve this goal given the rarity of certain histotypes. This is currently being conduction by intergroup studies, and international networks such as EURACAN. This work also confirms the important of national registries to investigate these rare subtypes.

An intriguing observation is that the incidence of these tumor may vary over time, and this was observed to be significant for 8 histotypes. While etiologic reasons may account fgor the reduction of Kaposi sarcoma in this time period, there is no obvious explanation for the seven other histotypes. Given the stability of the pathology team over this period this is not likely resulting from the pathology review. Epidemiological studies in other countries may be useful to confirm these variations, which may guide research on etiology of these most often rare sarcomas and TIM.

Another observation, expected by clinicians, is the link between the incidence and the availability of published prospective clinical research work to guide the management of individual subtypes. For decades the medical treatment of sarcomas used a one-size-fits-all approach for phase II to III clinical trials. Since 15 years, dedicated randomized phase II, III and phase II studies were implemented for specific histological subtypes, starting with GIST. This is more the exception of the rule though. The majority of histotypes described in this work, expecially those with an incidence under $1/10^6$/year have not had a dedicated phase II, randomized phase II or phase III clinical trial to guide clinical practice guidelines. This represents the majority of these patients for phase III, and still about 25% of the patients for phase II. This calls for a revision of the criterias to define standard treatment for such rare tumors where phase III are not feasible. Health authorities and reimbursement bodies should adapt their decisions on approval and reimbursement on the feasible level of evidence which could be reached for tumors with and incidence $<1/10^e6$ per year in order not to discriminate against patients with rare cancers. It is important to remember that altogether patient with rare cancers represent 22% of all patient swith cnacers, and about 30% of the mortality due to cancer (26).

This study has many limitations. We can not exclude that patients may not reach our network despite the administrative incentive. This is true in particular for bone sarcoma and TIM (e.g. chondroblastomas, osteoblastoma, aneurysmatic bone cyst, etc..) which were collected more recently. The work must also adapt the the rapidly evolving classification of sarcomas, including now molecular subclassifications , which are not described here (for instance GIST,

the novel NTRK sarcoma subgroup, BCOR, CIC-DUX4 sarcomas). To further explore the exhaustivity of the NETSARC+ bases, an ongoing project connects this base to the social security data base (SNDS) the single payer in France covering all citizens for all diseases (the Deepsarc project). This should enable a further refinement of these numbers. Nevertheless, the observation that the incidence of sarcomas and TIM was higher than previously reported in this work during this time period provides a valuable information for this group of tumors.

In conclusion, this nationwide registry describes the incidence of sarcoma and TIM at a nationwide level over a 4 year period, with a central sarcoma pathologist expert review. It provides a benchmark for comparison with other registries worldwide and confirm the limitations of clinical research in sarcomas with an incidence $<10^6$ per year. The observation of variable incidence for specific histological suibtype is intringuing and should be compared with data from other countries. Geographical research on the distribution of these cases over the national territory are ongoing.

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Legends to the Figures

Figure 1 : Published clinical trials in sarcoma and TMI histotypes.

Tabular presentation of different sarcoma histotypes and groups of histotypes by decreasing order together with the documented published clinical trials in Pubmed : if phase III clinical trials are published, the box is highlighted in light green, if randomized phase II trials are published the box is highlighted in dark blue, if uncontrolled phase II trials are published the box is highlighted in light blue.

Supplementary Figure: Variable incidence of sarcoma subtypes between 2013 to 2016

Presentation of the yearly variation of the eight different histotypes with significantly variable incidence in the period of observation.

Table 1: incidence of soft tissue and visceral sarcomas

	2013	2014	2015	2016	Total	Incidence /10^6/year
Adipocytic tumours	**744**	**821**	**817**	**865**	**3247**	**12,299**
Atypical lipomatous tumour / well-differentiated liposarcoma	289	304	314	357	1266	4,795
Liposarcoma – dedifferentiated	304	344	341	356	1345	5,095
Myxoid Round Cell LPS	**99**	**106**	**108**	**96**	**409**	**1,549**
Liposarcoma - myxoid	81	90	95	89	355	1,345
Liposarcoma - round cell	18	16	13	7	54	0,205
Liposarcoma - pleomorphic	31	41	36	31	139	0,527
Lipomatous spindle cell/pleomorphic	0	1	0	0	1	0,004
Liposarcoma NOS	21	25	17	22	85	0,322
Liposarcoma - mixed type	0	0	1	1	2	0,008
Fibroblastic & myofibroblastic tumours	**1041**	**1047**	**1115**	**1147**	**4349**	**16,473**
Desmoid fibromatosis	307	295	357	381	1340	5,072
Lipofibromatosis	3	0	5	0	8	0,030
Giant cell Fibroblastoma	2	4	4	1	11	0,042
Dermatofibrosarcoma Protuberans	261	270	258	251	1040	3,939
Solitary fibrous tumour (all)	**210**	**222**	**242**	**252**	**925**	**3,504**
Solitary fibrous tumor	166	178	193	214	751	2,845
High risk SFT	44	43	49	38	174	0,659
Inflammatory myofibroblastic Tum.	32	39	33	41	145	0,549
Low grade Myofibroblastic Sarc.	3	5	3	2	13	0,049
Myxoinflammatory Fibroblastic Sarc.	6	6	6	5	23	0,087
Infantile fibrosarcoma	3	2	1	4	10	0,038
Adult fibrosarcoma	11	4	9	4	28	0,106
Myxofibrosarcoma	162	160	152	156	630	2,386
Low grade fibromyxoid sarcoma	33	30	35	38	136	0,515
Sclerosing epithelioid fibrosarcoma	8	11	10	12	41	0,155
So-called fibrohistiocytic tumours	**29**	**16**	**37**	**24**	**106**	**0,402**
Intermediate fibrohistiocytic tumors	0	0	2	3	5	0,019
Malignant tenosynovial giant cell tum.	1	0	0	1	2	0,008
Plexiform fibrohistiocytic tumors	7	7	9	6	29	0,110
Giant cell tumour of soft tissue	21	9	26	14	70	0,265
Vascular tumours	**398**	**377**	**381**	**364**	**1520**	**5,758**
Retiform hemangio-endothelioma	1	3	3	2	9	0,034
Papillary intralymphatic angioendothelioma	0	0	0	1	1	0,004
Composite hemangioendothelioma	1	1	1	0	3	0,011
Kaposi sarcoma	191	165	162	145	663	2,511
Kaposiform hemangioendothelioma	1	1	1	1	4	0,015
Pseudomyogenic hemangioendothelioma	1	3	0	2	6	0,023
Epithelioid hemangioEndothelioma	27	20	30	23	100	0,379
Angiosarcoma	176	183	182	187	728	2,758
Intermediate vascular tumours	0	1	2	3	6	0,023
Pericytic (perivascular) tumours	**4**	**4**	**1**	**1**	**10**	**0,038**
Malignant glomus tumour						
Smooth muscle (SM) tumours	**646**	**698**	**669**	**666**	**2679**	**10,148**
SM tumor of undetermined malignancy	20	47	23	32	122	0,462

Metastatic leiomyoma	0	0	0	2	2	0,008
Leiomyosarcoma	247	263	287	297	1094	4,144
Leiomyosarcoma -differentiated	245	243	240	217	945	3,580
Leiomyosarcoma – poorly differentiated	134	145	119	118	516	1,955
Skeletal muscle sarcoma (RMS)	**145**	**157**	**173**	**133**	**608**	**2,303**
Embryonal RMS	**50**	**45**	**60**	**34**	**179**	**0,678**
Embryonal RMS sarcoma - botryoid type	8	6	6	3	23	0,087
Embryonal rhabdomyosarcoma usual type	35	31	47	24	137	0,519
Embryonal rhabdomyosarcoma spindle cell	7	8	7	7	29	0,110
Alveolar RMS	27	36	35	25	123	0,466
Pleomorphic RMS	28	38	42	36	144	0,545
Sclerosing RMS	2	3	3	3	11	0,042
Spindle cell RMS	13	8	9	9	39	0,148
Adult spindle cell RMS	0	0	1	4	5	0,019
RMS NOS	21	25	23	19	88	0,333
Ectomesenchymoma: Mal. mesenchymoma	4	2	0	3	9	0,034
Gastrointestinal stromal tumors (GIST).	**736**	**792**	**913**	**831**	**3272**	**12,394**
Chondro-osseous tumours						
Extraskeletal osteosarcoma	**25**	**25**	**32**	**14**	**96**	**0,364**
Peripheral nerve sheath tumours	**75**	**68**	**69**	**74**	**286**	**1,083**
MPNST - epithelioid type	0	2	1	3	6	0,023
MPNST - usual type	36	7	14	28	85	0,322
Malignant peripheral nerve sheath tumour	36	55	47	35	173	0,655
Malignant Triton tumour	0	2	3	5	10	0,038
Malignant granular cell Tumour	3	2	4	0	9	0,034
Malignant perineurioma	0	0	0	3	3	0,011

Table 1 (part 2): incidence of soft tissue and visceral sarcomas

	2013	2014	2015	2016	Total	Incidence /10e6/year
Tumours of uncertain differentiation						
Atypical fibroxanthoma	114	107	89	119	429	1,625
Angiomatoid fibrous histiocytoma	9	15	10	9	43	0,163
Ossifying fibromyxoid Tumour	7	7	5	13	32	0,121
Myoepithelioma, myoepithelial carcinoma, & mixed tumour	**31**	**26**	**18**	**18**	**96**	**0,364**
Myoepithelioma	30	26	15	14	85	0,322
Malignant myoepithelial Tumour	0	0	1	1	2	0,008
Mixed tumour	1	0	2	3	6	0,023
Haemosiderotic fibrolipomatous tumour	0	2	0	7	9	0,034
Phosphaturic mesenchymal tumour	0	1	2	2	5	0,019
NTRK-rearranged spindle cell neoplasm (emerging)	Not reported in NETSARC (so far)					
Synovial sarcoma	**103**	**101**	**133**	**105**	**442**	**1,674**
Synovial sarcoma – NOS	23	18	29	21	91	0,345
Synovial sarcoma - biphasic	11	19	23	17	70	0,265
Synovial sarcoma – monophasic	60	57	67	60	244	0,924
Synovial sarcoma - poorly Differentiated	9	7	14	7	37	0,140
Epithelioid sarcoma (all)	**29**	**30**	**28**	**33**	**120**	**0,455**
Epithelioid sarcoma	23	28	25	22	98	0,371
Undifferentiated epithelioid sarcoma	6	2	3	11	22	0,083
Alveolar soft part sarcoma	10	7	8	6	31	0,117
Clear cell sarcoma of soft tissue 13	16	26	16	71	0,269	
Extraskeletal myxoid chondrosarcoma	15	12	20	11	58	0,220
Desmoplastic small round cell tumour	14	9	12	17	52	0,197
Extrarenal rhabdoid tumour	6	13	16	16	51	0,193
SMARCA4-deficient thoracic sarcoma	0	0	6	9	15	0,057
PEComa, including angiomyolipoma	**13**	**27**	**15**	**29**	**86**	**0,326**
PECOMA - NOS	13	25	11	18	67	0,254
Malignant PECOMA	0	2	4	13	19	0,072
Intimal sarcoma	14	12	11	9	46	0,174
Undifferentiated sarcoma (all)	**566**	**627**	**784**	**740**	**2717**	**10,292**
Undifferentiated pleomorphic sarcoma	290	367	470	429	1556	5,894
Undifferentiated sarcoma	110	87	154	79	430	1,629
Undifferentiated sarcoma -NOS	125	130	111	57	423	1,602
Undifferentiated spindle cell sarcoma	41	43	49	175	308	1,167
Low grade sinonasal sarcoma	2	0	0	3	5	0,019
Melanotic neuroectodermal tumour infancy	0	0	0	1	1	0,004
Phyllode sarcoma	**32**	**25**	**46**	**35**	**138**	**0,523**
Sarcomas or TIM NOS						
- Sarcoma NOS	166	197	259	189	809	3,064
- Tumors of intermediate malignancy	7	15	13	17	52	0,197

Table 2: Incidence of bone sarcomas in NETSARC+ (2013-2016)

	2013	2014	2015	2016	Total	Incidence /10^6/year
Undifferentiated small round cell sarcomas (SRCS) of bone and soft tissue						
Ewing sarcoma	151	163	153	147	614	2,326
SRCS with EWSR1-non-ETS fusions	6	6	8	36	56	0,212
CIC-rearranged sarcoma	1	3	3	4	11	0,042
BCOR-rearranged Sarcoma	2	0	2	3	7	0,027
Bone tumours						
Chondrogenic tumours						
Chondroblastoma	11	16	9	16	52	0,197
Chondromyxoid fibroma	4	7	12	3	26	0,098
entral atypical cartilaginous tumour/chondrosarcoma, gd 1	2	10	19	45	76	0,288
Central chondroS grades 2 and 3	22	33	35	27	117	0,443
Chondrosarcoma NOS	164	125	143	140	572	2,167
Peripheral chondrosarcoma	5	6	8	20	39	0,148
Periosteal chondrosarcoma	8	4	6	7	25	0,095
Clear cell chondrosarcoma	4	3	2	5	14	0,053
Mesenchymal chondrosarcoma	3	7	11	10	31	0,117
Dedifferentiated chondrosarcoma	19	23	20	31	93	0,352
Osteogenic tumors						
Osteoblastoma	5	9	8	10	32	0,121
Low grade central osteosarcoma	4	4	4	7	19	0,072
Low-grade central osteosarcoma	2	1	1	3	7	0,027
Dediff. ow grade central osteosarcoma	2	3	3	4	12	0,045
Osteosarcoma	154	169	170	168	661	2,504
Osteosarcoma NOS	39	57	62	72	230	1,106
Conventional osteosarcoma	111	105	105	96	417	1,580
Osteoblastoma-like osteosarcoma	1	0	0	1	2	0,008
Telangiectasic osteosarcoma	2	7	2	5	16	0,061
Small cell osteosarcoma	1	0	1	2	4	0,015
Parosteal osteosarcoma	7	7	16	10	40	0,152
- Parosteal osteosarcoma	6	4	10	7	27	0,102
- Dedifferentiated parosteal osteoSarc	1	3	6	3	13	0,049
Periosteal osteosarcoma	1	4	0	0	5	0,019
High-grade surface osteosarcoma	6	5	6	8	25	0,095
Fibrogenic tumors						
Desmoplastic fibroma of bone	0	0	2	4	6	0,023
Fibrosarcoma of the bone	0	1	3	0	4	0,015
Vascular tumor of bone						
Epithelioid haemangioendothelioma	1	2	5	0	8	0,030
Angiosarcoma of bone	7	6	7	9	29	0,110
Osteoclastic giant-cell rich						
Aneurysmal bone cyst	14	9	22	8	53	0,201
Giant cell tumour of bone	76	88	87	67	318	1,204
Malignant/dedifferentiated GCTB	0	0	2	4	6	0,023
Notochordal tumours						
- Conventional chordoma	35	33	42	54	164	0,621
- Dedifferentiated chordoma	0	1	1	0	2	0,008
Adamantinoma	8	1	2	8	19	0,072
Langerhans cell histiocytosis	4	8	4	4	20	0,076

Table 3: Incidence of uterine and rare bone sarcomas & genetic syndromes

	2013	2014	2015	2016	Total	Incidence /10e6/year
Uterine sarcoma	**242**	**311**	**285**	**300**	**1138**	**4,311**
Endometrial stromal sarcoma, low grade	**57**	**64**	**55**	**62**	**238**	**0,902**
Endometrial stromal nodule	2	1	5	8	16	0,061
Endometrial stromal sarcoma	0	3	2	5	10	0,038
Endometrial stromal sarcoma-low grade	55	60	48	49	212	0,803
Endometrial stromal sarcoma - high-grade	1	5	13	22	41	0,155
Adenosarcoma	28	35	42	51	156	0,591
Undifferentiated uterine sarcoma	37	49	38	17	141	0,534
Uterine tumour resembling ovarian sex cord	5	1	4	7	17	0,064
Uterine leiomyosarcoma (extracted from the LMS group above)	**114**	**157**	**133**	**141**	**545**	**2,064**
Rare bone sarcomas (extracted from the histological groups in Table 1)						
All undifferentiated sarcoma of bone	**36**	**31**	**38**	**47**	**152**	**0,576**
Undifferentiated pleomorphic sarcoma of bone	16	20	12	21	69	0,261
Undifferentiated sarcoma	16	11	21	8	56	0,212
Undifferentiated spindle cell sarcoma	4	0	5	17	26	0,098
Undifferentiated epithelioid sarcoma	0	0	0	1	1	0,004
Leiomyosarcoma of bone	11	15	5	9	40	0,152
Synovial sarcoma of bone	4	2	2	1	9	0,034
Rhabdomyosarcoma of bone	2	2	1	4	9	0,034
BCOR Sarcoma of bone	1	0	2	3	6	0,023
Myoepithelioma of bone	1	1	1	1	4	0,015
Liposarcoma of bone	0	2	0	2	4	0,015
Other histological syubtypes of bone sarcomas	33	42	46	50	171	0,648
Genetic predisposition of soft tissue and bone or HIV						
Enchondromatosis	5	2	6	4	17	0,064
Li Fraumeni syndrome	3	3	4	4	14	0,053
Retinoblastoma	1	0	3	1	5	0,019
Multiple osteochondroma	2	2	11	5	20	0,076
Neurofibromatosis	28	28	24	25	105	0,398
Rothmund-Thomson	0	1	0	0	1	0,004
HIV	4	12	10	6	32	0,121
Other immunosuppression	3	13	4	5	25	0,095

Table 4: Age, gender, sites of histotypes

Histotypes	Mean Age	F/H Ratio	Sites (%)*							
			GI	Gyn	H&N	I. trnk	L. limb	Trnk w	U. limb	Others
Adamantinoma	29,1	1,71	0,0	0,0	0,0	0,0	100,0	0,0	0,0	0,0
Adenosarcoma	61,3	51,00	1,9	89,7	0,0	3,8	0,6	0,6	0,0	3,2
Adult fibrosarcoma	69,5	1,15	0,0	7,1	7,1	10,7	17,9	28,6	17,9	10,7
Adult spindle cell rhabdomyosarcoma	52,4	0,25	0,0	0,0	20,0	0,0	20,0	40,0	20,0	0,0
Alveolar rhabdomyosarcoma	22,7	1,05	0,0	0,8	40,7	16,3	13,8	9,8	13,8	4,9
Alveolar soft part sarcoma	30,5	1,21	0,0	0,0	9,7	6,5	51,6	22,6	6,5	3,2
Aneurysmal bone cyst	30,2	1,12	0,0	0,0	3,8	1,9	39,6	32,1	20,8	1,9
Angiomatoid fibrous histiocytoma	27,1	0,87	0,0	0,0	7,0	11,6	37,2	18,6	25,6	0,0
Angiosarcoma	67,2	1,57	1,2	0,5	14,1	7,0	9,9	21,4	3,3	42,4
Atypical cartilaginous Tumour/ChondroS G1	45	1,38	0,0	0,0	3,9	0,0	36,8	14,5	43,4	1,3
Atypical fibroxanthoma	78,7	0,20	0,2	0,0	12,8	0,0	1,6	82,1	1,6	1,6
Atypical lipomatous tumor/WDLPS	64,2	0,84	0,9	0,1	2,7	29,8	44,3	14,9	5,8	1,4
BCOR sarcoma	18,9	0,40	0,0	0,0	0,0	28,6	28,6	42,9	0,0	0,0
Central chondrosarcoma	56,4	0,98	0,0	0,0	7,7	13,7	35,0	17,1	26,5	0,0
Chondroblastoma	24,2	0,44	0,0	0,0	5,8	0,0	63,5	17,3	13,5	0,0
Chondromyxoid fibroma	34,1	0,73	0,0	0,0	3,8	0,0	42,3	30,8	23,1	0,0
Chondrosarcoma NOS	54,1	0,91	0,3	0,3	13,5	20,6	25,5	21,3	17,0	1,4
Chordoma	61,7	0,71	0,0	0,0	13,4	0,6	0,0	85,4	0,0	0,6
CIC-DUX sarcoma	24,1	0,38	9,1	0,0	9,1	0,0	45,5	27,3	0,0	9,1
Clear cell chondrosarcoma	42,5	0,27	0,0	0,0	0,0	7,1	64,3	7,1	21,4	0,0
Clear cell sarcoma	42,3	0,87	12,7	0,0	5,6	2,8	46,5	14,1	14,1	4,2
Composite hemangioendothelioma	33,3	0,50	0,0	0,0	0,0	0,0	33,3	66,7	0,0	0,0
Conventional osteosarcoma	32,6	0,80	0,0	0,0	12,5	3,1	60,2	14,4	9,6	0,2

Dedifferentiated chondrosarcoma	64	0,94	0,0	0,0	1,1	11,8	48,4	30,1	7,5	1,1
Dedifferentiated chordoma	53	NA	0,0	0,0	0,0	0,0	0,0	100,0	0,0	0,0
Dedifferentiated low-grade central osteo	36,2	1,40	0,0	0,0	0,0	0,0	83,3	8,3	8,3	0,0
Dedifferentiated parosteal osteosarcoma	43,8	2,25	0,0	0,0	7,7	0,0	76,9	7,7	7,7	0,0
Dermatofibrosarcoma protuberans	45	1,02	0,0	0,1	3,0	0,5	19,7	61,3	13,8	1,5
Desmoid-type fibromatosis	43,8	2,17	15,9	0,1	3,3	7,7	7,4	59,0	6,3	0,4
Desmoplastic fibroma of bone	27,5	1,00	0,0	0,0	0,0	0,0	66,7	16,7	16,7	0,0
Desmoplastic round cell tumour	24,3	0,30	3,8	0,0	0,0	84,6	0,0	0,0	0,0	11,5
Embryonal rhabdomyosarcoma - botryoid type	10,7	2,29	0,0	43,5	21,7	0,0	0,0	0,0	0,0	34,8
Embryonal rhabdomyosarcoma - NOS	20,3	0,71	0,0	16,7	41,7	8,3	0,0	8,3	0,0	25,0
Embryonal rhabdomyosarcoma - spindle cell	19	0,45	0,0	6,9	31,0	37,9	0,0	6,9	3,4	13,8
Embryonal rhabdomyosarcoma - usual type	14,4	0,57	0,9	4,4	35,4	38,9	3,5	3,5	0,9	12,4
Endometrial stromal nodule	50,7	NA	0,0	81,3	0,0	0,0	0,0	18,8	0,0	0,0
Endometrial stromal sarcoma NOS	56,2	NA	0,0	80,0	0,0	20,0	0,0	0,0	0,0	0,0
Endometrial stromal sarcoma - high-grade	60	NA	0,0	95,1	0,0	4,9	0,0	0,0	0,0	0,0
Endometrial stromal sarcoma - low-grade	53	211,00	0,5	88,7	0,0	9,4	0,0	0,5	0,0	0,9
Epithelioid hemangioendothelioma	52,1	1,56	2,0	0,0	9,0	11,0	14,0	14,0	5,0	45,0
Epithelioid sarcoma	40,1	0,85	1,0	6,1	2,0	12,2	22,4	19,4	29,6	7,1
Ewing sarcoma	26	0,68	1,0	0,5	5,7	16,6	28,2	33,6	7,8	6,7
Extraskeletal myxoid chondrosarcoma	58,2	0,81	0,0	0,0	0,0	1,7	58,6	27,6	8,6	3,4
Extraskeletal osteosarcoma	63,1	0,78	0,0	1,0	1,0	1,0	44,8	24,0	19,8	8,3
Fibro-osseous tumour of bone NOS	36	NA	0,0	0,0	0,0	0,0	0,0	100,0	0,0	0,0
Fibrosarcomatous dermatofibrosarcoma prot.	45,6	0,65	0,0	0,0	3,4	1,7	18,8	65,0	10,3	0,9
Gastrointestinal stromal tumour (GIST),	65,4	0,94	94,8	0,1	0,0	4,8	0,0	0,2	0,0	0,1
Giant cell fibroblastoma	22	0,38	0,0	0,0	0,0	0,0	54,5	45,5	0,0	0,0
Giant cell tumour of bone	37,8	1,13	0,0	0,0	0,9	0,0	58,3	14,4	25,1	1,3
Giant cell tumour of soft tissues	47,5	1,41	0,0	0,0	7,1	1,4	47,1	8,6	35,7	0,0
Hemosiderotic fibrolipomatous tumour	45,4	3,50	0,0	0,0	0,0	0,0	100,0	0,0	0,0	0,0
High risk solitary fibrous tumour	64,4	0,85	2,9	0,6	8,0	31,0	6,3	13,8	1,7	35,6

High-grade surface osteosarcoma	44,6	0,92	0,0	0,0	24,0	12,0	44,0	20,0	0,0	0,0
Infantile fibrosarcoma	5,9	2,33	10,0	0,0	20,0	10,0	20,0	20,0	0,0	20,0
Inflammatory myofibroblastic tumour	39,3	1,10	11,0	4,1	11,7	54,5	6,2	6,9	5,5	0,0
Intermediate fibrohistiocytic tumours	41	0,25	0,0	0,0	0,0	0,0	60,0	0,0	40,0	0,0
Intermediate vascular tumours	64,7	5,00	0,0	0,0	16,7	0,0	0,0	83,3	0,0	0,0
Intimal sarcoma	58,9	0,92	0,0	0,0	0,0	39,1	2,2	0,0	0,0	58,7
Kaposi sarcoma	65,8	0,22	1,1	0,0	3,2	1,1	65,8	11,5	13,4	4,1
Kaposiform hemangioendothelioma	6	3,00	0,0	0,0	0,0	0,0	50,0	50,0	0,0	0,0
Langerhans cell histiocytosis	29,5	4,00	0,0	0,0	10,0	5,0	5,0	75,0	5,0	0,0
Leiomyosarcoma	63,5	2,18	4,8	35,3	7,1	18,7	15,1	8,0	4,9	5,9
Leiomyosarcoma - differentiated	63,1	1,23	4,9	18,2	6,1	24,2	18,4	11,5	9,7	6,9
Leiomyosarcoma - poorly-differentiated	70,3	0,73	3,7	8,9	29,7	9,7	19,4	15,3	7,6	5,8
Lipofibromatosis	10,3	1,00	12,5	0,0	12,5	0,0	12,5	50,0	12,5	0,0
Lipomatous spindle cell/pleomorphic tum	33	NA	0,0	0,0	0,0	0,0	100,0	0,0	0,0	0,0
Liposarcoma - dedifferentiated	67,9	0,60	2,0	0,3	1,6	69,5	11,4	9,5	2,2	3,5
Liposarcoma - mixed type	61	1,00	0,0	0,0	0,0	50,0	50,0	0,0	0,0	0,0
Liposarcoma - myxoid	47,8	0,81	0,3	0,3	0,0	4,8	77,5	14,4	2,3	0,6
Liposarcoma - NOS	64,2	0,57	1,2	1,2	2,4	38,8	31,8	11,8	8,2	4,7
Liposarcoma - pleomorphic	63,1	0,78	0,7	0,7	3,6	15,1	38,1	22,3	15,8	3,6
Liposarcoma - round cell	49,2	0,59	0,0	0,0	0,0	14,8	63,0	14,8	7,4	0,0
Low grade fibromyxoid sarcoma	42,5	0,97	0,0	0,0	9,6	5,9	34,6	36,8	11,0	2,2
Low grade myofibroblastic sarcoma	40,5	1,17	7,7	0,0	46,2	0,0	23,1	23,1	0,0	0,0
Low grade sinonasal sarcoma	37,6	1,50	0,0	20,0	80,0	0,0	0,0	0,0	0,0	0,0
Low-grade central osteosarcoma	33,6	2,50	0,0	0,0	0,0	14,3	71,4	0,0	14,3	0,0
Malignant glomus tumour	54,2	0,67	20,0	10,0	10,0	10,0	30,0	0,0	20,0	0,0
Malignant granular cell tumour	46,1	1,25	0,0	0,0	0,0	0,0	0,0	55,6	44,4	0,0
Malignant mesenchymoma	61,1	1,25	0,0	11,1	0,0	11,1	33,3	0,0	33,3	11,1
Malignant mixed tumor	67,5	NA	25,0	75,0	0,0	0,0	0,0	0,0	0,0	0,0
Malignant myoepithelial tumour	49,5	1,00	0,0	0,0	0,0	0,0	0,0	50,0	50,0	0,0
Malignant PECOMA	60,1	1,71	15,8	21,1	0,0	26,3	10,5	10,5	0,0	15,8

Malignant perineurioma	46,3	2,00	0,0	0,0	0,0	0,0	33,3	33,3	0,0	33,3
Malignant peripheral nerve sheath tumour	46,4	0,86	0,6	0,0	11,6	17,3	24,9	31,2	9,8	4,6
Malignant rhabdoid tumour	24,3	0,89	2,8	8,3	13,9	16,7	5,6	16,7	0,0	36,1
Malignant tenosynovial giant cell tumour	68,5	0,00	0,0	0,0	0,0	50,0	0,0	50,0	0,0	0,0
Malignant Triton tumour	34,7	1,00	0,0	0,0	30,0	40,0	0,0	30,0	0,0	0,0
Malignant/dedifferentiated giant cell tumor of the bone	40	1,00	0,0	0,0	0,0	0,0	80,0	0,0	20,0	0,0
Melanotic neuroectodermal tumour of infa	38	NA	0,0	0,0	0,0	100,0	0,0	0,0	0,0	0,0
Mesenchymal chondrosarcoma	34,9	0,72	0,0	0,0	29,0	12,9	29,0	25,8	0,0	3,2
Metastatic leiomyoma	39	NA	0,0	0,0	0,0	50,0	0,0	50,0	0,0	0,0
Mixed tumour	66	NA	0,0	0,0	0,0	50,0	50,0	0,0	0,0	0,0
MPNST - epithelioid type	43,2	2,00	0,0	0,0	0,0	16,7	16,7	50,0	16,7	0,0
MPNST - usual type	45,4	0,77	1,2	1,2	14,1	12,9	27,1	27,1	11,8	4,7
Myoepithelioma	50,6	0,89	0,0	0,0	3,5	3,5	37,6	27,1	25,9	2,4
Myxofibrosarcoma	68,9	0,70	0,2	0,0	2,7	2,1	46,0	18,6	28,4	2,1
Myxoinflammatory fibroblastic sarcoma	54,3	0,53	0,0	0,0	0,0	0,0	39,1	0,0	60,9	0,0
Osseous tumour rich in giant cell NOS	40,5	1,00	0,0	0,0	0,0	0,0	50,0	50,0	0,0	0,0
Ossifying fibromyxoid tumour	49,8	1,13	0,0	0,0	9,4	6,3	12,5	37,5	34,4	0,0
Osteoblastoma	26,5	0,48	0,0	0,0	3,2	0,0	19,4	58,1	19,4	0,0
Osteoblastoma-like osteosarcoma	29	NA	0,0	0,0	0,0	0,0	100,0	0,0	0,0	0,0
Osteogenic tumor of uncertain prognosis	22	NA	0,0	0,0	0,0	0,0	0,0	100,0	0,0	0,0
Osteosarcoma NOS	38,3	0,64	0,0	0,0	15,7	2,6	51,3	19,1	9,1	2,2
Papillary intralymphatic angioendothelio	13	NA	0,0	0,0	0,0	0,0	0,0	100,0	0,0	0,0
Parosteal osteosarcoma	33,6	2,86	0,0	0,0	0,0	3,7	85,2	0,0	11,1	0,0
PECOMA - NOS	55,7	3,79	11,9	25,4	3,0	41,8	6,0	4,5	1,5	6,0
Periosteal chondrosarcoma	41,3	1,08	4,0	0,0	0,0	8,0	32,0	24,0	32,0	0,0
Periosteal osteosarcoma	19,8	4,00	0,0	0,0	0,0	20,0	80,0	0,0	0,0	0,0
Peripheral chondrosarcoma	37,3	0,63	0,0	0,0	0,0	10,3	33,3	33,3	23,1	0,0
Phosphaturic mesenchymal tumour	55,8	0,67	0,0	0,0	0,0	0,0	40,0	60,0	0,0	0,0
Phyllodes sarcoma	51,3	137,00	0,0	0,0	0,0	1,4	0,0	13,0	0,0	85,5

Pleomorphic rhabdomyosarcoma	67	0,58	1,4	7,6	5,6	11,8	36,1	19,4	11,1	6,9
Plexiform fibrohistiocytic tumour	23,1	1,23	0,0	0,0	6,9	3,4	34,5	24,1	31,0	0,0
Pseudomyogenic hemangioendothelioma	37,3	1,00	0,0	0,0	0,0	0,0	50,0	50,0	0,0	0,0
Retiform hemangioendothelioma	40,2	0,80	0,0	0,0	0,0	0,0	22,2	44,4	33,3	0,0
Rhabdomyosarcoma - NOS	41,7	0,80	1,1	13,6	17,0	23,9	11,4	4,5	5,7	22,7
Sclerosing epithelioid fibrosarcoma	55,8	1,05	0,0	0,0	9,8	17,1	14,6	41,5	9,8	7,3
Sclerosing rhabdomyosarcoma	45,2	0,38	0,0	0,0	9,1	0,0	72,7	0,0	9,1	9,1
Small cell osteosarcoma	21,8	0,33	0,0	0,0	0,0	25,0	25,0	0,0	25,0	25,0
SMARCA4-deficient thoracic sarcoma	48,3	0,25	13,3	0,0	0,0	40,0	0,0	0,0	0,0	46,7
Smooth muscle tumour of undetermined mal	50,6	4,30	6,6	59,8	0,8	15,6	5,7	7,4	4,1	0,0
Solitary fibrous tumour	58	1,25	1,2	1,1	15,4	21,0	13,3	18,6	4,3	25,0
Spindle cell rhabdomyosarcoma	38,8	0,63	5,1	2,6	17,9	20,5	28,2	10,3	12,8	2,6
Suspicion of giant cell tumour of bone	56,3	0,00	0,0	0,0	0,0	0,0	33,3	0,0	66,7	0,0
Sarcoma NOS	59,2	1,03	4,7	7,7	11,0	13,3	21,8	18,0	11,4	12,1
Synovial sarcoma - biphasic	41,2	0,84	1,4	0,0	5,7	5,7	52,9	17,1	10,0	7,1
Synovial sarcoma - monophasic	42,8	1,18	1,2	0,0	4,9	9,4	42,6	13,1	15,6	13,1
Synovial sarcoma NOS	45,6	1,22	0,0	1,1	5,5	8,8	34,1	13,2	16,5	20,9
Synovial sarcoma - poorly differentiated	45,2	0,85	0,0	0,0	5,4	10,8	29,7	18,9	8,1	27,0
Telangiectasic osteosarcoma	25,1	0,60	0,0	0,0	6,3	0,0	75,0	0,0	18,8	0,0
Tumour of intermediate malignancy NOS	47	1,14	5,8	3,8	13,5	13,5	21,2	19,2	21,2	1,9
Undifferentiated epithelioid sarcoma	70	0,47	0,0	0,0	13,6	18,2	22,7	13,6	27,3	4,5
Undifferentiated pleomorphic sarcoma	69,2	0,79	1,7	0,8	15,6	7,6	35,0	19,6	14,0	5,7
Undifferentiated round cell sarcoma	41,2	1,33	1,8	5,4	10,7	16,1	23,2	23,2	3,6	16,1
Undifferentiated sarcoma	66,7	0,89	1,4	3,3	15,8	13,0	29,5	21,4	8,8	6,7
Undifferentiated sarcoma - NOS	62,5	0,86	1,2	4,5	23,2	14,4	18,9	18,2	6,1	13,5
Undifferentiated spindle cell sarcoma	64,1	0,79	1,6	2,3	19,8	11,7	23,7	19,8	9,7	11,4
Undifferentiated uterine sarcoma	63,8	NA	0,0	96,1	0,0	2,9	0,0	1,0	0,0	0,0
Uterine tumour resembling ovarian sex co	48,1	NA	5,9	94,1	0,0	0,0	0,0	0,0	0,0	0,0

* : Sites : GI : gastrointestinal ; Gyn : Gynaecological sites ; H&N : head and neck ; I. trnk : Internal trunk ; L. Limb : lower limb ; Trnk w : trunk wall ; U. limb : upper limb

blished clinical trials and TMI histotypes

types	Total (2013-2016)	Incidence /10^6/year	Ph III	RPh II	Ph II
	25172	**95,104**			
umours	5274	19,977			
GIST).	3272	12,394			
	3247	12,299			
	2717	10,292			
	2679	10,148			
coma	1556	5,894			
	1520	5,758			
	1345	5,095			
	1339	5,072			
'S	1266	4,795			
	1138	4,311			
	1094	4,144			
s	1040	3,939			
	945	3,580			
	925	3,504			
	853	3,231			
	809	3,064			
	751	2,845			
	728	2,758			
	663	2,511			
	661	2,504			
	630	2,386			
	614	2,326			
	608	2,303			
	572	2,167			
	545	2,064			
tiated	516	1,955			
	442	1,674			
	429	1,625			
	409	1,549			
	417	1,580			
	355	1,345			
	330	1,250			
	324	1,227			
oma	308	1,167			
urs	286	1,083			

Histotypes	Total (2013-2016)	Incidence /10^6/year	Ph III	RPh II	Ph II
Incidence <1/10^6/year					
Synovial sarcoma - monophasic	244	0,924			
Endometrial stromal sarcoma, low grade	238	0,902			
Osteosarcoma NOS	230	0,860			
Embryonal RMS	179	0,678			
High risk SFT	174	0,659			
Malignant peripheral nerve sheath tumour	173	0,655			
Other histological subtypes of bone sarcomas	171	0,648			
Conventional chordoma	164	0,621			
Adenosarcoma	156	0,591			
All undifferentiated sarcoma of bone	152	0,576			
Inflammatory myofibroblastic Tumour	145	0,549			
Pleomorphic RMS	144	0,545			
Undifferentiated uterine sarcoma	141	0,534			
Liposarcoma - pleomorphic	139	0,527			
Phyllode sarcoma	138	0,523			
Embryonal rhabdomyosarcoma usual type	137	0,519			
Low grade fibromyxoid sarcoma	136	0,515			
Alveolar RMS	123	0,466			
Smooth muscle tumour of undetermined malignancy	122	0,462			
Epithelioid sarcoma (all)	120	0,455			
Central chondrosarcoma, grades 2and 3	117	0,443			
So-called fibrohistiocytic tumours	106	0,402			
EpithelioidhemangioEndothelioma	100	0,379			
Epithelioid sarcoma NOS	98	0,371			
Extraskeletal osteosarcoma	96	0,364			
Myoepithelioma, myoepithelial carcinoma, and mixed tumour	96	0,364			
Dedifferentiated chondrosarcoma	93	0,352			
Synovial sarcoma - NOS	91	0,345			
Rhabdomyosarcoma NOS	88	0,333			
Liposarcoma NOS	85	0,322			
MPNST - usual type	85	0,322			
Myoepithelioma	85	0,322			
Central atypical cartilaginous tumour / chondrosarcoma, grade 1	76	0,288			
Clear cell sarcoma of soft tissue	71	0,269			
Giant cell tumour of soft tissue	70	0,265			
Synovial sarcoma - biphasic	70	0,265			
Undifferentiated pleomorphic sarcoma of bone	69	0,261			
PECOMA - NOS	67	0,254			
Extraskeletal myxoid chondrosarcoma	58	0,220			
Round cell sarcoma with EWSR1-non-ETS fusions	56	0,212			
Liposarcoma - round cell	54	0,205			
Aneurysmal bone cyst	53	0,201			
Desmoplastic small round cell tumour	52	0,197			
All tumors of intermediate malignancy NOS	52	0,197			
Chondroblastoma	52	0,197			
Intimal sarcoma	46	0,174			
Angiomatoid fibrous histiocytoma	43	0,163			
Sclerosing epithelioid fibrosarcoma	41	0,155			
Endometrial stromal sarcoma - high-grade	41	0,155			
All parosteal osteosarcoma	40	0,152			
Leiomyosarcoma of bone	40	0,152			
Spindle cell RMS	39	0,148			
Peripheral chondrosarcoma	39	0,148			
Synovial sarcoma - poorly Differentiated	37	0,140			
Malignant rhabdoid tumor	36	0,136			
Ossifying fibromyxoid Tumour	32	0,121			
Alveolar soft part sarcoma	31	0,117			
Mesenchymal chondrosarcoma	31	0,117			
Osteoblastoma	31	0,117			
Plexiform fibrohistiocytic tumors	29	0,110			
Embryonal rhabdomyosarcoma spindle cell	29	0,110			
Angiosarcoma of bone	29	0,110			
Adult fibrosarcoma	28	0,106			
Parosteal osteosarcoma	27	0,102			

Histotypes	Total (2013-2016)	Inc /10
Incidence <0.1/10^6/year		
Chondromyxoid fibroma	26	
Undifferentiated spindle cell sarcoma	26	
Periosteal chondrosarcoma	25	
High-grade surface osteosarcoma	25	
Myxoinflammatory Fibroblastic Sarcoma	23	
Embryonal RMS sarcoma - botryoid type	23	
Undifferentiated epithelioid sarcoma	22	
Langerhans cell histiocytosis	20	
Malignant PECOMA	19	
Low grade central osteosarcoma (ALL)	19	
Adamantinoma	19	
UTROSC	17	
Endometrial stromal nodule	16	
Telangiectasic osteosarcoma	16	
SMARCA4-deficient thoracic sarcoma	15	
Clear cell chondrosarcoma	14	
Low grade Myofibroblastic Sarcoma	13	
Dedifferentiated parosteal osteosarcoma	13	
Dedifferentiated low grade central osteosarcoma	12	
Giant cell Fibroblastoma	11	
Sclerosing RMS	11	
CIC-rearranged sarcoma	11	
Infantile fibrosarcoma	10	
Pericytic (perivascular) tumours	10	
Malignant Triton tumour	10	
Endometrial stromal sarcoma	10	
Retiform hemangio-endothelioma	9	
Ectomesenchymoma : Malignant mesenchymoma	9	
Malignant granular cell Tumour	9	
Haemosiderotic fibrolipomatous tumour	9	
Synovial sarcoma of bone	9	
RMS of bone	9	
Lipofibromatosis	8	
Epithelioid hemangioendothelioma of bone	8	
Sarcoma with BCOR genetic alterations	7	
Low-grade central osteosarcoma	7	
Pseudomyogenic hemangioendothelioma	6	
Intermediate vascular tumours	6	
MPNST - epithelioid type	6	
Mixed tumour	6	
Desmoplastic fibroma of bone	6	
Malignant/dedifferentiated GCTB	6	
BCOR Sarcoma of bone	6	
Intermediate fibrohistiocytic tumors	5	
Adult spindle cell RMS	5	
Phosphaturic mesenchymal tumour	5	
Low grade sinonasal sarcoma	5	
Periosteal osteosarcoma	5	
Kaposiform hemangioendothelioma	4	
Small cell osteosarcoma	4	
Myoepithelioma of bone	4	
Liposarcoma of bone	4	
Composite hemangioendothelioma	3	
Malignant perineurioma	3	
Adult fibrosarcoma of bone	3	
Liposarcoma - mixed type	2	
Malignant tenosynovial giant cell tumors	2	
Metastatic leiomyoma	2	
Malignant myoepithelial Tumour	2	
Osteoblastoma-like osteosarcoma	2	
Dedifferentiated chordoma	2	
Lipomatous spindle cell/pleomorphic tum	1	
Papillary intralymphatic angioendothelioma	1	
Melanotic neuroectodermal tumour of infancy	1	
Osteogenic tumor of uncertain prognosis	1	
Fibro-osseous tumour of bone NOS	1	
Undifferentiated epithelioid sarcoma	1	