Survival in Patients With Uveal Melanoma in Europe

Gianni Virgili, MD; Gemma Gatta, MD; Laura Ciccolallo, MSc; Riccardo Capocaccia, MSc; Annibale Biggeri, MD; Emanuele Crocetti, MD; Jean-Michel Lutz, MD; Eugenio Paci, MD; for the EUROCARE Working Group

Objective: To estimate survival in patients in whom uveal melanoma was diagnosed between January 1, 1983, and December 31, 1994, in Europe.

Methods: Survival analysis of data from 32 cancer registries in 16 European countries adhering to the European Cancer Registry for 5788 patients with uveal melanoma diagnosed between January 1, 1983, and December 31, 1994, with follow-up to 1999.

Results: Five-year relative survival was 68.9% overall and remained stable with the period of diagnosis. Relative excess risk of death was 2.45 (95% confidence interval [CI], 2.10-2.86) in patients aged 75 years or older compared with patients aged 54 years or younger and was slightly higher in male patients (relative excess risk, 1.10; 95% CI, 1.02-1.19) than in female patients. Survival was similar in Nordic countries (relative excess risk, 1.03; 95% CI, 0.87-1.21) compared with the United Kingdom (reference country) and was lower in eastern and western European countries (1.26; 1.05-1.52, and 1.25; 0.90-1.60, respectively) compared with the reference country.

Conclusions: In this large series of patients with uveal melanoma, 5-year relative survival remained stable with the introduction of conservative treatment in individuals in whom uveal melanoma was diagnosed between 1983 and 1994. We found differences in survival between sexes and in European areas that should be investigated in studies that consider tumor characteristics at the individual level.

Arch Ophthalmol. 2008;126(10):1413-1418

Author Affiliations: Departments of Oto-Neuro-Ophthalmological Surgical Sciences (Dr Virgili) and Statistics "G. Parenti" (Dr Biggeri), University of Florence, and the Biostatistics Unit (Dr Biggeri) and the Clinical and Descriptive Epidemiology Unit (Drs Crocetti and Paci), Center for Study and Prevention of Cancer, Scientific Institute of the Tuscany Region, Florence; the Epidemiology Unit, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan (Dr Gatta and Ms Ciccolallo); Laboratory of Epidemiology, Istituto Superiore di Sanità, Rome (Mr Capocaccia), Italy; and Registre Genevois des Tumeurs, Geneva, Switzerland (Dr Lutz).

Group Information: A complete list of the members of the EUROCARE Working Group appears at the end of this article.

TREATMENTS OF UVEAL MELANOMA have changed with the progressive introduction of conservative management for smaller tumors during the 1980s.[1,2] Despite this therapeutic shift, 5-year relative survival (ie, the ratio of survival in patients with cancer to the survival expected from mortality in the general population) was reported to be stable at a level of approximately 80% of patients in a recent study based on the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) registries and conducted in the United States.[1] This 5-year rate is consistent with the results from the Collaborative Ocular Melanoma Study (COMS),[3] which found a similar survival rate after either enucleation or radiolabeled iodine 125 brachytherapy for medium-sized uveal melanomas.

CME available online at www.jamaarchivescme.com and questions on page 1335

The European Cancer Registry (EUROCARE)–based study of survival and care of patients with cancer, including data from 67 cancer registries with a combined population of 100 million persons in 22 European countries, offers a unique opportunity to study the epidemiology of rare cancers in a continental population. We recently reported the incidence of uveal melanoma using cancer registry data collected in the framework of the EUROCARE project from January 1, 1983, to December 31, 1994.[4] In the present study, we estimated survival and its possible temporal, demographic, and geographic variation in patients with uveal melanoma in the same cohort.

METHODS

DEFINITIONS AND INCLUSION CRITERIA

We analyzed data from 32 cancer registries for patients aged 15 to 99 years with a diagnosis of a selected rare cancer between 1983 and 1994. These data were from 16 European countries participating in EUROCARE.

Cases were defined as patients with ocular melanoma as identified by *International Classification of Diseases, Ninth Revision* (*ICD-9*) topography codes 190.0 (iris and ciliary body), 190.5 (retina), and 190.6 (choroid) and by *International Classification of Diseases for Oncology* morphology codes 8720 to 8780 (uveal melanoma). Based on the suggestion of Stang

Table 1. Registries Contributing Cases for the Present Study and Number of Patients With 5-Year Follow-up Data

Registry	No. of Cases	Registry	No. of Cases
United Kingdom		Western European area	
East Anglia	149	Bas Rhin	57
Mersey	146	Calvados Gen	32
Midlands	208	Eindhoven	49
Oxford	179	Geneva	21
Southwestern area	537	Latina	13
Thames	482	Mallorca	9
Trent	370	Navarra	15
Wales	200	Parma	22
Yorkshire	275	Ragusa	5
Nordic area		Saarland	66
Denmark	547	Tarragona	7
Finland	350	Turin	33
Iceland	14	Tuscany	47
Norway	442	Varese	35
Sweden	808	Eastern European area	
		Cracow	51
		Estonia	125
		Slovakia	345
		Slovenia	149

et al[5] and on an incidence study conducted by us in this same cohort,[4] we also included tumors with unspecified location (*ICD-9* code 190.9, part unspecified).

Contributing registries provided patient demographic data and vital statistics for 1983 to 1994 with follow-up to 1999. **Table 1** gives the registries and the number of cases for each. Verification of the diagnosis was classified as microscopic, clinical, or unknown. Microscopic verification is obtained when the eye is enucleated, whereas it can reasonably be assumed that the eye is treated conservatively with radiotherapy when the diagnosis is clinical. The number of tumors with unknown diagnostic verification was low (2.6%); thus, they were pooled with those clinically verified. Data were provided by 32 cancer registries (Table 1) in 16 countries. Because these countries differ noticeably in terms of economic development, social structure, and health care structure, we defined 4 geographic groups within which survival after common cancers are much the same[6-9]: United Kingdom; western Europe; eastern Europe; and the Nordic or Scandinavian area including Iceland. Data from the Scotland registry were eliminated as requested by the registry because of suspected undetected loss to follow-up. Therefore, the UK area includes only registries in England and Wales.

Only first occurring cancers at any site, as defined by *International Classification of Diseases for Oncology* morphology fifth-digit behavior code 3, were included in survival analyses. Both microscopically verified and nonverified cases were included, but cases known to registries by death certificate only or discovered incidentally at autopsy were excluded. Further details of the EUROCARE data set are available elsewhere.[6-9]

STATISTICAL ANALYSES OF RELATIVE SURVIVAL

Univariate 5-year relative survival obtained using SEER*Stat software (National Cancer Institute, Bethesda, Maryland)[10] is reported. For multivariate analysis of relative survival, we followed the approach for grouped data suggested by Hakulinen[11] and Dickman et al.[12] A relative survival model was used in the framework of generalized linear models to assess the effect of temporal, demographic, and geographic variables on risk of death to compute relative excess risk (RER) for categories of the same variable. The correlation of the data within registry was taken into account using a robust variance estimator.[13,14] Relative excess risk has also been referred to as excess hazard ratio and can be considered the excess hazard owing to diagnosis of cancer once the known baseline hazard, mortality in the general population, has been taken into account. Age was coded categorically in 3 bands in these models: 15 to 54 years, 55 to 74 years, and 75 years or older.

After temporal, demographic, and geographic variables were included in the regression model, the covariates coding for the type of diagnosis verification (microscopic vs clinical or unknown) and the tumor subsite were introduced into the model. Subsite was coded as typical uveal melanoma location (*ICD-9* codes 190.0, 190.5, and 190.6) or unspecified eye and orbit melanoma location (*ICD-9* code 190.9). Statistical analyses were made using commercially available software (STATA version 9.2; StataCorp LP, College Station, Texas).

RESULTS

Vital statistics for 5 years from diagnosis of uveal melanoma were obtained for 5788 incident melanomas during the 12 years of the study (1983-1994). Of the incident cohort of 6121 patients, 326 were excluded because they had other malignant lesions at baseline (n=269) or the diagnosis was made on the basis of the death certificate only (n=57). Seven additional patients were lost to follow-up.

UNIVARIATE ANALYSES OF 5-YEAR RELATIVE SURVIVAL

Table 2 gives the number of cases and 5-year relative survival by age, sex, period, geographic area, type of diagnosis verification, subsite, and year of follow-up. As expected, survival decreased with age and was lower in patients with tumors examined microscopically, which is a proxy of enucleation and, thus, of larger tumor size. Worse survival was also found for tumors with unspecified ocular subsite (*ICD-9* code 190.9). No substantial temporal trend could be identified; however, there were differences among geographic areas, with the UK and Nordic regions demonstrating better survival than the western and eastern European regions. **Table 3** gives 5-year relative survival rates for geographic areas across periods of diagnosis, which do not suggest a clear temporal trend in any of the 4 regions.

MULTIVARIATE ANALYSES

Table 4 gives the results of multivariate regression analyses for model 1, in which the covariates were age, sex, year of follow-up, and geographic area, and for model 2, in which the covariates tumor subsite and type of diagnosis verification were added. In model 1, RER was 10% higher in male patients and was about 2 and 2½ times higher, respectively, in the groups aged 55 to 64 years and 75 years or older compared with the group aged 54 years or younger. Mortality was much lower during the first year after diagnosis compared with later years; RER was about 1½ times higher for years 2 to 4 of follow-up compared with the first year. The period of diagnosis was

neither associated with survival nor is it an interaction with geographic area in any multiple regression models (data not shown). There were differences in survival among geographic areas (Table 4). Survival was similar in the Nordic area (RER, 1.03; 95% confidence interval [CI], 0.87-1.21) compared with the United Kingdom and in the eastern European area (RER, 1.01; 95% CI, 0.82-1.25) compared with the western European area. Survival was lower for the pooled western and eastern European areas compared with the pooled UK and Nordic areas (RER, 1.24; 95% CI, 1.09-1.41).

Model 2 shows that survival tended to be better for clinically verified tumors compared with microscopically verified tumors, as expected because enucleated tumors are typically larger at diagnosis. In addition, tumors with unspecified ocular location (*ICD-9* topography code 190.9) were associated with much higher mortality (RER, 1.46; 95% CI, 1.19-1.79), which suggests that this code is used for large tumors, for which the origin from typical uveal subsites (ie, iris and ciliary body vs choroid) is difficult or impossible to ascertain. This coding was more common in the United Kingdom (33.6% of all tumors) compared with the other areas (7.1%-13.3%). In this model, the difference between the United Kingdom and western Europe reached statistical significance ($P = .01$).

Table 2. Five-Year Relative Survival Rates

Variable	No. of Cases	5-Year Relative Survival, % (95% Confidence Interval)
Overall	5788	68.9 (67.4-70.4)
Age, y		
15-54	1681	79.0 (77.0-81.1)
55-74	2954	65.2 (63.2-67.3)
≥75	1153	58.8 (54.1-63.4)
Sex		
Female	2892	69.3 (67.2-71.4)
Male	2896	68.5 (66.3-70.7)
Study period		
1983-1985	1384	69.1 (66.0-72.2)
1986-1988	1455	69.2 (66.2-72.2)
1989-1991	1486	68.2 (65.2-71.2)
1992-1994	1463	69.1 (66.0-72.1)
Geographic region		
United Kingdom	2546	70.5 (68.2-72.8)
Nordic area	2161	69.2 (66.7-71.7)
Western European area	411	63.3 (57.7-69.0)
Eastern European area	670	65.4 (60.9-69.8)
Microscopic verification		
Yes	5113	67.9 (66.3-69.5)
No	675	76.7 (72.4-81.1)
Subsite (*ICD-9* code)		
Iris and ciliary body (190.0)	751	68.0 (63.8-72.2)
Choroid and retina (190.5-190.6)	4121	70.3 (68.6-72.1)
Unspecified ocular subsite (190.9)	916	63.0 (59.0-67.0)

Abbreviation: *ICD-9, International Classification of Diseases, Ninth Revision*.

COMMENT

We analyzed the largest published series of uveal melanomas to estimate relative survival based on 32 EUROCARE population-based cancer registries in 16 European countries, enabling us to study the effect of demographic characteristics and geographic area on survival as well as its temporal trend.

The 5-year relative survival rate was stable during the study period and was higher in the UK and Nordic areas compared with the western and eastern European areas. Lower survival rates were found for older age, male sex, and follow-up years 2 to 4. These results can be compared with those of 3 population-based studies that investigated 5-year relative survival in patients with uveal melanoma in the United States,[1] Sweden,[15] Denmark,[16] and England and Wales (UK study)[17] (**Table 5**). Although the samples in the 3 European studies overlap in part with our sample, the inclusion criteria differ, and we suggest that a comparison is useful.

OVERALL 5-YEAR RELATIVE SURVIVAL

Five-year relative survival in the present study was close to that of the 2 European studies[15,16] and was lower than in the US study[1] owing to differences in the inclusion criteria. The authors of the US study did not include melanomas with unspecified ocular location (*ICD-9* code 190.9), accounting for 31% of all cases of ocular melanoma in the earliest period (1973-1977) to less than 5% in the recent period of the study (1993-1997). However, there was indirect evidence from the present study and from an incidence report based on this same cohort[4] that this code was probably used for large uveal melanomas that were difficult to ascribe to a specific subsite. Tumors with unspecified ocular location were included in the Danish study,[16] whereas Bergman et al[15] did not include them but performed an extensive search of hospital files to determine all incident melanomas. Nevertheless, although better survival might have been the result, in part, of underascertainment of advanced cases in the US study as compared with the European studies, such a large difference is unlikely to be attributable to only this potential factor because in our study, 5-year relative survival was 70% for tumors located in the iris and ciliary body (*ICD-9* code 190.0) and was 68% for those located in the choroid and retina (*ICD-9* codes 190.6 and 190-5), which is still largely less than the relative survival in the US study. The findings in the UK study[17] confirm these observations; lack of inclusion of the unspecified site in the UK study led to an estimate of 5-year relative survival (72%) that was similar to ours. The authors observed that the differences may be attributable, in part, to how clinicians classify uveal melanoma and report to the cancer registries because survival in the United States is higher than in the United Kingdom for most major cancers.

TEMPORAL DIFFERENCES IN SURVIVAL

No temporal trend for change in relative survival was detected during our 12-year study, consistent with the results of the US,[10] Danish,[16] and UK[17] studies. Singh and Topham[1] reported that increasing frequency of globe conservation in primary uveal melanoma has not led to improvement in survival. However, the stability of population-

Table 3. Five-Year Relative Survival by Geographic Area Across Period of Diagnosis and Overall

Period of Diagnosis	Geographic Region: United Kingdom, No. (%)	Nordic Area, No. (%)	Western European Area, No. (%)	Eastern European Area, No. (%)	Total, No. (%)
1983-1985	612 (66.6)	522 (71.5)	86 (65.5)	164 (72.7)	**1384** (69.1)
1986-1988	643 (73.7)	547 (66.2)	94 (65.9)	171 (64.0)	**1455** (69.2)
1989-1991	672 (71.7)	527 (68.6)	113 (56.3)	174 (61.6)	**1486** (68.2)
1992-1994	619 (69.7)	565 (70.4)	118 (66.6)	161 (63.7)	**1463** (69.1)
Overall	**2546** (70.5)	**2161** (69.2)	**411** (63.3)	**670** (65.4)	**5788** (68.9)

Table 4. Relative Excess Risk of Death: Model 1 vs Model 2

Variable	Relative Excess Risk (No. [95% CI]): Model 1	Model 2	*P* Value
Follow-up year			<.001
1	1 [Reference]	1 [Reference]	
2	1.50 (1.14-1.96)	1.49 (1.11-1.98)	
3	1.67 (1.28-2.17)	1.66 (1.26-2.19)	
4	1.58 (1.12-2.23)	1.58 (1.10-2.27)	
5	1.25 (0.86-1.81)	1.25 (0.85-1.83)	
Age, categorical, y			<.001
15-54	1 [Reference]	1 [Reference]	
55-74	1.84 (1.61-2.10)	1.81 (1.59-2.06)	
≥75	2.45 (2.10-2.86)	2.41 (2.07-2.82)	
Sex			
Female	1 [Reference]	1 [Reference]	
Male	1.10 (1.02-1.19)	1.11 (1.03-1.20)	
Geographic region			<.001
United Kingdom	1 [Reference]	1 [Reference]	
Nordic area	1.03 (0.87-1.21)	1.09 (0.94-1.25)	
Western European area	1.25 (0.90-1.60)	1.34 (1.06-1.69)	
Eastern European area	1.26 (1.05-1.52)	1.33 (1.14-1.56)	
Linear trend per 4 years	0.99 (0.95-1.04)	1.00 (0.95-1.06)	
Type of verification[a]			.16
Microscopic		1 [Reference]	
Clinical or unknown		0.69 (0.41-1.17)	
Subsite (*ICD-9* code)			<.001
Ciliary body, retina, choroid (190.0, 190.5, 190.6)		1 [Reference]	
Unspecified (190.9)		1.46 (1.19-1.79)	

Abbreviations: CI, confidence interval; *ICD-9, International Classification of Diseases, Ninth Revision*.

[a] Tumor subsite and type of diagnosis verification have been introduced in model 2 as compared with model 1.

based survival suggests that the equal efficacy of enucleation and brachytherapy in the COMS,[3] which was a randomized clinical trial, has been translated into similar effectiveness when the eyeball-preserving technique was used in different health care settings in Europe and the United States.

Unlike the studies cited, Bergman et al[15] reported an improvement in 5-year relative survival in Sweden (RER, 0.58; 95% CI, 0.43-0.78) for 1980-1989 compared with 1960-1969. They hypothesized that more individuals sought medical advice earlier because of decreasing vision or underwent eye screening in recent years. However, they observed that incidence decreased during the same period[15]; thus, increased survival as a result of early tumor detection is unlikely. They concluded that the reason for the improvement in survival remains unclear. The finding was not confirmed in the Danish study, which is similar to ours as far as sample size, race/ethnicity, and temporal extension.[1]

Although our study was much shorter than other population-based studies, we could exclude a trend of relative survival exceeding the interval −1.3% to +1% per year on the basis of the width of the 95% CI of our estimate. We confirm the finding of Bergman et al[15] that peak excess mortality occurs during years 2 to 4 after diagnosis. This could be owing to cases with metastatic melanoma at diagnosis, even if undetected.

DEMOGRAPHIC DIFFERENCES IN SURVIVAL

We have shown that 5-year relative survival in patients with uveal melanoma decreased with increasing age at diagnosis, as for most common cancers. This finding is consistent with the findings in the Swedish,[15] Danish,[16] and UK[17] cohorts.

There was also a difference between sexes in our study, with male patients having 10% higher mortality. The lack of difference in survival by sex at univariate compared with multivariate analysis can be explained by confounding by age because of a higher percentage of older women compared with men. The statistical significance of the sex difference in survival is a new finding in population-based studies. Better survival in female patients previously was suggested in Sweden,[15] Denmark,[16] and the United Kingdom[17]; however, sex differences were not statistically significant in those studies, possibly because they included about half as many cases as in our study over a longer period. The potential causes of a sex difference in survival are unclear. No sex differences in survival were found in the COMS,[3,18] which is the largest randomized multicenter trial on the treatment of uveal melanoma. The COMS survival rates are adjusted for important individual tumor-specific variables, in particular, maximum basal tumor diameter, which, together with age, is the strongest predictor of mortality. That no sex difference was found in the COMS may suggest that a later diagnosis could cause lower survival in men in population-based studies.

GEOGRAPHIC DIFFERENCES IN SURVIVAL

There may be multiple explanations for the differences found by us among broad European areas. Not only could unknown genetic or environmental factors affect mortality, but also clinical factors such as late diagnosis might influence the estimate of relative survival. Different treatment patterns

Table 5. Characteristics of Previous Population-Based Survival Studies on Uveal and Ocular Melanoma

Characteristic	Source				
	Singh and Topham,[1] 2003	Bergman et al,[15] 2002	Isager et al,[16] 2006	Burr et al,[17] 2007	Present Study
Geographic region	United States	Sweden	Denmark	England and Wales	Europe
Sources of data and type of study	SEER program database; population-based study	Swedish Cancer Registry, hospital files from the 2 centers performing eye-sparing treatments; hospital-based study	Danish Cancer Registry; population-based study	Population-based cancer registries	EUROCARE-based study of survival and care of cancer patients; population-based study
Period of diagnosis	1973-1993	1960-1998	1943-1997	1986-2001	1983-1994
No. of cases	2054	2997	2504	2876	5788
Topographic inclusion criteria: subsite	Choroid, iris, ciliary body	Choroid, iris, ciliary body	Ocular region, ie, eyeball; orbit; lacrimal gland, duct, or sac; conjunctiva (excluding skin melanoma)	Choroid, retina, iris, ciliary body	Iris and ciliary body, choroid, retina, unspecified ocular part
5-Year relative survival, %	77-84	70.1	67-71	72.4	68.9
Survival by sex	Not reported	In male patients, 12% worse but not statistically significant; multivariate relative survival in male vs female patients, 0.88 (95% CI, 0.73-1.05)	In male patients, 6% worse but not statistically significant; 5-year relative survival, 71% in male patients vs 67% in female patients	Better in women at 5 years (RER, 0.90 compared with men) but not statistically significant	In male patients, 10% worse and statistically significant; multivariate RER 1.10 (95% CI, 1.02-1.19
Survival by period	Stable	Improved from 1980-1989 vs 1960-1969	Stable	Stable	Stable

Abbreviations: CI, confidence interval; EUROCARE, European Cancer Registry; RER, relative excess risk; SEER, National Cancer Institute Surveillance Epidemiology and End Results.

may have influenced survival rates. Against this hypothesis is the observation that enucleation and brachytherapy did not produce different outcomes in the COMS.[3]

INCLUSION CRITERIA AND CASE DETECTION IN POPULATION-BASED STUDIES OF UVEAL MELANOMA

The issue of inclusion criteria was proved important when the incidence of uveal melanoma was studied in registry-based research, as has also been recently pointed out by Stang et al.[5] In the incidence study based on these same data,[4] we found that the inclusion of melanomas with unspecified ocular location (*ICD-9* topography code 190.9) decreased the heterogeneity of incidence rates among registries in the United Kingdom, where this coding is common, and in Europe overall. In the present study, melanomas with unspecified ocular location were associated with worse prognosis, which is consistent with the hypothesis that registrars use this code for large tumors, the origin of which cannot be ascribed to a specific uveal subsite. We recommend that further population-based investigations of survival in patients with uveal melanoma be reported with the inclusion of tumors with unspecified location (*ICD-9* code 190.9). Although tumors with unspecified location should be included in the analysis, we recommend caution in RER interpretation when adjusting for this variable. For example, the RER in the western European area was statistically significant compared with in the United Kingdom when adjusting for tumor subsite, but the interpretation of this finding is unclear given the large difference in the use of this code in the United Kingdom compared with continental Europe, which suggests heterogeneity of diagnostic criteria.

In conclusion, 5-year relative survival remained stable during the study period, a finding that confirms at the general population level that the increase in conservative therapy during the years of the study did not negatively affect the prognosis of the disease. However, survival rates did not improve at the population level, which is the primary goal of treatment of malignant tumors. We found differences in survival rates between sexes and among European areas that should be investigated in studies that take into account tumor characteristics at the individual level.

Submitted for Publication: December 31, 2007; final revision received February 11, 2008; accepted March 15, 2008.
Correspondence: Gianni Virgili, MD, Department of Oto-Neuro-Ophthalmological Surgical Sciences, University of Florence, Viale Morgagni 85, Florence 50134, Italy (gianni.virgili@unifi.it).
Group Information: The members of the EUROCARE Working Group are as follows: *Austria:* W. Oberaigner (Tyrol Cancer Registry, Innsbruck); *Denmark:* H. H. Storm (Danish Cancer Society, Department of Cancer Prevention & Documentation, Copenhagen); *Estonia:* T. Aareleid (Estonian Cancer Registry, Tallinn); *Czech Republic:* M. Jechova and M. Rousarova (IHIS and West Bohemia Cancer Registry, Prague); *Finland:* T. Hakulinen (Finnish Cancer Registry, Helsinki); *France:* G. Hédelin (Bas-Rhin Cancer Registry, Strasbourg), J. Macé-Lesec'h (Calvados General Cancer Registry, Caen), A. Danzon (Doubs Cancer Registry, Besancon), B. Tretarre (Hérault Cancer Registry, Mont-

pellier), M. Colonna (Isère Cancer Registry, Meylan), N. Raverdy (Somme Cancer Registry, Amiens), P. Grosclaude (Tarn Cancer Registry, Albi), J. Estève (University of Lyon, Lyon), and H. Ziegler (Saarland Cancer Registry, Saarbrucken); *Iceland:* L. Tryggvadottir (Icelandic Cancer Registry, Reykjavik); *Italy:* F. Berrino, C. Allemani, P. Baili, L. Ciccolallo, P. Crosignani, G. Gatta, A. Micheli, M. Sant, E. Taussig, and S. Sowe (Istituto Nazionale per lo Studio e la Cura dei Tumori, Lombardy Cancer Registry, Milano), S. Ferretti (Ferrara Cancer Registry, Ferrara), V. Ramazzotti and M. C. Cercato (Latina Cancer Registry, Roma), M. Vercelli and A. Quaglia (Liguria Region Cancer Registry–Department of Oncology, Biology, and Genetics [DOBIGO] of the University of Genova, Genova), F. Pannelli (Macerata Cancer Registry, Camerino), M. Federico and M. E. Artioli (Modena Cancer Registry, Modena), V. De Lisi and L. Servente (Parma Cancer Registry, Parma), R. Zanetti and S. Patriarca (Piedmont Cancer Registry, Torino), L. Gafà and R. Tumino (Ragusa Cancer Registry, Ragusa), F. Falcini (Romagna Cancer Registry, Forli), M. Budroni (Sassari Cancer Registry, Sassari), E. Paci and E. Crocetti (Tuscan Cancer Registry, Firenze), P. Zambon and S. Guzzinati (Venetian Cancer Registry, Padova), and R. Capocaccia, E. Carrani, R. De Angelis, P. Roazzi, M. Santaquilani, A. Tavilla, F. Valente, and A. Verdecchia (Istituto Superiore di Sanità, Roma); *Malta:* M. Dalmas (Malta National Cancer Registry, Valletta); *Norway:* F. Langmark and A. Andersen (Cancer Registry of Norway, Institute of Population-based Cancer Research, Oslo); *Portugal*: P. Pinheiro (Southern Portugal Cancer Registry, Lisboa); *Poland:* J. Rachtan (Cracow Cancer Registry, Cracow) and M. Bielska–Lasota, Z. Wronkowski, and M. Zwierko (Warsaw Cancer Registry, Warsaw); *Slovakia:* I. Pleško and A. Obsitníková (National Cancer Registry of Slovakia, Bratislava); *Slovenia:* V. Pompe–Kirn and M. Primic-Žakelj (Cancer Registry of Slovenia, Ljubljana); *Spain:* I. Izarzugaza (Basque Country Cancer Registry, Vitoria-Gasteiz), C. Martinez-Garcia (Granada Cancer Registry, Granada), I. Garau (Mallorca Cancer Registry, Palma de Mallorca), C. Navarro and M. D. Chirlaque (Murcia Cancer Registry, Murcia), E. Ardanaz and C. Moreno (Navarra Cancer Registry, Pamplona, Navarra), and J. Galceran (Tarragona Cancer Registry, Reus); *Sweden:* L. Barlow (Cancer Registry of Sweden, Stockholm) and T. Möller (Southern Swedish Regional Tumour Registry, Lund University Hospital, Lund); *Switzerland:* G. Jundt (Basel Cancer Registry, Basel) and J. M. Lutz and C. Bouchardy (Geneva Cancer Registry, Geneva); *the Netherlands:* J. W. W. Coebergh (Eindhoven Cancer Registry, Eindhoven) and O. Visser (Amsterdam Cancer Registry, Amsterdam); *England:* S. Godward (East Anglian Cancer Registry, Cambridge), M. P. Coleman (London School of Hygiene and Tropical Medicine, London), E. M. I. Williams (Merseyside and Cheshire Cancer Registry, Liverpool), D. Forman (Northern and Yorkshire Cancer Registry and Information Service, Leeds), M. J. Quinn (Office for National Statistics, London), M. Roche and S. Edwards (Oxford Cancer Intelligence Unit, Oxford), C. Stiller (Childhood Cancer Research Group, Oxford), J. Verne (South West Cancer Intelligence Services, Bristol), H. Møller and J. Bell (Thames Cancer Registry, London), H. Botha (Trent Cancer Registry, Sheffield), and G. Lawrence (West Midlands Cancer Intelligence Unit, Birmingham); *Scotland:* R. Black (Scottish Cancer Intelligence Unit, Edinburgh); *Wales:* J. A. Steward (Welsh Cancer Intelligence and Surveillance Unit, Cardiff).

Financial Disclosure: None reported.

Funding/Support: This study was supported by EUROCARE-3 BIOMED-2 programme contract BMH4-CT98–3390; the Compagnia di San Paolo, Torino, Italy; and European Community grant SPC.2002303–DEP/01/19, "European Network of Cancer Registries: Survival of Adult Patients With Rare Tumours."

Additional Information: This article is partly based on Dr Virgili's master's thesis in epidemiology at the University of Turin and the Institute for Scientific Interchange (ISI) Foundation, Turin.

Additional Contributions: Sarah Harvey, MD, PhD, MS, edited the submitted manuscript.

REFERENCES

1. Singh AD, Topham A. Survival rates with uveal melanoma in the United States: 1973–1997. *Ophthalmology*. 2003;110(5):962-965.
2. Robertson DM. Changing concepts in the management of choroidal melanoma. *Am J Ophthalmol*. 2003;136(1):161-170.
3. Collaborative Ocular Melanoma Study Group. The COMS randomized trial of iodine 125 brachytherapy for choroidal melanoma, V: twelve-year mortality rates and prognostic factors: COMS report No. 28. *Arch Ophthalmol*. 2006;124(12):1684-1693.
4. Virgili G, Gatta G, Ciccolallo L, Capocaccia R, Biggeri A, Crocetti E, et al; EUROCARE Working Group. Incidence of uveal melanoma in Europe [published online ahead of print May 11, 2007]. *Ophthalmology*. 2007;114(12):2309-2315. doi:10.1015/j.ophtha.2007.01.032.
5. Stang A, Parkin DM, Ferlay J, Jöckel KH. International uveal melanoma incidence trends in view of a decreasing proportion of morphological verification. *Int J Cancer*. 2005;114(1):114-123.
6. Coleman MP, Gatta G, Verdecchia A, et al; EUROCARE Working Group. EUROCARE-3 summary: cancer survival in Europe at the end of the 20th century. *Ann Oncol*. 2003;14(suppl 5):128-149. doi:10.1093/annonc/mdg756.
7. Berrino F, Capocaccia R, Estève J, et al. *Survival of Cancer Patients in Europe: The EUROCARE-2 Study*. Lyon, France: International Agency for Research on Cancer; 1999:1-572. International Agency for Research on Cancer scientific publication No. 151.
8. Berrino F. The EUROCARE Study: strengths, limitations and perspectives of population-based comparative survival studies. *Ann Oncol*. 2003;14(suppl 5):v9-v13.
9. Berrino F, Sant M, Verdecchia A, et al. *Survival of Cancer Patients in Europe: The EUROCARE Study*. Lyon, France: International Agency for Research on Cancer; 1995:1-463. IARC Scientific Publication No. 132.
10. *SEER: Surveillance Epidemiology and End Results, Version 5.3.1*. Washington, DC: National Cancer Institute; 2004.
11. Hakulinen T. Cancer survival corrected for heterogeneity in patient withdrawal. *Biometrics*. 1982;38(4):933-942.
12. Dickman PW, Sloggett A, Hills M, Hakulinen T. Regression models for relative survival. *Stat Med*. 2004;23(1):51-64.
13. White H. Maximum likelihood estimation of misspecified models. *Econometrica*. 1982;50(1):1-25. doi:10.2307/1912526..
14. Rabe-Hesketh S, Skrondal A. *Multilevel and Longitudinal Modeling Using STATA*. College Station, TX: StataCorp LP; 2005.
15. Bergman L, Seregard S, Nilsson B, Ringborg U, Lundell G, Ragnarsson-Olding B. Incidence of uveal melanoma in Sweden from 1960 to 1998. *Invest Ophthalmol Vis Sci*. 2002;43(8):2579-2583.
16. Isager P, Engholm G, Overgaard J, Storm H. Uveal and conjunctival malignant melanoma in Denmark 1943-97: observed and relative survival of patients followed through 2002. *Ophthalmic Epidemiol*. 2006;13(2):85-96.
17. Burr JM, Mitry E, Rachet B, Coleman MP. Survival from uveal melanoma in England and Wales 1986 to 2001. *Ophthalmic Epidemiol*. 2007;14(1):3-8.
18. Hawkins BS; Collaborative Ocular Melanoma Study Group. The Collaborative Ocular Melanoma Study (COMS) randomized trial of pre-enucleation radiation of large choroidal melanoma, IV: ten-year mortality findings and prognostic factors: COMS report No. 24. *Am J Ophthalmol*. 2004;138(6):936-951.