

October 4, 2016

**HEALTHCARE/BIO TECHNOLOGY**

## Cancer Market

### Growing International Opportunity for Drug Development

#### SUMMARY

We estimate the global market for biotechnology cancer drugs (defined as the United States, Europe and Japan) is 36.9 million patients and is growing at 11.5% per year. These markets are detailed by geography and cancer type in this report. This is a large and growing market, with a need for new products addressing unmet medical need. We estimate the addressable market for front-line therapies (for newly diagnosed patients) is 6.5 million globally and growing at 2.4% per year. The market size for second-line and higher (relapsed/refractory patients) is 30.5 million and growing at 13.5% per year.

#### KEY POINTS

- We believe the market estimates in this report are unique tools for estimating the potential sales for cancer drugs. The estimates for incidence, prevalence and death rates in this report were calculated using the most reliable original sources, SEER for the US and IRAC for the rest of world. These estimates are differentiated and non-derivative.
- We estimate the most attractive opportunities for the front-line market occur where individual cancer incidence is growing faster than the overall market. Based on analysis of the data in this report, acute myeloid leukemia in the US market; larynx and oral cancer, bladder cancer and multiple myeloma in the European market; and leukemias and prostate cancer in the Japanese market.
- For the relapsed or second-line market to grow for an individual cancer, typically newly diagnosed patients are increasing and the death rate for these individual cancers is not declining. From our analysis of the data in this report, we estimate the fastest growing second-line or relapsed cancer markets are acute myeloid leukemia, lung cancer, stomach cancer and breast cancer in the US; and Hodgkins disease and brain cancer in Japan.

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**For analyst certification and important disclosures, see the Disclosure Appendix.**

## Estimating the size of the cancer market by analyzing incidence, survival and prevalence

**We believe incidence and prevalence best define the addressable cancer market. Based on the data in this study, we estimate overall global cancer prevalence will grow 8% per year from 2014-18 and overall international cancer incidence will grow 2.4% per year.**

### Defining incidence, death and prevalence

Prevalence is defined as the number of patients living with a specific disease. The US prevalence estimates for 2013 used in this report were obtained from the National Cancer Institute (NCI). The European and Japanese estimates for 2012 used in this report are based on data from the International Agency for Research on Cancer.

The NCI maintains Surveillance, Epidemiology, and End Results (SEER) for patients in the United States, which is used to estimate prevalence in a given year. Incidence is defined as the number of new cases of the disease in a given year. The incidence estimates for 2009 and 2013 used in this report were provided by the American Cancer Society, which collects the information from SEER. Death in this study is defined as death from the cancer being discussed. The number of deaths for 2009 and 2013 were provided by the American Cancer Society and are based on US Mortality Public Data Tapes and SEER data. This study includes the 35 cancers, and based on NCI data, we estimate they account for approximately 94% of the entire cancer market.

The International Agency for Research on Cancer's database has from the Descriptive Epidemiology Group of the International Association of Cancer Registries (IARC). The International Association of Cancer Registries (IACR) was founded in 1966, and is primarily for population-based registries, which collect information on the occurrence and outcome of cancer in defined population groups. The most recent database is based on populations, incidence and deaths for the year 2012. Our European study includes 27 major cancers and our Japanese study includes 23 major cancers.

### Incidence

Based on the data in this report, overall US cancer incidence has decreased 8% during 2009-13, or an average of 2% per year (**Table 1**). In the US nearly 50% of the cancers studied had incidence decreasing at an annual rate that was in line with this average. Approximately 30% of the cancers studied had incidence growth rates that varied significantly from the average. Colorectal cancer incidence decreased 13% from 2009-13, or 3% per year. Prostate cancer incidence decreased 28% from 2009-13, or 8% per year. Non-Hodgkin's lymphoma (NHL) incidence decreased 4.7% from 2009-13. Head and neck cancer incidence decreased slightly, and oral cancer incidence increased slightly from 2009-13. Bone cancer incidence decreased 9% from 2009-13, or 2% per year and myelodysplastic syndrome (MDS) decreased 15% from 2009-13, or 4% per year. Chronic myelogenous leukemia (CML) incidence decreased 6% from 2009-13, or 1% per year. Small cell lung cancer incidence decreased 12%, or 3% per year. Lastly, Leukemia (AML), Thyroid cancer and male breast cancer increased 16%, 8% and 6% from 2009-13, respectively, or 4%, 2% and 1.5% per year. Our estimates assume that these trends will continue from 2014-18.

Overall European cancer incidence was slightly over 3.1 million patients in 2012 and is expected to increase at 4.6% per year from 2012-18 (**Table 4**). All cancer incidence measured in Europe increased from 2005-10, with Larynx cancer increasing 11.2% per year. Bladder cancer, lung cancer and multiple myeloma increased 7.9%, 8.5% and 7.8% per year, respectively. Our estimates assume that these trends will continue from 2013-18. In Japan, cancer incidence was at 680,000 patients in 2012 and is expected to increase at 2% from 2012-18 (**Table 7**). All cancer incidence measured in Japan was growing at 0.5-4% per year with the exception of testicular cancer, which is declining slightly. Our estimates assume that these trends will continue from 2013-18.

**Table 1** US Incidence

Cancer type	Incidence 2009	Incidence 2013	Change in incidence	% change 2009-2013	% change per year	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2013-2018)
Breast, Female Total	356,522	352,838	(3,683)	-1.0%	-0.3%	351,923	351,011	350,101	349,193	348,288	-0.3%
<i>HR Positive (66%)</i>	196,087	194,061	(2,026)	-1.0%	-0.3%	193,558	193,056	192,555	192,056	191,558	-0.3%
<i>HER2 Positive (20-25%)</i>	80,217	79,389	(829)	-1.0%	-0.3%	79,183	78,977	78,773	78,568	78,365	-0.3%
<i>TNBC (10-20%)</i>	53,478	52,926	(552)	-1.0%	-0.3%	52,789	52,652	52,515	52,379	52,243	-0.3%
<i>BRCA1/2 (5-10%)</i>	26,739	26,463	(276)	-1.0%	-0.3%	26,394	26,326	26,258	26,189	26,122	-0.3%
In situ, female	92,852	88,970	(3,882)	-4.2%	-1.1%	88,025	87,090	86,165	85,250	84,345	-1.1%
Breast, Male	3,110	3,300	190	6.1%	1.5%	3,349	3,399	3,449	3,501	3,553	1.5%
Thyroid & other endocrine neoplasms											
Thyroid cancer	37,698	40,743	3,044	8.1%	2.0%	41,541	42,356	43,186	44,033	44,896	2.0%
Gastrointestinal											
Anal	5,244	5,014	(230)	-4.4%	-1.1%	4,958	4,902	4,848	4,793	4,740	-1.1%
Liver and Intrahepatic	22,949	24,240	1,291	5.6%	1.4%	24,574	24,912	25,256	25,604	25,956	1.4%
Colorectal	124,396	108,393	(16,003)	-12.9%	-3.4%	104,725	101,181	97,757	94,448	91,252	-3.4%
Small Intestine	5,924	6,412	488	8.2%	2.0%	6,540	6,671	6,804	6,940	7,079	2.0%
Esophagus	12,439	11,148	(1,291)	-10.4%	-2.7%	10,846	10,553	10,268	9,991	9,721	-2.7%
Gall bladder	3,291	3,295	4	0.1%	0.0%	3,297	3,298	3,299	3,300	3,301	0.0%
Pancreatic	34,995	35,038	43	0.1%	0.0%	35,049	35,060	35,070	35,081	35,092	0.0%
Stomach	21,599	20,077	(1,522)	-7.0%	-1.8%	19,713	19,356	19,006	18,662	18,324	-1.8%
Genitourinary											
Bladder	57,764	53,928	(3,836)	-6.6%	-1.7%	53,009	52,106	51,219	50,346	49,489	-1.7%
Kidney	45,055	43,862	(1,193)	-2.6%	-0.7%	43,569	43,277	42,988	42,700	42,415	-0.7%
Prostate	418,165	301,133	(117,032)	-28.0%	-7.9%	277,403	255,542	235,405	216,854	199,766	-7.9%
Testicular	16,033	16,086	53	0.3%	0.1%	16,099	16,113	16,126	16,140	16,153	0.1%
Gynecological											
Cervical	22,237	19,759	(2,478)	-11.1%	-2.9%	19,184	18,626	18,084	17,557	17,046	-2.9%
Corpus and Uterus	70,699	71,686	987	1.4%	0.3%	71,935	72,185	72,435	72,687	72,939	0.3%
Ovarian	34,998	31,750	(3,248)	-9.3%	-2.4%	30,986	30,241	29,514	28,804	28,111	-2.4%
Vaginal	2,148	1,945	(203)	-9.4%	-2.4%	1,898	1,851	1,806	1,762	1,719	-2.4%
Vulvar	6,821	6,886	65	1.0%	0.2%	6,902	6,919	6,935	6,952	6,968	0.2%
Head & neck											
Larynx	9,255	8,253	(1,002)	-10.8%	-2.8%	8,020	7,793	7,573	7,359	7,151	-2.8%
Oral Cancer	31,499	31,635	136	0.4%	0.1%	31,669	31,704	31,738	31,772	31,807	0.1%
Eye and Orbit	2,194	2,463	269	12.3%	2.9%	2,535	2,610	2,686	2,765	2,846	2.9%
Lymphoma & myeloma											
All leukemias combined	26,271	27,006	735	2.8%	0.7%	27,193	27,381	27,571	27,762	27,954	0.7%
Leukemia -ALL Total	4,751	4,680	(70)	-1.5%	-0.4%	4,663	4,646	4,628	4,611	4,594	-0.4%
<i>Leukemia- ALL BCR-ABLE Positive (25%)</i>	1,188	1,170	(18)	-1.5%	-0.4%	1,166	1,161	1,157	1,153	1,148	-0.4%
Leukemia -CLL Total	15,744	12,543	(3,201)	-20.3%	-5.5%	11,850	11,195	10,577	9,992	9,440	-5.5%
<i>Leukemia- CLL 17p positive (10-20%)</i>	2,362	1,881	(480)	-20.3%	-5.5%	1,777	1,679	1,587	1,499	1,416	-5.5%
Leukemia -AML Total	10,179	11,863	1,685	16.6%	3.9%	12,326	12,807	13,307	13,827	14,366	3.9%
<i>Leukemia- AML- FLT3 Mutant (33%)</i>	3,359	3,915	556	16.6%	3.9%	4,068	4,226	4,391	4,563	4,741	3.9%
<i>Leukemia-AML-IDH mutations (15-20%)</i>	1,730	2,017	286	16.6%	3.9%	2,095	2,177	2,262	2,351	2,442	3.9%
Leukemia -CML	4,971	4,956	(15)	-0.3%	-0.1%	4,952	4,948	4,944	4,940	4,936	-0.1%
Leukemia- AMoL	650	594	(57)	-8.7%	-2.3%	580	567	554	542	529	-2.3%
Hodgkin's disease	7,643	6,923	(720)	-9.4%	-2.4%	6,754	6,589	6,428	6,270	6,117	-2.4%
Non-Hodgkin's lymphoma Total	56,040	53,379	(2,661)	-4.7%	-1.2%	52,733	52,096	51,466	50,844	50,230	-1.2%
<i>Diffuse large B-cell (30%)</i>	16,812	16,014	(798)	-4.7%	-1.2%	15,820	15,629	15,440	15,253	15,069	-1.2%
Multiple myeloma	17,739	18,108	368	2.1%	0.5%	18,201	18,295	18,389	18,484	18,579	0.5%
Myelodysplastic syndrome- MDS	14,477	12,242	(2,235)	-15.4%	-4.1%	11,740	11,258	10,796	10,353	9,928	-4.1%
Chronic Myeloproliferative disorders- CMD	7,803	7,116	(687)	-8.8%	-2.3%	6,954	6,796	6,641	6,490	6,342	-2.3%
Chronic Myelomonocytic Leukemia- CMML	1,347	1,271	(76)	-5.7%	-1.4%	1,253	1,235	1,217	1,199	1,182	-1.4%
Neuro-oncology											
Brain and other nervous system	18,645	17,858	(787)	-4.2%	-1.1%	17,667	17,477	17,290	17,104	16,921	-1.1%
Soft tissue & musculoskeletal											
Bone and joints	2,724	2,491	(233)	-8.6%	-2.2%	2,436	2,382	2,329	2,278	2,227	-2.2%
Kaposi Sarcoma	1,577	1,324	(253)	-16.0%	-4.3%	1,267	1,213	1,161	1,112	1,064	-4.3%
Mesothelioma	3,013	2,566	(447)	-14.8%	-3.9%	2,465	2,368	2,274	2,185	2,099	-3.9%
Soft tissue	9,395	9,561	166	1.8%	0.4%	9,603	9,646	9,688	9,731	9,773	0.4%
Skin cancer											
Melanoma Total	60,064	62,968	2,904	4.8%	1.2%	63,716	64,472	65,238	66,012	66,796	1.2%
<i>BRAF mutant (40-60%)</i>	30,032	31,484	1,452	4.8%	1.2%	31,858	32,236	32,619	33,006	33,398	1.2%
Thoracic neoplasms											
Lung and Bronchus Total	168,645	151,926	(16,718)	-9.9%	-2.6%	148,013	144,199	140,485	136,865	133,339	-2.6%
<i>Adenocarcinoma (40%)</i>	67,458	60,771	(6,687)	-9.9%	-2.6%	59,205	57,680	56,194	54,746	53,336	-2.6%
<i>Squamous (25-30%)</i>	45,534	41,020	(4,514)	-9.9%	-2.6%	39,963	38,934	37,931	36,954	36,002	-2.6%
<i>Large Cell Carcinoma (10-15%)</i>	25,297	22,789	(2,508)	-9.9%	-2.6%	22,202	21,630	21,073	20,530	20,001	-2.6%
<i>Small cell Carcinoma (15%)</i>	25,297	22,789	(2,508)	-9.9%	-2.6%	22,202	21,630	21,073	20,530	20,001	-2.6%
Total	2,255,297	2,080,541	(174,756)	-7.7%	-2.0%	2,043,630	2,009,065	1,976,687	1,946,352	1,917,923	-1.6%
<i>Solid Tumors</i>	2,088,502	1,921,870	(166,632)	-8.0%	-2.1%	1,886,697	1,853,760	1,822,903	1,793,981	1,766,863	-1.7%
<i>Liquid Tumors</i>	166,795	158,672	(8,124)	-4.9%	-1.2%	156,933	155,304	153,784	152,371	151,061	-1.0%

Source: National Cancer Institute SEER (Surveillance, Epidemiology, and End Results) database.

## Deaths from cancer

Total deaths in 2014 were 479,141, down from 519,784 in 2008. Based on the data in this report, the overall number of US deaths from cancer decreased 6% from 2009-13, or an average of almost 1.5% per year (**Table 2**). Nearly 88% of cancers where death statistics were available (90%) had numbers of deaths growing at an annual rate that was in line with this average. Approximately 11% of cancers with death statistics had deaths growing at rates that varied significantly from the average. The most notable decreases in deaths were in the hematologic cancers. Deaths from NHL decreased 10% from 2009-13, or 3% per year. Deaths from chronic lymphocytic leukemia (CLL) decreased 7% from 2009-13, or 2% per year. This correlates with the introduction of effective therapies in this setting. Deaths from acute myelogenous leukemia (AML) decreased 3% from 2009-13, or 0.5% per year. AML is a setting with no improvements in therapies during that time frame. Unfortunately, liver and intrahepatic bile duct and corpus and uterus cancer deaths both increased 11%, or 3% per year. Anal and vaginal cancer deaths both increased from 2009-13 2%, or 0.5% per year. Our estimates assume that all these trends for deaths will continue from 2014-18.

The overall number of European cancer deaths was 1.5 million people in 2012 and is expected to increase at 1.3% per year from 2012-18 (**Table 5**). All cancer deaths measured in Europe were growing at 1-2% per year from 2005-10, with the exception of testicular cancer which was slightly less. Our estimates assume that these trends will continue from 2012-18. In Japan, the overall number of cancer deaths was 360,000 people in 2012 and is expected to increase at 2.3% per year from 2012-18 (**Table 8**). All cancer deaths in Japan were growing at 1-3% per year. Our estimates assume that these trends will continue from 2013-18.

**Table 2 US Deaths from Cancer**

Cancer type	Deaths 2009	Deaths 2013	Change in deaths	% change 2009-2013	% change per year	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2014-2018)
Breast, Female Total	62,594	58,299	(4,294)	-6.9%	-1.8%	57,273	56,264	55,273	54,300	53,343	-1.8%
<i>HR Positive</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<i>HER2 Positive</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<i>TNBC</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<i>BRCA1/2</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Breast (In situ), female	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Breast, Male	788	846	58	7.4%	1.8%	861	876	892	908	924	1.8%
Thyroid & other endocrine neoplasms											
Thyroid cancer	1,471	1,453	(18)	-1.2%	-0.3%	1,448	1,444	1,439	1,435	1,430	-0.3%
Gastrointestinal											
Anal	686	696	10	1.5%	0.4%	699	701	704	707	709	0.4%
Liver and intrahepatic bile duct	16,263	18,185	1,922	11.8%	2.8%	18,701	19,230	19,775	20,335	20,911	2.8%
Colorectal	44,480	40,668	(3,812)	-8.6%	-2.2%	39,767	38,886	38,025	37,183	36,359	-2.2%
Small intestine	1,027	1,001	(26)	-2.5%	-0.6%	995	988	982	976	969	-0.6%
Esophagus	11,752	11,304	(449)	-3.8%	-1.0%	11,194	11,086	10,978	10,872	10,767	-1.0%
Gall bladder	1,762	1,700	(62)	-3.5%	-0.9%	1,685	1,670	1,655	1,640	1,625	-0.9%
Pancreatic	30,501	30,399	(102)	-0.3%	-0.1%	30,373	30,348	30,322	30,297	30,272	-0.1%
Stomach	9,658	8,920	(738)	-7.6%	-2.0%	8,744	8,572	8,403	8,238	8,076	-2.0%
Genitourinary											
Bladder	12,307	12,445	138	1.1%	0.3%	12,480	12,515	12,549	12,584	12,620	0.3%
Kidney	11,070	10,847	(223)	-2.0%	-0.5%	10,792	10,737	10,683	10,628	10,574	-0.5%
Prostate	62,264	54,101	(8,163)	-13.1%	-3.5%	52,234	50,431	48,690	47,009	45,386	-3.5%
Testicular	704	685	(19)	-2.7%	-0.7%	680	676	671	666	662	-0.7%
Gynecological											
Cervical	6,433	6,551	118	1.8%	0.5%	6,581	6,611	6,641	6,671	6,701	0.5%
Corpus and Uterus	11,748	13,058	1,309	11.1%	2.7%	13,407	13,766	14,135	14,513	14,902	2.7%
Ovarian	22,094	20,238	(1,857)	-8.4%	-2.2%	19,798	19,369	18,948	18,537	18,135	-2.2%
Vaginal	600	609	9	1.5%	0.4%	611	614	616	618	620	NA
Vulvar	1,405	1,378	(27)	-1.9%	-0.5%	1,372	1,365	1,358	1,352	1,345	NA
Head & neck											
Larynx	3,055	2,842	(212)	-7.0%	-1.8%	2,792	2,742	2,693	2,645	2,597	-1.8%
Oral Cancer	6,668	6,778	109	1.6%	0.4%	6,805	6,833	6,861	6,889	6,917	0.4%
Eye	243	252	8	3.5%	0.9%	254	256	258	260	263	0.9%
Lymphoma & myeloma											
All leukemias combined	15,399	14,508	(891)	-5.8%	-1.5%	14,293	14,081	13,873	13,668	13,466	-1.5%
Leukemia -ALL Total	1,279	1,208	(71)	-5.5%	-1.4%	1,191	1,174	1,158	1,141	1,125	-1.4%
<i>Leukemia- ALL BCR-ABLE Positive</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CLL Total	3,951	3,674	(277)	-7.0%	-1.8%	3,608	3,543	3,479	3,417	3,355	-1.8%
<i>Leukemia- CLL 17p positive</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -AML Total	8,088	7,850	(238)	-2.9%	-0.7%	7,792	7,734	7,676	7,619	7,563	-0.7%
<i>Leukemia- AML- FLT3 Mutant</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<i>Leukemia-AML-IDH mutations</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CML	874	801	(73)	-8.3%	-2.2%	784	767	751	735	719	-2.2%
Leukemia -AMoL	95	76	(18)	-19.3%	-5.2%	72	68	65	62	58	NA
Hodgkin's disease	1,112	897	(214)	-19.3%	-5.2%	850	806	764	724	686	-5.2%
Non-Hodgkin's lymphoma	17,722	16,035	(1,687)	-9.5%	-2.5%	15,639	15,252	14,875	14,508	14,150	-2.5%
<i>Diffuse large B-cell</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Multiple myeloma	9,268	9,323	55	0.6%	0.1%	9,336	9,350	9,364	9,378	9,392	0.1%
Myelodysplastic syndrome- MDS	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myeloproliferative disorders- CMD	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myelomonocytic Leukemia- CMML	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Neuro-oncology											
Brain and other nervous system	12,234	12,258	24	0.2%	0.0%	12,264	12,270	12,277	12,283	12,289	0.0%
Soft tissue & musculoskeletal											
Bone and joints	1,225	1,206	(19)	-1.5%	-0.4%	1,202	1,197	1,193	1,188	1,184	-0.4%
Kaposi sarcoma	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mesothelioma	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Soft tissue	3,662	3,688	26	0.7%	0.2%	3,695	3,701	3,708	3,714	3,721	0.2%
Skin cancer											
Melanoma Total	7,728	7,306	(422)	-5.5%	-1.4%	7,204	7,103	7,004	6,907	6,810	-1.4%
<i>BRAF mutant</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Thoracic neoplasms											
Lung and Bronchus Total	132,972	119,177	(13,795)	-10.4%	-2.7%	115,958	112,826	109,778	106,813	103,928	-2.7%
<i>Adenocarcinoma</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<i>Squamous</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<i>Large Cell acrcinoma</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<i>Small cell carcinoma</i>	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Total	519,784	486,755	(33,029)	-6.4%	-1.6%	479,141	471,772	464,644	457,751	451,088	-1.5%
<i>Solid Tumors</i>	478,675	448,098	(30,506)	-6.4%	-1.6%	441,059	434,251	427,669	421,309	415,165	-1.5%
<i>Liquid Tumors</i>	41,109	38,656	(26,236)	-6.0%	-1.5%	38,082	37,521	36,975	36,442	35,923	-1.5%

Source: National Cancer Institute SEER (Surveillance, Epidemiology, and End Results) database.

## Prevalence

Based on the data in this report, overall US cancer prevalence is expected to increase to nearly 20 million patients by 2018, or 7% per year from 2013-18 (**Table 3**). Only 12% of cancers with these prevalence statistics had prevalence growing at rates that varied significantly from the average. The prevalence of lung and bronchus cancer is expected to increase by 110% from 2013-18, or 22% per year. Female and male breast cancer incidence is expected to increase from 2013-18 by 33% and 50%, respectively, or 8% and 13% per year. Esophagus is the one cancer expected to decline in prevalence from 2013-18 by 10%, or 2% per year.

Overall European cancer prevalence was at 8.5 million patients in 2012 and is expected to increase at an average of 16% per year from 2012-18 (**Table 6**). Prevalence for most cancers is expected to be in line with this average. Notable exceptions are liver and pancreatic cancers, both expected to decline more than 4% per year; and lung and bronchus cancer, which is expected to increase 23% per year. Overall Japanese cancer prevalence was at 1.6 million patients and is expected to increase 13% per year from 2012-18 (**Table 9**). Prevalence for most cancers is expected to be in line with this average. Notable exceptions are brain cancer, expected to increase 21% per year; and liver and multiple myeloma cancer, expected to increase only 5% per year.

**Table 3 US Prevalence**

Cancer type	Prevalence 2013	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2014-2018)
Breast, Female	3,053,450	3,348,101	3,642,848	3,937,676	4,232,570	4,527,514	8.2%
<i>HR Positive</i>	NA	NA	NA	NA	NA	NA	NA
<i>HER2 Positive</i>	NA	NA	NA	NA	NA	NA	NA
<i>TNBC</i>	NA	NA	NA	NA	NA	NA	NA
<i>BRCA1/2</i>	NA	NA	NA	NA	NA	NA	NA
Breast (In situ), female	NA	NA	NA	NA	NA	NA	NA
Breast, Male	15,781	18,269	20,792	23,349	25,942	28,571	12.6%
Thyroid & other endocrine neoplasms							
Thyroid cancer	637,115	677,208	718,120	759,866	802,464	845,929	5.8%
Gastrointestinal							
Anal	46,884	51,143	55,344	59,488	63,575	67,605	7.6%
Liver and intrahepatic bile duct	54,954	60,827	66,509	71,990	77,259	82,305	8.4%
Colorectal	1,177,556	1,242,513	1,304,808	1,364,539	1,421,805	1,476,698	4.6%
Small intestine	47,853	53,399	59,081	64,904	70,869	76,979	10.0%
Esophagus	36,857	36,509	35,977	35,266	34,385	33,338	-2.0%
Gall bladder	8,626	10,238	11,865	13,509	15,169	16,844	14.3%
Pancreatic	49,620	54,295	59,007	63,755	68,539	73,360	8.1%
Stomach	79,843	90,812	101,596	112,199	122,623	132,871	10.7%
Genitourinary							
Bladder	587,426	627,955	667,547	706,217	743,979	780,848	5.9%
Kidney	394,336	427,113	459,653	491,958	524,030	555,870	7.1%
Prostate	2,850,139	3,075,308	3,280,420	3,467,135	3,636,981	3,791,360	5.9%
Testicular	240,372	255,791	271,228	286,684	302,157	317,649	5.7%
Gynecological							
Cervical	248,920	261,523	273,538	284,981	295,867	306,212	4.2%
Corpus and Uterus	635,437	693,965	752,383	810,684	868,858	926,896	7.8%
Ovarian	195,767	206,955	217,827	228,393	238,659	248,636	4.9%
Vaginal	NA	NA	NA	NA	NA	NA	NA
Vulvar	NA	NA	NA	NA	NA	NA	NA
Head & neck							
Larynx	89,081	94,309	99,361	104,241	108,956	113,509	5.0%
Oral Cancer	300,682	325,546	350,416	375,293	400,177	425,066	7.2%
Eye	46,722	49,004	51,357	53,785	56,290	58,874	4.7%
Lymphoma & myeloma							
All leukemias combined	305,915	318,815	332,115	345,813	359,907	374,396	4.1%
Leukemia -ALL Total	77,855	81,327	84,798	88,268	91,738	95,206	4.1%
<i>Leukemia- ALL BCR-ABLE Positive</i>	NA	NA	NA	NA	NA	NA	NA
Leukemia -CLL Total	140,139	148,381	156,033	163,130	169,706	175,791	4.6%
<i>Leukemia- CLL 17p positive</i>	NA	NA	NA	NA	NA	NA	NA
Leukemia -AML Total	44,885	49,420	54,493	60,125	66,332	73,136	10.3%
<i>Leukemia- AML- FLT3 Mutant</i>	NA	NA	NA	NA	NA	NA	NA
<i>Leukemia-AML-IDH mutations</i>	NA	NA	NA	NA	NA	NA	NA
Leukemia -CML	40,043	44,210	48,391	52,584	56,790	61,007	8.8%
Leukemia -AMoL	2,993	NA	NA	NA	NA	NA	NA
Hodgkin's disease	193,545	199,448	205,231	210,895	216,441	221,872	2.8%
Non-Hodgkin's Lymphoma Total	569,536	606,631	643,475	680,066	716,402	752,482	5.7%
<i>Diffuse large B-cell</i>	NA	NA	NA	NA	NA	NA	NA
Multiple myeloma	95,688	104,553	113,497	122,522	131,628	140,816	8.0%
Myelodysplastic syndrome- MDS	NA	NA	NA	NA	NA	NA	NA
Chronic Myeloproliferative disorders- CMD	NA	NA	NA	NA	NA	NA	NA
Chronic Myelomonocytic Leukemia- CMML	NA	NA	NA	NA	NA	NA	NA
Neuro-oncology							
Brain and other nervous system	152,751	158,153	163,360	168,373	173,195	177,827	3.1%
Soft tissue & musculoskeletal							
Bones and joints	46,387	47,621	48,806	49,942	51,032	52,076	2.3%
Kaposi sarcoma	NA	NA	NA	NA	NA	NA	NA
Mesothelioma	NA	NA	NA	NA	NA	NA	NA
Soft tissue	119,052	124,961	130,905	136,885	142,901	148,954	4.6%
Skin cancer							
Melanoma Total	1,034,460	1,098,176	1,162,648	1,227,885	1,293,898	1,360,694	5.6%
<i>BRAF mutant</i>	NA	NA	NA	NA	NA	NA	NA
Thoracic neoplasms							
Lung and Bronchus Total	415,707	563,720	707,919	848,404	985,269	1,118,608	21.9%
<i>Adenocarcinoma</i>	NA	NA	NA	NA	NA	NA	NA
<i>Squamous</i>	NA	NA	NA	NA	NA	NA	NA
<i>Large Cell Carcinoma</i>	NA	NA	NA	NA	NA	NA	NA
<i>Small cell Carcinoma</i>	NA	NA	NA	NA	NA	NA	NA
Total available for calculation	14,036,377	15,206,198	16,351,349	17,470,804	18,566,389	19,639,796	6.9%
Total available for calculation - Solid tumors	12,871,693	13,972,228	15,045,431	16,093,215	17,117,353	18,119,487	7.1%
Total available for calculation - Liquid Tumors	1,164,684	1,233,969	1,305,918	1,377,589	1,449,036	1,520,309	5.5%

Source: National Cancer Institute SEER (Surveillance, Epidemiology, and End Results) database.

## Market size

We believe estimated prevalence is the best measure of the overall cancer market's size. We have estimated future prevalence for 2014-2018 (**Tables 3, 6, 9**). To arrive at these estimates, we used the 2012 or 2013 estimate and added estimated incidence (**Tables 1, 4, 7**) and subtracted estimated deaths (**Tables 2, 5, 8**) for each year. Exceptions included cancers that did not have prevalence data for 2012 or 2013. In cases where 2013 prevalence was not available for US patients, we used the 2009 prevalence estimate for 2013 or the incidence estimate. For these same exceptions outside the United States, we estimated 2012 or 2013 prevalence as a ratio to incidence that was consistent with US data.

Based on prevalence, we estimate the overall market for cancer therapies in the United States is slightly over 14 million patients growing at 7% per year. In Europe, we estimate the overall market is composed of 8 million patients and is growing at 16% per year. In Japan, we estimate the market is nearly 2 million patients and is growing 13% per year.

We believe incidence is the best measure of front-line (newly treated) cancer market's size (**Tables 1, 4, 7**). Therefore, we conclude the market for front-line therapies in the US is currently 2 million patients and is decreasing at 8% per year. In Europe, we estimate the market for front-line therapies is approximately 3.1 million patients and is growing at 4.5% per year. In Japan, we estimate the market for front-line therapies is currently 680,000 patients and is growing at 2% per year.

We believe the best measure of the market size for second-line and greater (relapsed/refractory) therapies is prevalence less incidence, which should account for all living patients who are not newly diagnosed. Therefore, we conclude the market for relapsed therapies in the US is currently 15 million patients and is growing at 10% per year. In Europe, we estimate the market for relapsed therapies is approximately 10.8 million patients and is growing at 11% per year. In Japan, we estimate the market for relapsed therapies is currently 2.1 million patients and is growing at 8% per year.



**Table 4** **European Incidence**

Cancer type	Incidence 2012	% change per year (2005-2010)	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2013-2018)
Breast, Female	458,718	1.9%	476,187	485,170	494,322	503,646	513,147	1.9%
Breast (In situ), female	NA	NA	NA	NA	NA	NA	NA	NA
Breast, Male	NA	NA	NA	NA	NA	NA	NA	NA
Thyroid & other endocrine neoplasms								
Thyroid cancer	52,956	1.3%	54,298	54,982	55,674	56,375	57,085	1.3%
Gastrointestinal								
Small Intestine	NA	NA	NA	NA	NA	NA	NA	NA
Anal	NA	NA	NA	NA	NA	NA	NA	NA
Colorectal	447,136	4.1%	484,126	503,754	524,177	545,428	567,540	4.1%
Esophagus	45,893	2.0%	47,748	48,703	49,677	50,671	51,685	2.0%
Gall bladder	29,744		29,744	29,744	29,744	29,744	29,744	0.0%
Liver and Intrahepatic	63,462		63,462	63,462	63,462	63,462	63,462	0.0%
Pancreatic	103,845	1.0%	105,917	106,968	108,030	109,103	110,186	1.0%
Stomach	139,667	5.3%	155,000	163,286	172,015	181,212	190,899	5.3%
Genitourinary								
Bladder	151,297	7.9%	176,069	189,937	204,898	221,036	238,446	7.9%
Kidney and renal pelvis	115,252	5.8%	129,088	136,617	144,586	153,018	161,943	5.8%
Prostate	400,364	5.3%	443,612	466,958	491,532	517,400	544,629	5.3%
Testicular	21,548	4.2%	23,384	24,360	25,377	26,436	27,540	4.2%
Gynecological								
Cervical	58,373	1.4%	60,070	60,937	61,817	62,709	63,614	1.4%
Corpus and Uterus	98,984	1.7%	102,396	104,146	105,926	107,737	109,578	1.7%
Ovarian	65,584	1.3%	67,274	68,136	69,008	69,892	70,787	1.3%
Vaginal	NA	NA	NA	NA	NA	NA	NA	NA
Vulvar	NA	NA	NA	NA	NA	NA	NA	NA
Head & neck								
Larynx	39,921	11.2%	49,374	54,910	61,067	67,913	75,527	11.2%
Oral Cancer	61,416	5.7%	68,575	72,462	76,569	80,909	85,495	5.7%
Nasopharynx	4,172		4,172	4,172	4,172	4,172	4,172	0.0%
Other pharynx	34,094		34,094	34,094	34,094	34,094	34,094	0.0%
Eye and Orbit	NA	NA	NA	NA	NA	NA	NA	NA
Lymphoma & myeloma								
All leukemias combined	82,329	4.6%	90,087	94,236	98,576	103,116	107,866	4.6%
Leukemia -ALL	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CLL	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -AML	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CML	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia- AMoL	NA	NA	NA	NA	NA	NA	NA	NA
Hodgkin's disease	17,584	3.1%	18,680	19,253	19,843	20,452	21,080	3.1%
Non-Hodgkin's lymphoma	93,518	4.0%	101,149	105,194	109,402	113,777	118,328	4.0%
Multiple myeloma	38,956	7.5%	44,984	48,339	51,945	55,819	59,983	7.5%
Myelodysplastic syndrome- MDS	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myeloproliferative disorders- CMD	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myelomonocytic Leukemia- CMML	NA	NA	NA	NA	NA	NA	NA	NA
Neuro-oncology								
Brain and other Nervous System	57,132	2.1%	59,597	60,868	62,167	63,494	64,849	2.1%
Soft tissue & musculoskeletal								
Bone and joints cancer	NA	NA	NA	NA	NA	NA	NA	NA
Kaposi Sarcoma	2,100		2,100	2,100	2,100	2,100	2,100	0.0%
Mesothelioma	NA	NA	NA	NA	NA	NA	NA	NA
Soft tissue	NA	NA	NA	NA	NA	NA	NA	NA
Skin cancer								
Melanoma	100,442	4.6%	109,946	115,031	120,350	125,915	131,738	4.6%
Thoracic neoplasms								
Lung and Bronchus	410,220	8.5%	482,528	523,330	567,582	615,576	667,628	8.5%
Total	3,112,378		3,393,576	3,546,914	3,709,536	3,882,092	4,065,279	4.6%
<i>Solid Tumors</i>	<i>2,879,991</i>		<i>3,138,676</i>	<i>3,279,892</i>	<i>3,429,770</i>	<i>3,588,926</i>	<i>3,758,023</i>	<i>4.5%</i>
<i>Liquid Tumors</i>	<i>232,387</i>		<i>254,899</i>	<i>267,022</i>	<i>279,766</i>	<i>293,166</i>	<i>307,256</i>	<i>4.8%</i>

Source: Historical data in this table was obtained from the International Agency for Research on Cancer's database. This Agency derives these data from the Descriptive Epidemiology Group of the International Association of Cancer Registries (IARC). We estimated incidence for 2014-2018, by using the IARC 2012 estimate and growing it at the historical growth rate (2005-10).

**Table 5** European Deaths from Cancer

Cancer type	Death 2012	% change per year (2005-2010)	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2013-2018)
Breast, Female	131,347	1.1%	134,155	135,581	137,023	138,480	139,952	1.1%
Breast (In situ), female	NA	NA	NA	NA	NA	NA	NA	NA
Breast, Male	NA	NA	NA	NA	NA	NA	NA	NA
Thyroid & other endocrine neoplasms								
Thyroid cancer	6,336	1.4%	6,510	6,598	6,688	6,779	6,871	1.4%
Gastrointestinal								
Small Intestine	NA	NA	NA	NA	NA	NA	NA	NA
Anal	NA	NA	NA	NA	NA	NA	NA	NA
Colorectal	214,866	1.3%	220,649	223,599	226,588	229,617	232,686	1.3%
Esophagus	39,536	1.3%	40,563	41,087	41,617	42,154	42,698	1.3%
Gall bladder	20,887		20,887	20,887	20,887	20,887	20,887	0.0%
Liver and Intrahepatic	62,191	1.5%	64,128	65,119	66,125	67,147	68,185	1.5%
Pancreatic	104,554	1.4%	107,468	108,955	110,463	111,992	113,542	1.4%
Stomach	107,360	1.3%	110,149	111,571	113,011	114,470	115,947	1.3%
Genitourinary								
Bladder	52,411	1.6%	54,062	54,906	55,764	56,636	57,521	1.6%
Kidney and renal pelvis	49,025	1.5%	50,480	51,223	51,978	52,743	53,520	1.5%
Prostate	92,328	1.8%	95,593	97,269	98,973	100,708	102,473	1.8%
Testicular	1,612	0.5%	1,627	1,635	1,643	1,650	1,658	0.5%
Gynecological								
Cervical	24,404	1.0%	24,888	25,134	25,382	25,632	25,885	1.0%
Corpus and Uterus	23,738	1.2%	24,310	24,602	24,896	25,195	25,497	1.2%
Ovarian	42,749	1.1%	43,684	44,159	44,639	45,125	45,615	1.1%
Vaginal	NA	NA	NA	NA	NA	NA	NA	NA
Vulvar	NA	NA	NA	NA	NA	NA	NA	NA
Head & neck								
Larynx	19,772	1.4%	20,338	20,627	20,920	21,217	21,519	1.4%
Oral Cancer	23,656	1.3%	24,276	24,591	24,911	25,236	25,564	1.3%
Nasopharynx	2,134		2,134	2,134	2,134	2,134	2,134	0.0%
Other pharynx	17,922		17,922	17,922	17,922	17,922	17,922	0.0%
Eye and Orbit	NA	NA	NA	NA	NA	NA	NA	NA
Lymphoma & myeloma								
All leukemias combined	53,806	1.3%	55,206	55,919	56,642	57,373	58,115	1.3%
Leukemia -ALL	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CLL	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -AML	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CML	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia- AMoL	NA	NA	NA	NA	NA	NA	NA	NA
Hodgkin's disease	4,622	0.8%	4,695	4,732	4,770	4,807	4,845	0.8%
Non-Hodgkin's lymphoma	37,926	1.3%	38,918	39,424	39,936	40,455	40,981	1.3%
Multiple myeloma	24,300	1.4%	24,982	25,331	25,684	26,042	26,405	1.4%
Myelodysplastic syndrome- MDS	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myeloproliferative disorders- CMD	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myelomonocytic Leukemia- CMML	NA	NA	NA	NA	NA	NA	NA	NA
Neuro-oncology								
Brain and other Nervous System	44,991	1.1%	45,970	46,467	46,970	47,478	47,992	1.1%
Soft tissue & musculoskeletal								
Bone and joints cancer	NA	NA	NA	NA	NA	NA	NA	NA
Kaposi Sarcoma	290		290	290	290	290	290	0.0%
Mesothelioma	NA	NA	NA	NA	NA	NA	NA	NA
Soft tissue	NA	NA	NA	NA	NA	NA	NA	NA
Skin cancer								
Melanoma	22,211	1.1%	22,716	22,973	23,232	23,495	23,760	1.1%
Thoracic neoplasms								
Lung and Bronchus	353,848	1.2%	362,219	366,479	370,788	375,148	379,560	1.2%
Total	1,525,016		1,563,613	1,583,294	1,603,235	1,623,439	1,643,910	1.3%
<i>Solid Tumors</i>	<i>1,404,362</i>		<i>1,439,811</i>	<i>1,457,888</i>	<i>1,476,204</i>	<i>1,494,761</i>	<i>1,513,564</i>	<i>1.3%</i>
<i>Liquid Tumors</i>	<i>120,654</i>		<i>123,801</i>	<i>125,406</i>	<i>127,031</i>	<i>128,678</i>	<i>130,346</i>	<i>1.3%</i>

Source: Historical data in this table was obtained from the International Agency for Research on Cancer's database. This Agency derives these data from the Descriptive Epidemiology Group of the International Association of Cancer Registries (IARC). We estimated incidence for 2014-18, by using the IARC 2012 estimate and growing it at the historical growth rate (2005-10).

**Table 6** European Cancer Prevalence

Cancer type	Prevalence 2012	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2013-2018)
Breast, Female	1,814,572	2,498,637	2,848,225	3,205,524	3,570,691	3,943,886	13.8%
Breast (In situ), female	NA	NA	NA	NA	NA	NA	NA
Breast, Male	NA	NA	NA	NA	NA	NA	NA
Thyroid & other endocrine neoplasms							
Thyroid cancer	210,222	305,799	354,183	403,169	452,766	502,980	15.6%
Gastrointestinal							
Small Intestine	NA	NA	NA	NA	NA	NA	NA
Anal	NA	NA	NA	NA	NA	NA	NA
Colorectal	1,203,943	1,730,897	2,011,052	2,308,641	2,624,452	2,959,306	16.2%
Esophagus	46,742	61,111	68,727	76,787	85,304	94,291	12.4%
Gall bladder	28,029	45,743	54,600	63,457	72,314	81,171	19.4%
Liver and Intrahepatic	57,208	55,876	54,219	51,556	47,871	43,148	-4.6%
Pancreatic	56,336	53,234	51,247	48,814	45,924	42,568	-4.6%
Stomach	192,878	282,579	334,293	393,298	460,039	534,991	18.5%
Genitourinary							
Bladder	496,379	740,394	875,425	1,024,558	1,188,959	1,369,884	18.4%
Kidney and renal pelvis	333,293	490,510	575,904	668,511	768,787	877,210	17.5%
Prostate	1,459,628	2,155,667	2,525,356	2,917,915	3,334,607	3,776,762	17.2%
Testicular	92,507	136,021	158,747	182,481	207,267	233,149	16.7%
Gynecological							
Cervical	199,817	270,182	305,985	342,421	379,498	417,227	13.1%
Corpus and Uterus	374,807	530,979	610,524	691,554	774,095	858,177	14.8%
Ovarian	157,198	204,379	228,356	252,725	277,492	302,663	11.5%
Vaginal	NA	NA	NA	NA	NA	NA	NA
Vulvar	NA	NA	NA	NA	NA	NA	NA
Head & neck							
Larynx	128,652	186,725	221,009	261,155	307,851	361,860	18.8%
Oral Cancer	160,000	248,599	296,470	348,128	403,801	463,732	19.4%
Nasopharynx	11,558	15,634	17,672	19,710	21,748	23,786	12.8%
Other pharynx	82,988	115,332	131,504	147,676	163,848	180,020	13.8%
Eye and Orbit							
Lymphoma & myeloma							
All leukemias combined	177,460	247,223	285,540	327,475	373,218	422,969	15.6%
Leukemia -ALL	NA	NA	NA	NA	NA	NA	NA
Leukemia -CLL	NA	NA	NA	NA	NA	NA	NA
Leukemia -AML	NA	NA	NA	NA	NA	NA	NA
Leukemia -CML	NA	NA	NA	NA	NA	NA	NA
Leukemia- AMoL	NA	NA	NA	NA	NA	NA	NA
Hodgkin's disease	59,821	87,790	102,310	117,384	133,029	149,264	16.5%
Non-Hodgkin's lymphoma	248,844	373,305	439,075	508,540	581,862	659,209	17.6%
Multiple myeloma	89,187	129,191	152,199	178,461	208,238	241,816	18.1%
Myelodysplastic syndrome- MDS	NA	NA	NA	NA	NA	NA	NA
Chronic Myeloproliferative disorders- CMD	NA	NA	NA	NA	NA	NA	NA
Chronic Myelomonocytic Leukemia- CMML	NA	NA	NA	NA	NA	NA	NA
Neuro-oncology							
Brain and other Nervous System	62,491	89,745	104,146	119,344	135,360	152,218	16.0%
Soft tissue & musculoskeletal							
Bone and joints cancer							
Kaposi Sarcoma	5,807	9,427	11,237	13,047	14,857	16,667	19.2%
Mesothelioma	NA	NA	NA	NA	NA	NA	NA
Soft tissue	NA	NA	NA	NA	NA	NA	NA
Skin cancer							
Melanoma	391,315	565,776	657,834	754,952	857,372	965,350	16.2%
Thoracic neoplasms							
Lung and Bronchus	442,810	683,428	840,280	1,037,073	1,277,501	1,565,568	23.4%
Total	8,407,032	12,066,958	14,030,579	16,136,880	18,395,533	20,816,902	16.3%
Solid Tumors	7,831,720	11,229,450	13,051,454	15,005,020	17,099,185	19,343,644	16.3%
Liquid Tumors	575,312	837,508	979,125	1,131,860	1,296,348	1,473,258	17.0%

Source: Historical data in this table was obtained from the International Agency for Research on Cancer's database. This Agency derives these data from the Descriptive Epidemiology Group of the International Association of Cancer Registries (IARC). We estimated prevalence for 2014-18, by using the NCI 2005 estimate and then adjusting it by our estimated number of deaths and the estimated incidence for each year.

**Table 7** Japanese Incidence

Cancer type	Incidence 2012	% change per year (2005-2009)	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2012-2018)
Breast, Female	55,710	0.6%	56,432	56,796	57,163	57,532	57,903	0.65%
Breast (In situ), female	NA	NA	NA	NA	NA	NA	NA	NA
Breast, Male	NA	NA	NA	NA	NA	NA	NA	NA
Thyroid & other endocrine neoplasms								
Thyroid cancer	9,290	1.2%	9,509	9,621	9,733	9,848	9,963	1.17%
Gastrointestinal								
Small Intestine	NA	NA	NA	NA	NA	NA	NA	NA
Anal	NA	NA	NA	NA	NA	NA	NA	NA
Colorectal	112,675	2.3%	117,866	120,551	123,297	126,105	128,978	2.28%
Esophagus	19,683	2.4%	20,631	21,121	21,624	22,138	22,665	2.38%
Gall bladder	21,417		21,417	21,417	21,417	21,417	21,417	0.00%
Liver and Intrahepatic	36,168	2.5%	37,979	38,918	39,880	40,866	41,876	2.48%
Pancreatic	32,899	2.5%	34,556	35,415	36,296	37,198	38,124	2.49%
Stomach	107,898	2.3%	112,908	115,500	118,151	120,863	123,637	2.30%
Genitourinary								
Bladder	22,042	2.6%	23,209	23,816	24,439	25,077	25,733	2.62%
Kidney and renal pelvis	16,830	2.1%	17,528	17,888	18,256	18,631	19,014	2.06%
Prostate	55,970	3.0%	59,421	61,226	63,085	65,001	66,975	3.04%
Testicular	1,274	-0.5%	1,261	1,255	1,248	1,242	1,236	-0.51%
Gynecological								
Cervical	9,390	1.0%	9,571	9,663	9,755	9,849	9,943	0.96%
Corpus and Uterus	11,449	0.6%	11,581	11,647	11,714	11,782	11,849	0.58%
Ovarian	8,921	1.0%	9,092	9,178	9,266	9,354	9,443	0.95%
Vaginal	NA	NA	NA	NA	NA	NA	NA	NA
Vulvar	NA	NA	NA	NA	NA	NA	NA	NA
Head & neck								
Larynx	3,615	2.3%	3,786	3,875	3,965	4,058	4,153	2.34%
Oral Cancer	8,306	2.1%	8,661	8,844	9,031	9,222	9,416	2.12%
Nasopharynx	553		553	553	553	553	553	0.00%
Other pharynx	5,475		5,475	5,475	5,475	5,475	5,475	0.00%
Eye and Orbit	NA	NA	NA	NA	NA	NA	NA	NA
Lymphoma & myeloma								
All leukemias combined	10,182	3.8%	10,973	11,391	11,826	12,276	12,744	3.82%
Leukemia -ALL	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CLL	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -AML	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CML	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia- AMoL	NA	NA	NA	NA	NA	NA	NA	NA
Hodgkin's disease	1,061	0.8%	1,078	1,087	1,096	1,105	1,114	0.82%
Non-Hodgkin's lymphoma	20,978	2.0%	21,826	22,262	22,708	23,162	23,625	2.00%
Multiple myeloma	4,984	2.6%	5,243	5,377	5,514	5,656	5,801	2.57%
Myelodysplastic syndrome- MDS	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myeloproliferative disorders- CMD	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myelomonocytic Leukemia- CMML	NA	NA	NA	NA	NA	NA	NA	NA
Neuro-oncology								
Brain and other Nervous System	5,510	1.3%	5,654	5,728	5,803	5,878	5,955	1.31%
Soft tissue & musculoskeletal								
Bone and joints cancer	NA	NA	NA	NA	NA	NA	NA	NA
Kaposi Sarcoma	19		19	19	19	19	19	0.00%
Mesothelioma	NA	NA	NA	NA	NA	NA	NA	NA
Soft tissue	NA	NA	NA	NA	NA	NA	NA	NA
Skin cancer								
Melanoma	1,371	1.5%	1,412	1,433	1,455	1,476	1,498	1.49%
Thoracic neoplasms								
Lung and Bronchus	94,855	2.6%	99,807	102,378	105,016	107,723	110,498	2.58%
Total	678,525		707,447	722,435	737,784	753,505	769,607	2.13%
Solid Tumors	641,320		668,328	682,317	696,640	711,306	726,323	2.10%
Liquid Tumors	37,205		39,120	40,118	41,144	42,199	43,285	2.56%

Source: Historical data in this table was obtained from the International Agency for Research on Cancer's database. This Agency derives these data from the Descriptive Epidemiology Group of the International Association of Cancer Registries (IARC). We estimated deaths for 2014-18, by using the IARC estimate and growing it at the historical growth rate (2005-09).

**Table 8 Japanese Deaths from Cancer**

Cancer type	Death 2012	% change per year (2005-2009)	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2013-2018)
Breast, Female	13,801	1.1%	14,116	14,276	14,438	14,601	14,767	1.1%
Breast (In situ), female	NA	NA	NA	NA	NA	NA	NA	NA
Breast, Male	NA	NA	NA	NA	NA	NA	NA	NA
Thyroid & other endocrine neoplasms								
Thyroid cancer	1,764	2.6%	1,857	1,906	1,956	2,007	2,059	2.6%
Gastrointestinal								
Small Intestine	NA	NA	NA	NA	NA	NA	NA	NA
Anal	NA	NA	NA	NA	NA	NA	NA	NA
Colorectal	49,345	2.5%	51,810	53,089	54,399	55,741	57,116	2.5%
Esophagus	12,440	2.5%	13,067	13,393	13,727	14,068	14,419	2.5%
Gall bladder	19,309		19,309	19,309	19,309	19,309	19,309	0.0%
Liver and Intrahepatic	32,518	2.6%	34,198	35,071	35,965	36,883	37,823	2.6%
Pancreatic	31,046	2.5%	32,634	33,459	34,304	35,171	36,059	2.5%
Stomach	52,326	2.5%	54,965	56,335	57,738	59,176	60,650	2.5%
Genitourinary								
Bladder	7,630	2.8%	8,066	8,293	8,527	8,767	9,014	2.8%
Kidney and renal pelvis	8,124	2.6%	8,547	8,767	8,992	9,223	9,460	2.6%
Prostate	11,644	3.1%	12,368	12,747	13,138	13,540	13,955	3.1%
Testicular	86	0.5%	87	87	88	88	89	0.5%
Gynecological								
Cervical	3,645	1.7%	3,770	3,835	3,900	3,967	4,035	1.7%
Corpus and Uterus	2,783	2.2%	2,908	2,972	3,038	3,105	3,174	2.2%
Ovarian	4,986	1.6%	5,145	5,226	5,308	5,392	5,477	1.6%
Vaginal	NA	NA	NA	NA	NA	NA	NA	NA
Vulvar	NA	NA	NA	NA	NA	NA	NA	NA
Head & neck								
Larynx	977	2.4%	1,025	1,050	1,076	1,103	1,130	2.4%
Oral Cancer	3,994	2.3%	4,176	4,270	4,366	4,464	4,565	2.3%
Nasopharynx	324		324	324	324	324	324	0.0%
Other pharynx	3,132		3,132	3,132	3,132	3,132	3,132	0.0%
Eye and Orbit	NA	NA	NA	NA	NA	NA	NA	NA
Lymphoma & myeloma								
All leukemias combined	8,583	1.9%	8,907	9,074	9,244	9,417	9,593	1.9%
Leukemia -ALL	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CLL	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -AML	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia -CML	NA	NA	NA	NA	NA	NA	NA	NA
Leukemia- AMoL	NA	NA	NA	NA	NA	NA	NA	NA
Hodgkin's disease	148	2.0%	154	157	160	164	167	2.0%
Non-Hodgkin's lymphoma	11,157	2.3%	11,684	11,957	12,237	12,523	12,815	2.3%
Multiple myeloma	4,334	2.7%	4,568	4,689	4,814	4,942	5,073	2.7%
Myelodysplastic syndrome- MDS	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myeloproliferative disorders- CMD	NA	NA	NA	NA	NA	NA	NA	NA
Chronic Myelomonocytic Leukemia- CMML	NA	NA	NA	NA	NA	NA	NA	NA
Neuro-oncology								
Brain and other Nervous System	2,229	1.5%	2,295	2,329	2,363	2,397	2,433	1.5%
Soft tissue & musculoskeletal								
Bone and joints cancer	NA	NA	NA	NA	NA	NA	NA	NA
Kaposi Sarcoma	4		4	4	4	4	4	0.0%
Mesothelioma	NA	NA	NA	NA	NA	NA	NA	NA
Soft tissue	NA	NA	NA	NA	NA	NA	NA	NA
Skin cancer								
Melanoma	691	2.0%	719	733	747	762	777	2.0%
Thoracic neoplasms								
Lung and Bronchus	75,119	2.7%	79,195	81,315	83,492	85,727	88,022	2.7%
Total	362,139	2.5%	370,124	378,723	387,540	396,579	405,847	2.3%
<i>Solid Tumors</i>	337,917		353,718	361,920	370,329	378,951	387,792	2.8%
<i>Liquid Tumors</i>	24,222		16,406	16,804	17,211	17,628	18,055	-5.7%

Source: Historical data in this table was obtained from the National Cancer Institute (NCI). The NCI derives these data from its SEER data base. We estimated prevalence for 2014-18, by using the NCI 2012 estimate and then adjusting it by our estimated number of deaths and the estimated incidence for each year.

**Table 9 Japanese Prevalence**

Cancer type	Prevalence 2012	Estimated 2014	Estimated 2015	Estimated 2016	Estimated 2017	Estimated 2018	% change per year (2013-2018)
Breast, Female	246,101	330,733	373,253	415,978	458,909	502,045	12.6%
Breast (In situ), female	NA	NA	NA	NA	NA	NA	NA
Breast, Male	NA	NA	NA	NA	NA	NA	NA
Thyroid & other endocrine neoplasms							
Thyroid cancer	38,088	53,391	61,106	68,884	76,725	84,628	14.2%
Gastrointestinal							
Small Intestine	NA	NA	NA	NA	NA	NA	NA
Anal	NA	NA	NA	NA	NA	NA	NA
Colorectal	384,877	516,989	584,452	653,350	723,714	795,576	12.9%
Esophagus	42,681	57,807	65,536	73,433	81,502	89,748	13.2%
Gall bladder	30,104	34,320	36,428	38,536	40,644	42,752	6.0%
Liver and Intrahepatic	75,630	83,191	87,038	90,953	94,936	98,989	4.6%
Pancreatic	21,399	25,242	27,198	29,190	31,218	33,282	7.6%
Stomach	330,857	446,742	505,907	566,320	628,006	690,993	13.1%
Genitourinary							
Bladder	77,899	108,186	123,709	139,621	155,932	172,651	14.2%
Kidney and renal pelvis	51,524	69,487	78,609	87,872	97,280	106,833	12.9%
Prostate	224,822	318,928	367,407	417,354	468,815	521,836	15.1%
Testicular	4,939	7,287	8,455	9,615	10,769	11,916	15.8%
Gynecological							
Cervical	33,744	45,345	51,173	57,028	62,910	68,819	12.6%
Corpus and Uterus	44,460	61,807	70,482	79,158	87,835	96,510	13.8%
Ovarian	25,155	33,049	37,002	40,960	44,922	48,888	11.7%
Vaginal	NA	NA	NA	NA	NA	NA	NA
Vulvar	NA	NA	NA	NA	NA	NA	NA
Head & neck							
Larynx	14,246	19,767	22,591	25,480	28,436	31,459	14.1%
Oral Cancer	26,831	35,801	40,374	45,039	49,796	54,647	12.6%
Nasopharynx	1,693	2,151	2,380	2,609	2,838	3,067	10.4%
Other pharynx	14,438	19,124	21,467	23,810	26,153	28,496	12.0%
Eye and Orbit	NA	NA	NA	NA	NA	NA	NA
Lymphoma & myeloma							
All leukemias combined	14,771	18,903	21,220	23,802	26,661	29,813	12.4%
Leukemia -ALL	NA	NA	NA	NA	NA	NA	NA
Leukemia -CLL	NA	NA	NA	NA	NA	NA	NA
Leukemia -AML	NA	NA	NA	NA	NA	NA	NA
Leukemia -CML	NA	NA	NA	NA	NA	NA	NA
Leukemia- AMoL	NA	NA	NA	NA	NA	NA	NA
Hodgkin's disease	3,016	4,865	5,795	6,731	7,672	8,620	19.1%
Non-Hodgkin's lymphoma	52,950	73,233	83,538	94,009	104,648	115,458	13.9%
Multiple myeloma	10,624	11,974	12,662	13,363	14,077	14,804	5.7%
Myelodysplastic syndrome- MDS	NA	NA	NA	NA	NA	NA	NA
Chronic Myeloproliferative disorders- CMD	NA	NA	NA	NA	NA	NA	NA
Chronic Myelomonocytic Leukemia- CMML	NA	NA	NA	NA	NA	NA	NA
Neuro-oncology							
Brain and other Nervous System	9,318	16,037	19,437	22,877	26,358	29,880	21.4%
Soft tissue & musculoskeletal							
Bone and joints cancer	NA	NA	NA	NA	NA	NA	NA
Kaposi Sarcoma	66	96	111	126	141	156	15.4%
Mesothelioma	NA	NA	NA	NA	NA	NA	NA
Soft tissue	NA	NA	NA	NA	NA	NA	NA
Skin cancer							
Melanoma	4,753	6,140	6,840	7,547	8,261	8,982	11.2%
Thoracic neoplasms							
Lung and Bronchus	176,120	217,344	238,407	259,932	281,928	304,405	9.5%
Total	1,961,106	2,635,753	2,979,464	3,329,708	3,686,634	4,050,394	12.8%
<i>Solid Tumors</i>	<i>1,879,745</i>	<i>2,526,779</i>	<i>2,856,250</i>	<i>3,191,805</i>	<i>3,533,576</i>	<i>3,881,700</i>	<i>12.8%</i>
<i>Liquid Tumors</i>	<i>81,361</i>	<i>108,974</i>	<i>123,214</i>	<i>137,904</i>	<i>153,058</i>	<i>168,695</i>	<i>12.9%</i>

Source: Historical data in this table was obtained from the International Agency for Research on Cancer's database. This Agency derives these data from the Descriptive Epidemiology Group of the International Association of Cancer Registries (IARC). We estimated prevalence for 2014-18, by using the NCI 2012 estimate and then adjusting it by our estimated number of deaths and the estimated incidence for each year.

## Descriptions of cancers mentioned in this report

### Breast

Breast cancer is a malignant tumor that develops from cells of the breast. The most common forms of breast cancer are (1) adenocarcinoma, which is in glandular tissue, and (2) ductal carcinomas, which are noninvasive. Rarer types of breast cancer include: (1) medullary carcinoma, an infiltrating form of breast cancer with well-defined boundaries between tumor and normal tissue, and a concentration of cancer and immune system cells at the edges of the tumor; (2) mucinous carcinoma, an invasive form of breast cancer that results from mucus-producing cancer cells; (3) Paget's disease, which starts in the ducts and spreads to the exterior of the breast, (4) Phyllodes tumor, which forms from the stroma (connective tissue) of the breast, in contrast to carcinomas, which develop in the ducts or lobules; and (5) tubular carcinoma, which is infiltrating breast carcinoma.

### Thyroid and other endocrine neoplasms

**Thyroid cancer.** The thyroid gland is located in the front part of the neck and has two lobes: right and left, united by a narrow isthmus. This gland takes up iodine from the diet and the blood and makes thyroid hormone. The thyroid gland primarily contains two types of cells. The first type, the thyroid follicle cells, produce and store thyroid hormone and thyroglobulin. The second type, C-cells, produce the hormone calcitonin. Cancers can develop from each of these types of cells. Many types of tumors can develop in the thyroid gland. Because the thyroid gland is close to the skin, tumors often appear as bumps in the neck, called thyroid nodules.

The most common types of thyroid cancer are papillary carcinoma, a slow-growing cancer that develops from the follicle cells and follicular carcinoma. Papillary carcinoma is prone to metastasis. Less common forms of thyroid cancer are anaplastic carcinoma, insular carcinoma, and Medullary carcinoma, which develop from C-cells and make calcitonin and carcinoembryonic antigen (CEA), and Hurthle cell carcinoma, anaplastic carcinoma, and thyroid lymphoma.

### Gastrointestinal

**Anal cancer.** The anus is a complex structure, which is both internal and external to the body. The anus is composed of several types of tissues, each containing several types of cells. The external tissues are an extension of the skin and the internal tissues are glandular. Different cancers can develop from each type of tissue. As a result, many types of tumors can develop in the anus. Malignant anal tumors include (1) squamous cell carcinomas, also called Bowen's disease, which are the most common; (2) adenocarcinomas, which can develop in glands under the anal epithelium or in apocrine glands; and (3) Paget's disease, a type of apocrine gland carcinoma that spreads through the surface layer of the skin.

**Bile duct cancer.** The bile duct is a thin tube, about 4-5 inches long, that reaches from the liver to the small intestine. In the liver, it begins as many small channels that gather bile from the liver cells. These all join into one tube or duct (this part of the bile duct is called the hepatic duct). About one-third along the length of the bile duct, the gallbladder attaches by a small duct called the cystic duct. The combined duct is called the common bile duct. The end of this part of the bile duct empties into the earliest part of the small intestine, next to where the pancreatic duct also enters the small intestine. The major function of this system is to transport bile to the small intestine, where it aids in digesting food.

Cancers can develop in any part of the bile duct and are divided into three groups. According to the American Cancer Society, about two-thirds of bile duct cancers develop at juncture of the hepatic duct and the bile ducts, just as they leave the liver. These are called perihilar cancers. About one-fourth of bile duct cancers occur in the common bile duct nearest the intestine, called distal bile duct cancers. The remaining cancers develop in the interior of the liver and are called intrahepatic bile duct cancers.

**Colorectal cancer.** Colon and rectal cancers develop in the gastrointestinal system. The colon has four sections. The first section is called the ascending colon. The second section is called the transverse colon, since it goes across the body to the left side. There it joins the third section, the descending colon, which continues downward on the left side. The fourth section is known as the sigmoid colon because of its S-shape. Each of these sections is composed of several layers of tissue.

Colorectal cancers originate in the innermost layer and can grow through some or all of the other layers. Colon and rectal cancer share many features. Cancer can develop in any of the four sections of the colon or in the rectum. Colorectal cancers are thought to develop slowly over a period of several years. Most colorectal cancers begin as a polyp, also known as adenoma. Once a cancer forms in these polyps, instead of growing only into the center of the colon or rectum, it will also grow into the walls of these organs. Cells from the tumor can then break away and spread through the bloodstream or lymph system to other parts of the body. There, they can form “colony” tumors. This process is called metastasis.

**Esophagus cancer.** The esophagus is a muscular tube that connects the throat to the stomach. The wall of the esophagus has several layers. There are two main types of esophageal cancer: squamous cell carcinoma and adenocarcinoma. Since the entire esophagus is normally lined with squamous cells, squamous cell carcinoma can occur anywhere along the length of the esophagus. Adenocarcinoma originates in glandular tissue.

**Gall bladder cancer.** The gallbladder is a small, pear-shaped organ located underneath the right lobe of the liver. The gallbladder concentrates and stores bile, which aids in digesting fats in the small intestine. According to the American Cancer Society, more than 80% of gallbladder cancers are adenocarcinomas, which originate in the epithelial cells of a gland. Gallbladder cancers that grow along the connective tissue and blood vessels are called papillary cancers, which are unlikely to invade the liver or lymph nodes.

**Liver cancer.** The liver, unlike most other organs, receives blood from two sources. The hepatic artery supplies the liver with blood that is rich in oxygen. The portal vein carries nutrient-rich blood from the intestines. The liver is necessary for survival. This organ is made of several different types of cells, which can result in several types of malignant and benign tumors. Malignant tumors can be angiosarcomas or hemangiosarcomas. Angiosarcomas grow rapidly and are usually too widespread to be removed surgically. Cholangiocarcinoma (hemangiosarcoma), starts near the hilum and is generally too large or invasive to be removed by surgery. Generally, liver cancers are metastasis from another area of the body.

**Pancreatic cancer.** The pancreas is located behind the stomach and has two separate glands, the exocrine and endocrine. Exocrine glands release into ducts, while endocrine glands release into the bloodstream. The exocrine glands produce pancreatic fluid. The endocrine cells are arranged in small clusters called islets (or islets of Langerhans). The islets release two hormones, insulin and glucagon, which are important in controlling the amount of sugar in the blood. The exocrine cells and endocrine cells of the pancreas form completely different types of tumors. The most common cancers of the exocrine pancreas are adenocarcinomas, which originate in the ducts of the pancreas. Less common cancers of the exocrine pancreas include adenosquamous carcinomas, squamous cell carcinomas, and giant cell carcinomas. Cancerous tumors of the endocrine pancreas are less common than islet cell tumors carcinomas.

**Stomach cancer.** Stomach cancer originates in the stomach and is also known as gastric cancer. The stomach is a sack-like organ that holds food and begins the digestive process by secreting gastric juice. Cancer can develop in any of the five sections of the stomach, but most are reported to start in the mucosa. Stomach cancers are believed to develop slowly over many years and grow through the wall of the stomach, eventually invading nearby organs, or spreading to the lymph system.

## Genitourinary

### Bladder

Located in the lower part of the abdomen, the bladder stores waste collected from the kidneys until it is passed out of the body through the urethra. There are three types of



bladder cancer that begin in the cells lining the bladder: transitional cell carcinoma, squamous cell carcinoma, and adenocarcinoma. Transitional cells comprise the innermost tissue of the bladder. Cancers that originate here account for 90% of all bladder cancers. According to the American Cancer Society, the prevalence and incidence of bladder cancer in the United States is 499,199 and 63,210. We believe the discrepancy between these figures is due to the vast majority of bladder cancer patients being diagnosed early in their disease. Early-stage bladder cancer is highly treatable with surgery.

### **Kidney Cancer (renal cell carcinoma)**

Renal cell carcinoma is a type of kidney cancer, which accounts for more than 90% of malignant kidney tumors. Renal cell carcinoma usually grows as a single mass within the kidney. Sometimes tumors may be found in both kidneys simultaneously. Like most cancers, renal cell carcinoma is difficult to treat once it has metastasized.

According to the American Cancer Society, there are five main types of renal cell carcinoma that are identified by examining the tumor under a microscope: clear cell, papillary, chromophobe, collecting duct, and unclassified.

- Clear cell renal cell carcinoma appears very pale or clear and is the most common form of renal cell carcinoma. About 70% to 80% of patients with renal cell carcinoma have clear cell.
- Papillary renal cell carcinoma is the second most common type—affecting about 10% to 15% of patients. These cancers form little finger-like projections papillae in some if not most of the tumor. Some doctors call these cancers chromophilic because the cells take up certain dyes used in preparing the tissue to be viewed under the microscope, causing them to appear pink.
- Chromophobe renal carcinoma is the third most common type—accounting for about 5% of cases. The cells of these cancers are also pale, like the clear cells, but are much larger and have certain other features that can be recognized.
- Collecting duct renal carcinoma is very rare. The major feature is that the cancer cells can form irregular tubes.
- About 5% of renal cancers are unclassified because their appearance doesn't fit into any of the other categories.

Another aspect of a renal cell carcinoma is its grade. This refers to how closely the cancer cells' nuclei (part of a cell in which DNA is stored) look like normal kidney cells' nuclei. Renal cell cancers are usually graded on a scale of 1 through 4. Grade 1 renal cell cancers have cell nuclei that differ very little from normal kidney cell nuclei. These cancers usually grow and spread slowly and tend to have a good outlook (prognosis.) At the other extreme, grade 4 renal cell cancer nuclei look quite different from normal kidney cell nuclei and have a worse prognosis.

Although the cell type and grade are sometimes helpful in predicting a prognosis, the cancer's stage is by far the best predictor of survival. The stage describes the cancer's size and how far it has spread beyond the kidney. The letter T followed by a number from 0 to 3 describes the tumor's size and spread to nearby tissues. Some of these numbers are further subdivided with letters, such as T1a and T1b. Higher T numbers indicate a larger tumor and/or more extensive spread to tissues near the kidney. The letter N followed by a number from 0 to 2 indicates whether the cancer has spread to lymph nodes near the kidney and, if so, how many are affected. Lymph nodes are bean-sized collections of immune system cells that help fight infections and cancers. The letter M followed by a 0 or 1 indicates whether or not the cancer has spread (metastasized) to distant organs such as the lungs or bones, or to lymph nodes that are not near to the kidneys.

### **Prostate**

Male hormones cause the prostate gland to develop in the fetus and to grow in the adolescent male. In older men the part of the prostate around the urethra often continues to grow. This causes BPH (benign prostatic hyperplasia) which can result in problems with urinating.

Although there are several cell types in the prostate, nearly all prostate cancers start in the gland cells, resulting in an adenocarcinoma. Generally prostate cancer grows slowly; however, prostate cancer can grow and spread quickly. It is still difficult to tell which prostate cancers will grow slowly and which will grow quickly. In some cases it is believed that prostate cancer begins with a small change in the size and shape of the prostate gland cells, known as PIN (prostatic intraepithelial neoplasia). These changes can be either low-grade (almost normal) or high-grade (abnormal). Prostate cancer remains a leading cause of cancer death in American men. The American Cancer Society estimates that prostate cancer accounts for approximately 9% of cancer-related deaths in men.

### Testicular

The testicles contain several types of cells, each of which may develop into one or more types of cancer. It is important to distinguish these types of cancers from one another because they differ in their prognosis (the course of disease and the outlook for cure) and in the ways they are treated. The most common form of testicular cancer originates in the germ cells. It is estimated that over 90% of cancers of the testicle develop in the germ cells. The two main types of germ cell tumors (GCTs) are seminomas (60%) and nonseminomas (40%). Invasive testicular germ cell cancers can begin as a noninvasive form of the disease called carcinoma in situ or intratubular germ cell neoplasia. Testicular cancer is one of the most curable forms of cancer and has a 5-year relative survival rate that is greater than 96%.

### Gynecological

**Cervical cancer.** The cervix is the lower part of the uterus. Cancer of the cervix begins in the lining of the cervix. Cervical cancer develops slowly and is usually detected early. The two primary types of cervical cancers are squamous cell carcinoma and adenocarcinoma.

**Endometrial cancer.** Endometrial cancer develops from the inner lining of the uterus. The uterus is a hollow organ, about the size and shape of a medium-sized pear. Most endometrial cancers are adenocarcinomas.

**Ovarian cancer.** Ovarian cancer originates in the ovaries, which are the main source of female hormones, estrogen and progesterone. Generally, ovarian tumors are named according to the cells of origin. There are three main types of ovarian tumors: epithelial, which form from the cells covering the outer surface of the ovary; germ cell tumors, which start from the cells that produce the ova; and stromal tumors, which start from connective tissue cells. Ovarian cancer may cause an elevation in the tumor marker CA 125.

**Vaginal cancer.** The walls of the vagina are lined by a thin layer called the epithelium. According to the American Cancer Society there are several types of vaginal cancer, but 85-90% of vaginal cancers are squamous cell carcinomas that begin in the epithelial lining.

**Vulvar cancer.** The vulva is the external portion of the female reproductive system. According to the American Cancer Society, more than 90% of cancers of the vulva are squamous cell carcinomas. The second most common type of vulvar cancer is melanoma.

### Head and neck

**Laryngeal and Hypo-pharyngeal cancer.** The larynx, or voice box, is divided into three levels: the glottis (or vocal cords), the supraglottis (the area above the vocal cords including the epiglottis), and the subglottis (the area below the vocal cords). The larynx and vocal cords function for speaking and protecting the airway during swallowing. Several types of cancers can develop in the larynx and hypopharynx. The American Cancer Society reports that 95% of these cancers develop from squamous cells.

**Oral cancer.** Oral cancer starts in the mouth. Many types of tumors can develop in the oral cavity and oropharynx. More than 90% of cancers of the oral cavity and oropharynx are squamous cell carcinoma, also called squamous cell cancer.

### Lymphoma and Myeloma

**Leukemia.** This cancer starts in the bone marrow, but in most cases quickly moves into the blood. Leukemia can spread to other parts of the body, including the lymph nodes, liver, spleen, central nervous system, and testes. Acute leukemia develops quickly, and if

left untreated, is usually fatal in a few months. Leukemias are divided into four main types. The first distinction is acute versus chronic, referring to whether the abnormal cells are mature or immature. In acute leukemia, the bone marrow cells are unable to properly mature. Immature leukemic cells, which are often called blasts, continue to reproduce and accumulate. Left untreated, the American Cancer Society estimates that most patients with acute leukemia will live only a few months. In chronic leukemia, cells can mature, but are abnormal. These cells live much longer than normal white blood cells, resulting in accumulation of too many mature granulocytes or lymphocytes.

The second distinction of leukemias is myelogenous versus lymphocytic. This classification refers to the type of bone marrow cells that are involved. Leukemias that involve granulocytes or monocytes are classified as myelogenous. Leukemias that develop from bone marrow lymphocytes are lymphocytic. Malignant lymphomas are also cancers of lymphocytes, but develop from lymphocytes in lymph nodes or other organs.

In conclusion, the four main types of leukemias are as follows:

- Acute myelogenous leukemia (AML);
- Chronic myelogenous leukemia (CML);
- Acute lymphocytic leukemia (ALL); and
- Chronic lymphocytic leukemia (CLL).

**Hodgkin's Disease.** Hodgkin's disease, or Hodgkin's lymphoma, is a cancer that originates in lymphatic tissue--lymph nodes and related organs that are part of the body's immune and blood-forming systems. The cancer cells in Hodgkin's disease are called Reed-Sternberg cells, after the two doctors who first described them in detail. Under a microscope they look different from cells of non-Hodgkin's lymphomas and other cancers. Lymph nodes make and store lymphocytes, infection-fighting white blood cells. They are connected throughout the body by lymph vessels, which carry lymphatic fluid containing lymphocytes. The lymphatic tissue is present in many parts of the body; therefore, Hodgkin's disease can start almost anywhere, but most often starts in the lymph nodes.

**Non-Hodgkin's Lymphoma.** Non-Hodgkin's Lymphoma is cancer that starts in the lymphatic tissue. The lymphatic system functions to filter germs and cancer cells, as well as fluid from the extremities and internal organs. Lymphoid tissue is formed by several types of immune system cells that function to fight infections. Lymphoid tissue is found throughout the body, including the lymph nodes, the thymus, the spleen, the tonsils and adenoids, in the bone marrow, and other systems. Lymphoid tissue is composed of the lymphocyte cells, of which there are two main types: B cells and T cells. Both can develop into lymphomas, but B cell lymphomas are much more prevalent. B cells protect the body against bacteria by producing antibodies. The antibodies attach to substances on the cell surface of bacteria and attract an immune system cell that surrounds and digests the antibody-coated bacteria. Normal T cells help protect the body against viruses, fungi, and bacteria. T cells target specific substances found in virus-infected cells and destroy them. T cells release cytokines that attract white blood cells that digest the infected cells.

Non-Hodgkin's Lymphoma is classified based on the size and shape of the cancer cells under the microscope and their pattern of growth within the lymph node. Size is described as large or small and shape is described as cleaved or noncleaved (basically indented versus smooth and round). The growth pattern may be follicular (clustered cells), or diffuse (scattered). Non-Hodgkin's Lymphomas are grouped according to prognosis, which are divided into low, intermediate, and high-grade categories. Low-grade lymphomas tend to grow slowly, and patients with low-grade lymphoma often live for many years without problems from their disease. Intermediate and high-grade lymphomas grow more rapidly and, left untreated, patients' lifespans are estimated to be less than a few months.

In conclusion, non-Hodgkin's lymphoma is classified as follows:

- Low grade—small lymphocytic and follicular small-cleaved cell; follicular mixed (small-cleaved and large cell).

- Intermediate grade—follicular, large cell; diffuse small-cleaved cell; diffuse mixed (small and large cell); diffuse large cell.
- High grade—immunoblastic; lymphoblastic; small non-cleaved (Burkitt's and non-Burkitt's).
- Miscellaneous types—cutaneous T-cell lymphoma; adult T-cell Leukemia/lymphoma; diffuse intermediately differentiated lymphoma; malignant histiocytosis.

**Multiple myeloma.** Multiple myeloma is a type of cancer formed by malignant plasma cells. Plasma cells produce and release antibodies. When plasma cells grow out of control, they can produce tumors that can grow in several sites, particularly in the bone marrow. When these tumors grow in multiple sites they are referred to as multiple myeloma. Large growths of plasma cells can impair the blood-forming functions of the bone marrow, resulting in an anemia and leukopenia—a shortage of white blood cells. While normal plasma cells produce antibodies that attack specific infectious agents, myeloma cells produce an ineffective antibody that is unable to fight any infection.

**Myelodysplastic syndrome.** Myelodysplastic syndromes (MDS) are a group of conditions caused by abnormalities of the blood-forming cells of the bone marrow. These abnormal cells produce defective marrow, which are usually destroyed before leaving the bone marrow or shortly after entering the bloodstream, resulting in patients having shortages of blood cells. According to the American Cancer Society, in approximately 30% of cases of MDS, the bone marrow cells eventually develop into acute leukemia. Myelodysplastic syndromes are classified into five types—refractory anemia (RA); refractory anemia with ringed sideroblasts (RARS); refractory anemia with excess blasts (RAEB); refractory anemia with excess blasts in transformation (RAEB-T); and chronic myelomonocytic leukemia (CMML). In both RA and RARS, bone marrow abnormalities are limited to those cells that develop into red blood cells. The abnormality in refractory anemia with excess blasts (RAEB) and refractory anemia with excess blasts in transformation (RAEB-T) are not limited to bone marrow cells that form red blood cells. In both RAEB and RAEB-T, myeloblasts (the bone marrow cells that develop into white blood cells) also reproduce excessively and become too numerous. In chronic myelomonocytic leukemia (CMML), the bone marrow cells that form red blood cells are relatively unaffected.

### Neuro-oncology

**Brain and spinal cord cancer.** There are many types of cancers that start in the central nervous system (CNS). The CNS is composed of the brain, spinal cord, and cranial nerves. Tumors of different parts of the CNS disrupt different functions and cause a variety of symptoms. The brain consists of a number of kinds of tissues and cells, which give rise to various types of tumors. Any of the different types of tissues or cells within the brain or spinal cord can become cancerous. With a few exceptions, tumors of the brain or spinal cord are never benign. It is nearly impossible to completely remove brain or spinal cord tumors; therefore, they continue to grow and eventually cause death. CNS tumors include (1) astrocytomas, which arise within the brain itself; (2) oligodendrogliomas, which start in brain cells called oligodendrocytes and spread; (3) ependymomas, which arise from the ependymal cells and may spread along the cerebrospinal fluid pathways that do not spread outside the brain or spinal cord; (4) Gliomas, a general category that includes astrocytomas, oligodendrogliomas, and ependymomas; (5) tumors of neurons are rare; (6) medulloblastomas, which develop from neurons of the cerebellum and are fast-growing tumors that can be treated and are often cured by radiation therapy; (7) gangliogliomas, which contain both neurons and glial cells; (8) schwannomas (neurilemoma), which form near the cerebellum and in the cranial nerve; (9) chordomas, which start in the bone at the back of the skull or at the lower end of the spinal cord; and (10) germ cell tumors, germinoma, which are very rare in adults.

### Soft tissue and musculoskeletal

**Bone cancer.** There are several different types of bone tumors and their names are derived from the area of bone or surrounding tissue that is affected or the kind of cells forming the tumor. Bone tumors include (1) osteosarcoma, a cancerous tumor of the bone itself; (2) chondrosarcoma, a cancer of cartilage cells; (3) Ewing's tumor, which arises in

the long bones of the legs and arms, but may also develop in the pelvis and other bones; (4) fibrosarcoma and malignant fibrous histiocytoma, which develop from connective tissues other than bones; (5) giant cell tumor of bone, which can be malignant, but is usually benign; and (6) chordoma, which occurs in the base of the skull and bones of the spine.

**Sarcoma.** Soft tissue sarcomas are tumors that develop from fat, muscle, nerve, joint, blood vessel, or deep skin tissues. These cancers can develop in any part of the body. They include Lipomas; Liposarcomas; Leiomyosarcomas; Rhabdomyosarcomas, neurofibrosarcomas, Ewing's tumor, Synovial sarcoma, angiosarcomas, Kaposi's Sarcoma, a cancer formed by cells similar to those lining blood or lymph vessels and most common in AIDS patients; hemangioendothelioma, a blood vessel tumor that is less aggressive than hemangiosarcoma and usually invades nearby tissues; fibrosarcoma, a cancer of the fibrous tissue; Desmoid tumor, a fibrous tissue tumor; dermatofibrosarcoma protuberans (DFSP), a low-grade cancer of the fibrous tissue; malignant fibrous histiocytoma (MFH), the most common malignant soft tissue tumor; and Perivascular tissue tumor, hemangiopericytoma, a sarcoma of perivascular tissue that develops in the legs, pelvis, and retroperitoneum. Less common tumors include malignant, alveolar sarcoma, epithelioid sarcoma, clear cell sarcoma, and desmoplastic small cell tumor.

### Melanoma

Melanoma is a cancer that begins in the melanocytes, the cells that produce the skin coloring or pigment known as melanin. Because most melanoma cells still produce melanin, melanoma tumors are often brown or black. Melanoma is much less common than basal cell and squamous cell skin cancers, but far more serious. Melanoma most often appears on the trunk of fair-skinned men and on the lower legs of fair-skinned women.

### Thoracic neoplasms

The lungs are two sponge-like organs and are divided into three lobes. The left lung has two lobes and is smaller than the right lobe. Air goes into your lung via the trachea, which divides into tubes called the bronchi, and they divide into smaller branches—the bronchioles. At the end of the bronchioles are tiny air sacs known as alveoli. Many tiny blood vessels run through the alveoli, absorbing oxygen from the inhaled air into the bloodstream and releasing carbon dioxide. A lining, called the pleura, surrounds the lungs. This lining protects the lungs and facilitates their sliding motion as they expand and contract during breathing. Most lung cancers start in the lining of the bronchi. Less often, cancers begin in the trachea, bronchioles, or alveoli. Lung cancers are thought to develop over a period of many years.

**Small cell lung cancer.** Small-cell lung cancer (SCLC) accounts for about 20% of all lung cancers. These cancers are small-cell, named for the size and appearance of the cancer cells. These cells can multiply quickly and form large tumors, and can spread to lymph nodes and other organs such as the bones, brain, adrenal glands, and liver. This type of cancer often starts in the bronchi and toward the center of the lungs. Small-cell lung cancer is almost always caused by smoking.

**Non-small-cell lung cancer.** Non-small-cell lung cancer (NSCLC) includes sub-types that differ in size, shape, and chemical makeup. Squamous cell carcinoma accounts for about 30% of NSCLC, is associated with a history of smoking, and tends to start near a bronchus. Adenocarcinoma accounts for about 40% of NSCLC and is usually found in the outer region of the lung. Large-cell undifferentiated carcinoma accounts for about 10% of lung cancers. NSCLC may appear in any part of the lung, and it tends to grow and spread quickly, resulting in a poor prognosis.

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	Count	Percent	Count	Percent
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