Ejemplo de informe: Epidemiología del melanoma en Global Data (internacional) y en España incluyendo datos de mortalidad

<table>
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<tr>
<th>Solicitante</th>
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<tbody>
<tr>
<td>Proyecto</td>
<td>Revisión y análisis de literatura médica</td>
</tr>
<tr>
<td>Descripción</td>
<td>Búsqueda y selección de información sobre el tema de interés. Se empleará Global Data y Pharma eTrack así como otras fuentes de interés como valor añadido (PubMed, Scholar, bases de datos nacionales, Instituto Nacional de Estadística), ESPACENET.</td>
</tr>
</tbody>
</table>

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Epidemiología de melanoma en España incluyendo defunciones

INFORME GLOBAL DATA

PharmaPoint: Melanoma – Global Drug Forecast and Market Analysis to 2023

Reference Code: GDHC104PIDR  Publication Date: April 2015

EPIDEMIOLOGY

Disease Background

Melanoma is a malignant neoplasm of melanocytes, the pigment cells in the skin located on the epidermis, the most superficial layer of the body (WHO, 2014). Melanocytes are embryological derivatives of neural crest tissue, and as such, any region of the body that is a derivative of the neural crest and contains melanocytes — namely, areas of skin, meninges, mucous membranes, esophagus, and eyes — can develop melanoma (Komarnicky-Kocher and Alite, 2013). Accordingly, non-cutaneous melanomas, typically occurring in the eye and mucosa, account for only 4-5% of primary melanomas; this section focuses on melanoma of the skin, which is the deadliest form of skin cancer (CDC, 2014; Mayo Clinic, 2014). Melanoma typically presents as a mole (nevus) on the skin, and is characterized by the growth's asymmetry, irregular border, color variation, a diameter greater than 6mm, and an evolution in appearance over the past few weeks or months; these five diagnostic characteristics are known collectively by the acronym ABCDE (American Cancer Society, 2014; Goodman and Snyder, 2012; Melanoma, 2008). Melanoma may also present with itching and bleeding, or develop satellites (Mayo Clinic, 2014; Belvoir Media Group, 2008).

This report provides an overview of the risk factors, comorbidities, and the global and historical trends for melanoma of the skin in the eight major markets (BBM) (US, France, Germany, Italy, Spain, UK, Japan, and Australia). It includes a 10-year epidemiological forecast for the diagnosed incident cases of melanoma of the skin segmented by age (in 10-year age groups, beginning at 20 years and ending at ≥80 years), sex, and cancer stage at diagnosis (American Joint Commission on Cancer [AJCC] stages I, II, III, and IV). The forecast also includes a 10-year epidemiological forecast for the five-year diagnosed prevalent cases and the five-year diagnosed prevalent cases segmented by genetic aberrations (BRAF and c-KIT) in these markets.

Risk Factors and Comorbidities

Several studies have identified biological, genetic, behavioral and environmental risk factors that are associated with an increased risk of developing melanoma. These include increasing age, sex, fair complexion, excessive UV light exposure, history of sunburn, having many (≥50) moles, a personal history of cancer of the skin, a family history of melanoma, immunosuppression, and certain medical conditions including but not limited to xeroderma pigmentosum (XP) and atypical mole (dysplastic nevi) syndrome (Cho et al., 2005; Belvoir Media Group, 2008; NIH, 2010; Rivers and Rivers, 1996; US Department of Health and Human Services, 2014). The interaction between the nature and extent of sun exposure and skin type appear to influence the risk of melanoma (Lens and Dawes, 2004).

Compared with individuals with a darker complexion, those with fair skin, lighter hair color, or light eyes are at higher risk for developing melanoma of the skin due to these individuals' increased susceptibility to sunburn (Cho et al., 2005). The amount of UV exposure is typically higher at both lower and higher latitudes and is also dependent on the time and strength of rays the skin is exposed to (Bataille, 2009; NCI, 2011). Medical conditions such as XP and atypical mole (dysplastic nevi) syndrome are known precursors for the development of melanoma (NCI, 2011). Individuals with XP are genetically susceptible to DNA damage caused by sunlight and are at an increased risk of developing melanoma on sun-exposed areas of the skin (Kraemer et al., 1994). The number of moles present on an individual is indicative of the likelihood of developing melanoma (Psaty et al., 2010).
Melanoma is typically not associated with the development of any comorbidity. However, since the incidence of the disease increases with age, diseases that are common among older age groups can co-exist with melanoma (Grann et al., 2013). A higher prevalence of comorbidities is also associated with advancing cancer stage, the interaction of which also increases the mortality rate (Grann et al., 2013). The most common comorbid indications in patients with melanoma of the skin are congestive heart failure, vascular disease, diabetes mellitus, and pulmonary disease (Grann et al., 2013).
Table 1 lists the major risk factors and comorbidities for melanoma.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Description</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing age and sex</td>
<td>Historically, melanoma has been rare prior to puberty and increased in incidence as age increases. In recent years, epidemiology trends show that the incidence of melanoma in women is higher among those younger than 40 years, while the incidence in men is higher among those older than 40 years.</td>
<td>Diepgen and Mahler, 2002; Little and Eide, 2012</td>
</tr>
<tr>
<td>Fair complexion</td>
<td>Compared with those with a darker complexion, individuals with a fair complexion and poor tanning ability have a 40% increased risk of developing melanoma (RR=1.4; 95% CI=1.0–1.8), adjusting for the effects of other risk factors.</td>
<td>D’Arcy et al., 1984; Garbe et al., 1994; Gandini et al., 2005</td>
</tr>
<tr>
<td>Excessive UV light exposure</td>
<td>Excessive total UV exposure over a person’s lifetime increases the risk of melanoma by 32% (RR=1.32; 95% CI=1.02–1.77). UV exposure at lower latitudes significantly influences the estimated risk of developing melanoma.</td>
<td>Gandini et al., 2005</td>
</tr>
<tr>
<td>Having atypical nevi</td>
<td>The total number of nevi (moles) is the most important common independent risk factor for the development of melanoma. Individuals having ten or more raised nevi on the arms are 11 times more likely to develop melanoma compared with individuals without nevi on the arms (OR 11.31; 95% CI=4.92–25.98). Individuals with pre-malignant and skin cancer lesions have a 4.28 times greater risk of developing melanoma compared with those without pre-malignant and skin cancer lesions (RR=4.28; 95% CI=2.80–6.55).</td>
<td>D’Arcy et al., 1984; Gandini et al., 2005</td>
</tr>
<tr>
<td>A personal history of skin cancer</td>
<td>1–8% of melanoma patients will be diagnosed with another melanoma within the next few years. Having non-melanoma (including actinic damage) increases the risk of developing melanoma by 328% (RR = 4.28; 95% CI = 2.80–6.55).</td>
<td>Diepgen and Mahler, 2002; Psaty et al., 2010</td>
</tr>
<tr>
<td>Family history of melanoma</td>
<td>Individuals with one or more blood relative with a history of melanoma are more than twice as likely to develop melanoma as those without (OR = 2.32; 95% CI = 1.40–3.54). The risk increases to 5.00 times as high (95% CI = 1.45–17.27) with two or more affected blood relatives. This increased risk could be associated with similar lifestyle, similar sun exposure patterns, common characteristics of fair complexions, hereditary genetic mutations, or a combination of factors.</td>
<td>D’Arcy et al., 1984</td>
</tr>
<tr>
<td>Genetic predisposition</td>
<td>Mutations in CDKNA2A are the most common genetic abnormalities in individuals with melanoma, and increase the risk of melanoma 35–70-fold. Somatic mutations in p16, p53, BRAF, and c-KIT are also found in melanoma.</td>
<td>Bataille, 2009; Markovic et al., 2007; Psaty et al., 2010</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>Immunosuppressed patients such as those with acquired immunodeficiency syndrome (AIDS) and those receiving immunosuppressive agents after solid organ transplantation have increased risk of developing melanoma.</td>
<td>Markovic et al., 2007</td>
</tr>
<tr>
<td>Having XP</td>
<td>XP carries a 1000-fold increase in risk for melanoma. Approximately one in five XP patients will develop melanoma.</td>
<td>Psaty et al., 2010</td>
</tr>
<tr>
<td>Atypical mole syndrome</td>
<td>Studies have validated that the number of atypical nevi is a strong positive predictor of melanoma risk. 38% of those with multiple primary melanoma had dysplastic nevi compared with 18% of those with a single primary melanoma.</td>
<td>Psaty et al., 2010</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Description</td>
<td>Source</td>
</tr>
<tr>
<td>Diseases related to old age</td>
<td>Due to the association of melanoma to advancing age, several conditions common in old age such as congestive heart failure, vascular disease, diabetes mellitus, and pulmonary disease are comorbidities in individuals with melanoma as well.</td>
<td>Grann et al., 2013</td>
</tr>
</tbody>
</table>

Source: GlobalData (various sources listed above)

Note: OR = odds ratio; RR = relative risk; CI = confidence interval; XP = xeroderma pigmentosum
Global Trends

Melanoma of the skin is considered an epidemic in the US, Europe, and Australia because of the increased incidence of melanoma in these areas between 1950 and 2007 (Geller et al., 2013; Tucker, 2009). Global estimates of melanoma trends suggest a doubling of melanoma incidence every 10–20 years during the past several decades (Diepgen and Mahler, 2002). Although the annual increase in incidence rates varies between populations, the general temporal trend has been an annual increase in the order of 3–7% per year for populations with fair complexions (Garbe et al., 2000).

Melanoma is 20 times more common in individuals with fair complexions compared with populations with darker complexions (American Cancer Society, 2014). Much of the increase in incidence can be attributed to changes in sun-related behaviors. Melanoma incidence rates are highest in Australia, with levels matched only by New Zealand (Cancer Research UK, 2014b). In fair-skinned white populations worldwide, the number of deaths from melanoma has also increased in the past few decades (Garbe et al., 2000). Although the death rate from melanoma continues to increase faster compared with death rates of most other cancers, overall, mortality rates attributed to melanoma remain low (Lens and Dawes, 2004; WHO, 2014).

Age-specific incidence rates in men in the 5EU were similar across markets, though all are relatively lower compared with the US and Australia, which had the highest incidence rates for men and women. In 2007, the incidence of melanoma in men and women ages ≥20 years in Australia was 67 cases per 100,000 population (Ferlay et al., 2014). Overall, Japan reported the lowest age-specific incidence and prevalence of melanoma in both men and women ages ≥20 years (Ferlay et al., 2014). Although the 8MM have varying levels of incidence rates, GlobalData epidemiologists observed that they share a similar trend in that the diagnosed incidence increases with age.

The individual markets analysis in the following sections is based on the 10-year historical incidence in men and women ages ≥20 years for the years 1997–2007 as reported in the CI-5Plus, 2007 being the most recent year with available data (Ferlay et al., 2014).

US

The incidence of melanoma in men and women ages ≥20 years in the US in 2007 was 29.04 cases per 100,000 population (Ferlay et al., 2014). The incidence of melanoma in men and women ≥20 years in the US was lower than the reported incidence rates for melanoma in Australia, though higher than the other markets included in this analysis. Data from the US Surveillance, Epidemiology, and End Results (SEER) registry of the National Cancer Institute (NCI), which covers approximately 14% of the US population, showed that melanoma was the most rapidly increasing malignancy in both sexes (Lens and Dawes, 2004).

SEU

In 2007, the incidence of melanoma in men and women ages ≥20 years in the SEU varied across the markets. A review of the 10-year historical incidence in men and women ages ≥20 years reported by the CI-5Plus shows a steady increase of melanoma (Ferlay et al., 2014). The highest incidence of melanoma in men and women ≥20 years among the SEU in 2007 was observed in the UK where the crude rate was 23.88 cases per 100,000 population, followed by France with 21.97 cases per 100,000 population, and Italy with 20.28 cases per 100,000 population. This crude rate represents the number of diagnosed incident cases of melanoma in the given time period divided by the total number of individuals in the population. Germany and Spain reported the lowest incidence of melanoma in men and women ages ≥20 years, at 18.45 cases per 100,000 population and 14.28 cases per 100,000 for 2007, respectively.

Japan and Australia

Japan

In 2007, the incidence rate of melanoma in Japan was 1.10 cases per 100,000 population for men and women ≥20 years. This is considerably lower compared with other markets analyzed for this report. In the US for instance, the incidence of melanoma in 2007 was 29.04 cases per 100,000 population. The low incidence of melanoma in Japan may be due in part to ethnic differences in the presentation of melanoma in the population. Typically, the Japanese population has a higher number of melanocytes in the
skin, leading to a phenotypic expression not conducive to an elevated risk of developing melanoma. However, another possible contributing factor to the low incidence of melanoma in Japan may be underreporting.

**Australia**

Melanoma incidence rates are the highest in Australia compared with all the markets included in this analysis. In 2007, Australia’s incidence of melanoma for men and women ages ≥20 years was 67 cases per 100,000 population, compared with the US where the incidence of melanoma in men and women ages ≥20 years in 2007 was 29.04 cases per 100,000 population (Ferlay et al., 2014). Similar to other markets, Australia also has a higher incidence of melanoma in men than in women.

**Forecast Methodology**

This analysis used the International Classifications of Diseases, Tenth Revision (ICD-10) code for malignant neoplasm of the melanocytes (C43) definition of melanoma. Melanoma was defined as a malignant neoplasm which originates from melanocytes, the pigment cells in the skin.

For the purposes of this analysis, GlobalData epidemiologists excluded melanoma inside eyes (iris) and on the skin of genital organs. The clinical staging definitions across markets were standardized to follow AJCC staging definitions as defined in Table 2 below.

### Table 2: Melanoma of the Skin Staging Definition Equivalencies

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>TisN0M0</td>
<td>Presence of cancerous cells (<em>in situ</em>) that have not invaded or migrated.</td>
</tr>
<tr>
<td>IA</td>
<td>T1aN0M0</td>
<td>The tumor is no thicker than 1.0mm in the largest vertical diameter. There is no ulceration and the mitotic rate is &lt;1/mm². There is no evidence of regional lymph node or distant metastases.</td>
</tr>
<tr>
<td>IB</td>
<td>T1bN0M0</td>
<td>The tumor is no thicker than 1.0mm in the largest vertical diameter, with ulceration or mitotic rate &gt;1/mm². No evidence of regional lymph node or distant metastases. Or the tumor is 1.01–2.0mm in the largest vertical diameter and without ulceration. No evidence of regional lymph node or distant metastases.</td>
</tr>
<tr>
<td></td>
<td>T2aN0M0</td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>T(1-4)aN1aM0</td>
<td>The tumor is 1.01–2.0mm in the largest vertical diameter and with ulceration. No evidence of regional lymph node or distant metastases. Or the tumor is 2.01–4.0mm in the largest vertical diameter and without ulceration. No evidence of regional lymph node or distant metastases.</td>
</tr>
<tr>
<td></td>
<td>T(1-4)aN2aM0</td>
<td></td>
</tr>
<tr>
<td>IIB</td>
<td>T3bN0M0</td>
<td>The tumor is 2.01–4.0mm in the largest vertical diameter and with ulceration. No evidence of regional lymph node or distant metastases. Or the tumor is thicker than 4.0mm in the largest vertical diameter and without ulceration. No evidence of regional lymph node or distant metastases.</td>
</tr>
<tr>
<td></td>
<td>T4aN0M0</td>
<td></td>
</tr>
<tr>
<td>IIC</td>
<td>T4bN0M0</td>
<td>The tumor is thicker than 4.0mm in the largest vertical diameter and with ulceration. No evidence of regional lymph node or distant metastases.</td>
</tr>
<tr>
<td>Regional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td>T(1-4)aN1aM0</td>
<td>T(1-4)aN2aM0</td>
</tr>
<tr>
<td>-------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>IIIA</td>
<td>T(1-4)bN1aM0</td>
<td>T(1-4)bN2aM0</td>
</tr>
<tr>
<td></td>
<td>T(1-4)aN1bM0</td>
<td>T(1-4)aN2bM0</td>
</tr>
<tr>
<td>IIIB</td>
<td>T(1-4)bN1bM0</td>
<td>T(1-4)bN2cM0</td>
</tr>
<tr>
<td></td>
<td>TanyN3M0</td>
<td></td>
</tr>
<tr>
<td>IIIIC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>TanyNanyM1</td>
<td></td>
</tr>
</tbody>
</table>

Source: GlobalData; Dummer et al., 2012; National Comprehensive Cancer Network, 2014
Sources Used

Table 3 presents the sources used to obtain melanoma incidence rates for the 8MM.

<table>
<thead>
<tr>
<th>Markets</th>
<th>Source</th>
<th>Data Obtained/Calculated</th>
<th>Location of Study</th>
<th>Study Period</th>
<th>Ages of Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>Ferlay et al., 2014</td>
<td>Age-specific incidence of diagnosed melanoma for men and women: Crude annual average incidence (2007): 21.97 cases per 100,000 population</td>
<td>Eight registries, France</td>
<td>1997–2007</td>
<td>≥20 years</td>
</tr>
<tr>
<td>Germany</td>
<td>Ferlay et al., 2014</td>
<td>Age-specific incidence of diagnosed melanoma for men and women: Crude annual average incidence (2007): 18.45 cases per 100,000 population</td>
<td>The Saarland Region, Germany</td>
<td>1997–2007</td>
<td>≥20 years</td>
</tr>
<tr>
<td>Italy</td>
<td>Ferlay et al., 2014</td>
<td>Age-specific incidence of diagnosed melanoma for men and women: Crude annual average incidence (2007): 20.28 cases per 100,000 population</td>
<td>Eight registries, Italy</td>
<td>1997–2007</td>
<td>≥20 years</td>
</tr>
<tr>
<td>Spain</td>
<td>Ferlay et al., 2014</td>
<td>Age-specific incidence of diagnosed melanoma for men and women: Crude annual average incidence (2007): 14.28 cases per 100,000 population</td>
<td>Seven registries, Spain</td>
<td>1997–2007</td>
<td>≥20 years</td>
</tr>
<tr>
<td>UK</td>
<td>Ferlay et al., 2014</td>
<td>Age-specific incidence of diagnosed melanoma for men and women: Crude annual average incidence (2007): 23.88 cases per 100,000 population</td>
<td>UK (nine registries) and Northern Ireland</td>
<td>1997–2007</td>
<td>≥20 years</td>
</tr>
<tr>
<td>Japan</td>
<td>Ferlay et al., 2014</td>
<td>Age-specific incidence of diagnosed melanoma for men and women: Crude annual average incidence (2007): 1.03 cases per 100,000 population</td>
<td>Three registries: Miyagi, Nagasaki, and Osaka Prefectures.</td>
<td>1997–2007</td>
<td>≥20 years</td>
</tr>
<tr>
<td>Australia</td>
<td>Ferlay et al., 2014</td>
<td>Age-specific incidence of diagnosed melanoma for men and women: Crude annual average incidence (2007): 44.77 cases per 100,000 population</td>
<td>Six registries, Australia</td>
<td>1997–2007</td>
<td>≥20 years</td>
</tr>
</tbody>
</table>

Source: GlobalData (various sources listed above)

Table 4 below presents the sources used to calculate the incident cases by pathological stage at diagnosis.

<table>
<thead>
<tr>
<th>Markets</th>
<th>Source</th>
<th>Data Obtained/Calculated</th>
<th>Location of Study</th>
<th>Study Period</th>
<th>Ages of Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>Proxy from Germany and the UK</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
Table 5 presents the sources used to calculate the five-year diagnosed prevalent cases by stage in the 8MM. For each stage at diagnosis, relative survival data were used to calculate the number of persons diagnosed with melanoma who survived up to the fifth year following their diagnosis.

<table>
<thead>
<tr>
<th>Markets</th>
<th>Source</th>
<th>Data Obtained/Calculated</th>
<th>Location of Study</th>
<th>Study Period</th>
<th>Ages of Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>Proxy from Australia</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>SEU</td>
<td>Proxy from Australia</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Japan</td>
<td>Proxy from Australia</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Australia</td>
<td>Australian Cancer Network Melanoma Guidelines Revisions Working Party, 2008</td>
<td>Stage (relative survival for years 1, 2, 3, 4, 5 [%]): Stage I (99.67, 98.33, 95.30, 93.44, 91.73) Stage II (95.34, 93.44, 91.73) Stage III (95.34, 93.44, 91.73) Stage IV (95.34, 93.44, 91.73) Stage V (95.34, 93.44, 91.73)</td>
<td>Australia</td>
<td>1991–2002</td>
<td>All ages</td>
</tr>
</tbody>
</table>

Table 5: 8MM, Sources of Melanoma of the Skin Five–Year Diagnosed Prevalent Cases by Stage Data

France

Mazeau-Woynar et al., 2010

Incident cases by stage at diagnosis
Stage I and II: 86.00%
Stage III: 3.00%
Stage IV: 6.00%
Unstaged: 4.00%
PETRI study, France
All ages

Germany

German Guideline Program in Oncology, 2014

Incident cases by stage at diagnosis
Stage I: 49.98%
Stage II: 12.81%
Stage III: 5.60%
Stage IV: 1.61%

In situ: 30.00%
Germany
All ages

Italy

Proxy from Germany and the UK
–
–
–
–

Spain

Proxy from Germany and the UK
–
–
–
–

UK

Cancer Research UK, 2014b

Incident cases by stage at diagnosis
Stage I: 66.40%
Stage II: 19.10%
Stage III: 11.10%
Stage IV: 1.30%
Unknown: 2.10%
Former Anglia Cancer Network (5% of the population of England)
2006–2010
15–99 years

Japan

Fujisawa et al., 2008

Incident cases by stage at diagnosis
Stage I: 22.00%
Stage II: 28.00%
Stage III: 21.00%
Stage IV: 11.00%
In situ: 18.00%
160 selected institutions, Japan
2006–2007
5–98 years

Australia

Proxy from Germany and the UK
–
–
–
–

Source: GlobalData (various sources listed above)
<table>
<thead>
<tr>
<th></th>
<th>20.89, 16.76, 11.67)</th>
</tr>
</thead>
</table>

Source: GlobalData (various sources listed above)

Note: 5EU = France, Germany, Italy, Spain, and UK
Table 6 presents the sources used to calculate the number of diagnosed prevalent cases by genetic aberration in the 8MM.

<table>
<thead>
<tr>
<th>Markets</th>
<th>Source</th>
<th>Data Obtained/Calculated</th>
<th>Location of Study</th>
<th>Study Period</th>
<th>Ages of Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>Flaherty et al., 2012a</td>
<td>BRAF: 50.00 % KIT: 1.00 % NRAS: 20.00%</td>
<td>US</td>
<td>Unspecified</td>
<td>All ages</td>
</tr>
<tr>
<td>SEU</td>
<td>Proxy from the US</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Japan</td>
<td>Ashida et al., 2012 Uhara et al., 2014</td>
<td>BRAF: 26.70% KIT: 5.00% NRAS: 7.10%</td>
<td>Japan</td>
<td>Ashida et al., 2012: 2012 Uhara et al., 2014: 2004-2012</td>
<td>All ages</td>
</tr>
<tr>
<td>Australia</td>
<td>Proxy from the US</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Source: GlobalData (various sources listed above)

Note: SEU = France, Germany, Italy, Spain, and UK

8MM — Population

GlobalData epidemiologists obtained the most up-to-date, country-specific total population data from the United States Census Bureau’s (USCB) International Data Base for each country covered in the forecast. The USCB was chosen as the source for population data because population estimates are calculated using census and survey data, vital statistics, country-specific administrative statistics, and information from multinational organizations that collect and publish data for these countries. Additionally, the USCB uses a cohort-component projection method that incorporates fertility, mortality, and migration to forecast population estimates (USCB, 2013).

8MM — Diagnosed Incident Cases of Melanoma

In order to determine the number of incident cases of melanoma of the skin in the 8MM, GlobalData epidemiologists obtained the age-specific melanoma diagnosed incidence data for the 8MM from the CI-5Plus database which is published and maintained by the International Agency for Research on Cancer (IARC) of the WHO (Ferlay et al., 2014). The database, considered a gold-standard source for cancer statistics, provides validated annual diagnosed incidence data derived from country-specific registries (Ferlay et al., 2014).

8MM — Pathological Stage at Diagnosis of Diagnosed Incident Melanoma

In the US, GlobalData epidemiologists used the distribution of incident cases by pathological stage data provided by SEER. For melanoma, SEER provided the clinical stages of disease as follows: localized disease, regional disease, metastatic disease, and unstaged. The SEER disease staging descriptions correlate to the AJCC TNM staging system, as shown in Table 2.

The Association for the Prevention and Epidemiology of Tumors in the Ile-de-France region (PETRI) study provided the data for the pathological staging of melanoma in France. The study was conducted in the period from 1994–1999 (Mazeau-Woynar et al., 2010).

Data for the pathological staging of melanoma in Germany was obtained from the German Guideline Program in Oncology. The guideline is produced through a research partnership of the German Cancer Society (DKG), German Cancer Aid (DKH), and Association of Medical Scientific Societies (AMWF). The guideline provides evidence and consensus-based recommendations through the analysis of population-based studies representative of the German population (German Guideline Program in Oncology, 2014).

GlobalData epidemiologists used data from Cancer Research UK (CRU) for the segmentation of pathological stage of melanoma at diagnosis for the UK market. CRU conducts and funds research into the prevention, diagnosis, and treatment of cancer, primarily in the UK (Cancer Research UK, 2013).
For Japan, GlobalData epidemiologists used data from the study by Fujisawa and colleagues (2008). The study presented results from a period survey of malignant melanoma patients in Japan by the Prognosis and Statistical Investigation Committee of the Japanese Skin Cancer Society (Fujisawa et al., 2008). The committee is housed under the Japanese Skin Cancer Society, a reliable source of Japanese skin cancer data.

For the Italian, Spanish, and Australian markets, GlobalData epidemiologists were unable to locate an appropriate source for the pathological stage of melanoma at diagnosis. Data from Germany and the UK were averaged and used as proxies for these markets.

**8MM — Five-Year Diagnosed Prevalent Cases of Melanoma**

In order to determine the number of five-year diagnosed prevalent cases of melanoma, GlobalData epidemiologists used one-, two-, three-, four-, and five-year relative survival data by clinical stage at diagnosis from the Australian Cancer Network Melanoma Guidelines. The Australian Cancer Network, now known as Cancer Council Australia, has developed high standards for the preparation and evaluation of the best evidence in order to build recommendations for the prevention and diagnosis of cancer (Cancer Council Australia, 2014). These relative survival rates were proxied to the US, SEU, and Japan.

**8MM — Five-Year Diagnosed Prevalent Cases by Genetic Aberration of Melanoma**

The prevalence of genetic aberrations in diagnosed cases of melanoma was evaluated in this analysis. The proportion of prevalent cases with genetic anomalies in the BRAF (B-Raf proto-oncogene serine/threonine-protein kinase), KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) and NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) genes were extracted from scientific literature and applied to the populations of the markets included in this report (National Institutes of Health[NIH], 2014).

Flaherty and colleagues conducted a comprehensive review of current research and literature that focused on the analysis of recent advances in the strategy of molecularly targeted approaches to the therapy of melanoma in humans (Flaherty et al., 2012a). In this review, they noted the distributions of the prevalent cases that can be attributed to expressive disruption in BRAF, KIT, and NRAS genes. These distributions were used for the US, SEU, and Australia.

For the Japanese market, GlobalData epidemiologists obtained the distributions of BRAF and KIT genetic disruptions from a 2012 study by Ashida and colleagues (2012) and NRAS from Uhara and colleagues (2014). Uhara and colleagues examined NRAS mutation in primary and metastatic lesions of 127 Japanese melanoma patients in an effort to increase the amount of data on genetic mutations, specifically the characterization of the MAPK (mitogen-activated protein kinases) signaling pathway associated with the treatment of NRAS-mutated melanoma, in Asian populations (Uhara et al., 2014; NIH, 2014). Ashida et al., 2012 examined specimen from 101 melanoma patients at Shinshu University Hospital in order to assess the prevalence of KIT mutations in Japanese melanoma patients. This is because KIT mutations are more common in acral and mucosal melanomas, and because of pre–despondence of these genetic aberrations in melanoma in Asian populations, the authors noted (Ashida et al., 2012).
Sources Not Used

GlobalData epidemiologists did not use melanoma incidence data from any country-specific registries. GlobalData epidemiologists used data provided in the IARC extensive and comprehensive database. The data presented are of high quality and are comparable between markets.

Forecast Assumptions and Methods

Incident Cases

For the 8MM included in this report, GlobalData epidemiologists obtained age-specific melanoma incidence data from the CI-5Plus database published by the IARC of the WHO (Ferlay et al., 2014). Using 10 years of historical data on the incidence of melanoma, GlobalData epidemiologists forecast the incidence rates for melanoma to 2023 using linear regression analysis. Age-specific melanoma incidence rates were then multiplied by the USCB’s estimated populations for each year in the forecast period in order to determine the number of age-specific incident cases.

In order to ensure the precision of the forecast, GlobalData epidemiologists evaluated the coefficient of determination to assess the goodness of fit for the linear regression product. GlobalData epidemiologists chose a coefficient of determination cutoff of 0.4. For age groups that had coefficient of determination that fell below the pre-determined cutoff, the 2008 predicted value was held constant for the years 2009–2023.

For Japanese men aged 40–44 years, the incidence rate was low and reached 0 for many of the years during 1997–2000. As a result, the regression equation yielded a negative growth in the incidence rate. Therefore, GlobalData epidemiologists assumed the incidence rate for the time period 2008–2023 to equal the average of the ten–year historical values from 1997–2007.

For the Italian and Australian markets, CI-5Plus did not provide incidence data for the age group ≥85 years. Therefore, GlobalData epidemiologists extrapolated the incidence rate in the 80–84 year age group to the ≥85 years age group in both of these markets.

Pathological Stage at Diagnosis for the Diagnosed Incident Cases of Melanoma

In order to determine the number of incident cases by pathological stage at diagnosis for the US, GlobalData epidemiologists obtained the proportions of incident cases by clinical stage at diagnosis for men and women in the US from SEER. For melanoma, SEER data is presented using the clinical stages localized, regional, metastatic, and unstaged. GlobalData epidemiologists used the equivalencies presented in Table 2 to present the data using AJCC staging methodologies. GlobalData epidemiologists used the average of the UK and Germany stage I to stage I and stage II ratios to convert data presented using SEER staging methods to AJCC staging. The UK and Germany were chosen because reliable data were available for these markets and were averaged in order to reduce the bias of only using one market as proxy. For the purpose of the forecast model, GlobalData epidemiologists assumed that all the reported cases had a known stage at diagnosis. A normalization calculation was applied in order to remove the “unstaged” proportion presented in the SEER data.

For the French market, GlobalData epidemiologists obtained data for the incident cases by clinical stage at diagnosis for men and women from the PETRI study (Mazeau-Woynar et al., 2010). PETRI conducted a cohort study from 1994–1999 using a comprehensive collection of cases of incident cancers reported in Il-de-France to health insurance (27,080 patients) (Mazeau-Woynar et al., 2010). The data were presented using AJCC staging, except for stage I and stage II melanoma, which were combined together. The PETRI study also presented the proportion of melanoma cases that were unstaged. GlobalData epidemiologists used the average of the UK and Germany stage I to stage I and stage II ratios to determine the proportion of melanoma cases that were pathologically stage I as well as the proportion of cases that were pathologically stage II in France. The UK and Germany were chosen because reliable data were available for these markets and were averaged in order to reduce the bias of only using one market as proxy. For the purpose of the forecast model, GlobalData epidemiologists assumed that all the reported cases had a known stage at diagnosis. A normalization calculation was applied in order to remove the “unstaged” proportion presented in the data obtained from the PETRI study.

For Germany, GlobalData epidemiologists obtained the distribution of the incident cases by clinical stage at diagnosis for men and women from the German Guideline Program in Oncology (2014). Data was presented for stages I–IV as well for in situ cases. This
forecast does not include in situ melanoma skin cases; therefore, a normalization calculation was applied in order to remove the “in situ” proportion presented in the data obtained from the German Guideline Program in Oncology.

For Japan, GlobalData epidemiologists obtained data for the proportions of incident cases by clinical stage at diagnosis from a study conducted by Fujisawa and colleagues (2008). Data were presented for stages I–IV as well for in situ cases. This forecast does not include in situ melanoma cases; therefore, a normalization calculation was applied in order to remove the “in situ” proportion from the data presented (Fujisawa et al., 2008).

For the UK market, data for the proportion of incident cases by clinical stage were obtained from CRU. GlobalData epidemiologists presented both the proportions of incident cases for stages I–IV as well as the proportion of cases whose stage at diagnosis was unknown. GlobalData epidemiologists used a normalization calculation in order to remove the proportion of cases for which the stage at diagnosis of melanoma was unknown.

For the Italian, Spanish, and Australian markets, GlobalData epidemiologists were unable to locate an appropriate source for the pathological stage of melanoma at diagnosis. Data from Germany and the UK were averaged and used as a proxy for these markets.

**Five-Year Diagnosed Prevalent Cases**

GlobalData epidemiologists calculated the five-year diagnosed prevalent cases of melanoma using relative survival data by stage at diagnosis and incident cases of melanoma. Among the 8MM, Australia was the only market with robust data; therefore, GlobalData epidemiologists used Australian data as a proxy for all the other markets included in this report. GlobalData epidemiologists obtained zero-, one-, two-, five-, and 10-year relative survival data by pathological stage. Data points were then fitted to a linear regression of reciprocal second-order decay model to calculate the one-, two-, three-, four-, and five-year relative survival rates for stages I, II, III, and IV of melanoma.

GlobalData epidemiologists multiplied the one-year relative survival rate for stage I melanoma by the total number of incident cases of melanoma diagnosed as stage I in the same year to calculate the expected number of cases that survived past one year. The epidemiologists applied the two-year relative survival rate for stage I melanoma to the total number of stage I incident cases that were diagnosed one year ago to obtain the expected number of cases that survived past two years. The same calculations were repeated to obtain the three-, four-, and five-year survival cases, and the total of the expected number of stage I cases that survived past five years were summed to obtain the five-year prevalent cases of melanoma for stage I. The same steps were repeated for stage II, III, and IV melanoma cases.

**Genetic Aberrations**

For the US, in order to determine the number of cases with a *BRAF* or *NRAS* mutation, GlobalData epidemiologists applied percentage rates obtained from a US study conducted by Flaherty and colleagues (2012a). The expected percentage distributions of *BRAF* (50.00%) and *NRAS* (20.00%) mutations were applied to the number of five-year diagnosed prevalent cases for each year. The results were the number of expected five-year diagnosed prevalent cases with *BRAF* and *NRAS* mutations of melanoma in both sexes ages ≥20 years.

For the Japanese market, GlobalData epidemiologists obtained percentage rates for the distribution of *BRAF* and *NRAS* mutations within prevalent cases of melanoma from a study conducted by Ashida and colleagues (Ashida et al., 2012). For the Japanese market, the expected percentage distributions of *BRAF* (26.70%) and *NRAS* (7.10%) mutations were applied to the number of five-year diagnosed prevalent cases for each year. The results were the number of expected five-year diagnosed prevalent cases with *BRAF* and *NRAS* mutations of melanoma in both sexes ages ≥20 years.

The expected distributions of *BRAF* and *NRAS* mutations obtained from the US were used to proxy for the 5EU and Australia (Flaherty et al., 2012a).
Epidemiological Forecast for Melanoma (2013–2023)

Diagnosed Incident Cases of Melanoma

In 2013, there were 155,057 diagnosed incident cases of melanoma in the 8MM. GlobalData epidemiologists forecast that the diagnosed incident cases of melanoma in the 8MM will increase to 207,606 diagnosed incident cases in 2023. During the forecast period, the UK will have the highest growth in the diagnosed incident cases of melanoma at an AGR of 4.64%, while Germany will have the lowest growth with an AGR of 1.37%. 
Table 7 and Figure 1 show the number of diagnosed incident cases of melanoma of the skin in the 8MM.

### Table 7: 8MM, Diagnosed Incident Cases of Melanoma of the Skin, Both Sexes, Ages ≥20 Years, N, Select Years 2013–2023

<table>
<thead>
<tr>
<th>Market</th>
<th>2013</th>
<th>2015</th>
<th>2017</th>
<th>2019</th>
<th>2021</th>
<th>2023</th>
<th>AGR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>12,359</td>
<td>12,950</td>
<td>13,545</td>
<td>14,149</td>
<td>14,743</td>
<td>15,327</td>
<td>2.40</td>
</tr>
<tr>
<td>Germany</td>
<td>15,041</td>
<td>15,626</td>
<td>16,179</td>
<td>16,537</td>
<td>16,732</td>
<td>17,097</td>
<td>1.37</td>
</tr>
<tr>
<td>Italy</td>
<td>11,379</td>
<td>11,896</td>
<td>12,404</td>
<td>12,888</td>
<td>13,351</td>
<td>13,824</td>
<td>2.15</td>
</tr>
<tr>
<td>Spain</td>
<td>5,494</td>
<td>5,682</td>
<td>5,871</td>
<td>6,047</td>
<td>6,223</td>
<td>6,404</td>
<td>1.66</td>
</tr>
<tr>
<td>UK</td>
<td>14,939</td>
<td>16,222</td>
<td>17,576</td>
<td>18,982</td>
<td>20,411</td>
<td>21,875</td>
<td>4.64</td>
</tr>
<tr>
<td>Japan</td>
<td>1,340</td>
<td>1,427</td>
<td>1,518</td>
<td>1,613</td>
<td>1,709</td>
<td>1,815</td>
<td>3.54</td>
</tr>
<tr>
<td>Australia</td>
<td>12,224</td>
<td>12,761</td>
<td>13,307</td>
<td>13,862</td>
<td>14,434</td>
<td>15,030</td>
<td>2.30</td>
</tr>
<tr>
<td>SEU</td>
<td>59,212</td>
<td>62,376</td>
<td>65,575</td>
<td>68,603</td>
<td>71,460</td>
<td>74,527</td>
<td>2.59</td>
</tr>
<tr>
<td>8MM</td>
<td>155,057</td>
<td>164,920</td>
<td>175,188</td>
<td>185,683</td>
<td>196,277</td>
<td>207,606</td>
<td>3.39</td>
</tr>
</tbody>
</table>

Source: GlobalData; Ferlay et al., 2014
Note: Totals may not sum due to rounding
SEU = France, Germany, Italy, Spain, and UK; 8MM = US, SEU, Japan, and Australia; AGR = Annual Growth Rate, 2013–2023

### Figure 1: 8MM, Diagnosed Incident Cases of Melanoma of the Skin, Ages ≥20 Years, Both Sexes, N, 2013–2023

Source: GlobalData; Ferlay et al., 2014

### Age-Specific Diagnosed Incident Cases of Melanoma

In the 8MM, the proportion of diagnosed incident cases of melanoma in each age group generally increases with age up to ages 60–69 years, and then decreases afterwards. The age groups with the highest proportions of diagnosed incident cases of melanoma in 2013 consistently across the 8MM were individuals between 60–69 and 70–79 years. Japan is the only market that showed a continued increase in the diagnosed incident cases of melanoma with age through ages ≥80 years. For the age groups under 40 years, the highest incidence of melanoma were observed in the Spanish market with 12.14% of all diagnosed incident cases in 2013 reported in individuals between 30 and 39 years. This is most likely due to the popularity of sunbathing that can be observed in this population.
Table 8 and Figure 2 show the number of diagnosed incident cases of melanoma of the skin by age group in 2013.

### Table 8: 8MM, Age-Specific Diagnosed Incident Cases of Melanoma of the Skin, N (Row%), 2013

<table>
<thead>
<tr>
<th>Markets</th>
<th>20-29 Years</th>
<th>30-39 Years</th>
<th>40-49 Years</th>
<th>50-59 Years</th>
<th>60-69 Years</th>
<th>70-79 Years</th>
<th>80+ Years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>3,326 (4.04)</td>
<td>5,268 (6.40)</td>
<td>10,060 (12.23)</td>
<td>15,926 (19.36)</td>
<td>20,578 (25.01)</td>
<td>15,596 (18.95)</td>
<td>11,527 (14.01)</td>
<td>82,281 (100.00)</td>
</tr>
<tr>
<td>France</td>
<td>482 (3.90)</td>
<td>954 (7.72)</td>
<td>1,609 (13.02)</td>
<td>2,313 (18.72)</td>
<td>2,885 (23.34)</td>
<td>1,941 (15.71)</td>
<td>2,175 (17.60)</td>
<td>12,359 (100.00)</td>
</tr>
<tr>
<td>Germany</td>
<td>636 (4.23)</td>
<td>1,164 (7.74)</td>
<td>2,452 (16.30)</td>
<td>2,237 (14.87)</td>
<td>3,073 (20.43)</td>
<td>3,738 (24.85)</td>
<td>1,741 (11.58)</td>
<td>15,041 (100.00)</td>
</tr>
<tr>
<td>Italy</td>
<td>539 (4.74)</td>
<td>1,375 (12.08)</td>
<td>2,188 (19.23)</td>
<td>1,884 (16.56)</td>
<td>1,916 (16.84)</td>
<td>2,101 (18.46)</td>
<td>1,376 (12.09)</td>
<td>11,379 (100.00)</td>
</tr>
<tr>
<td>Spain</td>
<td>255 (4.64)</td>
<td>667 (12.14)</td>
<td>879 (16.00)</td>
<td>988 (17.98)</td>
<td>986 (17.95)</td>
<td>881 (16.04)</td>
<td>838 (15.25)</td>
<td>5,494 (100.00)</td>
</tr>
<tr>
<td>UK</td>
<td>689 (4.61)</td>
<td>1,359 (9.10)</td>
<td>2,088 (13.98)</td>
<td>2,576 (17.24)</td>
<td>3,309 (22.15)</td>
<td>2,745 (18.37)</td>
<td>2,173 (14.55)</td>
<td>14,939 (100.00)</td>
</tr>
<tr>
<td>Japan</td>
<td>43 (3.21)</td>
<td>58 (4.33)</td>
<td>63 (4.70)</td>
<td>146 (10.90)</td>
<td>242 (18.06)</td>
<td>286 (21.34)</td>
<td>502 (37.46)</td>
<td>1,340 (100.00)</td>
</tr>
<tr>
<td>Australia</td>
<td>354 (2.90)</td>
<td>768 (6.28)</td>
<td>1,408 (11.52)</td>
<td>2,336 (19.11)</td>
<td>2,913 (23.83)</td>
<td>2,448 (20.03)</td>
<td>1,997 (16.34)</td>
<td>12,224 (100.00)</td>
</tr>
<tr>
<td>SEU</td>
<td>2,601 (4.39)</td>
<td>5,519 (9.32)</td>
<td>9,216 (15.56)</td>
<td>9,998 (16.89)</td>
<td>12,169 (20.55)</td>
<td>11,406 (19.26)</td>
<td>8,303 (14.02)</td>
<td>59,212 (100.00)</td>
</tr>
<tr>
<td>8MM</td>
<td>6,324 (4.08)</td>
<td>11,613 (7.49)</td>
<td>20,747 (13.38)</td>
<td>28,406 (18.32)</td>
<td>35,902 (23.15)</td>
<td>29,736 (19.18)</td>
<td>22,329 (14.40)</td>
<td>155,057 (100.00)</td>
</tr>
</tbody>
</table>

Source: GlobalData; Ferlay at al., 2014

Note: Totals may not sum due to rounding

SEU = France, Germany, Italy, Spain, and UK; 8MM = US, SEU, Japan, and Australia

### Figure 2: Age-Specific Diagnosed Incident Cases of Melanoma of the Skin, Both Sexes, N, 2013

Source: GlobalData; Ferlay et al., 2014
Sex-Specific Diagnosed Incident Cases of Melanoma Skin Cancer

Historically, men have had a higher risk of developing melanoma (Diepgen and Mahler, 2002; Little and Eddie, 2012). However, in recent years, melanoma has become more likely to develop both in older men and younger women.

For the 8MM included in this report, of the estimated cases of melanoma in 2013, 54.86% were men and 45.14% were women. The historical trend of higher incidence of melanoma in men held true for men in the US and Italy in 2013; these population segments had a higher incidence of melanoma compared with women in their respective markets. Of the total number of diagnosed incident cases in the US, 58.91% of men compared with 41.09% of women had melanoma while in Italy, 50.36% of men and 49.64% of women were diagnosed with melanoma.

For the remaining six major markets, the sex-specific trend observed in recent years holds true; the proportion of the all the diagnosed incident cases of melanoma who were women was higher compared with the proportion of the diagnosed incident cases of melanoma who were men.
Table 9 and Figure 3 show the number of diagnosed incident cases of melanoma in 2013 by sex.

### Table 9: 8MM, Sex-Specific Diagnosed Incident Cases of Melanoma of the Skin, Ages ≥20 Years, N (Row %), 2013

<table>
<thead>
<tr>
<th>Markets</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>48,469 (58.91)</td>
<td>33,812 (41.09)</td>
<td>82,281 (100.00)</td>
</tr>
<tr>
<td>France</td>
<td>5,825 (47.13)</td>
<td>6,534 (52.87)</td>
<td>12,359 (100.00)</td>
</tr>
<tr>
<td>Germany</td>
<td>7,434 (49.42)</td>
<td>7,607 (50.58)</td>
<td>15,041 (100.00)</td>
</tr>
<tr>
<td>Italy</td>
<td>5,730 (50.36)</td>
<td>5,649 (49.64)</td>
<td>11,379 (100.00)</td>
</tr>
<tr>
<td>Spain</td>
<td>2,612 (47.54)</td>
<td>2,882 (52.46)</td>
<td>5,494 (100.00)</td>
</tr>
<tr>
<td>UK</td>
<td>7,180 (48.06)</td>
<td>7,759 (51.94)</td>
<td>14,939 (100.00)</td>
</tr>
<tr>
<td>Japan</td>
<td>562 (41.94)</td>
<td>778 (58.06)</td>
<td>1,340 (100.00)</td>
</tr>
<tr>
<td>Australia</td>
<td>7,253 (59.33)</td>
<td>4,971 (40.67)</td>
<td>12,224 (100.00)</td>
</tr>
<tr>
<td>SEU</td>
<td>28,781 (48.61)</td>
<td>30,431 (51.39)</td>
<td>59,212 (100.00)</td>
</tr>
<tr>
<td>8MM</td>
<td>85,065 (54.86)</td>
<td>69,992 (45.14)</td>
<td>155,057 (100.00)</td>
</tr>
</tbody>
</table>

Source: GlobalData; Ferlay et al., 2014
Note: Totals may not sum due to rounding
SEU = France, Germany, Italy, Spain, and UK; 8MM = US, SEU, Japan, and Australia

### Figure 3: Sex-Specific Diagnosed Incident Cases of Melanoma of the Skin (N), 2013

Source: GlobalData; Ferlay et al., 2014
Age-Standardized Diagnosed Incidence Rates

The age-standardized prevalence, or the age-adjusted prevalence, of a disease is the weighted average of the age-specific prevalence. Direct prevalence comparisons among countries are difficult because prevalence proportions may be affected by the various age distributions of different countries. The use of age-standardized prevalence allows for the comparison of prevalence among different countries as if they had the same underlying population structure. GlobalData epidemiologists calculated the age-standardized prevalence by multiplying the age-specific prevalence proportions from each country by the age-specific world standard population weights (Segi, 1960). However, it is important to note that the age-standardized prevalence is an artificial measure used for comparison purposes and should not be used to estimate the number of cases.

In the 8MM, the age-standardized diagnosed incidence rate for melanoma was higher in women compared with men in all of the markets with the exception of the US and Australian markets.
For all the eight markets assessed, Australia had the highest age-standardized diagnosed incidence of melanoma in both men (66.63 cases per 100,000 population) and women (45.85 cases per 100,000 population). Inversely, Japan had the lowest age-standardized diagnosed incidence of melanoma in men (0.62 cases per 100,000 population) and women (0.90 cases per 100,000 population).

In the 5EU the highest age-standardized diagnosed incidence rates of melanoma in 2013 were in the UK, with 27.02 cases per 100,000 population in men and 29.75 cases per 100,000 population in women. The lowest age-standardized diagnosed incidence rates in the 5EU were in Spain, with 11.42 cases per 100,000 population in men and 12.77 cases per 100,000 population in women.

Table 10 and Figure 4 present the age-standardized diagnosed incidence rates for melanoma in the 8MM for men and women, ages ≥20 years in 2013.

### Table 10: Age-Standardized Diagnosed Incidence Rate (ASR) of Melanoma of the Skin, Men and Women, Ages ≥20 Years, 2013

<table>
<thead>
<tr>
<th>Markets</th>
<th>US</th>
<th>France</th>
<th>Germany</th>
<th>Italy</th>
<th>Spain</th>
<th>UK</th>
<th>Japan</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>32.94</td>
<td>18.77</td>
<td>15.78</td>
<td>18.74</td>
<td>11.42</td>
<td>27.02</td>
<td>0.62</td>
<td>66.63</td>
</tr>
<tr>
<td>Women</td>
<td>24.14</td>
<td>19.95</td>
<td>19.78</td>
<td>20.75</td>
<td>12.77</td>
<td>29.74</td>
<td>0.90</td>
<td>45.85</td>
</tr>
</tbody>
</table>

Source: GlobalData; Ferlay et al., 2014

### Figure 4: Age-Standardized Diagnosed Incidence Rate (ASR) of Melanoma of the Skin, Men and Women, Ages ≥20 Years, 2013

Source: GlobalData; Ferlay et al., 2014

### Pathological Stage at Diagnosis

For all the markets included in this analysis except for Japan, most cases of melanoma are diagnosed during stage I.

In terms of cases of melanoma diagnosed in stage I, the US, 5EU, and Australia have similar percentages. In the US, 68.09% of all melanoma cases are diagnosed in stage I. The average proportion of melanoma cases in the 5EU that are diagnosed in stage I is 69.92%, whereas in Australia, 69.61% of all melanoma cases are diagnosed in stage I. In the 5EU, the highest rate of melanoma cases diagnosed in stage I was observed in Germany with 71.40%, while the lowest rate of melanoma cases diagnosed in stage I in the 5EU was observed in the UK with 67.82% of all cases.
On the other hand, Japan had the lowest proportion of cases of melanoma diagnosed in stage I (26.84%) and had the highest proportion of late stage diagnoses of melanoma with 13.39% of cases diagnosed at stage IV. Comparatively, in the US market, 4.12% of all melanoma cases were diagnosed in stage IV. On average for all markets in the 5EU, 2.71% of all melanoma cases were diagnosed in stage IV. In the 5EU, the rates of stage IV diagnosis ranged from 1.33% in the UK to 6.31% in France.

Currently, the Japanese Skin Cancer Society is working to increase awareness and screening for melanoma in Japan. These efforts should increase the proportion of cases with early stage diagnoses in the Japanese market.

Figure 5 shows the distribution of incident cases of melanoma by pathological stage at diagnosis in the 8MM in 2013.

Five-Year Diagnosed Prevalent Cases of Melanoma Skin Cancer

GlobalData epidemiologists forecast that the total number of five-year diagnosed prevalent melanoma cases in the 8MM will increase from 639,165 diagnosed prevalent cases in 2013 to 860,889 diagnosed prevalent cases in 2023, with an AGR of 3.47% for each year over the ten-year forecast period.

In 2013, the US had the highest number of five-year diagnosed prevalent cases of melanoma among the 8MM, with 334,374 diagnosed prevalent cases, which will increase to 474,802 diagnosed prevalent cases in 2023 with an AGR of 4.20% for each year over the ten-year period. Japan had the lowest number of five-year diagnosed prevalent cases of melanoma at 4,608 cases, which will increase over the next ten years with an AGR of 3.63% for each year over the ten-year forecast period to 6,279 five-year diagnosed prevalent cases in 2023.

In the 5EU, Germany had the highest number of diagnosed five-year prevalent melanoma cases at 64,676 diagnosed prevalent cases in 2013, but Germany will have the lowest AGR (1.51%) of the 8MM during the forecast period. In 2023, GlobalData epidemiologists forecast that the UK will have the highest number of diagnosed five-year prevalent cases of melanoma in the 5EU with 90,270 cases. The UK will also have the highest AGR (4.88%) of the 8MM during the forecast period.

Table 11 and Figure 6 show the five-year diagnosed prevalent cases of melanoma in the 8MM during the forecast period.
Table 11: BMM, Five-Year Diagnosed Prevalent Cases of Melanoma of the Skin, Both Sexes, ≥20 years, N, Select Years 2013–2023

<table>
<thead>
<tr>
<th>Markets</th>
<th>2013</th>
<th>2015</th>
<th>2017</th>
<th>2019</th>
<th>2021</th>
<th>2023</th>
<th>AGR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>334,374</td>
<td>359,385</td>
<td>385,898</td>
<td>414,040</td>
<td>443,667</td>
<td>474,802</td>
<td>4.20</td>
</tr>
<tr>
<td>France</td>
<td>51,307</td>
<td>54,009</td>
<td>56,623</td>
<td>59,224</td>
<td>61,843</td>
<td>64,429</td>
<td>2.56</td>
</tr>
<tr>
<td>Germany</td>
<td>64,676</td>
<td>66,907</td>
<td>69,386</td>
<td>71,625</td>
<td>73,201</td>
<td>74,468</td>
<td>1.51</td>
</tr>
<tr>
<td>Italy</td>
<td>48,060</td>
<td>50,401</td>
<td>52,689</td>
<td>54,907</td>
<td>57,046</td>
<td>59,133</td>
<td>2.30</td>
</tr>
<tr>
<td>Spain</td>
<td>23,601</td>
<td>24,346</td>
<td>25,156</td>
<td>25,979</td>
<td>26,770</td>
<td>27,554</td>
<td>1.67</td>
</tr>
<tr>
<td>UK</td>
<td>60,672</td>
<td>66,125</td>
<td>71,823</td>
<td>77,785</td>
<td>83,957</td>
<td>90,270</td>
<td>4.88</td>
</tr>
<tr>
<td>Japan</td>
<td>4,608</td>
<td>4,912</td>
<td>5,233</td>
<td>5,563</td>
<td>5,915</td>
<td>6,279</td>
<td>3.63</td>
</tr>
<tr>
<td>Australia</td>
<td>51,867</td>
<td>54,167</td>
<td>56,532</td>
<td>58,951</td>
<td>61,418</td>
<td>63,954</td>
<td>2.33</td>
</tr>
<tr>
<td>5EU</td>
<td>248,316</td>
<td>261,788</td>
<td>275,677</td>
<td>289,520</td>
<td>302,817</td>
<td>315,854</td>
<td>2.72</td>
</tr>
<tr>
<td>8MM</td>
<td>639,165</td>
<td>680,252</td>
<td>723,340</td>
<td>768,074</td>
<td>813,817</td>
<td>860,889</td>
<td>3.47</td>
</tr>
</tbody>
</table>

Source: GlobalData; Ferlay et al., 2014; Australian Cancer network Melanoma Guidelines Revisions Working Party, 2008
Note: Totals may not sum due to rounding

SEU = France, Germany, Italy, Spain, and the UK; 8MM = 5EU, US, Japan, and Australia; AGR = Annual Growth Rate, 2013–2023

Figure 6: BMM, Five-Year Diagnosed Prevalent Cases of Melanoma of the Skin, Both Sexes, Ages ≥20 Years, N, 2013–2023

Source: GlobalData; Ferlay et al., 2014; Australian Cancer network Melanoma Guidelines Revisions Working Party, 2008

Five-Year Diagnosed Prevalent Cases of Melanoma Skin Cancer by Genetic Aberrations

In 2013, the total number of five–year diagnosed prevalent cases of melanoma with a BRAF mutation in the 8MM was 318,510 in men and women ages ≥20 years.

The US had the largest number of melanoma cases with expected BRAF mutations in the 8MM, with 167,187 cases in 2013, whereas Japan had the lowest at 1,230 cases. In the 5EU, Germany had the highest number of prevalent cases with a BRAF mutation of 32,338 cases, whereas Spain had the lowest number, with 11,801 cases in 2013.
Figure 7 shows the number of five-year diagnosed prevalent cases of melanoma with a BRAF mutation in the 8MM in 2013.

The total number of five-year diagnosed prevalent cases of melanoma with a NRAS mutation in the 8MM was 127,237 in 2013.

The US had the largest proportion of melanoma cases with expected NRAS mutations in the 8MM, at 66,875 cases in 2013 for men and women ages ≥20 years, whereas Japan has the lowest at 327 cases. In the 5EU in 2013, Germany had the highest number of prevalent cases with a NRAS mutation with 12,935 cases, whereas Spain had the lowest number at 4,720 cases in men and women ages ≥20 years.
Figure 8 shows the number of five-year diagnosed cases of melanoma with a NRAS mutation in the 8MM in 2013.

**Figure 8:** Five-Year Diagnosed Prevalent Cases of Melanoma of the Skin with NRAS Mutations, Both Sexes, Ages ≥20 Years, 2013

![Bar chart showing five-year diagnosed prevalent cases of melanoma with NRAS mutations by market.](chart.png)

Source: GlobalData; Flaherty et al., 2012a; Uhara et al., 2014

### Discussion

#### Epidemiological Forecast Insight

GlobalData epidemiologists provided in this analysis the incident and five-year diagnosed prevalent cases of melanoma in the 8MM for 2013–2023. The incident cases are further segmented by age, sex, and pathological stage at diagnosis, and the diagnosed five-year prevalent cases are further segmented by genetic aberration (BRAF and NRAS). The forecast is based on strong historical, age-specific 10-year incidence data from 1997–2007 from the IARC’s CI-5Plus database.

Melanoma will likely remain underreported, as most in situ and superficial skin melanomas are treated in outpatient settings and are likely not reported to cancer registries. Current trends indicate that the majority of melanoma in the 8MM, except for in Japan, is diagnosed in the early stages. GlobalData epidemiologists expect this trend to hold true during the 10-year forecast period, as awareness of the risk factors associated with the disease increases through prevention campaigns targeting populations already at high risk and those individuals with increasing risk (such as young women ages ≤40 years). These disease awareness campaigns include education and public health awareness campaign efforts put forth by national and international public health organizations such as the CDC’s Choose Your Cover and the Burning Truth campaigns (Jorgensen et al., 2000). If the education and public awareness efforts put forth by national and international public health organizations such as the CDC and the WHO are successful, it is expected that this will lead to a reduction in the incidence of melanoma seen in several high-risk countries among recent birth cohorts. This could potentially change the forecast results, specifically the diagnosed incident cases.

#### Limitations of the Analysis

GlobalData epidemiologists came across several limitations in building this forecast. First, the literature uses several different staging systems. This required the establishing of an equivalency system in order to maintain consistency in disease definitions across the markets. The various disease staging systems included the AJCC stages and the SEER summary staging system. GlobalData epidemiologists defined the equivalencies between AJCC standardized stages and other the methods found in the literature in Table 2.
Secondly, rapidly changing genetic research and technology made it difficult to pinpoint the most accurate distributions of genetic aberrations in the five-year diagnosed prevalent cases included in the forecast. The most up-to-date data on the distribution of genetic aberrations in melanoma of the skin were used in this analysis. However, the distributions of genetic aberrations may need to be revised periodically to remain up-to-date with the research in this field.

Finally, the lack of robust and/or reliable data for certain markets or segmentations limited the integrity of the melanoma forecast. This limitation required that GlobalData epidemiologists perform multi-step calculations and use proxy data from markets with available data. GlobalData epidemiologists resolved this limitation by finding suitable sources for the data that could be used to extrapolate to other similar markets. For example, for most of the markets included in this report, relative survival by pathological stage was difficult to obtain. However, GlobalData epidemiologists extrapolated data from the Australian Cancer Network Melanoma Guideline and used within–stage exponential decay to calculate estimates for survival by pathological stage for all the other markets.

Future epidemiology research could include enhanced data collection for stage-specific data. For example, national and international cancer registries should collect and report data on survival by pathological stage. This would also require that staging for all cancers is required at diagnosis. AJCC staging for melanoma is a staging system that is reliable and precise with the potential for global application. Future epidemiology for melanoma should aim to follow AJCC staging for consistency across markets in order to alleviate the inconsistencies in the current available data on melanoma.

Strengths of the Analysis

This forecast is based on a thorough literature review and is supported by 10 years of historical data from IARC’s CI-5Plus database. The forecast for melanoma incident rates and diagnosed incident cases was based on detailed age-specific and sex-specific incidence trends in each of the 8MM from the CI-5Plus database published by the IARC of the WHO (Ferlay et al., 2014). The database provides validated annual diagnosed incidence data derived from country-specific registries and is considered a gold standard for international cancer data and related statistics (Ferlay et al., 2014).

GlobalData epidemiologists maintained consistent disease definition and forecasting methodology across all 8MM included in the report. This allowed for a meaningful comparison of the detailed segmentations of the melanoma patient populations included in this report. In addition, GlobalData epidemiologists provided a comprehensive review of disease statistics and a realistic trend based on insights gained through research and analysis.

GlobalData epidemiologists compared the diagnosed incident case estimates for melanoma from this forecast with the number of estimated incident cases from IARC’s Globocan 2012 to assess the validity of GlobalData’s epidemiological forecast. The comparison showed that the difference on average between the two sets of estimates was less than 12.52% (range: 0.14%–23.45%) (Ferlay et al., 2013b).

Frequency and characteristics of familial melanoma in Spain: the FAM-GEM-1 Study.


Abstract

INTRODUCTION:
Familial history of melanoma is a well-known risk factor for the disease, and 7% melanoma patients were reported to have a family history of melanoma. Data relating to the frequency and clinical and pathological characteristics of both familial and non-familial melanoma in Spain have been published, but these only include patients from specific areas of Spain and do not represent the data for the whole of Spain.

PATIENTS AND METHODS:
An observational study conducted by the Spanish Group of Melanoma (GEM) analyzed the family history of patients diagnosed with melanoma between 2011 and 2013 in the dermatology and oncology departments.

RESULTS:
In all, 1047 patients were analyzed, and 69 (6.6%) fulfilled criteria for classical familial melanoma (two or more first-degree relatives diagnosed with melanoma). Taking into account other risk factors for familial melanoma, such as multiple melanoma, pancreatic cancer in the family or second-degree relatives with melanoma, the number of patients fulfilling the criteria increased to 165 (15.8%). Using a univariate analysis, we determined that a Breslow index of less than 1 mm, negative mitosis, multiple melanoma, and a history of sunburns in childhood were more frequent in familial melanoma patients, but a multivariate analysis revealed no differences in any pathological or clinical factor between the two groups.

CONCLUSIONS:
Similar to that observed in other countries, familial melanoma accounts for 6.6% of melanoma diagnoses in Spain. Although no differences in the multivariate analysis were found, some better prognosis factors, such as Breslow index, seem more frequent in familial melanoma, which reflect a better early detection marker and/or a different biological behavior.

PMCID: PMC4395344 Free PMC Article

PMID: 25874698 [PubMed - indexed for MEDLINE]


Age-related characteristics of cutaneous melanoma in a Spanish Mediterranean population.

Montero I1, Requena C1, Traves V2, García-Casado F, Kumar R3, Nagore E1.

Author information: 1Department of Dermatology, Instituto Valenciano de Oncologia, Valencia, Spain. 2Department of Pathology, Instituto Valenciano de Oncologia, Valencia, Spain. 3Department of Molecular Biology, Instituto Valenciano de Oncologia, Valencia, Spain. 4Division of Molecular Genetic Epidemiology, German Cancer Research Center, Heidelberg, Germany. 5Universidad Católica de Valencia, Valencia, Spain.

Abstract

BACKGROUND:
Melanoma is considered a heterogeneous tumor with genetic and environmental factors involved in its pathogenesis. The impact of these factors varies depending on age.

OBJECTIVE:
The aim of this study was to characterize the epidemiological, phenotypic, and histological features of patients with melanoma according to three age groups: ≤40, 41-65, and >65 years.

METHODS:

A total of 1122 consecutive patients with invasive melanoma definitively treated in our institution since January 2000 were selected from our melanoma database. Epidemiological, phenotypic, and histological data were retrieved and analyzed as a function of age.

RESULTS:

Female patients predominated in the younger age group. The location of cutaneous malignant melanoma differed with age. In the younger and middle age groups, tumors presented mainly on the trunk, while in the older group they were mainly found on the head/neck. Signs of actinic damage such as actinic keratoses, solar lentigines, or other skin tumors increased with age, while genetic factors such as family history of melanoma or a high number of common melanocytic nevi were more frequent in the younger group.

CONCLUSION:

Our results suggest that melanoma development in younger patients is the result of genetic factors, particularly related to multiple nevi, whereas in older patients environmental factors such as severe chronic sun exposure play a major role.

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PMID: 25771683 [PubMed - indexed for MEDLINE]

Similar articles


Author information:

1 Melanoma Unit, Dermatology Department, Hospital Clinic of Barcelona, University of Barcelona, IDIBAPS, ES-08036 Barcelona, Spain. spuig@clinic.ub.es, susipuig@gmail.com.

Abstract

All cases of MM diagnosed in 23 hospitals in Catalonia, from 2000 to 2007 were recorded and melanoma incidence calculated and adjusted for the European standard population via the direct method. The age standardised rate/100,000 inhabitants varied from 6.74 in 2000 to 8.64 in 2007 for all melanomas and from 4.79 to 5.80 for invasive MMs; the Breslow thickness was stable during the period. The increase in invasive melanoma incidence in the elderly was remarkable, the crude rate/100,000 inhabitants increasing from 11.04 (2000) to 15.49 (2007) in the 60-64 year population, while remaining more stable in the 30-34 year range, from 3.97 in 2000 to 4.55 in 2007, and with a tendency to decrease from 5.1 in 2000 to 2.5 in 2007 for the age range of 25-29 years. These lower age ranges are much more affected by immigration. Despite the large immigrant population (nearly one million immigrants arrived in Catalonia during the study period from countries with a low melanoma incidence), melanoma incidence in our region has risen considerably and this trend is likely to persist in the near future.

PMCID: PMC4753069 Free PMC Article

PMID: 25367888 [PubMed - indexed for MEDLINE]
Spain.

Abstract

Several MC1R variants are associated with increased risk of malignant melanoma (MM) in a variety of populations. We aim to examine the influence of the MC1R variants (RHC: D84E, R151C, R160W; NRHC: V60L, R163Q and the synonymous polymorphism T314T) on the MM risk in a population from the Canary Islands. Overall, 1,046 Caucasian individuals were included in the study. A thousand of them were genotyped for MC1R variants: 509 were sporadic MM patients and 491 were healthy control subjects from general population. The analysis was adjusted for age, sex, hair colour, eye colour, skin phototype and ancestry. We found that carriers of the R151C and R163Q variants were at an increased risk for melanoma OR 2.76 (1.59-4.78) and OR 5.62 (2.54-12.42), respectively. The risk of carrying RHC variants was 3.04 (1.90-4.86). Current study confirms the increased MM risk for R151C carriers. It also supports the association between R163Q variant and MM risk in the population on the Canary Islands, as opposed to reported on northern populations. These results highlight the importance of the sample population selection in this kind of studies.

PMID: 24170137 [PubMed - indexed for MEDLINE]

Similar articles


Melanoma characteristics at diagnosis from the Spanish National Cutaneous Melanoma Registry: 15 years of experience
[Article in English, Spanish]


Author information: 1Servicio de Dermatología, Hospital Ramón y Cajal, Madrid, España.

Abstract

BACKGROUND AND OBJECTIVES:

The Spanish National Cutaneous Melanoma Registry (Registro Nacional de Melanoma Cutáneo [RNMC]) was created in 1997 to record the characteristics of melanoma at diagnosis. In this article, we describe the characteristics of these tumors at diagnosis.

PATIENTS AND METHODS:

This was a cross-sectional observational study of prevalent and incident cases of melanoma for which initial biopsy results were available in the population-based RNMC.

RESULTS:

The RNMC contains information on 14,039 patients. We analyzed the characteristics of 13,628 melanomas diagnosed between 1997 and 2011. In total, 56.5% of the patients studied were women and 43.5% were men. The mean age of the group was 57 years (95% CI, 56.4-57 years) while median age was 58 years. The most common tumor site was the trunk (37.1%), followed by the lower limbs (27.3%). The most frequent clinical-pathologic subtype was superficial spreading melanoma (n=7481, 62.6%), followed by nodular melanoma (n=2014, 16.8%). Localized disease was observed in 86.2% of cases (n=10,382), regional metastasis in 9.9% (n=1188), and distant metastasis in 3.9% (n=479). Independently of age at diagnosis, men had thicker tumors, more ulceration, higher lactate dehydrogenase levels, and a higher rate of metastasis than women (P<.001).

CONCLUSIONS:

Based on our findings, melanoma prevention campaigns should primarily target men over 50 years old because they tend to develop thicker tumors and therefore have a worse prognosis.

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PMID: 23622931 [PubMed - indexed for MEDLINE]

Similar articles

NRAS and BRAF mutations in cutaneous melanoma and the association with MC1R genotype: findings from Spanish and Austrian populations.

Hacker E1, Nagore E, Cerrore L, Woods SL, Hayward NK, Chapman B, Montgomery GW, Soyer HP, Whiteman DC.

Author information: 1Genetics and Computational Biology Department, Queensland Institute of Medical Research, Brisbane, Queensland, Australia.

Comment in


Abstract

There is increasing epidemiologic and molecular evidence that cutaneous melanomas arise through multiple causal pathways. To further define the pathways to melanoma, we explored the relationship between germline and somatic mutations in a series of melanomas collected from 134 Spanish and 241 Austrian patients. Tumor samples were analyzed for melanocortin-1 receptor (MC1R) variants and mutations in the BRAF and NRAS genes. Detailed clinical data were systematically collected from patients. We found that NRAS-mutant melanomas were significantly more likely from older patients and BRAF-mutant melanomas were more frequent in melanomas from the trunk. We observed a nonsignificant association between germline MC1R status and somatic BRAF mutations in melanomas from trunk sites (odds ratio (OR) 1.8 (0.8-4.1), P=0.1), whereas we observed a significant inverse association between MC1R and BRAF for melanomas of the head and neck (OR 0.3 (0.1-0.8), P=0.02). This trend was observed in both the Spanish and Austrian populations.

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PMID: 23096702 [PubMed - indexed for MEDLINE]

Similar articles


Epidemiological changes in cutaneous melanoma: retrospective study of 969 cases (1996-2010).
(Article in English, Spanish)


Author information: 1Servicio de Dermatología, Hospital General Universitario Gregorio Marañón, Madrid, Spain. jaavilesizquierdo@gmail.com

Abstract

BACKGROUND:

The incidence of malignant melanoma has increased over recent decades all over the world; however, we are not aware if this also occurs in Madrid. Our objective was to analyze epidemiological changes in cutaneous malignant melanomas diagnosed over a 15-year period.

PATIENTS AND METHODS:

Retrospective analysis of data of patients with primary cutaneous melanomas attended at Hospital Gregorio Marañón, Madrid, Spain, between 1996 and 2010, divided into three periods: 1996-2000; 2001-2005; 2006-2010, was obtained.

RESULTS:

In total, 969 melanomas were histologically diagnosed. The mean age at the moment of diagnosis was 58.5 years old. The mean tumor thickness was 1.61 mm. The most common histological type was surface-spread melanoma and the most common site was the trunk. There were statistically significant differences (P < .05) between the three periods of the study: older age at diagnoses (P < .001); larger number of head and neck melanomas (P < .001); more melanomas on trunk in women (P < .001); increase of lentigo maligna melanoma (P < .001); thinner mean tumor thickness (Breast index) (P < .001); larger number of melanomas in situ (P < .001). However, thick melanomas (tumor thickness over 2 mm) ratio was still over 20% in all periods, especially in males and in those over 65 years old.

CONCLUSIONS:

Diagnosis of cutaneous melanoma in Spain is made increasingly with a thinner mean tumor thickness, although thick melanomas are still diagnosed in men and in individuals over 65 years.

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INTRODUCTION:

It is important to identify subgroups within the general population that have an elevated risk of developing cutaneous melanoma because preventive and early-detection measures are useful in this setting. The findings of most studies that have evaluated risk factors for cutaneous melanoma are of limited application in Spain because the populations studied have different pigmentary traits and are subject to different environmental factors.

OBJECTIVE:

To identify the phenotypic characteristics and amount of exposure to sunlight that constitute risk factors for cutaneous melanoma in the population of the Autonomous Community of Valencia, Spain.

METHODS:

We performed a multicenter observational case-control study. In total, the study included 242 patients with melanoma undergoing treatment in 5 hospitals and 173 controls enrolled from among the companions of the patients between January 2007 and June 2008. The information was collected by means of a standardized, validated questionnaire. The odds ratio (OR) was calculated for each variable and adjusted using a multiple logistic regression model.

RESULTS:

The risk factors found to be statistically significant were skin phototypes I and II, blond or red hair, light eye color, abundant melanocytic nevi, and a personal history of actinic keratosis or nonmelanoma skin cancer. After the multivariate analysis, only blond or red hair (OR=1.9), multiple melanocytic nevi (OR=3.1), skin phototypes I a and II (OR=2.1), and a personal history of actinic keratosis (OR=3.5) or nonmelanoma skin cancer (OR=8.1) maintained significance in the model as independent predictive variables for melanoma.

CONCLUSIONS:

Our study supports the importance of certain factors that indicate genetic predisposition (hair color and skin phototype) and environmental factors associated with exposure to sunlight. Patients with multiple acquired melanocytic nevi and patients with markers of chronic skin sun damage (actinic keratosis and nonmelanoma cancer) presented a significant increase in risk.

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PMID: 22626452 [PubMed - indexed for MEDLINE]
A divergent pathway model to cutaneous melanoma is commonly accepted: sun sensitivity/chronic sun exposure and melanocytic instability. Although this dual model explains the development of most melanomas, clinical experience suggests other possible routes. The aim of this study was to explore the characteristics of patients who do not fit with these two pathways. We selected 818 patients with nonacral cutaneous melanoma and defined three groups: nevus-prone individuals, sun-sensitive individuals, and non-nevus-prone and non-sun-sensitive individuals. This group included patients without identifiable melanoma risk factors and comprised 52 patients (5.5% of the overall nonacral melanoma population). These patients were more frequently women, were more likely to present melanoma at a very young age (13.5% before 25 years), to have less frequent personal history of melanoma and remnants of pre-existing nevi, and to present tumors on the trunk and legs. We have identified a group of patients with fewer risk factors for melanoma that needs further studies to increase our understanding of melanoma development.

PMID: 22516967 [PubMed - indexed for MEDLINE]


Prevalence of ocular and oculodermal melanocytosis in Spanish population with uveal melanoma.
Carreño E1, Saenil MA, García-Alvarez C, López-Lara F, De Frutos-Baraja JM, Almaraz A.

Author information: 1Ophthalmology Department, Hospital Clinico Universitario, Valladolid, Spain.

Abstract

PURPOSE:
The aim of this study was to determine the prevalence of ocular and oculodermal melanocytosis (ODM) among patients with uveal melanoma (UM) in a Spanish population.

METHODS:
Retrospective review of the medical records of patients with ODM among patients with UM.

RESULTS:
Ten (11 eyes) of 400 patients (2.7%) with UM associated had ODM. The mean age at diagnosis of UM among patients with ODM was 62 years. One patient had bilateral tumours. UM was diagnosed during a routine-examination in two cases. All tumours were medium (7/11) or large (4/11) in size, with a mean maximum base of 13 mm and height of 7 mm. No patient had extraocular extension or metastatic disease at diagnosis. Enucleation was done in five cases and I-125-brachytherapy in six. The mean follow-up was 43 months. One patient died because of metastasis 2 years after enucleation; one patient is currently on treatment of systemic metastasis 11 years after.

CONCLUSIONS:
ODM is more frequent in Spanish population with UM than in American population. Despite the risk of UM in ODM, it is often diagnosed late when a conservative treatment is not indicated.

PMCID: PMC3259590 Free PMC Article

PMID: 22020174 [PubMed - indexed for MEDLINE]


Analysis of phenotypic characteristics and exposure to UV radiation in a group of patients with cutaneous melanoma.
Fagundo E1, Rodríguez-García C, Rodríguez-G, González S, Sánchez B, Jiménez A.

Author information: 1Departamento de Dermatología, Hospital Universitario de Canarias, España.
Abstract

BACKGROUND:

Melanoma is the most serious type of skin cancer and is caused by a combination of endogenous and exogenous risk factors. Here we describe the clinical and anatomical characteristics of melanoma along with the endogenous and exogenous risk factors in 120 patients diagnosed with cutaneous melanoma in a health care area of the province of Santa Cruz de Tenerife in Spain.

PATIENTS AND METHODS:

A descriptive, cross-sectional study was undertaken in patients diagnosed with melanoma between January 1999 and July 2005 in the health care area served by Hospital Universitario de Canarias. Data were collected on demographic characteristics, phenotype, sun exposure, sun protection, and actinic damage.

RESULTS:

Melanoma was most commonly diagnosed in women (62.5%) and lesions were most frequently located on the trunk. The most frequent tumor subtype was superficial spreading melanoma (63.3%) and 51.5% of patients were classified as having skin phototype II. Intermittent sun exposure was reported by 81.8% of patients and 50% had a moderate cumulative sun exposure (50-120 h/y). Multiple melanomas were present in 3.3% of patients. In 43% of patients, the time to diagnosis of melanoma was more than 24 months.

CONCLUSIONS:

A substantial percentage of melanomas were associated with actinic damage. Differences were observed in the level of sun exposure according to melanoma subtype. The most common causes for concern were growth and color changes in the lesion, and a substantial number of patients waited for some time between observing these changes and consulting a doctor.

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Similar articles


Phenotypic and histologic characteristics of cutaneous melanoma in patients with melanocortin-1 receptor polymorphisms.
Avilés JA, Lázaro P, Fernández LP, Benítez J, Ibarrola-Villava M, Ribas G.

Author information:
Servicio de Dermatología, Hospital General Universitario Gregorio Marañón, Madrid, Spain. jaavilesizquierdo@gmail.com

Abstract

BACKGROUND:

The melanocortin-1 receptor (MC1R) is an important risk factor for melanoma due to its role in the production of melanin in response to sun exposure.

OBJECTIVES:

To analyze the phenotypic and histologic characteristics of cutaneous melanoma in patients carrying mutations in MC1R and assess the influence of sun exposure on the occurrence of melanoma.

MATERIAL AND METHODS:

A total of 224 patients with a diagnosis of melanoma seen in the Department of Dermatology at Hospital General Universitario Gregorio Marañón in Madrid, Spain between September 2004 and December 2009 were included in the study. The genomic sequence of MC1R was analyzed by polymerase chain reaction.
RESULTS:

At least one of the following MC1R variants was present in 58% of the patients: V60L, V92M, I155T, R160W, D294H, and R163Q. Carriers of those variants had a history of sunburn (P=.018) and melanomas located on areas with intermittent sun exposure (P=.019), and the majority had a diagnosis of superficial spreading melanoma. These associations were especially significant in patients with the R160W and D294H variants. Carriers of R160W also had melanomas associated with melanocytic nevi (P=.028).

CONCLUSIONS:

The results of our study suggest that there may be a relationship between the expression of certain MC1R variants and sun exposure, history of sunburn, and skin type. They also indicate a higher frequency of superficial spreading melanomas and melanomas associated with melanocytic nevi in patients carrying certain mutations in MC1R.
In-transit metastases have been associated with a variety of negative prognostic factors in patients with cutaneous melanoma. It has recently been suggested that sentinel lymph node biopsy (SLNB) may lead to an increase in the incidence of this particular type of metastasis. In this study, we analyzed risk factors for the appearance of in-transit metastasis and its potential association with the use of SLNB.

MATERIAL AND METHODS:

A prospective study was undertaken in a cohort of 404 patients with cutaneous melanoma seen in the melanoma unit of Hospital San Cecilio in Granada, Spain. Statistical analysis was performed with SPSS 15.0 and Epidat 3.1 using the χ² and Fisher exact tests.

RESULTS:

Out of 93 (23%) patients with recurrence at any time, 28 (6.9%) had in-transit metastases. The occurrence of in-transit metastasis was associated with age greater than 50 years, greater Breslow depth and Clark level, the presence of ulceration, positive SLNB, and the presence of other types of recurrence (local recurrence, lymph node metastasis, or distant metastasis). There was no relationship between surgical treatment or performing SLNB and the presence of in-transit metastasis.

CONCLUSIONS:

The risk factors for in-transit metastases are the same as those for any type of recurrence and coincide with factors linked to poor prognosis. Given that in-transit metastases are much more common in patients with positive SLNB, while the technique itself is not linked to their occurrence, these findings suggest that the appearance of in-transit metastasis is linked to biological characteristics of the tumor cells rather than an influence of the surgical technique.

e-education salud 2016

PMID: 21559390 [PubMed - indexed for MEDLINE]

Similar articles


Malignoma, altitude, and UV-B radiation.
[Article in Spanish]

Aceituno-Madera P1, Buendía-Eisman A, Olmo FJ, Jiménez-Moleón JJ, Serrano-Ortega S.

Author information: 1Servicio de Dermatología, Hospital Clínico Universitario San Cecilio, Granada, España. pedroaceituno40@hotmail.com

Abstract

BACKGROUND AND OBJECTIVES:

UV radiation is the main modifiable risk factor for the development of cutaneous melanoma. Many people in the Spanish province of Granada live at high altitudes and, therefore, receive high doses of UV-B radiation. The aims of this study were to assess the possible association between melanoma and altitude and to measure the daily erythemal dose at different altitudes.

MATERIAL AND METHODS:

An epidemiological study was carried out between 1982 and 2007 to assess the relationship between altitude, daily erythemal dose, and the prevalence of melanoma. We calculated the prevalence of melanoma in patients with a clinical and histological diagnosis of melanoma at Hospital Clínico Universitario San Cecilio in Granada, Spain. All individuals were required to be residents of the province of Granada in order to be included in the study. The prevalence of melanoma was calculated for altitude intervals of 100 m. Daily erythemal dose was estimated using measures of UV-B radiation obtained with pyranometers at altitudes of 0, 680, 1200, and 3398 m above sea level during the Evaluation of the Effects of Elevation and Aerosols on UV Radiation (VELETA) 2002 field campaign.

RESULTS:

The highest prevalence of melanoma was found between 1400 and 1499 m above sea level (the interval at which the highest settlements are found), with a rate of 2.36 cases per 1000 inhabitants (95% confidence interval, 0.64-6.03). Above 700 m, the daily erythemal dose increased exponentially with increasing altitude.

CONCLUSIONS:

We observed a tendency toward increased prevalence of melanoma at higher altitude, with higher prevalences observed beyond 700 m above sea level.

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PMID: 21334587 [PubMed - indexed for MEDLINE]

Similar articles


Defining fast-growing melanomas: reappraisal of epidemiological, clinical, and histological features.


Author information: 1Instituto Valenciano de Oncología, c/Profesor Beltrán Báguesa 8, Valencia, Spain.

Abstract

The growth rate (GR) of melanomas is not uniform. A fast-growing subtype has been identified and seems to have a role in the stabilization of the mortality rates because of melanoma. To examine features associated with fast-growing melanomas (FGMs) and to determine the relationship between the GR and well-recognized prognostic factors of melanoma, a series of 386 new invasive cutaneous melanomas seen during 2004-2009
were retrieved from our database. The GR was calculated according to earlier published studies. FGMs were defined as those whose GR was greater than 0.49 mm per month. Differences in clinical, epidemiological, and pathological features were evaluated. Correlations between the GR, tumor thickness, and mitotic rate were also analyzed. FGMs were significantly more prevalent among patients aged over 65 years and with a higher rate of past personal history of nonmelanoma skin cancer. This subtype was over-represented among melanomas located on both nonexposed and usually exposed skin and was less related to earlier sunburns. Patients with FGMs presented with more aggressive pathological features and had more advanced disease with sentinel node analysis affected in up to 35% of cases. There was a strong positive correlation between the GR and tumor thickness (r=0.762), and mitotic rate (r=0.542). This study was limited by being retrospective in nature. FGMs are a highly aggressive subtype of melanomas that seem to develop after at least two routes, one related to chronic sun exposure and another unrelated to the sun. Older patients have a higher predisposition to develop this kind of tumor. This variant warrants specific strategies to improve primary and secondary prevention.

PMID: 21183860 [PubMed - indexed for MEDLINE]

Similar articles


Rapid increase in incidence of melanoma in situ in Girona (Spain), 1994-2005: Effectiveness of public education campaigns about early detection.

[Article in Spanish]


PMID: 20738982 [PubMed - indexed for MEDLINE]

Similar articles


Rising trends in incidence of cutaneous malignant melanoma and their future projections in Catalonia, Spain: increasing impact or future epidemic?


Author information: 1 Girona Cancer Registry and Catalan Cancer Plan, Department of Health, Regional Government of Catalonia, Barcelona, Girona. rmarcos@ico.scs.es

Abstract

BACKGROUND:

During the past decades, there has been a substantial increase in the incidence of cutaneous malignant melanoma (CMM) among all Caucasian populations. Spain presents one of Europe's lowest incidence and mortality rates.

OBJECTIVE:

The aim of this study was to analyse the recent trends of CMM incidence and mortality in a region with lower incidence as well as to project their future trends.

METHODS:

Cutaneous malignant melanoma incidence data were provided by the Tarragona and Girona population-based cancer registries and mortality data were provided by the Mortality Registry of Catalonia. Time trends of incidence and mortality rates by CMM were assessed through the estimated annual percentages of change of the incidence and mortality age-standardized rates to the World Standard Population. Projections were based on a Bayesian age-period-cohort model using second order autoregressive effects on age.

RESULTS:

During the last 20 years CMM incidence has increased substantially at a faster rate than any other neoplasms in Catalonia, particularly among
women and this trend will probably continue for the next several years. Nevertheless, CMM mortality trends have been and probably will remain stable during this period.

CONCLUSION:

Improvements in preventive activities should be implemented to decrease incidence and mortality from this cancer. Monitoring stage-specific trends in CMM incidence can assess the impact of preventive strategies; for this reason more complete information on diagnostic features of CMM patients in the Spanish population-based cancer registries are necessary.

PMID: 20236382 [PubMed - indexed for MEDLINE]


Melanocortin receptor 1 variants and melanoma risk: a study of 2 European populations.


Author information: 1Division of Molecular Genetic Epidemiology, German Cancer Research Center, 69120 Heidelberg, Germany.
d.scherer@dkfz.de

Abstract

Variation within the melanocortin receptor 1 (MC1R) gene, that influences phenotypic traits and susceptibility to melanoma, is abundant across the populations. We assessed and compared the risk of melanoma in 2 European populations, German and Spanish, by genotyping MC1R variants through direct DNA sequencing from 1,185 melanoma cases and 1,582 controls. The presence of any variant in both populations was associated with a significantly increased risk of melanoma (odds ratio OR = 1.67, 95% confidence interval CI 1.40-1.99). The population attributable fractions (PAF) associated with the MC1R variants in both populations was over 25%. However, the results showed a statistically significant (p < 0.0001) higher frequency of MC1R variants in the German (70%) than in the Spanish population (60%). The red hair colour (RHC) variants, though associated with increased risk in both populations, were more common in the German than in the Spanish population (p < 0.0001). Interestingly, non-RHC variants increased the disease risk in the Spanish (OR = 1.60, 95% CI 1.20-2.14) but not in the German population (OR = 1.07, 95% CI 0.80-1.44). Although RHC variants explained a major proportion of the observed PAF in the German population, in the Spanish population the major contributor to the PAF was the non-RHC V60L variant. We also observed reduced historic linkage disequilibrium between the variants V92M and T314T in the gene in German melanoma cases. In conclusion, our data underscored the unambiguous importance of the MC1R variants towards the population burden of melanoma. However, the variants that are associated with the disease differ between the investigated populations.

Free Article

PMID: 19585506 [PubMed - indexed for MEDLINE]


Germline variation of the melanocortin-1 receptor does not explain shared risk for melanoma and thyroid cancer.

Bauer J, Weng J, Kebebew E, Soares P, Trovisco V, Bastian BC.

Author information: 1Department of Dermatology, Eberhard Karls University, Tübingen, Germany.

Abstract

BACKGROUND:

Recently, germline variants of the melanocortin-1 receptor (MC1R) have been shown to be associated with an increased risk for BRAF mutant but not BRAF wild-type cutaneous melanoma. Similar to melanoma, BRAF mutations are also commonly found in papillary thyroid carcinomas. Furthermore, patients with melanoma have an increased risk for thyroid carcinoma and vice versa.

METHODS:
To determine whether MC1R variation also represents a risk factor for BRAF mutant thyroid carcinomas, we sequenced BRAF and MC1R in two separate case-control cohorts.

RESULTS:

We demonstrate that MC1R is expressed in normal and neoplastic thyroid epithelial cells, albeit at lower levels than in melanocytes. In the first cohort of 66 follicular and 62 papillary thyroid carcinomas (PTC), and 128 matched controls from the San Francisco Bay Area we found no association between the number of MC1R variant alleles and thyroid cancer. Patients with BRAF-mutated tumors had a higher frequency of MC1R variant alleles than their matched controls (P = 0.039). However, contrary to the findings in melanoma, the odds ratio for having a BRAF mutant cancer decreased from 3.9 for carriers of one MC1R allele to 1.5 for carriers of two or more alleles. As the frequency of MC1R alleles varies highly among different ethnic populations, we analysed a second, ethnically more homogeneous cohort from Spain and Portugal, and found no association with PTC nor with BRAF-mutated PTC.

CONCLUSION:

Our data indicate that the strong association between BRAF mutations and MC1R variants previously found in melanoma does not extend to thyroid cancer.

PMCID: PMC2862686 Free PMC Article

PMID: 19493000 [PubMed - indexed for MEDLINE]

Similar articles
INTRODUCTION:

The incidence of melanoma has increased more than that of any other type of malignant tumor. Our aim was to analyze the changes in incidence of cutaneous melanoma in recent years in a Mediterranean population.

MATERIAL AND METHODS:

Patients with melanoma diagnosed between 1988 and 2006 were included in the study. Data from the first half of this period were compared with data from the second half.

RESULTS:

The number of in situ melanomas increased from 36/302 cases (11.92 %) in the first half of the period to 224/724 (30.94 %) in the second half. Melanomas measuring more than 4 mm increased from 29/302 cases (9.60 %) to 62/724 (8.56 %). The mean maximum thickness for the whole study period was 1.91 mm and was similar for both halves.

CONCLUSIONS:

The increase in incidence of melanoma in our population was due mainly to an increase in incipient cases. The proportion of melanomas larger than 4 mm remained constant, although, in absolute terms, twice as many such melanomas were detected per year. We believe that campaigns for prevention and early detection must continue, and should focus in particular on the older population.

PMID: 18558054 [PubMed - indexed for MEDLINE]
Abstract

BACKGROUND:

The incidence of melanoma and its associated mortality has stabilized over the recent years, due in part to efforts directed at better prevention and detection of these lesions. We analysed the trends in the distribution of melanomas, mainly according to their thickness.

METHODS:

Data from the Dermatology Service of ‘Virgen de la Victoria’ University Hospital in Malaga (Spain) showed a total of 459 cases of melanoma between 1990 and 2005, both inclusive. The lesions were stratified according to year of diagnosis (1990-96 and 1997-2005), sex, age (0-49, > or = 50), thickness (0-0.99, 1.00-1.99, and > or = 2 mm) and the histological subtype (lentigo maligna melanoma (LMM), superficial spreading melanoma (SSM), nodular melanoma (NM) and acral lentiginous melanoma (ALM)). Particular attention was given to the distribution of the groups according to thickness.

RESULTS:

The number of new cases rose by 92% between the two study periods (1990-1996 and 1997-2005). However, the number of new cases of thick melanoma remained almost constant over the two periods, being associated with persons over 50 years of age (65.1% vs. 64.3%), with men having half the cases (48.4% vs. 47%). The proportion of nodular melanomas within the group of thick melanomas was high in both periods (36.5% and 39.3%, respectively).

CONCLUSIONS:

This study shows that despite the large increase in new melanomas, the diagnosis of thick melanomas has remained constant, mainly in persons over the age 50 years, with a relative increase in men. New strategies and education programmes are, therefore, required for the early detection of this type of tumour to reduce its incidence in these patients.

PMID: 18081751 [PubMed - indexed for MEDLINE]
Abstract

Epidemiological studies on cutaneous melanoma in Mediterranean countries are scarce. Our aim was to perform a descriptive analysis of melanoma cases diagnosed in Valencia, Spain, and to evaluate the relationship between Breslow thickness and some clinical features. A total of 1571 patients with histologically confirmed cutaneous malignant melanoma diagnosed at the two main referral melanoma centres were evaluated retrospectively. For each patient the following clinical and pathological characteristics were selected: age, gender, anatomic site, histogenetic type, Breslow thickness, presence of ulceration, the stage, and symptoms such as bleeding, changes in size and colour, altered sensations and previous traumas. Chi-squared tests were performed together with logistic regression to evaluate the relationship of variables with tumour thickness. Tumour thickness was independently correlated with increasing age, presence of bleeding, location on hand or foot, and presence of altered sensations. Female sex and presence of a change in colour were associated with thin melanomas. Ideally, public awareness campaigns concerning the risks that exist should be aimed at subgroups such as men and people of an advanced age who generally present with thicker tumours. Emphasis should be placed on irregularities or changes in pigmentation, as these appear to be the first indicators of the development of a melanoma.

PMID: 16585990 [PubMed - indexed for MEDLINE]
RESULTADOS DE GOOGLE SCHOLAR

1. Estimación de las proyecciones de las tasas de incidencia, prevalencia y mortalidad por melanoma en España Projections of incidence, prevalence and mortality from melanoma in Spain

Bernal M, Bezerra DL, Gómez FJ, Gómez

Med Cutan Iber Lat Am 2014; 42 (1-3): 23-29


RESUMEN

Las tasas de incidencia y de mortalidad por melanoma cutáneo se incrementaron notablemente en los últimos años en todo el mundo, representando en España tasas medias del global general. Material y métodos: Como fuente de datos se han utilizado las estadísticas de mortalidad del Instituto Nacional de Estadística. El método utilizado ha sido MIAMOD. Resultados: Solamente se han observado incrementos en la mortalidad por melanoma cutáneo en las mujeres. Tanto en las tasas de incidencia en mujeres como en las tasas de incidencia y mortalidad en hombres no se aprecian variaciones estadísticamente significativas. Conclusiones: Es necesario mantener la prevención primaria y secundaria para esta enfermedad porque se espera tener incrementos en la mortalidad en hombres.

2. Comportamiento epidemiológico del cáncer de piel en Nariño.

Ceballos YF, Arellano NM, Argoty YL, España ZY, Arroyo CG.


Resumen

El carcinoma (Ca) de piel es la neoplasia maligna más frecuente, de crecimiento lento y alta morbilidad. Aquí se describe su comportamiento epidemiológico en pacientes atendidos en el Hospital Universitario Departamental de Nariño (H.U.D.N.) y la Fundación Hospital San Pedro (F.H.S.P.). Este estudio descriptivo-retrospectivo con enfoque cuantitativo, se realizó con una población total de 393 casos de cáncer de piel diagnosticados histopatológicamente, atendidos entre los años 2005 y 2007, de los cuales 218 fueron registrados en el H.U.D.N para una proporción del 55.5% y 175 registrados en la F.H.S.P para una proporción del 44.5%. El promedio general de edad de los pacientes es de 64,8 años: una mediana de 68,5 y un 75% por encima de los 54. En relación a la altura sobre el nivel del mar, sólo el 12% reside en municipios que quedan por debajo de los 1500 msnm, proporción que sube al 35% cuando se incluye los residentes en municipios ubicados por debajo de los 2000 msnm. El hecho de vivir en la zona centro del departamento tiene una baja asociación con la impasividad del cáncer de piel (OR cercano a 1) aunque sea estadísticamente significativo. La residencia en la zona sur se presenta como un factor de riesgo. Según el tipo histológico, el Ca. basocelular es el tipo más frecuente con el 56.7% de casos, seguido por el Ca. escamocelular con un 25%. En todos los tipos hay una mayor proporción de casos en mujeres que en hombres, siendo más homogénea esta proporción para el Ca. escamocelular.

3. Cytogenetic analysis of choroidal melanoma

Filloy A, Caminal JM, Varela MM, Gomà M, Arias L, Arruga J.

Archivos de la Sociedad Española de Oftalmología (English Edition), Volume 89, Issue 1, January 2014, Pages 17-21

Resumen

Objetivo

Investigar la presencia de las alteraciones citogenéticas conocidas del melanoma de coroides en una serie de pacientes diagnostcados y tratados en nuestra Unidad de Oncología Ocular. También exponemos una revisión de la literatura actual sobre este tema.

Método

Durante dos años se han estudiado muestras procedentes de piezas de enucleación o de resección de melanoma corioideo de un total de 27 pacientes mediante análisis de microsatélites (MSA) para estudio de pérdida de heterocigosidad (LOH) del cromosoma 3 y mediante multiplex-ligation-prove amplification (MLPA) para los cromosomas 1, 3, 6 y 8.

Resultados

Entre los casos estudiados, 20 mostraron como mínimo una de las alteraciones citogenéticas que se buscaban, 11 LOH del cromosoma 3 (44%), 8 ganancias del cromosoma 6 p (30%), 8 ganancias en cromosoma 8 (30%) y 7 pérdidas totales o parciales del cromosoma 1 (26%).

Conclusiones

Este es el primer estudio citogenético del melanoma de úvea en nuestro país. La presencia y preponderancia de las distintas alteraciones citogenéticas se corresponden con las de las series publicadas en la literatura.
El análisis citogenético nos permite conocer mejor el pronóstico vital individualizado. También puede resultar una herramienta valiosa para establecer el protocolo de seguimiento más adecuado y la necesidad de tratamientos adyuvantes en estos pacientes.

4. Melanoma Characteristics at Diagnosis From The Spanish National Cutaneous Melanoma Registry: 15 Years of Experience

Resumen
Introducción y objetivos
El registro nacional de melanoma cutáneo (RNMC) se creó en el año 1997 con el objetivo de conocer las características del melanoma en el momento del diagnóstico. Se muestran las características de los tumores en el momento de su diagnóstico inicial.

Pacientes y métodos
Registro observacional transversal, con base poblacional. Se incluyeron casos incidentes y prevalentes de melanoma con resultados de la primera biopsia disponibles.

Resultados
El RNMC contiene información de 14.039 pacientes. Se analizaron las características del melanoma en los pacientes diagnosticados en el periodo 1997-2011, sumando un total de 13.628 melanomas. El 56,5% de los pacientes eran mujeres y el 43,5% hombres. La edad media fue de 57 años (IC 95%: 56,4 a 57), con mediana de 58 años. La localización más frecuente fue en el tronco (37,1%), seguido de la extremidad inferior (27,3%). El tipo clínico-patológico más observado fue el melanoma de extensión superficial en un 62,6% (n = 7.481), seguido del melanoma nodular en un 16,8% de los casos (n = 2.014). El 86,2% (n = 10.382) tenían enfermedad localizada, el 9,9% metástasis regionales (n = 1.188) y el 3,9% (n = 479) a distancia. Se observó en los hombres, independientemente de la edad de diagnóstico, un mayor espesor del tumor y una mayor proporción de tumores ulcerados, con niveles de lactatodeshidrogenasa elevados y con enfermedad metastásica (p < 0,0001).

Conclusiones
Con los resultados observados las campañas preventivas deberían orientarse al colectivo masculino mayor de 50 años, en el que se observan tumores de mayor espesor, y por lo tanto de peor pronóstico.

5. Melanoma maligno cutáneo: Estudio de su prevalencia en España en los últimos años y elaboración de medidas de prevención y diagnóstico precoz
Bondía M, Anguas A. Publication Date Apr 24, 2012.
https://www.mysciencework.com/publication/show/9cf5ee8d626c7dd260b2c5f6d64314a

Abstract
El melanoma maligno cutáneo (MMC) ha experimentado un aumento considerable a lo largo de los últimos años a nivel mundial. España sufre un periodo de continuo aumento de la incidencia de MMC en la época comprendida entre los años 1978-2002, alcanzando la tasa más alta en el periodo 1998-2002. A pesar de ello, nuestro país está considerado como uno de los países con cifras más bajas de incidencia y mortalidad de Europa. El número de campañas de prevención y promoción de salud han aumentado con el fin de conseguir que la población tome conciencia de la importancia de esta patología y adopte hábitos de vida saludable, si bien es verdad que estas campañas continúan siendo escasas hasta la fecha. Mediante la información recopilada se han realizado dos protocolos tipo de valoración de riesgo de melanoma maligno y de seguimiento de lunar maligno, con objeto de empezar a tomar medidas de prevención desde las consultas de Atención Primaria, puerta de acceso al sistema sanitario.

6. Perfil clínico y epidemiológico de los pacientes con melanoma cutáneo según el grado de exposición solar de la localización del melanoma
Actas Dermosifiliográficas. 2009; 10 (3):205–211

Resumen
Introducción
Se ha observado que los melanomas tienen un perfil genético similar según el patrón de exposición al sol de la área cutánea donde asientan. El objetivo de este estudio ha sido caracterizar desde el punto de vista clínico los pacientes con melanoma según su patrón de exposición al sol: crónico, intermitente y ausencia de exposición.

Material y métodos
Se seleccionaron 789 pacientes con melanoma diagnosticados en nuestro centro de forma consecutiva desde enero del año 2000 a partir de la base de datos de melanoma. Se obtuvieron los datos referentes a las características epidemiológicas, fenotípicas y los antecedentes personales y familiares de cáncer. Se compararon las frecuencias observadas de cada una de las variables estudiadas.
Resultados

Se observó que la mayoría de los pacientes tienen los melanomas en localizaciones expuestas al sol de forma intermitente. Además, estos pacientes tienen más nevus melanocíticos tanto comunes como atípicos y su melanoma se asocia con una elevada frecuencia a un nevus preexistente. Por otra parte, el segundo grupo en número está constituido por el grupo de pacientes con melanomas en áreas cutáneas expuestas al sol de forma crónica que presentaron todas las lesiones (lentigos solares y queratosis actínicas) y antecedentes típicos de esta localización. Finalmente, el grupo de melanomas que se presenta en áreas de piel no expuestas al sol tiene, al igual que el anterior, una edad de diagnóstico mayor y se diagnostican en fases avanzadas de la enfermedad.

Conclusiones

La presencia de un elevado número de pacientes que no sigue ninguno de los patrones mencionados suscita la necesidad de caracterizarlos clínicamente y biológicamente para conocer vías alternativas de desarrollo de un melanoma, y así poder establecer medidas preventivas adecuadas.
ÁREA DE ANÁLISIS EPIDEMIOLÓGICO Y SITUACIÓN DE SALUD. INSTITUTO DE SALUD CARLOS III

TENDENCIA TEMPORAL
Mortalidad por Melanoma
Entre los años 1990 Y 2014
Grupo de edad Todas edades
Territorio España
Número de defunciones

SERVIDOR INTERACTIVO DE INFORMACIÓN EPIDEMIOLÓGICA (ARIADNA)

1) Mujeres
Figura 1. Tasa ajustada a la población europea de melanoma en mujeres en España (2014)

Figura 2. Tasa ajustada de ranking de incidencia de melanoma en mujeres por provincias (2014)

2) Hombres
Figura 3. Tasa ajustada a la población europea de melanoma en hombres en España (2014)

Figura 4. Tasa ajustada de ranking de incidencia de melanoma en hombres por provincias (2014)
La Red Española de Registros de Cáncer (REDECAN), ha realizado el informe sobre las Estimaciones de la Incidencia y la Supervivencia del Cáncer en España y su Situación en Europa. El objetivo de este trabajo es describir la situación del cáncer en nuestro país, a partir de los datos de incidencia disponibles en la base de datos de la Red Española de Registros de Cáncer (REDECAN), los datos de mortalidad proporcionados por el Instituto Nacional de Estadística (INE) hasta el año 2011 y los datos de supervivencia de los registros españoles participantes en el proyecto European Cancer Registry Based Study on Survival and Care of Cancer Patients en su quinta fase (EUROCARE-5).

Podemos destacar la siguiente tabla:
### Tabla 1: Estimaciones de la incidencia de cáncer en España para el año 2014

<table>
<thead>
<tr>
<th>Tipo tumoral</th>
<th>N Casos</th>
<th>IC 95%</th>
<th>TB IC 95%</th>
<th>TAm IC 95%</th>
<th>T Ae IC 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labio, Cavidad oral y Faringe</td>
<td>4,661</td>
<td>(3,884 - 6,103)</td>
<td>21,8</td>
<td>(17,1 - 27,2)</td>
<td>12,7</td>
</tr>
<tr>
<td>Esófago</td>
<td>1,960</td>
<td>(1,736 - 2,209)</td>
<td>6,6</td>
<td>(7,6 - 9,7)</td>
<td>4,8</td>
</tr>
<tr>
<td>Estómago</td>
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<td>(4,649 - 5,601)</td>
<td>22,8</td>
<td>(20,4 - 24,6)</td>
<td>11,0</td>
</tr>
<tr>
<td>Colon</td>
<td>15,198</td>
<td>(13,121 - 17,622)</td>
<td>59,6</td>
<td>(57,7 - 70,0)</td>
<td>31,5</td>
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<tr>
<td>Recto</td>
<td>2,816</td>
<td>(2,377 - 2,604)</td>
<td>39,4</td>
<td>(34,2 - 40,7)</td>
<td>18,3</td>
</tr>
<tr>
<td>Colonrectal</td>
<td>23,482</td>
<td>(21,264 - 26,031)</td>
<td>103,2</td>
<td>(93,2 - 114,3)</td>
<td>49,8</td>
</tr>
<tr>
<td>Hígado</td>
<td>4,076</td>
<td>(3,496 - 4,709)</td>
<td>17,9</td>
<td>(15,4 - 20,7)</td>
<td>9,5</td>
</tr>
<tr>
<td>Vescícu y vías biliareyes</td>
<td>1,061</td>
<td>(0,611 - 1,366)</td>
<td>4,6</td>
<td>(3,6 - 5,9)</td>
<td>2,1</td>
</tr>
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<td>Páncreas</td>
<td>3,405</td>
<td>(3,060 - 3,781)</td>
<td>15,0</td>
<td>(13,5 - 16,6)</td>
<td>7,5</td>
</tr>
<tr>
<td>Laringe</td>
<td>3,442</td>
<td>(3,003 - 3,918)</td>
<td>15,1</td>
<td>(13,2 - 17,2)</td>
<td>8,9</td>
</tr>
<tr>
<td>Pulmón</td>
<td>22,455</td>
<td>(19,952 - 25,212)</td>
<td>86,7</td>
<td>(87,7 - 110,8)</td>
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<tr>
<td>Melanoma cutáneo</td>
<td>2,512</td>
<td>(2,160 - 2505)</td>
<td>11,1</td>
<td>(9,5 - 12,8)</td>
<td>6,1</td>
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<tr>
<td>Próstata</td>
<td>32,041</td>
<td>(28,906 - 35,066)</td>
<td>143,5</td>
<td>(116,6 - 171,4)</td>
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<td>Testículo</td>
<td>997</td>
<td>(803 - 1,196)</td>
<td>4,4</td>
<td>(3,9 - 4,9)</td>
<td>4,3</td>
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<td>Riñón</td>
<td>3,523</td>
<td>(3,128 - 3,952)</td>
<td>15,5</td>
<td>(13,8 - 17,4)</td>
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<td>Vejiga urinaria</td>
<td>16,794</td>
<td>(15,091 - 18,534)</td>
<td>73,7</td>
<td>(66,3 - 81,5)</td>
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<td>Encéfalo y SNC</td>
<td>2,317</td>
<td>(2,078 - 2,578)</td>
<td>10,2</td>
<td>(9,1 - 11,3)</td>
<td>6,8</td>
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<td>Tiroides</td>
<td>801</td>
<td>(709 - 902)</td>
<td>3,5</td>
<td>(3,1 - 4,0)</td>
<td>2,3</td>
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<tr>
<td>Linfoma de Hodgkin</td>
<td>933</td>
<td>(819 - 1,032)</td>
<td>4,1</td>
<td>(3,6 - 4,5)</td>
<td>3,7</td>
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<td>Linfomas no hodgkinianos</td>
<td>8,185</td>
<td>(3,600 - 4,752)</td>
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<td>(16,1 - 20,9)</td>
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<td>Melanoma</td>
<td>1,465</td>
<td>(1,013 - 2,110)</td>
<td>6,4</td>
<td>(4,5 - 9,3)</td>
<td>3,0</td>
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<tr>
<td>Leucemias</td>
<td>3,653</td>
<td>(3,044 - 4,305)</td>
<td>16,0</td>
<td>(15,6 - 18,9)</td>
<td>9,4</td>
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<tr>
<td>Otros cánceres</td>
<td>6,084</td>
<td>(5,205 - 7,049)</td>
<td>26,7</td>
<td>(22,9 - 31,1)</td>
<td>14,3</td>
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<tr>
<td>Total exc. pial no melanoma</td>
<td>145,813</td>
<td>(138,709 - 153,734)</td>
<td>641,0</td>
<td>(606,8 - 676,8)</td>
<td>531,0</td>
</tr>
</tbody>
</table>

**Fuente:** Red Española de Registros de Cáncer

### RESULTADOS BASE DE DATOS ESPACENET

#### 1. SISTEMA DE RECOGIDA DE VARIABLES DE PARTICIPANTES EN ESTUDIOS EPIDEMIOLOGICOS

<table>
<thead>
<tr>
<th>Inventor:</th>
<th>Solicitante:</th>
<th>CPC:</th>
<th>IPC:</th>
<th>Información de publicación:</th>
<th>Fecha de prioridad:</th>
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<tbody>
<tr>
<td>BEJAR PRADO LUIS MARIA</td>
<td>UNIV SEVILLA</td>
<td>A61B5/00</td>
<td>A61B5/00</td>
<td>ES2399303 (A2)</td>
<td>2011-09-13</td>
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<td>BASTIAN BORIS CURTIN JOHN</td>
<td>REGENTS OF THE UNIV OF CALIFORNIA</td>
<td>C12Q1/6886 C12Q2600/106 C12Q2600/118 (+3)</td>
<td>C07H21/0/2 C07K14/435 (+3)</td>
<td>ES2577535 (T3)</td>
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**Tabla 1**: Estimaciones de la incidencia de cáncer en España para el año 2014
<table>
<thead>
<tr>
<th>Número</th>
<th>Tema</th>
<th>Autor(a)</th>
<th>Solicitante</th>
<th>CPC</th>
<th>IPC</th>
<th>Información de publicación</th>
<th>Fecha de prioridad</th>
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<td><strong>11. MELANOMA ANTIGENS</strong></td>
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</tbody>
</table>

| **12. Method for preventing or treating malignant melanoma** |   |   |   |
| Solicitante: |   | IPC: | A61K38/18 A61K38/57 (IPC1-7): A61K38/18 |

| **13. Method for reducing the risk of cancer** |   |   |   |
| Inventor: | [US] HOCK JANET M | CPC: | A61K2300/00 A61K38/29 |
| Solicitante: | HOCK JANET M | IPC: | A61K38/29 A61P9/08 A61P35/04 (+1) |

| **14. COMPOSITIONS TO REDUCE OR PREVENT SKIN CANCER** |   |   |   |
| Inventor: | [US] KISS ZOLTAN | CPC: | A61K2300/00 (+17) |