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### CANCER AMONG ADOLESCENTS AND YOUNG ADULTS BETWEEN 2000 AND 2016 IN FRANCE: INCIDENCE AND IMPROVED SURVIVAL

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#### 1 CANCER AMONG ADOLESCENTS AND YOUNG ADULTS BETWEEN 2000 AND 2016 IN FRANCE:

- 2 INCIDENCE AND IMPROVED SURVIVAL
- 3 ABSTRACT
- 4 **Purpose:** This study was undertaken to determine cancer survival and describe the spectrum
- 5 of cancers diagnosed among French adolescent and young adult (AYA) population.
- 6 Methods: All cases of cancer diagnosed in 15-24 years, recorded by all French population-
- based registries (18% of the French population), over the 2000-2016 period, were included.
- 8 Age-standardized incidences rates (ASR), conventional annual percentage change (cAPC) of
- 9 incidence over time, and 5-year overall survival (5yOS) were calculated.
- 10 Results: We analyzed 2,734 cancer diagnoses in adolescents and 4,199 in young adults.
- Overall incidence rates were  $231.9/10^6$  in 15-19 year olds and  $354.0/10^6$  in 20-24 year olds.
- 12 The most frequently diagnosed cancers in male AYA were malignant gonadal germ-cell
- tumors (GCT), Hodgkin lymphoma (HL), and malignant melanoma, and were HL, thyroid
- 14 carcinoma, and malignant melanoma in females. Cancer incidence was stable over time with a
- 15 cAPC of 0.8% (p=0.72). For all cancers combined, 5yOS was 86.6% (95%CI: 85.8-87.4),
- greater than 85% for HL, non-Hodgkin lymphomas (NHL), GCT, thyroid carcinomas, and
- 17 malignant melanomas, and around 60% and lower for osteosarcomas, Ewing tumors, hepatic
- carcinomas, and rhabdomyosarcomas. The 5yOS has significantly improved from 2000-2007
- to 2008-2015 for all cancers pooled, with a substantial gain of 4% for 15-19 year-olds, and
- 20 3% for 20-24 year-olds.
- 21 Conclusion: Notwithstanding the encouraging results for some cancers, and overall,
- 22 persistent poorer survivals in AYA were shown compared to children for acute lymphoblastic
- 23 leukemia, osteosarcoma, Ewing tumor, rhabdomyosarcoma and malignant hepatic tumors.
- 24 These disparities require further investigation to identify and address the causes of these
- 25 inferior outcomes.

#### Introduction

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28	Incidence and survival within the adolescents and young adults (AYA) population can be
29	misleading when assessed across all tumor streams. The latest French report (2000-2008) <sup>1</sup>
30	described an overall incidence rate (IR) 219.4 per million adolescents (age 15-19 years) and
31	293.1 per million young adults (age 20-24 years). For all cancers combined, substantial
32	survival gains were achieved, with an increase of 5-year overall survival (OS) from 62.0%
33	(95%CI: 57.5-66.5) in the 1978-1982 period to 81.8% (95%CI: 79.5-83.9) in the 2000-2004
34	period. An improvement in survival was found for leukemia, lymphoma, and central nervous
35	system (CNS) tumors in subgroup analysis. Conversely, no increase in survival over time was
36	observed for malignant bone tumors. <sup>1,2</sup> AYA had significantly worse 5-year OS, during the
37	2000s, than children (0-14 years) for acute lymphoblastic leukemia (ALL, 62.8% vs. 89.8%),
38	non-Hodgkin lymphomas (NHL, 78.9% vs. 88.3%), CNS tumors (67.3% vs. 71.9%), and
39	bone sarcomas (50.0% vs. 74.4%). <sup>1,3</sup> To improve cancer outcomes for AYA, various
40	initiatives have been implemented in France since 2011,4 including promoting collaboration
41	between pediatric and adult oncologists, developing French national policies for managing
42	AYA with cancer, and setting up specific treatment units. Nevertheless it is unclear whether
43	the adoption of pediatric-based protocols in adult centers has abolished disparities in AYA
44	outcomes between pediatric and adult centers and improved outcomes at a population-level.
45	Using a population-based cohort of AYA in France, the objectives were to provide updated
46	statistics covering incidence and survival and to describe incidence and survival trends of
47	these patients from 2000 to 2016.

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#### Methods

50 Source of data

The registration of cancers in AYA is ensured by eighteen general and specialized population-based registries of the Francim network, covering 18% of the French population. Medico-administrative sources (health institution claims databases of public or private health institutions used to obtain hospital patient information coded on discharge, and health insurance schemes databases) and medical sources (multidisciplinary team meetings databases in oncology, histology reports databases) were used to identify cases. Vital status was obtained by active search in medical records and by matching the French Cancer Registries files and the national population register "Repertoire National d'Identification des Personnes Physiques" sorted by date and place of birth to obtain the mention of death and the date of death. The cut-off date was defined as June 30, 2018.

#### 62 Population

Data were taken from the common database of all Francim network registries, and included gender, age at diagnosis, and diagnostic information. In line with the recommendations of the European Network of Cancer Registries<sup>5</sup> and the third version of the International Classification of Childhood Cancer (ICCC-3),<sup>6</sup> eligibility criteria were: diagnosis of cancer, for CNS localization according to the first revision of the third edition of the International Classification of Disease for Oncology (ICDO-3),<sup>7</sup> benign and borderline tumors were also considered; from 15 to 24 years of age at diagnosis; and period of diagnosis between January

#### 72 Statistical Analyses

All data were retrieved, tabulated by tumor type and categorized using the ICCC-3 levels: 12

1, 2000 and December 31, 2016. Cutaneous carcinomas were excluded.

- main diagnostic groups, 47 diagnostic subgroups, and 2-11 divisions of selected subgroups.<sup>6</sup>
- 75 The males/females (M/F) ratio was the ratio of number of cases in males to that in females.

The IR were calculated for the 17-year period, 2000-2016, and based on person-years derived from the annual estimates of population by age and sex provided by the Institute of Statistics and Economic Studies. Crude and age-specific IR were calculated and age-standardized rates (ASR) were estimated by the direct method using the world population for the age 15-24 years. 8 Methods based on Poisson distribution were used to specify the 95% confidence interval (95%CI) for the IR.9 Time trend in the incidence was estimated by the conventional annual percent change (cAPC) calculated as the slope of the linear regression used to model the natural logarithm of the IR as a function of the calendar year. <sup>10</sup> Survival analysis was performed on a dataset containing all cases diagnosed between January 1, 2000 and December 31, 2015 and followed-up until June 30, 2018. The probability of OS was estimated using the Kaplan–Meier method. 11 The endpoint of interest was death from any cause for OS, with the date of diagnosis acting as the time origin. Survival curves between groups were compared using the log-rank test and the trend in survival over time periods was estimated using the logrank test for trend. 12,13 Cox models were used to calculate the hazard ratios of death (HRs) and their 95%CI.<sup>14</sup> Statistical tests were two-sided with a significant level of 0.05. All statistical analyses were performed using the SAS version 9.4 (SAS Institute Inc., Cary, North Carolina, USA, 2013).

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#### Results

95 Patient characteristics

Table 1 shows the number of cancers in AYA, diagnosed from 2000 to 2016, with main data quality indicators by French administrative areas where a French Cancer Registry is established. Most cancers were microscopically verified (98.6%) and only 2% had unspecified morphology. A total of 2,734 15-19-year-old adolescents (39.4%) and 4,199 20-24-year-old young adults (60.6%) were included. Table 2 shows the distribution of tumors by

age group and diagnostic group and the M/F ratios for each tumor type. The most common diagnoses in 15-19 year olds were lymphomas (27.7%): Hodgkin lymphoma (HL) 20.4%, NHL 6.0%. In young adults (20-24 years), the most frequent tumors were malignant epithelial tumors (33.8%): thyroid carcinomas (13.5%), malignant melanomas (10.2%). In 15-24-year-olds, approximately 30.7% of cancers were tumors of adulthood, especially thyroid carcinomas 11.6% and malignant melanomas 8.5%. Embryonal malignancies, including Wilms tumor, hepatoblastoma, neuroblastoma, and medulloblastoma, were rare accounting for less than 1% of cases. For all cancers combined, the M/F ratios were 1.0 for adolescents, for young adults, and for both. In male AYA, the most common cancers were malignant germ-cell tumors (GCT), malignant bone tumors, soft-tissue sarcomas, and leukemia, with M/F ratio of 5.0, 1.5, 1.4, and 1.4 respectively. Conversely, malignant melanomas and thyroid carcinomas were more frequent in female AYA (M/F ratio 0.6 and 0.2, respectively).

#### Incidence

Table 2 shows the specific IR and ASR from 2000 to 2016 for the main tumor types by age group, computed with both genders. The ASR for the 15-24-year-old population was 289.4 per million (95%CI%: 279.8-299.2). The incidence (rate per million) was lowest in 15-19 year olds: 232.2 (males) and 231.7 (females). This incidence increased to 351.4 (males) and 372.2 (females) in 20-24 year olds. The highest ASR in males aged from 15 to 24 years was seen for malignant gonadal GCT (ASR = 89.2, 95%CI: 82.8-96.1). HL was the second most frequent tumor type in males (ASR = 51.7, 95%CI: 46.8-56.9), followed by malignant melanoma (ASR = 21.7, 95%CI: 18.5-25.2). In AYA females, HL represented the most frequent cancer type with an ASR of 58.6(95%CI: 52.6-65.2), thyroid carcinoma the second (ASR=54.1, 95%CI: 48.4-60.2), and malignant melanoma the third (ASR=30.7 95%CI: 26.6-35.4). Cancer incidence in AYA for both genders was stable over time with a cAPC of 0.8%

126 (95%CI: -3.5%;+5.3%, p=0.72, Fig.1). No variation in incidence was observed by age group,

127 gender, or each ICCC-3 diagnostic group.

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Overall Survival

129 130 Table 3 describes the 1-, 2-, and 5-year OS among AYA with cancer from 2000 to 2015 by 131 ICCC-3 diagnostic groups and subgroups (n=6,480). With 2.9% lost to follow-up (Table 1), 132 the median follow-up time in the cohort was 103 months (min-max: 0-222 months). At the 133 end time, 983 AYA had died with a median time after diagnosis of 21 months (min-max: 0-134 194 months). For all cancers combined, OS was 95.3% (95%CI: 94.8-95.8) at 1 year, 91.3% 135 (95%CI: 90.6-92.0) at 2 years, and 86.6% (95%CI: 85.8-87.4) at 5 years. The 5-year OS 136 greater than 85% were observed for HL, NHL, GCT, thyroid carcinomas, cervix uteri 137 carcinomas, and malignant melanomas whereas 5-year OS was around 60% and lower for 138 osteosarcomas, Ewing tumors, hepatic carcinomas, and rhabdomyosarcomas. The 5-year OS 139 were close to 65-80% for ALL, acute myeloid leukemia (AML), CNS tumors, and malignant 140 renal tumors. 141 A comparison of 5-year OS in the studied periods (2000-2007 and 2008-2015) with those in earlier time periods (1972-1982, 1983-1987, 1988-1992, and 1993-1997 data from reference<sup>2</sup>) 142 143 indicated that substantial survival gains were achieved for all tumors pooled (Table 4), with 144 an increase from 62.0% (95%CI:57.5-66.5) in the 1978-82 period to 88.0% (95%CI:86.9-145 89.0) in the 2008-15 period. Since 1997, survival improvement was especially seen in 146 leukemia and CNS tumors. For malignant bone tumors, the increase in survival was only 147 observed during the last analyzed period (2008-15). Since 1993, survival was stable for soft-148 tissue sarcomas. 149 The 5-year OS has significantly improved from 2000-2007 to 2008-2015 for all cancers 150 pooled, with a substantial gain of about 4% for 15-19 year-olds, and 3% for 20-24 year-olds 151 (Table 5). Increases in 5-year OS concerned most of diagnostic groups and were especially 152 apparent for osteosarcomas in both age groups (p<0.01), and carcinomas in 20-24 year-olds 153 (p=0.04). Conversely, a significant decrease over time was observed for astrocytomas in 20-154 24 year-olds (p=0.01), due to differences in percentage of pilocytic astrocytoma and glioblastoma, respectively 51% vs. 12% during the 2000-2007 period, and 24% vs. 45% 155 156 during the 2008-2015 period. 157 During the 2000-2007 period, there were no statistically significant differences in 5-year OS 158 between adolescents (15-19 years) and young adults (20-24 years) whatever the main 159 diagnostic group (Table 5). However, during the latest studied period, young adults (20-24 160 years) diagnosed with ALL, astrocytoma, or Ewing's sarcoma had significantly a higher risk 161 of dying from the disease compared to adolescents (15-19 years): HR=2.0 (IC95%: 1.1-3.5), 162 HR=2.2 (IC95%: 1.2-3.9), and HR=2.3 (IC95%: 1.1-4.8), respectively. The histologic 163 distribution of pilocytic astrocytoma and glioblastoma were significantly different between 164 adolescents and young adults: 61% and 12% in 15- to 19-year-olds, vs. 24% and 45% in 20-165 to 24-year-olds (p<0.01).

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#### Discussion

Considering the emergence of interest in oncology in the AYA group, we examined incidence and survival of 15-24 year olds in order to better define the burden of the cancer for this age group. The two major findings in the present study were that cancer incidence in AYA remained stable during the 2000-2016 period, and the 5-year OS combined has significantly improved over time, especially for osteosarcoma. Another major finding of our study was that, during the latest studied period, adolescents had significantly better 5-year OS than young adults for ALL, Ewing's sarcomas, and astrocytomas.

The major strength of this study is its homogenization of compulsory registration based to various sources of notification of 18 population-based cancer registries providing a nonbiased and valid view of the situation in France during the studied period, compared to clinical series which report better survival than population-based studies. The coverage is 18% of the whole country. However, these registries have provided the estimates of national rates for decades and they are the gold standard referred to by all descriptive studies. Roughly 2,300 new cases of cancers in AYA are currently diagnosed each year in France (900 in adolescents and 1,400 in young adults). Several studies have described cancer incidence and survival in AYA, but few of them were based on the same period and the same age ranges. 10,15-21 Our incidence rates in 15-19 year olds were comparable to those reported in other countries. 10,15-18 In 20-24 year olds, highest incidence was observed in the United States (US): 386 per million. <sup>10</sup> Marked differences between France and the US occurred for thyroid carcinoma (IR per million: 78 versus 122 for young females, no difference for males) and for melanoma (IR per million: 47 versus 57 for young white females, no difference for males). In the US, the incidence of thyroid carcinoma in AYA population increased by 4.0% per year from 1988 to 2006, 8.6% per year from 2006 to 2009, and 1.4% from 2009 to 2016, likely a consequence of ultrasound screening.<sup>22</sup> For melanoma, this suggests that American white female young adults may share high exposures that are associated with malignant melanoma. Jones et al<sup>23</sup> have reported that, during 1999-2009, the percentage of white American students who never or rarely wore sunscreen when outside on a sunny day for >1 hour increased from 57.5% to 69.4% (with an increase most pronounced among white female students). We reported a non-significant increase of +0.8 in incidence for all malignancies over time in 15- to 24-year olds. Vast differences between countries were observed in the incidence trend for all cancers combined. Gupta et al<sup>24</sup> have reported that the incidence of AYA (15-39 years) cancer rose over the 1998-2012 period in 23

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200 countries, decreased in two countries, and remained stable in the other 16. Striking increases were noted for thyroid and testicular in 33 and 22 countries respectively, including France. 201 202 The 5-year observed survivals in this study were similar to those reported for AYA in the US (2009-2015)<sup>10</sup>, in Australia (2000-2014)<sup>18</sup>, in the United-Kingdom (UK: 2005-2010)<sup>19</sup>, and in 203 27 European countries participating in EUROCARE-5 (2000-2007)<sup>21</sup>. However marked 204 differences between France and the UK occurred for NHL (88% vs. 79%), bone sarcomas 205 206 (65% vs. 56%), soft-tissue sarcomas (67% vs. 61%), and GCT (93% vs. 82%). Compared to EUROCARE-5 study<sup>21</sup>, we reported higher survival for ALL, CNS tumors, Ewing's sarcoma, 207 and soft-tissue sarcomas especially in 15-19 years. These survival disparities may be due to 208 209 differences in tumor classification used (ICDO-2 vs. ICDO-3), in tumor selection (inclusion 210 or not of benign/borderline CNS tumors), in distribution of cases by stages at diagnosis, by 211 histological or biological subtypes, or by grades of neoplasm, and in treatment strategies by 212 age over time. Compared to results of the latest French reports among AYA, 1,2 we found an improvement in 213 survival from 1978 to 2015, to achieve a 5-year OS of 88.0% (95%CI: 86.9-89.0) for all 214 215 cancers combined during the 2008-2015 period. Increases in survival over time have been observed for all diagnostic groups, except for soft-tissue sarcomas with a 5-year OS around 216 70% since the mid-90s. Compared to children and older adults, AYA with soft-tissue 217 sarcomas have not experienced an improvement in survival. <sup>25,26</sup> The reasons for this disparity 218 219 remain unclear, but following issues have been mentioned: delays in diagnosis, trial 220 availability and participation, aspects of the organization of care, national centralization of sarcoma care, international consortia, and factors related to tumor biology.<sup>27</sup> In our series, 221 222 comparison of 5-year OS of osteosarcoma AYA treated during 2000 to 2007 and 2008 to 223 2015 revealed a significant improvement of 14% in adolescents and 40% in young adults. 224 One of the most crucial factors contributing to the increase in survival is the setting up of the

225 French OS2006/sarcome-09 study using methotrexate-etoposide-ifosfamide based regimen, 226 randomized to receive or not high doses of zoledronic acid adapted from those given for pediatric osteosarcoma patients.<sup>28,29</sup> 227 228 During the latest studied period, 5-year OS was worse in young adults than in adolescents and 229 in children<sup>3</sup> for ALL (63.2%, 79.3%, and 89.8%, respectively), for astrocytoma (49.6%, 74.8%, and 87.0%, respectively), and Ewing tumor (38.1%, 70.4%, and 73.8%, respectively). 230 231 Interest has recently been paid to AYA with ALL, particularly because all reports so far 232 published indicate that these patients have a better outcome when treated with pediatric rather than adult therapeutic protocols.<sup>30</sup> In France since 2003, adolescents with ALL have been 233 234 treated in or according to pediatric trials (either the FRALLE-2000 or EORTC-58951 trials)<sup>31</sup> 235 and young adults markedly benefited from a pediatric approach by the Group for Research on 236 Adult Acute Lymphoblastic Leukemia (GRAALL). 32,33 This may explain the difference in 237 survival between adolescents and young adults. Although the inclusion of asparaginase in 238 pediatric-inspired chemotherapy regimens has a positive impact on survival in AYA patients, 239 factors accounting for differences in outcome compared to children include incidence of adverse events<sup>34</sup> and heterogeneity in ALL biology.<sup>35</sup> Differences in survival between 240 children, adolescents and young adults with astrocytoma result of different distribution of 241 242 gliomas with varying prognosis depending on tumor grade. Low-grade astrocytomas (WHO 243 grades I and II including especially pilocytic astrocytomas) are the most frequently 244 encountered brain tumors in early childhood and adolescence, while high-grade astrocytomas 245 (WHO grades III and IV, such as anaplastic astrocytomas and glioblastomas) tend to occur at increasing rates with increasing age.<sup>36</sup> Several studies have analyzed potential correlations 246 247 between Ewing sarcoma patients' ages and prognosis, but results have been inconsistent, and it remains unproven whether age in the AYA range by itself truly confers inferior survival.<sup>37</sup> 248 249 For this reason, European cooperative group trials have included patients up to the age of 50 years.<sup>38</sup> Moreover, in the EURO-EWING99 clinical trial, it has been observed that some toxicities (neutropenia, thrombocytopenia and stomatitis) may even decrease with age.<sup>38</sup> It remains to be determined whether less toxicity represents less treatment administered to older patients, or whether age distribution of biologic factors and Ewing-like tumor entities, treated as Ewing sarcoma and having different clinical behavior, can be held responsible.<sup>39</sup> Even though the survival between adolescents and young adults seemed to be similar for the other cancers, these AYA patients had persistent worse 5-year overall survival than children for osteosarcoma, rhabdomyosarcoma, and malignant hepatic tumors.<sup>1,3</sup> Several factors are believed to have influenced the lack of survival improvement noted for AYA: access to clinical trials, biologic characteristics of these cancers, access to health-care professionals and services, and specific treatment strategies.<sup>4,40,41</sup>

#### Conclusion

We have presented updated data representing a comprehensive analysis of cancer incidence and survival in AYA in France during the 2000-2016 period. Notwithstanding the encouraging results for some cancers, and overall, persistent poorer survivals in AYA were shown compared to children for ALL, osteosarcoma, Ewing tumor, rhabdomyosarcoma and malignant hepatic tumors. These survival disparities observed require further investigation to identify and address the causes of these inferior outcomes.

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396 19 French Administrative Areas, with data quality indicators 397 Abbreviations: ICCC-3, third version of the International Classification of Childhood Cancer. 398 399 TABLE 2. NUMBER OF TUMORS, SEX RATIO, AND CANCER IRS PER MILLION IN AYA IN FRANCE 400 FROM 2000 TO 2016 DETAILED BY DIAGNOSTIC GROUPS AND SUBGROUPS 401 Abbreviations: AYA, adolescents and young adults; ICCC-3, third version of the International 402 Classification of Childhood Cancer; GCT, Germ-Cell tumors; cPNET, central primitive 403 neuroectodermal tumors; pPNET, peripheral primitive neuroectodermal tumors; M/F ratio, 404 Male/Female ratio; IR, Incidence rates per million; ASR, age-standardized incidence rates per 405 million; 95%CI, 95% confidence interval. 406 407 FIG. 1. Time trend in age-standardized incidence rates estimated by the conventional annual 408 percent change, in AYA (15-24 years) in France between 2000 and 2016 409 Abbreviations: cAPC, conventional annual percent change; ASR, age-standardized incidence 410 rates per million; AYA, adolescents and young adults. 411 412 TABLE 3. ONE-, TWO-, AND FIVE-YEAR OVERALL SURVIVAL AMONG AYA WITH CANCER 413 FROM 2000 TO 2015 BY ICCC-3 DIAGNOSTIC GROUPS 414 Abbreviations: AYA, adolescents and young adults; ICCC-3, third version of the International 415 Classification of Childhood Cancer; GCT, Germ-Cell tumors; cPNET, central primitive 416 neuroectodermal tumors; pPNET, peripheral primitive neuroectodermal tumors; OS, Overall 417 Survival; 95%CI, 95% confidence interval.

TABLE 1. CANCER CASES IN ADOLESCENTS AND YOUNG ADULTS DIAGNOSED IN 2000–2016, IN

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419 TABLE 4. TRENDS IN FIVE-YEAR OVERALL SURVIVAL AMONG ADOLESCENTS AND YOUNG 420 ADULTS WITH CANCER FROM 1978 TO 2015 BY ICCC-3 DIAGNOSTIC GROUPS 421 Abbreviations: ICCC-3: third version of the International Classification of Childhood Cancer; 422 OS: Overall Survival; 95%CI: 95% confidence interval 423 \* Data from reference <sup>2</sup> # Only malignant CNS tumors were included (exclusion of benign or borderline tumors) 424 <sup>a</sup> p<0.05 Comparison between diagnostic periods (2000-2007 vs 2008-2015) 425 426 TABLE 5. TRENDS IN FIVE-YEAR OVERALL SURVIVAL AMONG ADOLESCENTS AND YOUNG 427 428 ADULTS WITH CANCER FROM 2000-2007 TO 2008-2015 BY ICCC-3 DIAGNOSTIC GROUPS 429 Abbreviations: ICCC-3, third version of the International Classification of Childhood Cancer; 430 5yOS, Five-year Overall Survival; 95%CI, 95% confidence interval. 431 <sup>a</sup> p<0.05 Comparison between diagnostic periods (2000-2007 vs 2008-2015) 432 <sup>b</sup> p<0.05 Comparison between age groups (15-19 years vs 20-24 years)

TABLE 1. CANCER CASES IN ADOLESCENTS AND YOUNG ADULTS DIAGNOSED IN 2000-2016, IN 19 FRENCH ADMINISTRATIVE AREAS, WITH DATA

QUALITY INDICATORS

French Administrative Areas	Registered period	П	Incidence analysis (2000-2016)	00-2016)	Survival analysis (2000-2015)	is (2000-2015)
		Patient included N	Microscopically Verified N (%)	Unspecified cases according to ICCC-3 N (%)	Patient included N	Lost to follow-up N (%)
14-Calvados	2000-2015	396	391 (98.7)	6 (1.5)	392	5 (1.3)
16-Charente	2008-2016	123	120 (97.6)	1 (0.8)	110	5 (4.5)
17-Charente/Maritime	2008-2016	189	187 (98.9)	2 (1.1)	164	19 (11.6)
25-Doubs	2000-2016	336	326 (97.0)	10 (3.0)	320	0 (0.0)
33-Gironde	2005,2008-2016	594	579 (97.5)	7 (1.2)	532	18 (3.4)
34-Hérault	2000-2016	632	624 (98.7)	12 (1.9)	573	25 (4.4)
38-Isère	2000-2016	816	810 (99.3)	7 (0.9)	775	17 (2.2)
44-Loire Atlantique	2000-2016	836	830 (99.3)	10 (1.2)	780	22 (2.8)
50-Manche	2000-2016	245	242 (98.8)	4 (1.6)	234	14 (6.0)
59-Lille Area	2008-2016	315	313 (99.4)	4 (1.3)	284	4 (1.4)
67- Bas Rhin	2000-2014	644	631 (98.0)	10 (1.6)	642	13 (2.0)
68- Haut Rhin	2000-2016	457	454 (99.3)	1 (0.2)	429	19 (4.4)
79-Deux-Sèvres	2008-2016	124	122 (98.4)	3 (2.4)	108	2 (1.9)
80-Somme	2000-2016	325	320 (98.5)	7 (2.2)	309	9 (2.9)
81-Tam	2000-2016	173	171 (98.8)	1 (0.6)	157	3 (1.9)
85-Vendée	2000-2016	429	427 (99.5)	3 (0.7)	404	7 (1.7)
86-Vienne	2008-2016	151	146 (96.7)	2 (1.3)	133	3 (2.3)
87-Haute Vienne	2009-2016	66	97 (98.0)	2 (2.0)	68	2 (2.2)
90- Territoire de Belfort	2007-2016	49	48 (98.0)	1 (2.0)	45	1 (2.2)
Total	2000-2016	6933	(9838 (98.6)	93 (1.3)	6480	188 (2.9)

TABLE 2. NUMBER OF TUMORS, SEX RATIO, AND CANCER IRS PER MILLION IN AYA IN FRANCE FROM 2000 TO 2016 DETAILED BY DIAGNOSTIC

## GROUPS AND SUBGROUPS

Diagnostic groups and subgroups (ICCC-3)	Adol	escents (1:	Adolescents (15-19 years)	Young	g adults (	Young adults (20–24 years)	AY	AYA (15-24 years)	4 years)
	(%) u	M/F ratio	IR [95%CI]	n (%)	M/F ratio	IR [95%CI]	(%) u	M/F ratio	ASR [95%CI]
I. Leukemias, myeloproliferative/dysplastic diseases	365 (13.4)	1.5	31.0 [27.9-34.3]	318 (7.6)	1.2	26.8 [23.9-29.9]	(6.6) (89)	1.4	29.0 [26.0-32.2]
Ia. Lymphoblastic leukemias	196 (7.2)	2.1	16.6 [14.4-19.1]	111 (2.6)	2.2	9.4 [7.7-11.3]	307 (4.4)	2.1	13.2 [11.2-15.4]
Ial. Precursor cell leukemias	195 (7.1)	2.1	16.5 [14.3-19]	100 (2.4)	2.2	8.4 [6.9-10.3]	295 (4.3)	2.1	12.7 [10.8-14.9]
Ia2. Mature B-cell leukemias	1 (0.0)	0.0	0.1[0.0-0.5]	8 (0.2)	3.0	0.7 [0.3-1.3]	9 (0.1)	2.0	0.4 [0.1-0.9]
Ia3. Mature T-cell and NK cell leukemias	0 (0.0)		0.0[0.1-0.3]	3 (0.1)	0.5	0.3 [0.0-0.7]	3 (0.0)	0.5	0.1 [0.1-0.5]
Ib. Acute myeloid leukemias	102 (3.7)	1.1	8.7 [7.1-10.5]	87 (2.1)	6.0	7.3 [5.9-9.0]	189 (2.7)	1.0	8.0 [6.5-9.8]
Ic. Chronic myeloproliferative diseases	42 (1.5)	1.0	3.6 [2.6-4.8]	96 (2.3)	1.0	8.1 [6.6-9.9]	138 (2.0)	1.0	5.7 [4.4-7.2]
Id. Myelodysplastic diseases	16 (0.6)	8.0	1.4 [0.8-2.2]	19 (0.5)	0.7	1.6 [1.0-2.5]	35 (0.5)	8.0	1.5 [0.9-2.3]
Ie. Unspecified and other specified leukemias	9 (0.3)	3.5	0.8[0.3-1.5]	5 (0.1)	0.3	0.4 [0.1-1.0]	14 (0.2)	1.3	0.6 [0.2-1.2]
II. Lymphomas and lymphoreticular neoplasms	758 (27.7)	6.0	64.3 [59.8-69.1]	956 (22.8)	1.0	80.6 [75.6-85.9]	1714 (24.7)	6.0	72.0 [67.2-77.0]
IIa. Hodgkin disease	557 (20.4)	8.0	47.3 [43.4-51.3]	703 (16.7)	6.0	59.3 [55-63.8]	1260 (18.2)	8.0	52.9 [48.8-57.2]
IIb. Non-Hodgkin lymphomas	164 (6.0)	1.0	13.9 [11.9-16.2]	227 (5.4)	1.2	19.1 [16.7-21.8]	391 (5.6)	1.1	16.4 [14.2-18.8]
IIb1. Precursor-cell lymphomas	12 (0.4)	5.0	1.0[0.5 - 1.8]	14 (0.3)	2.5	1.2 [0.6-2.0]	26 (0.4)	3.3	1.1 [0.6-1.9]
IIb2. Mature B-cell lymphomas	101 (3.7)	6.0	8.6 [7.0-10.4]	160 (3.8)	1.3	13.5 [11.5-15.8]	261 (3.8)	1.1	10.9 [9.1-12.9]
IIb3. Mature T-cell and NK-cell lymphomas	47 (1.7)	1.0	4.0 [2.9-5.3]	46 (1.1)	8.0	3.9 [2.8-5.2]	93 (1.3)	6.0	3.9 [2.9-5.2]
IIb4. Unspecified Non-Hodgkin lymphomas	4 (0.1)	0.0	0.3[0.1-0.9]	7 (0.2)	8.0	0.6 [0.2-1.2]	11 (0.2)	0.4	0.5[0.2-1.0]
IIc. Burkitt lymphoma	23 (0.8)	3.6	2.0 [1.2-2.9]	15 (0.4)	4.0	1.3 [0.7-2.1]	38 (0.5)	3.8	1.6 [1.0-2.5]
IId. Miscellaneous lymphoreticular neoplasms	13 (0.5)	3.3	1.1[0.6-1.9]	8 (0.2)	1.0	0.7 [0.3-1.3]	21 (0.3)	2.0	0.9 [0.4-1.6]
IIe. Unspecified lymphoma	1 (0.0)	0.0	0.1[0.0-0.5]	3 (0.1)	0.0	0.3 [0.0-0.7]	4 (0.1)	0.0	0.2 [0.0-0.6]

TABLE 2. (CONTINUED)

Diagnostic groups and subgroups (ICCC-3)	Adole	scents (1:	Adolescents (15–19 years)	Your	g adults (	Young adults (20–24 years)	AY	A (15–2	AYA (15-24 years)
	(%) u	M/F ratio	IR [95%CI]	(%) u	M/F ratio	IR [95%CI]	(%) u	M/F ratio	ASR [95%CI]
III. Central nervous system tumors	332 (12.1)	1.1	28.2 [25.2-31.4]	411 (9.8)	1.3	34.6 [31.4-38.2]	743 (10.7)	1.2	31.2 [28.1-34.6]
IIIa. Ependymomas and choroid plexus tumor	31 (1.1)	1.6	2.6 [1.8-3.7]	25 (0.6)	1.5	2.1 [1.4-3.1]	56 (0.8)	1.5	2.4 [1.6-3.4]
IIIa1. Ependymomas	26 (1.0)	1.9	2.2 [1.4-3.2]	23 (0.5)	1.3	1.9 [1.2-2.9]	49 (0.7)	1.6	2.1 [1.3-3.1]
IIIa2. Choroid plexus tumor	5 (0.2)	0.7	0.4[0.1-1.0]	2 (0.0)	,	0.2 [0.0-0.6]	7 (0.1)	1.3	0.3 [0.1-0.8]
IIIb. Astrocytomas	106 (3.9)	1.3	9.0 [7.4-10.9]	122 (2.9)	1.7	10.3 [8.5-12.3]	228 (3.3)	1.5	9.6 [7.9-11.5]
IIIc. Intracranial and intraspinal embryonal tumors	26 (1.0)	2.3	2.2 [1.4-3.2]	25 (0.6)	5.3	2.1 [1.4-3.1]	51 (0.7)	3.3	2.2 [1.4-3.2]
IIIc1.Medulloblastomas	18 (0.7)	3.5	1.5 [0.9-2.4]	19 (0.5)	8.5	1.6 [1.0-2.5]	37 (0.5)	5.2	1.6 [0.9-2.5]
IIIc2. cPNET	5 (0.2)	0.7	0.4 [0.1-1.0]	5 (0.1)	4.0	0.4 [0.1-1.0]	10 (0.1)	1.5	0.4 [0.1-1.0]
IIIc3. Medulloepithelioma	1 (0.0)	0.0	0.1[0.0-0.5]	1 (0.0)	0.0	0.1 [0.0-0.5]	2 (0.0)	0.0	0.1 [0.0-0.5]
IIIc4. Atypical teratoid/rhabdoid tumor	2 (0.1)	,	0.2[0.0-0.6]	0 (0.0)	,	0.0 [0.1-0.3]	2 (0.0)		0.1 [0.0-0.5]
IIId. Other gliomas	43 (1.6)	0.7	3.6 [2.6-4.9]	101 (2.4)	1.2	8.5 [6.9-10.3]	144 (2.1)	1:1	5.9 [4.7-7.5]
IIId1. Oligodendrogliomas	20 (0.7)	8.0	1.7 [1.0-2.6]	58 (1.4)	1.2	4.9 [3.7-6.3]	78 (1.1)	1:1	3.2 [2.3-4.4]
IIId2. Mixed and unspecified gliomas	22 (0.8)	0.7	1.9 [1.2-2.8]	42 (1)	1.2	3.5 [2.6-4.8]	64 (0.9)	1.0	2.7 [1.8-3.8]
IIId3. Neuroepithelial glial tumors	1 (0.0)	0.0	0.1[0.0-0.5]	1 (0.0)	,	0.1 [0.0-0.5]	2 (0.0)	1.0	0.1[0.0-0.5]
IIIe. Other specified intracranial and intraspinal tumors	115 (4.2)	6.0	9.8 [8.1-11.7]	121 (2.9)	8.0	10.2 [8.5-12.2]	236 (3.4)	6.0	10.0 [8.2-11.9]
IIIe1. Pituitary adenomas and carcinomas	6 (0.2)	2.0	0.5[0.2 - 1.1]	4 (0.1)	0.3	0.3 [0.1-0.9]	10 (0.1)	1.0	0.4 [0.1-1.0]
IIIe2. Tumors of sellar region	10 (0.4)	0.7	0.8[0.4-1.6]	20 (0.5)	1.2	1.7 [1.0-2.6]	30 (0.4)	1.0	1.2 [0.7-2.1]
IIIe3. Pineal parenchymal tumors	2 (0.1)	1.0	0.2[0.0-0.6]	1 (0.0)	0.0	0.1 [0.0-0.5]	3 (0.0)	0.5	0.1[0.0-0.6]
IIIe4. Neuronal and mixed neuronal-glial tumors	68 (2.5)	6.0	5.8 [4.5-7.3]	51 (1.2)	1.0	4.3 [3.2-5.7]	119 (1.7)	6.0	5.1 [3.9-6.5]
IIIe5. Meningiomas	29 (1.1)	6.0	2.5 [1.6-3.5]	45 (1.1)	0.7	3.8 [2.8-5.1]	74 (1.1)	8.0	3.1 [2.2-4.3]
IIIf. Unspecified intracranial and intraspinal neoplasms	11 (0.4)	8.0	0.9 [0.5-1.7]	17 (0.4)	1.4	1.4 [0.8-2.3]	28 (0.4)	1.2	1.2 [0.6-2.0]
IV. Neuroblastoma	13 (0.5)	1.6	1.1[0.6-1.9]	12 (0.3)	0.3	1.0 [0.5-1.8]	25 (0.4)	8.0	1.1[0.6-1.8]
IVa. Neuroblastoma and ganglioneuroblastoma	6 (0.2)	2.0	0.5[0.2-1.1]	3 (0.1)	0.5	0.3 [0.0-0.7]	9 (0.1)	1.3	0.4[0.1-0.9]
IVb. Other peripheral nervous cell tumors	7 (0.3)	1.3	0.6[0.2 - 1.2]	9 (0.2)	0.3	0.8 [0.3-1.4]	16 (0.2)	9.0	0.7 [0.3-1.3]
VI. Renal tumors	20 (0.7)	0.7	1.7 [1.0-2.6]	42 (1)	1.2	3.5 [2.6-4.8]	62 (0.9)	1.0	2.6 [1.7-3.6]
VIa. Nephroblastoma. other nonepithelial renal tumors	6 (0.2)	0.0	0.5[0.2 - 1.1]	7 (0.2)	1.3	0.6 [0.2-1.2]	13 (0.2)	9.4	0.5 [0.2-1.2]
VIa1. Nephroblastoma	4 (0.1)	0.0	0.3[0.1-0.9]	6 (0.1)	2.0	0.5 [0.2-1.1]	10 (0.1)	0.7	0.4[0.1-1.0]
VIa2. Rhabdoid renal tumors	1 (0.0)	0.0	0.1[0.0-0.5]	1 (0.0)	0.0	0.1 [0.0-0.5]	2 (0.0)	0.0	0.1[0.0-0.5]
VIa4. pPNET of kidney	1 (0.0)	0.0	0.1[0.0-0.5]	0 (0.0)		0.0 [0.1-0.3]	1 (0.0)	0.0	0.0[0.0-0.4]
VIb. Renal carcinoma	14 (0.5)	1.3	1.2[0.6-2.0]	34 (0.8)	1.3	2.9 [2.0-4.0]	48 (0.7)	1.3	2.0 [1.3-2.9]
VIc. Unspecified malignant renal tumors	0.00)		0.0 [0.1-0.3]	1 (0.0)	0.0	0.1 [0.0-0.5]	1 (0.0)	0.0	0.0 [0.0-0.4]

TABLE 2. (CONTINUED)

Diagnostic groups and subgroup

Diagnostic groups and subgroups (ICCC-3)	Adole	scents (15	Adolescents (15–19 years)	Youn	g adults (	Young adults (20–24 years)	AY	AYA (15-24 years)	4 years)
	(%) u	M/F ratio	IR [95%CI]	(%) u	M/F ratio	IR [95%CI]	(%) u	M/F ratio	ASR [95%CI]
VII. Hepatic tumors	11 (0.4)	8.0	0.9 [0.5-1.7]	20 (0.5)	1.9	1.7 [1.0-2.6]	31 (0.4)	1.4	1.3 [0.7-2.1]
VIIa. Hepatoblastoma	1 (0.0)		0.1[0.0-0.5]	0.00)		0.0 [0.1-0.3]	1 (0.0)		0.0 [0.0-0.4]
VIIb. Hepatic carcinoma	9 (0.3)	0.5	0.8[0.3-1.5]	20 (0.5)	1.9	1.7 [1.0-2.6]	29 (0.4)	1.2	1.2 [0.7-2.0]
VIIc. Unspecified malignant hepatic tumors	1 (0.0)		0.1[0.0-0.5]	0 (0.0)		0.0 [0.1-0.3]	1 (0.0)		0.0 [0.0-0.4]
VIII. Malignant bone tumors	217 (7.9)	1.5	18.4 [16.0-21.0]	122 (2.9)	1.6	10.3 [8.5-12.3]	339 (4.9)	1.5	14.6 [12.5-16.9]
VIIIa. Osteosarcomas	107 (3.9)	1.7	9.1 [7.4-11.0]	48 (1.1)	1.4	4.0 [3.0-5.4]	155 (2.2)	1.6	6.7 [5.3-8.3]
VIIIb. Chondrosarcomas	17 (0.6)	6.0	1.4 [0.8-2.3]	32 (0.8)	6.0	2.7 [1.8-3.8]	49 (0.7)	6.0	2.0 [1.3-3.0]
VIIIc. Ewing tumor and related sarcomas of bone	83 (3.0)	1.5	7.0 [5.6-8.7]	36 (0.9)	3.5	3.0 [2.1-4.2]	119 (1.7)	1.9	5.2 [4.0-6.6]
VIIId. Other specified malignant bone tumors	8 (0.3)	0.3	0.7 [0.3-1.3]	6 (0.1)	2.0	0.5 [0.2-1.1]	14 (0.2)	8.0	0.6 [0.2-1.2]
VIIId2. Malignant chordomas	6 (0.2)	0.0	0.5 [0.2-1.1]	2 (0.0)		0.2 [0.0-0.6]	8 (0.1)	0.3	0.3 [0.1-0.9]
VIIId3. Odotongenic malignant tumors	1 (0.0)		0.1[0.0-0.5]	0.00)		0.0 [0.1-0.3]	1 (0.0)		0.0 [0.0-0.4]
VIIId4. Miscellaneous malignant bone tumors	1 (0.0)		0.1[0.0-0.5]	4 (0.1)	1.0	0.3 [0.1-0.9]	5 (0.1)	1.5	0.2 [0.0-0.7]
VIIIe. Unspecified malignant bone tumors	2 (0.1)		0.2[0.0-0.6]	0 (0.0)		0.0 [0.1-0.3]	2 (0.0)		0.1[0.0-0.5]
IX. Soft tissue and other extraosseous sarcomas	134 (4.9)	1.4	11.4 [9.5-13.5]	165 (3.9)	1.4	13.9 [11.9-16.2]	299 (4.3)	1.4	12.6 [10.6-14.8]
IXa.Rhabdomyosarcomas	33 (1.2)	1.5	2.8 [1.9-3.9]	23 (0.5)	2.8	1.9 [1.2-2.9]	56 (0.8)	1.9	2.4 [1.6-3.5]
IXb.Fibrosarcomas. and other fibrous neoplasms	26 (1.0)	6.0	2.2 [1.4-3.2]	26 (0.6)	6.0	2.2 [1.4-3.2]	52 (0.8)	6.0	2.2 [1.4-3.2]
IXb1. Fibroblastic and myofibroblastic tumors	17 (0.6)	1.4	1.4 [0.8-2.3]	13 (0.3)	9.0	1.1 [0.6-1.9]	30 (0.4)	1.0	1.3 [0.7-2.1]
IXb2.Nerve sheath tumors	9 (0.3)	0.3	0.8[0.3-1.5]	13 (0.3)	1.2	1.1 [0.6-1.9]	22 (0.3)	0.7	0.9 [0.5-1.7]
IXc. Kaposi sarcoma	0 (0.0)		0.0[0.1-0.3]	1 (0.0)	0.0	0.1[0.0-0.5]	1 (0.0)	0.0	0.0 [0.0-0.4]
IXd.Other specified soft tissue sarcomas	62 (2.3)	1.6	5.3 [4.0-6.7]	87 (2.1)	1.4	7.3 [5.9-9.0]	149 (2.1)	1.4	6.2 [4.9-7.8]
IXd1-2. Ewing tumors and pPNET of soft tissue	16 (0.6)	1.7	1.4 [0.8-2.2]	11 (0.3)	1.8	0.9 [0.5-1.7]	27 (0.4)	1.7	1.2 [0.6-2.0]
IXd3.Extrarenal rhabdoid tumor	0 (0.0)	1	0.0[0.1-0.3]	3 (0.1)	0.5	0.3 [0.0-0.7]	3 (0.0)	0.5	0.1 [0.1-0.5]
IXd4.Liposarcomas	8 (0.3)	9.0	0.7 [0.3-1.3]	14 (0.3)	1.3	1.2 [0.6-2.0]	22 (0.3)	1.0	0.9 [0.5-1.6]
IXd5.Fibrohistiocytic tumors	2 (0.1)	1.0	0.2[0.0-0.6]	5 (0.1)	0.7	0.4 [0.1-1.0]	7 (0.1)	8.0	0.3 [0.1-0.8]
IXd6.Meiomyosarcomas	6 (0.2)		0.5[0.2-1.1]	10 (0.2)	1.0	0.8 [0.4-1.6]	16 (0.2)	2.2	0.7 [0.3-1.3]
IXd7.Synovial sarcomas	19 (0.7)	1.4	1.6[1.0-2.5]	23 (0.5)	1.9	1.9 [1.2-2.9]	42 (0.6)	1.6	1.8 [1.1-2.7]
IXd8. Blood vessel tumors	4 (0.1)	0.3	0.3[0.1-0.9]	5 (0.1)	0.3	0.4 [0.1-1.0]	9 (0.1)	0.3	0.4 [0.1-0.9]
IXd9. Osseous and chondromatous neoplasms	1 (0.0)	,	0.1[0.0-0.5]	5 (0.1)	0.7	0.4 [0.1-1.0]	6 (0.1)	1.0	0.2 [0.1-0.7]
IXd10. Alveolar soft parts sarcoma	1 (0.0)	0.0	0.1[0.0-0.5]	4 (0.1)	1	0.3 [0.1-0.9]	5 (0.1)	4.0	0.2 [0.0-0.7]
IXd11. Miscellaneous soft tissue sarcomas	5 (0.2)		0.4[0.1-1.0]	7 (0.2)	2.5	0.6 [0.2-1.2]	12 (0.2)	5.0	0.5 [0.2-1.1]
IXe Unspecified soft tissue sarcomas	13 (0.5)	2.3	1.1 [0.6-1.9]	28 (0.7)	1.5	2.4 [1.6-3.4]	41 (0.6)	1.7	1.7 [1.0-2.6]

TABLE 2. (CONTINUED)

Diagnostic groups and subgroups (ICCC-3)	Adole	scents (1:	Adolescents (15-19 years)	Youn	g adults (	Young adults (20–24 years)	AY	'A (15–2	AYA (15–24 years)
	u (%)	M/F ratio	IR [95%CI]	u (%)	M/F ratio	IR [95%CI]	(%) u	M/F ratio	ASR [95%CI]
X. Germ-cell tumors. and other neoplasms of gonads	292 (10.7)	2.7	24.8 [22.0-27.8]	721 (17.2)	7.0	60.8 [56.4-65.4]	1013 (14.6)	5.0	41.7 [38.2-45.5]
Xa. Intracranial and intraspinal germ cell tumors	31 (1.1)	8.9	2.6 [1.8-3.7]	16 (0.4)	7.0	1.3 [0.8-2.2]	47 (0.7)	8.9	2.0[1.3-3.0]
Xa1. germinomas	20 (0.7)	19.0	1.7 [1-2.6.0]	9 (0.2)	,	0.8 [0.3-1.4]	29 (0.4)	28.0	1.3 [0.7-2.1]
Xa2. teratomas	3 (0.1)	0.5	0.3 [0.0-0.8]	5 (0.1)	1.5	0.4 [0.1-1.0]	8 (0.1)	1.0	0.3 [0.1-0.9]
Xa3. embryonal carcinomas	0 (0.0)		0.0 [0.1-0.3]	1 (0.0)	,	0.1 [0.0-0.5]	1 (0.0)		0.0[0.0-0.4]
Xa4. yolk sac tumor	1 (0.0)	,	0.1[0.0-0.5]	0.00)	,	0.0 [0.1-0.3]	1 (0.0)		0.0[0.0-0.4]
Xa5. choriocarcinomas	3 (0.1)	2.0	0.3 [0.0-0.8]	1 (0.0)	,	0.1 [0.0-0.5]	4 (0.1)	3.0	0.2[0.0-0.6]
Xa6. tumors of mixed forms	4 (0.1)		0.3[0.1-0.9]	0.00)	,	0.0 [0.1-0.3]	4 (0.1)		0.2[0.1-0.6]
Xb. Malignant extracranial and extragonadal GCT	14 (0.5)	2.5	1.2 [0.6-2.0]	35 (0.8)	2.5	3.0 [2.1-4.1]	49 (0.7)	2.5	2.0 [1.3-3.0]
Xb1. germinomas	8 (0.3)	1.7	0.7 [0.3-1.3]	10 (0.2)	0.6	0.8[0.4-1.6]	18 (0.3)	3.5	0.8 [0.3-1.4]
Xb2. teratomas	3 (0.1)		0.3[0.0-0.8]	3 (0.1)	2.0	0.3 [0.0-0.7]	6 (0.1)	5.0	0.3 [0.0-0.8]
Xb3. Embryonal carcinomas	0 (0.0)		0.0[0.1-0.3]	1 (0.0)	,	0.1 [0.0-0.5]	1 (0.0)		0.0[0.0-0.4]
Xb4. Yolk sac tumor	0 (0.0)	,	0.0[0.1-0.3]	7 (0.2)	,	0.6 [0.2-1.2]	7 (0.1)		0.3 [0.2-0.8]
Xb5. Choriocarcinomas	1 (0.0)	0.0	0.1[0.0-0.5]	10 (0.2)	0.4	0.8[0.4-1.6]	11 (0.2)	9.4	0.4 [0.2-1.0]
Xb6. Other and unspecified malignant mixed GCT	2 (0.1)		0.2[0.0-0.6]	4 (0.1)	3.0	0.3 [0.1-0.9]	6 (0.1)	5.0	0.2 [0.0-0.7]
Xc. Malignant gonadal germ cell tumors	224 (8.2)	3.5	19.0 [16.6-21.7]	626 (14.9)	15.1	52.8 [48.7-57.1]	850 (12.3)	9.8	34.9 [31.7-38.3]
Xc1. germinomas	48 (1.8)	1.2	4.1 [3.0-5.4]	189 (4.5)	9.5	15.9 [13.7-18.4]	237 (3.4)	4.9	9.7 [8.1-11.5]
Xc2. teratomas	49 (1.8)	2.3	4.2 [3.1-5.5]	106 (2.5)	9.8	8.9 [7.3-10.8]	155 (2.2)	5.0	6.4 [5.1-8.0]
Xc3. embryonal carcinomas	37 (1.4)	36.0	3.1 [2.2-4.3]	133 (3.2)	132.0	11.2 [9.4-13.3]	170 (2.5)	84.0	6.9 [5.6-8.5]
Xc4. yolk sac tumor	12 (0.4)	1.4	1.0[0.5-1.8]	20 (0.5)	2.3	1.7 [1.0-2.6]	32 (0.5)	1.9	1.3 [0.8-2.2]
Xc5. choriocarcinomas	7 (0.3)	2.5	0.6 [0.2-1.2]	9 (0.2)	,	0.8 [0.3-1.4]	16 (0.2)	7.0	0.7 [0.3-1.3]
Xc6. tumors of mixed forms	71 (2.6)	13.2	6.0 [4.7-7.6]	169 (4.0)	55.3	14.2 [12.2-16.6]	240 (3.5)	29.0	9.9 [8.2-11.8]
Xd. Gonadal carcinoma	17 (0.6)	0.0	1.4 [0.8-2.3]	38 (0.9)	0.0	3.2 [2.3-4.4]	55 (0.8)	0.0	2.3 [1.5-3.3]
Xe. Other and unspecified malignant gonadal tumors	6 (0.2)	0.5	0.5 [0.2-1.1]	6 (0.1)	2.0	0.5 [0.2-1.1]	12 (0.2)	1.0	0.5 [0.2-1.1]

TABLE 2. (CONTINUED)

Diagnostic groups and subgroups (ICCC-3)	Adole	scents (1	Adolescents (15-19 years)	Young	adults (	Young adults (20–24 years)	AY	A (15–2	AYA (15–24 years)
	(%) u	M/F ratio	IR [95%CI]	(%) u	M/F ratio	IR [95%CI]	(%) u	M/F ratio	ASR [95%CI]
XI. Epithelial neoplasms and malignant melanomas	580 (21.2)	6.5	49.2 [45.3-53.4]	1419 (33.8)	6.4	119.6 [113.5-126]	1999 (28.8)	9.4	82.3 [77.4-87.6]
XIa. Adrenocartical carcinomas	4 (0.1)	1.0	0.3[0.1-0.9]	10 (0.2)	0.4	0.8 [0.4-1.6]	14 (0.2)	9.0	0.6 [0.2-1.2]
XIb. Thyroid carcinomas	241 (8.8)	0.3	20.4 [17.9-23.2]	566 (13.5)	0.2	47.7 [43.9-51.8]	807 (11.6)	0.2	33.3 [30.1-36.7]
XIc. Nasopharyngeal carcinomas	21 (0.8)	3.2	1.8 [1.1-2.7]	14 (0.3)	1.0	1.2 [0.6-2.0]	35 (0.5)	1.9	1.5 [0.9-2.4]
XId.Malignant melanomas	156 (5.7)	0.7	13.2 [11.2-15.5]	430 (10.2)	0.5	36.3 [32.9-39.8]	586 (8.5)	9.0	24.1 [21.4-26.9]
XIf. Other and unspecified carcinomas	158 (5.8)	9.0	13.4 [11.4-15.7]	399 (9.5)	9.4	33.6 [30.4-37.1]	557 (8)	9.4	22.9 [20.3-25.8]
XIf1. Carcinomas of salivary glands	21 (0.8)	0.4	1.8 [1.1-2.7]	22 (0.5)	0.7	1.9 [1.2-2.8]	43 (0.6)	0.5	1.8 [1.1-2.8]
XIf2. Carcinomas of colon and rectum	16 (0.6)	0.3	1.4 [0.8-2.2]	49 (1.2)	0.5	4.1 [3.1-5.5]	65 (0.9)	0.5	2.7 [1.8-3.7]
XIf3. Carcinomas of appendix	67 (2.5)	0.7	5.7 [4.4-7.2]	55 (1.3)	0.4	4.6 [3.5-6.0]	122 (1.8)	9.0	5.2 [4.0-6.7]
XIf4. Carcinomas of lung	13 (0.5)	1.2	1.1[0.6-1.9]	41 (1.0)	1.0	3.5 [2.5-4.7]	54 (0.8)	1.0	2.2 [1.5-3.2]
XIf5. Carcinomas of thymus	5 (0.2)	0.7	0.4 [0.1-1.0]	6 (0.1)	1.0	0.5 [0.2-1.1]	11 (0.2)	8.0	0.5 [0.2-1.0]
XIf6. Carcinomas of breast	4 (0.1)	0.0	0.3[0.1-0.9]	90 (2.1)	0.0	7.6 [6.1-9.3]	94 (1.4)	0.0	3.8 [2.9-4.9]
XIf7. Carcinomas of cervix uteri	1 (0.0)	0.0	0.1[0.0-0.5]	40(1)	0.0	3.4 [2.4-4.6]	41 (0.6)	0.0	1.6 [1.1-2.4]
XIf8. Carcinomas of bladder	1 (0.0)	,	0.1[0.0-0.5]	1 (0.0)	,	0.1[0.0-0.5]	2 (0.0)		0.1[0.0-0.5]
XIf9. Carcinomas of eye	0 (0.0)	ı	0.0[0.1-0.3]	2 (0.0)	1.0	0.2 [0.0-0.6]	2 (0.0)	1.0	0.1 [0.1-0.5]
XIf10. Carcinomas of other specified sites	29 (1.1)	0.7	2.5 [1.6-3.5]	82 (2.0)	9.0	6.9 [5.5-8.6]	111 (1.6)	9.0	4.6 [3.5-5.9]
XIf11. Carcinomas of unspecified sites	1 (0)	,	0.1[0.0-0.5]	11 (0.3)	2.7	0.9 [0.5-1.7]	12 (0.2)	3.0	0.5[0.2 - 1.0]
XII. Other and unspecified malignant neoplasms	12 (0.4)	3.0	1.0 [0.5-1.8]	13 (0.3)	1.2	1.1 [0.6-1.9]	25 (0.4)	1.8	1.1 [0.6-1.8]
XIIa. Other specified malignant tumors	9 (0.3)	3.5	0.8[0.3-1.5]	6 (0.1)	1.0	0.5 [0.2-1.1]	15 (0.2)	2.0	0.6 [0.3-1.3]
XIIa1. Gastrointestinal stromal tumor	5 (0.2)	4.0	0.4[0.1-1.0]	2 (0.0)	1.0	0.2 [0.0-0.6]	7 (0.1)	2.5	0.3 [0.1-0.8]
XIIa4. Other complex mixed and stromal neoplams	1 (0.0)	0.0	0.1[0.0-0.5]	1 (0.0)	0.0	0.1[0.0-0.5]	2 (0.0)	0.0	0.1[0.0-0.5]
XIIa5. Mesothelioma	3 (0.1)		0.3 [0.0-0.8]	3 (0.1)	2.0	0.3 [0.0-0.7]	6 (0.1)	5.0	0.3 [0.0-0.8]
XIIb. Other unspecified malignant tumors	3 (0.1)	2.0	0.3 [0.0-0.8]	7 (0.2)	1.3	0.6 [0.2-1.2]	10 (0.1)	1.5	0.4 [0.1-1.0]
Total	2734 (100.0)	1.0	231.9 [223.3-240.8]	4199 (100.0)	1.0	354.0 [343.4-364.9]	6933 (100.0)	1.0	289.4 [279.8-299.2]

Abbreviations: AYA, adolescents and young adults; ICCC-3, third version of the International Classification of Childhood Cancer; GCT, Germ-Cell tumors; cPNET, central primitive neuroectodermal tumors; M/F ratio, Male/Female ratio; IR, Incidence rates per million; ASR, age-standardized incidence rates per million; 95%CI, 95% confidence interval.

TABLE 3. ONE-, TWO-, AND FIVE-YEAR OVERALL SURVIVAL AMONG AYA WITH CANCER FROM 2000 TO 2015 BY ICCC-3 DIAGNOSTIC GROUPS

ICCC-3 diagnostic groups and subgroups	n	1-year OS % [95%CI]	2-year OS % [95%CI]	5-year OS % [95%CI]
I. Leukemias, myeloproliferative/dysplastic diseases	645	88.4 [85.6-90.6]	80.4 [77.1-83.3]	73.4 [69.7-76.6]
Ia. Lymphoblastic leukemias	292	87.3 [82.9-90.6]	78.7 [73.5-83.0]	69.6 [63.9-74.6]
Ia1. Precursor cell leukemias	280	87.8 [83.4-91.2]	79.2 [74.0-83.5]	69.8 [63.9-74.9]
Ia2. Mature B-cell leukemias	9	77.8 [36.5-93.9]	66.7 [28.2-87.8]	66.7 [28.2-87.8]
Ia3. Mature T-cell and NK cell leukemias	3	66.7 [5.4-94.5]	66.7 [5.4-94.5]	66.7 [5.4-94.5]
Ib. Acute myeloid leukemias	176	83 [76.5-87.8]	72.2 [64.9-78.2]	64.4 [56.8-71.0]
Ic. Chronic myeloproliferative diseases	130	100.0 [-]	99.2 [94.7-99.9]	96.8 [91.7-98.8]
Id. Myelodysplastic diseases	34	91.2 [75.1-97.1]	82.1 [64.3-91.5]	75.6 [57.0-87.0]
Ie. Unspecified and other specified leukemias	14	64.3 [34.3-83.3]	42.9 [17.7-66.0]	42.9 [17.7-66.0]
II. Lymphomas and reticuloendothelial neoplasms	1594	98.1 [97.3-98.7]	96.0 [94.9-96.8]	94.1 [92.8-95.1]
IIa. Hodgkin disease	1170	99.7 [99.1-99.9]	98.0 [97.0-98.7]	96.5 [95.3-97.4]
IIb. Non-Hodgkin lymphomas	365	94.5 [91.5-96.4]	91.1 [87.7-93.6]	87.6 [83.7-90.6]
IIb1. Precursor-cell lymphomas	25	84 [62.8-93.7]	76.0 [54.2-88.4]	68.0 [46.1-82.5]
IIb2. Mature B-cell lymphomas	239	95.3 [91.7-97.4]	92.4 [88.1-95.1]	88.7 [83.8-92.2]
IIb3. Mature T-cell and NK-cell lymphomas	91	95.5 [88.5-98.3]	93.3 [85.7-96.9]	91.0 [82.8-95.4]
IIb4. Unspecified Non-Hodgkin lymphomas	10	90.0 [47.3-98.5]	80.0 [40.9-94.6]	80.0 [40.9-94.6]
IIc. Burkitt lymphoma	38	94.7 [80.6-98.7]	89.5 [74.3-95.9]	89.5 [74.3-95.9]
IId. Miscellaneous lymphoreticular neoplasms	17	88.2 [60.6-96.9]	82.4 [54.7-93.9]	82.4 [54.7-93.9]
IIe. Unspecified lymphoma	4	50.0 [5.8-84.5]	50.0 [5.8-84.5]	50.0 [5.8-84.5]
III. Central nervous system tumors	695	92.7 [90.5-94.4]	86.4 [83.6-88.7]	78.1 [74.7-81]
IIIa. Ependymomas and choroid plexus tumor	52	98 [86.9-99.7]	96.1 [85.2-99.0]	89.2 [76.0-95.4]
IIIa1. Ependymomas	45	100.0 [-]	97.7 [84.9-99.7]	90.0 [75.4-96.1]
IIIa2. Choroid plexus tumor	7	85.7 [33.4-97.9]	85.7 [33.4-97.9]	85.7 [33.4-97.9]
IIIb. Astrocytomas	213	90.9 [86.2-94.1]	78.0 [71.7-83.0]	66.7 [59.8-72.8]
IIIc. Intracranial and intraspinal embryonal tumors	47	89.4 [76.3-95.4]	85.1 [71.3-92.6]	71.1 [55.3-82.1]
IIIc1.Medulloblastomas	34	97.1 [80.9-99.6]	91.2 [75.1-97.1]	81.7 [63.6-91.4]
IIIc2. cPNET	9	66.7 [28.2-87.8]	66.7 [28.2-87.8]	20.0 [1.2-55.7]
IIIc3. Medulloepithelioma	2	100.0 [-]	100.0 [-]	100.0 [-]
IIIc4. Atypical teratoid/rhabdoid tumor	2	50.0 [0.6-91.0]	50.0 [0.6-91.0]	50.0 [0.6-91.0]
IIId. Other gliomas	141	85.6 [78.6-90.5]	77.7 [69.8-83.8]	63.7 [55.0-71.1]
IIId1. Oligodendrogliomas	78	85.5 [75.4-91.7]	78.9 [68.0-86.5]	68.4 [56.7-77.6]
IIId2. Mixed and unspecified gliomas	61	85.2 [73.6-92.0]	77.0 [64.3-85.7]	59.7 [46.1-71.0]
IIId3. Neuroepithelial glial tumors	2	100.0 [-]	50.0 [0.6-91.0]	50.0 [0.6-91.0]
IIIe. Other intracranial and intraspinal tumors	217	98.1 [95.1-99.3]	97.2 [93.9-98.7]	96.1 [92.4-98]
IIIe1. Pituitary adenomas and carcinomas	10	100.0 [-]	100.0 [-]	100 [100-100]
IIIe2. Tumors of sellar region	29	100.0 [-]	100.0 [-]	95.5 [71.9-99.3]
IIIe3. Pineal parenchymal tumors	3	100.0 [-]	100.0 [-]	100.0 [-]
IIIe4. Neuronal and mixed neuronal-glial tumors	112	98.2 [93.0-99.5]	97.3 [91.8-99.1]	96.3 [90.4-98.6]
IIIe5. Meningiomas	63	96.8 [87.8-99.2]	95.2 [85.8-98.4]	95.2 [85.8-98.4]
IIIf. Unspecified neoplasms	27	92.3 [72.6-98.0]	92.3 [72.6-98.0]	88.5 [68.4-96.1]
IV. Neuroblastoma	24	87.5 [66.1-95.8]	83.3 [61.5-93.4]	79.2 [57.0-90.8]
IVa. Neuroblastoma and ganglioneuroblastoma	9	66.7 [28.2-87.8]	66.7 [28.2-87.8]	55.6 [20.4-80.5]
IVb. Other peripheral nervous cell tumors	15	100 -	93.3 [61.3-99.0]	93.3 [61.3-99.0]

Table 3. (CONTINUED)

ICCC-3 diagnostic groups and subgroups	n	1-year OS % [95%CI]	2-year OS % [95%CI]	5-year OS % [95%CI]
VI. Renal tumors	55	90.7 [79.2-96.0]	88.9 [76.9-94.8]	79.1 [65.4-87.9]
VIa. Nephroblastoma and other nonepithelial tumors	11	81.8 [44.7-95.1]	81.8 [44.7-95.1]	71.6 [35.0-89.9]
VIa1. Nephroblastoma	8	100.0 [-]	100.0 [-]	85.7 [33.4-97.9]
VIa2. Rhabdoid renal tumors	2	0.0 [-]	0.0 [-]	0.0 [-]
VIa4. pPNET of kidney	1	100.0 [-]	100.0 [-]	100.0 [-]
VIb. Renal carcinoma	43	92.9 [79.5-97.6]	90.5 [76.6-96.3]	80.5 [64.6-89.7]
VIc. Unspecified malignant renal tumors	1	100.0 [-]	100.0 [-]	100.0 [-]
VII. Hepatic tumors	31	71.0 [51.6-83.7]	58.1 [39.0-73.1]	33.4 [17.3-50.4]
VIIa. Hepatoblastoma	1	100.0 [-]	100.0 [-]	100.0 [-]
VIIb. Hepatic carcinoma	29	69.0 [48.8-82.5]	55.2 [35.6-71.0]	28.4 [13.0-46.0]
VIIc. Unspecified malignant hepatic tumors	1	100.0 [-]	100.0 [-]	100.0 [-]
VIII. Malignant bone tumors	313	94.2 [90.9-96.3]	82.2 [77.5-86.1]	65.1 [59.4-70.3]
VIIIa. Osteosarcomas	145	93.8 [88.3-96.7]	82.6 [75.3-87.9]	60.3 [51.5-67.9]
VIIIb. Chondrosarcomas	42	100.0 [-]	92.7 [79.0-97.6]	90.0 [75.6-96.1]
VIIIc. Ewing tumor and related sarcomas of bone	113	92.9 [86.3-96.4]	77.0 [68.1-83.7]	61.1 [51.3-69.5]
VIIId. Other specified malignant bone tumors	12	90.9 [50.8-98.7]	90.9 [50.8-98.7]	72.7 [37.1-90.3]
VIIId2. Malignant chordomas	6	80.0 [20.4-96.9]	80.0 [20.4-96.9]	40.0 [5.2-75.3]
VIIId3. Odotongenic malignant tumors	1	100.0 [-]	100.0 [-]	100.0 [-]
VIIId4. Miscellaneous malignant bone tumors	5	100.0 [-]	100.0 [-]	100.0 [-]
VIIIe. Unspecified malignant bone tumors	1	100.0 [-]	100.0 [-]	100.0 [-]
IX. Soft tissue and other extraosseous sarcomas	288	90.5 [86.5-93.4]	79.9 [74.8-84.2]	66.8 [60.9-72.1]
IXa.Rhabdomyosarcomas	52	84.6 [71.6-92.0]	61.5 [47.0-73.2]	48.1 [34.1-60.8]
IXb.Fibrosarcomas, and other fibrous neoplasms	50	89.8 [77.2-95.6]	85.7 [72.4-92.9]	79.1 [64.6-88.2]
IXb1.Fibroblastic and myofibroblastic tumors	29	100.0 [-]	96.4 [77.2-99.5]	89.0 [69.7-96.3]
IXb2.Nerve sheath tumors	21	76.2 [51.9-89.3]	71.4 [47.2-86.0]	66.7 [42.5-82.5]
IXc. Kaposi sarcoma	1	100.0 [-]	100.0 [-]	100.0 [-]
IXd.Other specified soft tissue sarcomas	144	93.6 [88.1-96.6]	84.4 [77.3-89.5]	70.6 [62.1-77.6]
IXd1-2.Ewing tumors and pPNET of soft tissue	27	92.6 [73.5-98.1]	74.1 [53.2-86.7]	58.3 [37.4-74.4]
IXd3.Extrarenal rhabdoid tumor	3	33.3 [0.9-77.4]	0.0 [-]	0.0 [-]
IXd4.Liposarcomas	22	100.0 [-]	100.0 [-]	95.2 [70.7-99.3]
IXd5.Fibrohistiocytic tumors	7	100.0 [-]	100.0 [-]	100.0 [-]
IXd6.Meiomyosarcomas	16	100.0 [-]	100.0 [-]	87.5 [58.6-96.7]
IXd7.Synovial sarcomas	39	97.4 [82.8-99.6]	89.3 [73.8-95.8]	65.7 [47.3-78.9]
IXd8. Blood vessel tumors	8	75 [31.5-93.1]	62.5 [22.9-86.1]	50.0 [15.2-77.5]
IXd9. Osseous and chondromatous neoplasms	6	100.0 [-]	100.0 [-]	100.0 [-]
IXd10. Alveolar soft parts sarcoma	4	100.0 [-]	100.0 [-]	100.0 [-]
IXd11. Miscellaneous soft tissue sarcomas	12	81.8 [44.7-95.1]	54.5 [22.9-78.0]	36.4 [11.2-62.7]
IXe Unspecified soft tissue sarcomas	41	87.8 [73.2-94.7]	80.5 [64.8-89.7]	62.6 [45.7-75.6]

Table 3. (CONTINUED)

ICCC-3 diagnostic groups and subgroups	n	1-year OS	2-year OS	5-year OS
X. Germ-cell tumors, and other neoplasms of gonads	948	% [95%CI] 97.0 [95.7-97.9]	% [95%CI] 94.5 [92.9-95.8]	% [95%CI] 92.9 [91-94.4]
Xa. Intracranial and intraspinal germ cell tumors	42	97.6 [84.3-99.7]	88.1 [73.7-94.9]	83.3 [68.2-91.7]
Xa1. germinomas	26	100.0 [-]	92.3 [72.6-98.0]	88.5 [68.4-96.1]
Xa2. teratomas	7	100.0 [-]	100.0 [-]	100.0 [-]
Xa4. yolk sac tumor	1	100.0 [-]	0.0 [-]	0.0 [-]
Xa5. choriocarcinomas	4	75.0 [12.8-96.1]	75.0 [12.8-96.1]	75.0 [12.8-96.1]
Xa6. tumors of mixed forms	4	100.0 [-]	75.0 [12.8-96.1]	50.0 [5.8-84.5]
Xb. Malignant extracranial and extragonadal GCT	<del>4</del> 7	85.1 [71.3-92.6]	72.3 [57.2-82.9]	69.4 [53.8-80.7]
Xb1. germinomas	17	88.2 [60.6-96.9]	88.2 [60.6-96.9]	88.2 [60.6-96.9]
Xb2. teratomas	6	66.7 [19.5-90.4]	33.3 [4.6-67.6]	33.3 [4.6-67.6]
Xb3. Embryonal carcinomas	1	100.0 [-]	100.0 [-]	100.0 [-]
Xb4. Yolk sac tumor	6	= =	50.0 [11.1-80.4]	= =
Xb5. Choriocarcinomas	11	100.0 [-] 81.8 [44.7-95.1]	72.7 [37.1-90.3]	50.0 [11.1-80.4] 72.7 [37.1-90.3]
Xb6. Other and unspecified malignant mixed GCT	6		83.3 [27.3-97.5]	
	798	83.3 [27.3-97.5]		62.5 [14.2-89.3] 95.7 [94.0-96.9]
Xc. Malignant gonadal germ cell tumors Xc1. germinomas		98.2 [97.0-98.9]	96.9 [95.5-97.9] 99.1 [96.3-99.8]	
Xc2. teratomas	220	99.5 [96.7-99.9]	. ,	99.1 [96.3-99.8]
	148	99.3 [95.2-99.9]	96.6 [91.9-98.6] 99.4 [95.5-99.9]	93.5 [87.9-96.6]
Xc3. embryonal carcinomas	159	100.0 [-]		98.0 [94.1-99.4]
Xc4. yolk sac tumor	29	96.4 [77.2-99.5]	96.4 [77.2-99.5]	96.4 [77.2-99.5]
Xc5. choriocarcinomas	16	87.1 [57.3-96.6]	73.7 [44.1-89.2]	73.7 [44.1-89.2]
Xc6. tumors of mixed forms	226	96.0 [92.4-97.9]	95.1 [91.3-97.2]	93.7 [89.6-96.2]
Xd. Gonadal carcinoma	50	88.0 [75.2-94.4]	82.0 [68.3-90.2]	77.9 [63.6-87.1]
Xe. Other and unspecified malignant gonadal tumors	11	100.0 [-]	100.0 [-]	100.0 [-]
XI. Epithelial neoplasms and malignant melanomas	1883	97.1 [96.2-97.8]	95.3 [94.2-96.1]	92.5 [91.2-93.7]
XIa. Adrenocartical carcinomas	14	78.6 [47.2-92.5]	57.1 [28.4-78.0]	57.1 [28.4-78.0]
XIb. Thyroid carcinomas	746	99.7 [98.9-99.9]	99.7 [98.9-99.9]	99.4 [98.5-99.8]
XIc. Nasopharyngeal carcinomas	33	90.9 [74.4-97.0]	84.8 [67.4-93.4]	77.8 [58.7-88.8]
XId.Malignant melanomas	560	98.9 [97.6-99.5]	97.8 [96.2-98.7]	95.3 [93.1-96.8]
XIf. Other and unspecified carcinomas	531	92.3 [89.7-94.3]	87.9 [84.8-90.4]	81.7 [78.1-84.8]
XIf1. Carcinomas of salivary glands	40	100.0 [-]	100.0 [-]	100.0 [-]
XIf2. Carcinomas of colon and rectum	64	92.2 [82.2-96.7]	85.9 [74.7-92.4]	67.9 [54.7-78.0]
XIf3. Carcinomas of appendix	109	100.0 [-]	100.0 [-]	100.0 [-]
XIf4. Carcinomas of lung	54	90.6 [78.8-96.0]	88.6 [76.4-94.7]	82.7 [69.4-90.6]
XIf5. Carcinomas of thymus	11	100.0 [-]	90.9 [50.8-98.7]	81.8 [44.7-95.1]
XIf6. Carcinomas of breast	91	94.5 [87.3-97.7]	91.2 [83.2-95.5]	82.7 [73.0-89.2]
XIf7. Carcinomas of cervix uteri	40	97.5 [83.5-99.6]	87.5 [72.5-94.6]	87.5 [72.5-94.6]
XIf8. Carcinomas of bladder	2	50.0 [0.6-91.0]	50.0 [0.6-91.0]	50.0 [0.6-91.0]
XIf9. Carcinomas of eye	2	100.0 [-]	100.0 [-]	100.0 [-]
XIf10. Carcinomas of other specified sites	107	84.1 [75.7-89.8]	75.7 [66.4-82.8]	70.7 [61.0-78.4]
XIf11. Carcinomas of unspecified sites	11	40.9 [12.7-67.9]	30.7 [7.3-58.6]	0.0 [-]
XII. Other and unspecified malignant neoplasms	24	74.6 [51.9-87.7]	70.2 [47.4-84.5]	65.5 [42.6-81.1]
XIIa. Other specified malignant tumors	14	92.9 [59.1-99.0]	92.9 [59.1-99.0]	85.1 [52.3-96.1]
XIIa1. Gastrointestinal stromal tumor	6	100.0 [-]	100.0 [-]	100.0 [-]
XIIa4. Other complex mixed and stromal neoplams	2	50.0 [0.6-91.0]	50.0 [0.6-91.0]	50.0 [0.6-91.0]
XIIa5. Mesothelioma	6	100.0 [-]	100.0 [-]	83.3 [27.3-97.5]
XIIb. Other unspecified malignant tumors	10	46.7 [15.0-73.7]	35.0 [8.5-64.0]	35.0 [8.5-64.0]
Total  Abbreviations: AVA adolescents and young adults: ICCC 3, this	6480	95.3 [94.8-95.8]	91.3 [90.6-92.0]	86.6 [85.8-87.4]

Abbreviations: AYA, adolescents and young adults; ICCC-3, third version of the International Classification of Childhood Cancer; GCT, Germ-Cell tumors; cPNET, central primitive neuroectodermal tumors; pPNET, peripheral primitive neuroectodermal tumors; OS, Overall Survival; 95%CI, 95% confidence interval.

Table 4. Trends in Five-year Overall Survival among adolescents and young adults with Cancer from 1978 to 2015 by ICCC-3 DIAGNOSTIC GROUPS

ICCC-3 diagnostic groups			5-year OS			
			% (95%CI)			
	1978-82*	1983-87*	1988-92*	1993-97*	2000-07	2008-15
I. Leukemia	28.6 (16.1-41.1)	25.3 (13.9-36.7)	30.3 (20.3-40.3)	49.5 (38.9-60.1)	49.5 (38.9-60.1) 69.5 (63.5-74.7) 76.2 (71.5-80.2)	76.2 (71.5-80.2)
II. Lymphomas	72.0 (63.8-80.2)	77.9 (71.4-84.4)	86 (80.3-91.7)	87.6 (82.9-92.3)	93.4 (91.6-95.5) 94.2 (92.5-95.5)	94.2 (92.5-95.5)
III. Central Nervous System tumors	47.4 (32.5-62.3)#	61.7 (46.4-77.0)#	63.3 (51.3-75.3)#	60.1 (47.9-72.3)#	77.6 (72.1-82.2)	77.6 (72.1-82.2) 78.3 (73.9-82.1)
VIII. Malignant bone tumors	59.3 (40.7-77.9)	48.4 (30.8-66.0)	58.6 (43.5-73.7)	60.3 (47.2-73.4)	58.2 (48.9-66.4)	58.2 (48.9-66.4) 70.0 (62.7-76.2) <sup>a</sup>
IX. Soft tissue and other extraosseous	56.1 (36.3-75.9)	50.7 (33.8-67.6)	49.2 (35.7-62.7)	73.1 (60.0-86.2)	65.6 (56.6-73.2) 67.5 (59.3-74.5)	67.5 (59.3-74.5)
sarcomas						
X. Germ-cell tumors	73.2 (63.4-83.0)	78 (69.4-86.6)	88.5 (83.2-93.8)	91.1 (86.6-95.6)	91.1 (86.6-95.6) 91.2 (87.9-93.6) 94.3 (91.9-96.0) <sup>a</sup>	$94.3 (91.9-96.0)^a$
XI. epithelial neoplasms and melanomas	75.9 (66.7-85.1)	74.6 (66.6-82.6)	85.7 (80.4-91.0)	89.9 (86.2-93.6)	90.9 (88.5-92.9)	90.9 (88.5-92.9) 93.5 (91.8-94.7) <sup>a</sup>
All tumors	62.0 (57.5-66.5)	66.0 (61.9-70.1)	73.2 (70.1-76.3)	80.2 (77.7-82.8)	80.2 (77.7-82.8) 81.8 (79.5-83.9) 88.0 (86.9-89.0) <sup>a</sup>	$88.0 (86.9-89.0)^a$
Abharintians ICCC 3. Hind remains afthe Intermedianel Classification of Childhood Canon OC. Oremall Committed 1050/Cl. 1050/ confidenced intermed	tomotional Closestic	Little Little	OC. Organia	1. 050/CI. 050/	Larmotai conclustan	

Abbreviations: ICCC-3: third version of the International Classification of Childhood Cancer; OS: Overall Survival; 95% confidence interval \* Data from reference 2 # Only malignant CNS tumors were included (exclusion of benign or borderline tumors) a p<0.05 Comparison between diagnostic periods (2000-2007 vs 2008-2015)

TABLE 5. TRENDS IN FIVE-YEAR OVERALL SURVIVAL AMONG ADOLESCENTS AND YOUNG ADULTS WITH CANCER FROM 2000-2007 TO 2008-2015 BY

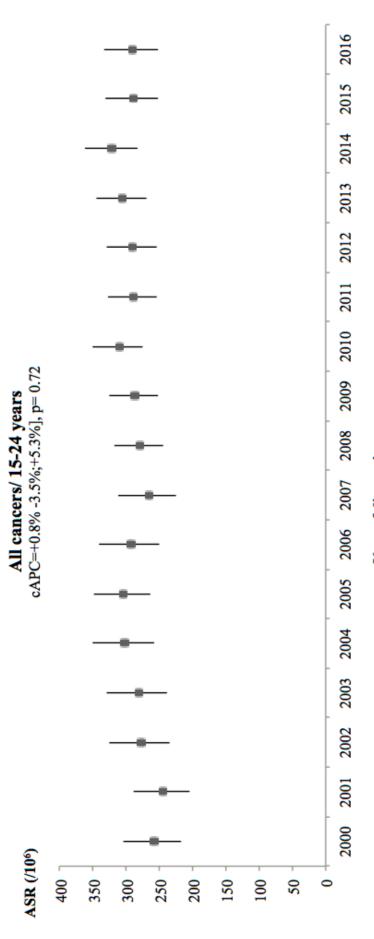
# ICCC-3 DIAGNOSTIC GROUPS

ICCC-3 diagnostic groups and subgroups		Adolescents (15-19 years)	15-19 ye	ars)		Young adults (20-24 years)	(20-24 y	ears)
1		2000-2007		2008-2015		2000-2007		2008-2015
	u	5yOS [95%CI]	u	5yOS [95%CI]	п	5yOS [95%CI]	¤	5yOS [95%CI]
I. Leukemias, myeloproliferative/myelodysplastic diseases	141	67.9 [59.5-74.9]	201	76.4 [69.7-81.8]	122	71.3 [62.4-78.5]	181	76.1 [69.0-81.8]
Ia. Lymphoblastic leukemias	83	69.6 [58.4-78.3]	100	79.3 [69.8-86.2] <sup>b</sup>	39	59.0 [42.0-72.5]	70	$63.2 [50.4-73.5]^{b}$
Ib. Acute myeloid leukemias	39	59.0 [42.0-72.5]	55	62.4 [47.7-74.0]	36	63.9 [46.1-77.2]	46	71.4 [55.9-82.3]
Ic. Chronic myeloproliferative diseases	15	93.3 [61.3-99.0]	26	100.0 [-]	35	94.3 [79.0-98.5]	54	98.1 [87.6-99.7]
Id. Myelodysplastic / myeloproliferative diseases	2	50.0 [0.6-91.0]	14	77.9 [45.9-92.3]	6	77.8 [36.5-93.9]	6	76.2 [33.2-93.5]
Ie. Unspecified and other specified leukemias	3	33.3 [0.9-77.4]	9	50.0 [11.1-80.4]	3	33.3 [0.9-77.4]	7	50.0 [0.6-91.0]
II. Lymphomas and reticuloendothelial neoplasms	286	94.4 [91.0-96.5]	409	95.0 [92.4-96.8]	335	93.4 [90.2-95.6]	564	93.6 [91.2-95.4]
IIa. Hodgkin disease	210	97.6 [94.3-99.0]	300	98.0 [95.5-99.1]	241	95.8 [92.4-97.7]	419	95.5 [93.0-97.2]
IIb. Non-Hodgkin lymphomas	99	86.2 [75.1-92.5]	85	86.8 [77.5-92.5]	82	87.8 [78.5-93.2]	132	88.2 [80.8-92.9]
IIc. Burkitt lymphoma	7	100.0 [-]	16	81.3 [52.5-93.5]	∞	100.0 [-]	7	85.7 [33.4-97.9]
IId. Miscellaneous lymphoreticular neoplasms	33	33.3 [0.9-77.4]	7	100.0 [-]	33	66.7 [5.4-94.5]	4	100.0 [-]
IIe. Unspecified lymphoma	1		1	1	_	0.0 [-]	7	50.0 [0.6-91.0]
III. Central nervous system tumors	119	80.3 [71.9-86.5]	187	81.3 [74.7-86.4]	151	75.4 [67.6-81.6]	238	76.0 [69.8-81.1]
IIIa. Ependymomas and choroid plexus tumor	9	83.3 [27.3-97.5]	22	85.7 [53.9-96.2]	9	83.3 [27.3-97.5]	18	94.4 [66.6-99.2]
IIIb. Astrocytomas	37	77.8 [60.4-88.2]	61	$74.8 [61.6-84.0]^{b}$	43	73.7 [57.5-84.5] <sup>a</sup>	72	$49.6[37.0-61.0]^{a,b}$
IIIc. Intracranial and intraspinal embryonal tumors	6	66.7 [28.2-87.8]	14	85.7 [53.9-96.2]	10	50.0 [18.4-75.3]	14	76.6 [43.3-91.9]
IIId. Other gliomas	16	43.8 [19.8-65.6]	24	47.8 [26.8-66.1]	20	67.3 [52.3-78.6]	51	73.6 [58.7-83.9]
IIIe. Other specified intracranial and intraspinal neoplasms	45	97.7 [84.9-99.7]	61	96.7 [87.3-99.2]	38	94.4 [79.5-98.6]	73	95.3 [85.9-98.5]
IIIf. Unspecified intracranial and intraspinal neoplasms	9	83.3 [27.3-97.5]	5	100.0 [-]	S	80.0 [20.4-96.9]	11	90.0 [47.3-98.5]
IV. Neuroblastoma, other peripheral nervous cell tumors	S	60.0 [12.6-88.2]	7	100.0 [-]	9	66.7 [19.5-90.4]	9	83.3 [27.3-97.5]
IVa. Neuroblastoma and ganglioneuroblastoma	7	0.0 [-]	4	100.0 [-]	_	100.0 [-]	7	50.0[0.6-91.0]
IVb. Other peripheral nervous cell tumors	33	100.0 [-]	3	100.0 [-]	5	80.0 [20.4-96.9]	4	100.0 [-]
VI. Renal tumors	12	81.8 [44.7-95.1]	w	80.0 [20.4-96.9]	13	84.6 [51.2-95.9]	25	74.4 [51.3-87.7]
VIa. Nephroblastoma and other nonepithelial renal tumors	1	ı	1	ı	П	100.0 [-]	4	37.5 [1.1-80.8]
VIb. Renal carcinoma	9	80.0 [20.4-96.9]	5	80.0 [20.4-96.9]	11	81.8 [44.7-95.1]	21	80.0 [54.9-92.0]
VII. Hepatic tumors	9	33.3 [4.6-67.6]	S	60.0[12.6-88.2]	9	16.7 [0.8-51.7]	14	35.7 [13.0-59.4]
VIIb. Hepatic carcinoma	S	20.0 [0.8-58.2]	4	50.0 [5.8-84.5]	9	16.7 [0.8-51.7]	4	35.7 [13.0-59.4]

TABLE 5. (CONTINUED)

ICCC-3 diagnostic groups and subgroups		15-19 years	ears			20-24	20-24 years	
		2000-2007		2008-2015		2000-2007		2008-2015
	n	5yOS [95%CI]	n	5yOS [95%CI]	n	5yOS [95%CI]	n	5yOS [95%CI]
VIII. Malignant bone tumors	82	$60.5 [49.0-70.2]^a$	120	72.1 [62.8-79.4] <sup>a</sup>	41	53.7 [37.4-67.4]	70	66.5 [53.7-76.6]
VIIIa. Osteosarcomas	46	$55.6 [40-68.6]^a$	99	$69.8 [55.3-80.4]^a$	14	$28.6 [8.8-52.4]^a$	29	68.4 [47.9-82.2] <sup>a</sup>
VIIIb. Chondrosarcomas	∞	75.0 [31.5-93.1]	7	100.0 [-]	8	100.0 [-]	19	87.7 [58.8-96.8]
VIIIc. Ewing tumor and related sarcomas of bone	25	64.0 [42.2-79.4]	53	70.4 [55.6-81.1] <sup>b</sup>	17	52.9 [27.6-73.0]	18	38.1 [16.6-59.5] <sup>b</sup>
VIIId. Other specified malignant bone tumors	$\epsilon$	66.7 [5.4-94.5]	3	66.7 [5.4-94.5]	2	50.0 [0.6-91.0]	4	100.0 [-]
IX. Soft tissue and other extraosseous sarcomas	25	70.6 [56.0-81.1]	9/	67.7 [55.3-77.4]	74	62.2 [50.1-72.1]	98	67.4 [55.7-76.6]
IXa.Rhabdomyosarcomas	12	41.7 [15.2-66.5]	17	58.8 [32.5-77.8]	13	38.5 [14.1-62.8]	10	50.0 [18.4-75.3]
IXb.Fibrosarcomas, and other fibrous neoplasms	10	77.8 [36.5-93.9]	16	80.8 [51.4-93.4]	13	76.9 [44.2-91.9]	11	81.8 [44.7-95.1]
IXd.Other specified soft tissue sarcomas	24	79.2 [57.0-90.8]	36	66.8 [47.6-80.3]	37	70.3 [52.8-82.3]	47	67.9 [50.8-80.2]
IXe Unspecified soft tissue sarcomas	9	83.3 [27.3-97.5]	7	68.6 [21.3-91.2]	10	40.0 [12.3-67.0]	18	65.8 [39.1-83.0]
X. Germ-cell tumors, and other neoplasms of gonads	112	88.0 [80.2-92.8]	156	93.4 [88.1-96.4]	293	92.4 [88.7-94.9]	387	94.6 [91.8-96.5]
Xa. Intracranial and intraspinal germ cell tumors	12	75.0 [40.8-91.2]	17	82.4 [54.7-93.9]	S	80.0 [20.4-96.9]	∞	100.0 [-]
Xb. Malignant extracranial and extragonadal germ cell tumors	7	71.4 [25.8-92.0]	9	66.7 [19.5-90.4]	12	66.7 [33.7-86.0]	22	72.7 [49.1-86.7]
Xc. Malignant gonadal germ cell tumors	88	92.9 [84.9-96.8]	118	96.4 [90.7-98.6]	255	94.4 [90.7-96.6]	337	97.2 [94.7-98.5]
Xd. Gonadal carcinoma	S	60.0[12.6-88.2]	10	90.0 [47.3-98.5]	16	81.3 [52.5-93.5]	19	73.3 [47.2-87.9]
Xe. Other and unspecified malignant gonadal tumors	1	1	1	1	5	100.0 [-]	П	100.0 [-]
XI. Other malignant epithelial neoplasms and melanomas	207	92.1 [87.5-95.1]	342	93.7 [90.3-95.9]	463	90.4 [87.3-92.8] <sup>a</sup>	871	93.4 [91.4-94.9] <sup>a</sup>
XIa. Adrenocartical carcinomas	7	0.0 [-]	7	0.0 [-]	2	50.0 [0.6-91.0]	8	87.5 [38.7-98.1]
XIb. Thyroid carcinomas	94	100.0 [-]	136	100.0 [-]	166	99.4 [95.8-99.9]	350	99.1 [97.3-99.7]
XIc. Nasopharyngeal carcinomas	5	60.0[12.6-88.2]	15	78.0 [45.5-92.5]	4	75.0 [12.8-96.1]	6	87.5 [38.7-98.1]
XId.Malignant melanomas	61	94.9 [85.1-98.3]	98	95.9 [87.8-98.7]	168	93.4 [88.4-96.3]	245	96.4 [93.0-98.2]
XIf. Other and unspecified carcinomas	45	79.8 [64.8-89.0]	103	87.3 [78.6-92.6]	123	75.4 [66.7-82.1]	260	83.2 [78.0-87.3]
XII. Other and unspecified malignant neoplasms	7	71.4 [25.8-92.0]	S	80.0 [20.4-96.9]	7	51.4 [11.8-81.3]	S	60.0 [12.6-88.2]
XIIa. Other specified malignant tumors	S	100.0 [-]	4	100.0 [-]	1	0.0 [-]	4	75.0 [12.8-96.1]
XIIb. Other unspecified malignant tumors	7	0.0 [-]	_	0.0 [-]	9	62.5 [14.2-89.3]	-	0.0 [-]
Total	1028	83.3 [80.8-85.5] <sup>a</sup>	1511	87.0 [85.2-88.7] <sup>a</sup>	1509	85.5 [83.6-87.2] <sup>a</sup>	2432	88.6 [87.2-89.8] <sup>a</sup>
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Abbreviations: ICCC-3, third version of the International Classification of Childhood Cancer; 5yOS, Five-year Overall Survival; 95%CI, 95% confidence interval. a p<0.05 Comparison between diagnostic periods (2000-2007 vs 2008-2015) b p<0.05 Comparison between age groups (15-19 years vs 20-24 years)



Year of diagnosis