

**Advisory Board (Work Package 3)****Evaluation of RARECARE project to March 2009 (end of Year 2)**

The Advisory Board met on 27 March 2009 at the London School of Hygiene and Tropical Medicine. Present:

**Advisory Board members**

Michel Coleman (Chair, LSHTM)  
Jan Geissler (ECPC)  
Markus Wartenberg (Das Lebenshaus)  
**Apologies:** Ulrik Ringborg (Karolinska)

**RARECARE personnel (observers)**

Gemma Gatta (Principal Investigator)  
Riccardo Capocaccia  
Samba Sowe

Jan Geissler represented ECPC on behalf of Lynn Faulds Wood

**Abbreviations:**

AIRTUM	Association of Italian Tumour Registries	ICD-O	International Classification of Diseases for Oncology (WHO)
ASCO	American Society for Clinical Oncology	LSHTM	London School of Hygiene and Tropical Medicine (UK)
CML	Chronic myeloid leukaemia	MAC	MEPs Against Cancer group (EU)
ECCO	European CanCER Organisation	MEP	Member of the European Parliament
ECPC	European Cancer Patient Coalition	OECD	Organisation for Economic Co-operation and Development
EORTC	European Organisation for Research and Treatment on Cancer	SEER	Surveillance Epidemiology and End Results program (USA)
ESMO	European Society for Medical Oncology	TNEH	Total National Expenditure on Health (OECD)
ESO	European School of Oncology	UKACR	UK Association of Cancer Registries (OECD)
GDP	Gross Domestic Product (OECD)		
GIST	Gastro-intestinal stromal tumour		
GRELL	Groupe pour l'enregistrement des cancers dans les pays de langue latine		

The Advisory Board met to evaluate progress in the RARECARE project to the end of Year 2 (31 March 2009). Functions of the Board were reviewed. Dr Gatta presented an overview of recent progress, and supporting documents were available from all the WorkPackage leaders.

The initial list of indicators was presented in our September 2008 response to comments from the Commission on the first interim report (June 2008). We noted then that the indicators would be subject to revision during Year 2 (Appendix 1). Progress on each major Work Package was discussed. Performance against the revised set of indicators (below) was assessed. The Advisory Board's evaluation of progress toward these objectives is documented.

A publication plan was established (Appendix 2).

Overall progress is considered excellent. The Advisory Board commended the organisers of the RARECARE project for innovation, extensive new collaborations, and steady progress toward the overall goals of the project.

## **List of rare tumours (Work Package 4)**

### **1. Establish an Expert Advisory Group on rare tumours**

This objective has been achieved. The list of members is attached (Appendix 3). The Expert Advisory Group met in Brussels, Belgium, in January 2008 and Treviso, Italy, in June 2008. The agenda and minutes are available on request. A third meeting is planned for 10 June 2009 to endorse the final version of the list of rare tumours.

### **2. Produce a frequency distribution of all tumours by ICD-O site (topography) and morphology**

This objective was achieved. The list was derived from population-based cancer registry data in both the RARECARE database and the US SEER Program of cancer registries. It was used as the basis for the discussions of the Expert Advisory Group.

### **3. Reach a consensus on the definition of a rare tumour and the list of rare tumours.**

This objective was achieved. The proposed list of rare tumours was discussed in detail and consensus was reached. All scientific societies that come under the umbrella of the European CanCer Organisation (ECCO) were contacted to seek comments on the draft list. Most of them responded. Those that responded gave positive evaluations of RARECARE. The European Organisation for Research and Treatment on Cancer (EORTC) also proposed a joint meeting to discuss further development and deployment of the list of rare tumours. This meeting is now being planned.

### **4. Disseminate the results of RARECARE in scientific publications, communications to scientific congresses and patient advocacy groups and at other meetings, and evaluate public access to the RARECARE web site.**

Good progress toward this objective has been made. A scientific paper on the rare tumour list, with its rationale, is now in preparation. Presentations at congresses have been made:

AIRTUM, Mantova, Italy, 2008

European Society for Medical Oncology (ESMO), Brussels, November 2008

Italian Health Ministry international conference on rare diseases, Rome, November 2008

Other communications are planned:

ECCO, Berlin, September 2009

Advocacy group for GIST and CML, Germany, June 2009

European Cancer Patient Coalition (ECPC), October 2009

3<sup>rd</sup> International Cancer Control Congress, Cernobbio, Italy, November 2009

Italian Health Ministry international conference on rare diseases, Rome, November 2009

American Society for Clinical Oncology (ASCO), Chicago, USA, June 2010

The RARECARE web-site received over 1,000 hits from 540 unique persons who downloaded an average of 4.14 pages per visit during the period up to March 2009 (Appendix 4).

## **RARECARE Indicators (Work Package 5)**

### **1. Identify and list the cancer registries from which data are to be analysed**

This objective was achieved: 75 population-based cancer registries agreed to participate. The list is available on request.

### **2. Specify the number of rare cancers for which data have been analysed**

This objective was achieved: 261 rare tumour entities were defined as unique combinations of ICD-O-3 codes for topography (site) and morphology. These entities, the most detailed definition possible with routinely collected data, have been grouped into 185 rare disease entities, as perceived and treated by clinicians. Disease entities have been further grouped into 41 rare tumour families, as defined by their referral patterns (see Appendix 5). These groupings are based on detailed examination of 8.85 million cancer patient records provided by the 75 participating cancer registries.

### **3. Define the layout of tables for the presentation of results.**

This objective was achieved: see example in Appendix 6.

### **4. Define the list of variables to be analysed**

This objective was achieved: data on incidence, prevalence, survival and mortality will be analysed by age (broad age bands), sex (males, females, persons), European Region (north, south, east, west, central), time since diagnosis (for survival only: 1 and 5 years) and by three levels of two macro-economic indicators obtained from the OECD, namely the gross domestic product (GDP) and the total national expenditure on health (TNEH).

## **Data quality (Work Package 6)**

### **1. Identify scientists to participate in the data quality working group**

This objective was achieved: see Appendix 7.

### **2. Schedule a series of meetings**

This objective was achieved: meetings were held 7-8 January 2008, Brussels, Belgium and 26-27 May 2008, Treviso, Italy.

### **3. Identify specific data quality problems**

This objective was achieved: problems were identified with the data for some tumours with unusually high (or low) values for:

- the proportion for which morphological verification was available (MV%)

- the proportion registered only from a death certificate (DCO%)

- the proportion of patients lost to follow-up

- the proportion for which morphology was specified in a broad category such as “Sarcoma, Not Otherwise Specified (NOS)”

- the proportion of long-term survivors (e.g. over 3 years) for tumours known to be particularly lethal, such as mesothelioma and angiosarcoma of the liver

### **4. Identify those rare tumours most affected by data quality problems**

A short-list of rare tumours was identified for which data quality (and other) problems were considered worthy of more detailed attention (see Appendix 8)

### **5. Identify cancer registries able to perform a detailed review of data quality**

This objective was achieved: 8 regional and 5 national registries in 11 countries (Appendix 7).

### **6. Propose training courses to European Network of Cancer Registries and national associations of cancer registries**

This objective was achieved: one training course on rare tumours has been accepted:

- GRELL (Latin language cancer registry group), Zaragoza, Spain, May 2010

Other courses have been proposed and are awaiting confirmation:

- European School of Oncology (ESO)

- Nordic group of Cancer Registries

- Italian Association of Tumour Registries (AIRTUM)

- UK Association of Cancer Registries (UKACR)

### **7. Improve the contribution to RARECARE by cancer registries from Eastern Europe**

This objective has only been partially achieved. Participation by Estonia and Poland (Kielce, Silesia) is balanced by the fact that both Slovakia and the Czech Republic declined to participate, in the latter case because clinicians have objected strongly to the survival comparisons in EURO CARE. Slovenia also participates but is now classified as being in Southern Europe.

**Provisional performance indicators specified in first Interim Report (September 2008)**

“For the task of definition and list of rare tumours, the markers of progress will be:

- definition of a list of specialist and establishment of the specific working group (a list)
- in order to identify the frequency of rare tumours a preliminary frequency analysis by ICD-O cancer topography and morphology is needed: availability of frequency tables by cancer sites and morphology
- schedule a series of meetings (agenda of meetings)
- number of the working group meetings held
- final agreement on definition and list of rare tumours
- to disseminate the results: number of scientific publications or communications to congress; number of pages made available from the specific and connected web site.

“In order to evaluate whether the objectives of estimating frequency (incidence and prevalence) and outcome (survival) of rare tumours have been achieved, the markers of progress will be:

- a list of registries from which data are to be analysed, after evaluation of the quality of their data
- number of rare cancers that have been analysed
- a definition of tables layout for the presentation of results
- a list of variables to be analysed
- to disseminate the results: number of scientific publications or communications to congress; number of pages made available from the specific and connected web site.

“To improve data quality in the definition of rare cancers (accuracy of diagnosis), completeness of registration (for incidence) and standardization of coding practice, progress markers will include:

- identification of a group of people for the specific working group (a list)
- schedule a series of meetings (agenda of meetings)
- identification of specific data quality problems (a list)
- identification of which rare tumours are affected by quality problems (a list)
- identification of cancer registries able to carry out a special review of their data quality (a list)
- report on this task
- proposal of training courses to European Network of Cancer Registries and national associations of cancer registries
- to disseminate the results: number of scientific publications or communications to congress; number of pages made available from the specific and connected web site.
- coverage of East of Europe by participating CRs

“During the course of the second year these indicators will be improved.”

## **Appendix 2 RARECARE publication plan**

Various methods of disseminating the findings of the RARECARE project have been or will be used. The strategy is outlined in the publication plan below. The Principal Investigator and the Chair of the Advisory Board are in regular contact to ensure the most effective means and timing of dissemination of the results.

**Scientific publication** - a first article on the rationale for the project is being prepared for submission to a peer-reviewed journal. It will include the full list of rare tumours. Other articles will be prepared as determined by participants in each Work Package or by the principal investigator.

**Web access** - the web-site [www.rarecare.eu](http://www.rarecare.eu) has been created. The site is accessible now. It is under continuous development by collaborators in Edinburgh. Translation of key pages into several European languages is being actively explored. Automated translation has been tried and rejected. The key pages are already available in English and Polish, and will shortly be available in Spanish, Italian, French, German and possibly other languages. The problem is neither feasibility nor cost, but assuring maintenance after updates.

**Congresses** - the RARECARE project has been presented at several congresses. Abstracts requesting oral presentation have been submitted or will soon be submitted to several other congresses in Europe and the USA.

**European Parliament** - a submission has been made to the EU draft Communication on Rare Diseases ([http://ec.europa.eu/health-eu/news/raredis\\_cons/raredis\\_cons\\_en.htm](http://ec.europa.eu/health-eu/news/raredis_cons/raredis_cons_en.htm)). Opportunities to present the findings of RARECARE to MEPs will be explored through ECPC, which holds the secretariat for MEPs Against Cancer (the MAC group).

**Press** - the print, electronic and broadcast media will all be used to secure publicity for the key findings of the RARECARE project when the work is largely complete, toward month 36 (March 2010). A press release will be prepared to coincide with publication of the first scientific article, in conjunction with the journal's editorial staff. A press conference will be held if that is judged desirable at the time; the preferred location would be in Brussels, in the European Parliament.

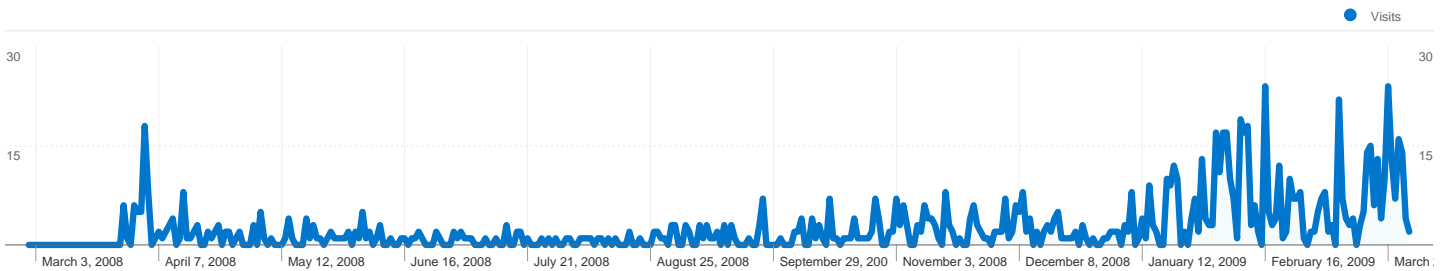
**Patient advocacy groups** - two members of the Advisory Board are cancer patients actively involved in advocacy, and members of cancer patient organisations. They will continue to advise on the cancer patient's perspective, and to assist in ensuring that key messages from RARECARE reach the cancer patient community in a suitable form and in a timely manner.

### Appendix 3 Expert Advisory Group on rare tumours - list of members

NAME	SURNAME	ORGANISATION	COUNTRY
Pascale	Blaes	ESMO	Belgium
Sandrine	Marreaud	EORTC	Belgium
Dirk	Schrijvers	Ziekenhuisnetwerk Antwerpen	Belgium
Hildrun	Sundseth	European Cancer Patient Coalition	Belgium
Jan-Willem	Van De Loo	European Commission	Belgium
Ellen	Benhamou	Institut Gustave Roussy	France
Isabelle Ray	Coquard	Centre Léon Bérard	France
Jean-Pierre	Droz	Centre Léon Bérard	France
Marc	Maynadié	Haematological Malignancies Registry	France
Marine	Grossgoupil	Institut Gustave Roussy	France
Ségolène	Aymè	ORPHANET	France
Simon	Baconnier	CONTICANET	France
Rudiger	Hehlmann	Leukemia Network	Germany
Sandra	Deady	National Cancer Registry of Ireland	Ireland
Alba	Brandes	Bellaria Maggiore Hospital	Italy
Alessandro	Gronchi	Fondazione IRCCS	Italy
Angelo Paolo	Dei Tos	ULSS No.9, Regione Veneto	Italy
Franco	Berrino	Fondazione IRCCS	Italy
Lisa	Licitra	Fondazione IRCCS, INT	Italy
Paolo	Casali	Fondazione IRCCS, INT	Italy
Patrizia	Olmi	Fondazione IRCCS, INT	Italy
Riccardo	Capocaccia	Istituto Superiore di Sanità	Italy
Stefano	Ferretti	Ferrara Cancer Registry	Italy
Andres	Cervantes	University of Valencia	Spain
Torgil	Möller	University of Lund	Sweden
Harry	Schouten	University of Maastricht	The Netherlands
Annet	Sollie	CINEAS	The Netherlands
Ian	Kunkler	University of Edinburgh	UK
James	Mackay	University College of London	UK

## **Appendix 4 Summary report of traffic to RARECARE web-site**





## Site Usage

1,000 Visits

29.80% Bounce Rate

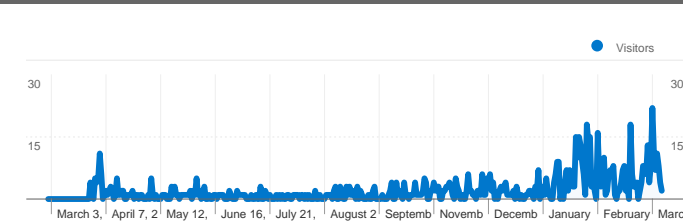
4,142 Pageviews

00:03:32 Avg. Time on Site

4.14 Pages/Visit

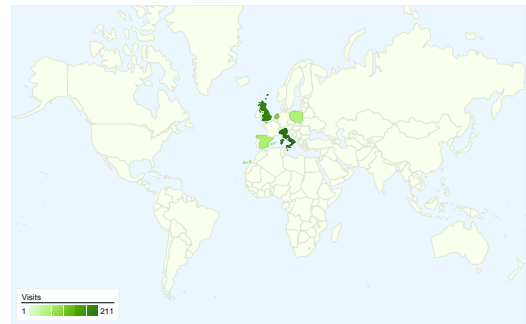
53.90% % New Visits

## Visitors Overview

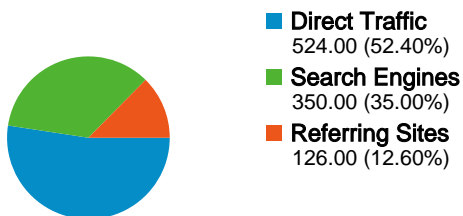


Visitors  
540

## Map Overlay world

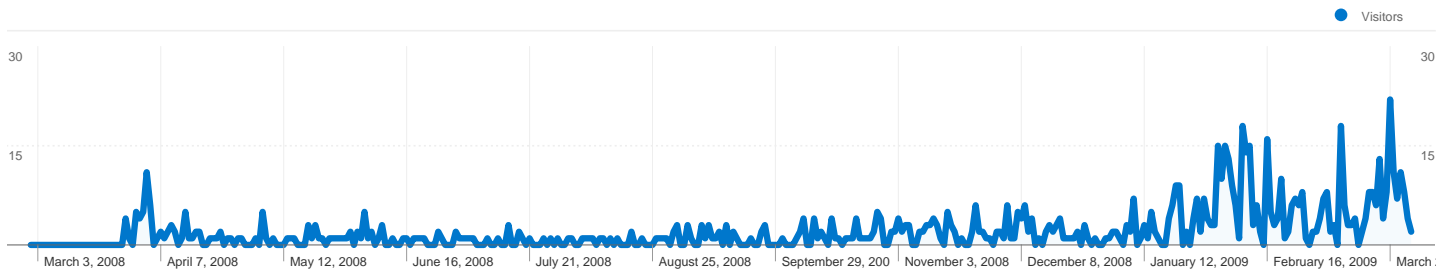


## Traffic Sources Overview



## Content Overview

Pages	Pageviews	% Pageviews
/activities/activities.asp	764	18.45%
/aims/aims.asp	731	17.65%
/	663	16.01%
/default.asp	593	14.32%
/rarecancers/rarecancers.asp	557	13.45%



**540 people visited this site**

**1,000 Visits**

**540 Absolute Unique Visitors**

**4,142 Pageviews**

**4.14 Average Pageviews**

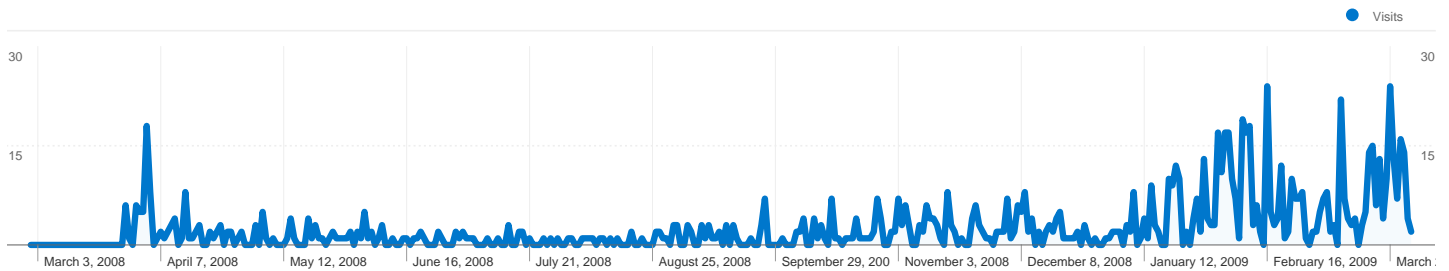
**00:03:32 Time on Site**

**29.80% Bounce Rate**

**53.90% New Visits**

## Technical Profile

Browser	Visits	% visits	Connection Speed	Visits	% visits
Internet Explorer	782	78.20%	Unknown	461	46.10%
Firefox	176	17.60%	T1	224	22.40%
Safari	32	3.20%	DSL	207	20.70%
Chrome	4	0.40%	Cable	70	7.00%
Netscape	2	0.20%	Dialup	24	2.40%



All traffic sources sent a total of 1,000 visits



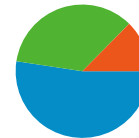
52.40% Direct Traffic



12.60% Referring Sites



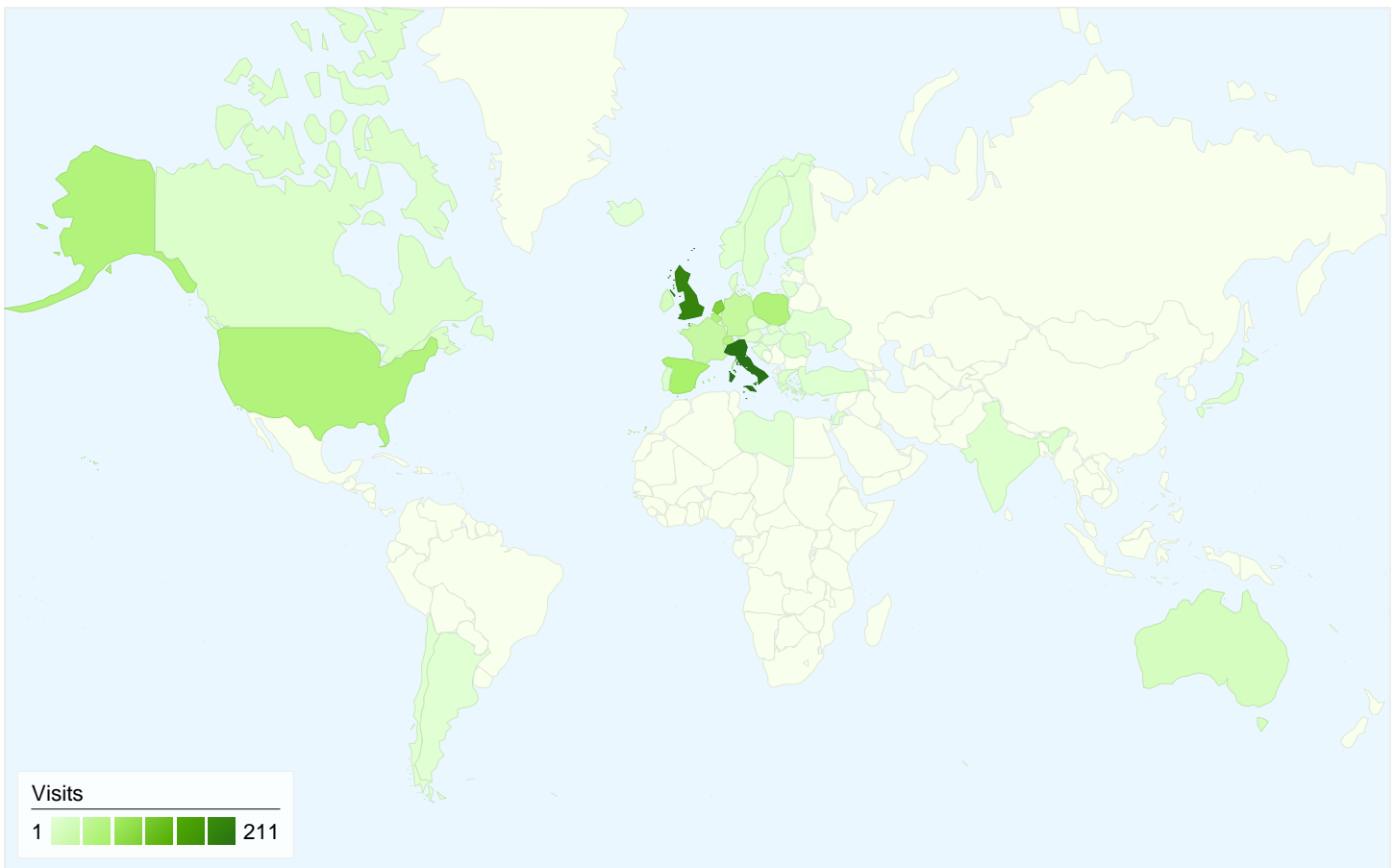
35.00% Search Engines



■ Direct Traffic  
524.00 (52.40%)  
■ Search Engines  
350.00 (35.00%)  
■ Referring Sites  
126.00 (12.60%)

## Top Traffic Sources

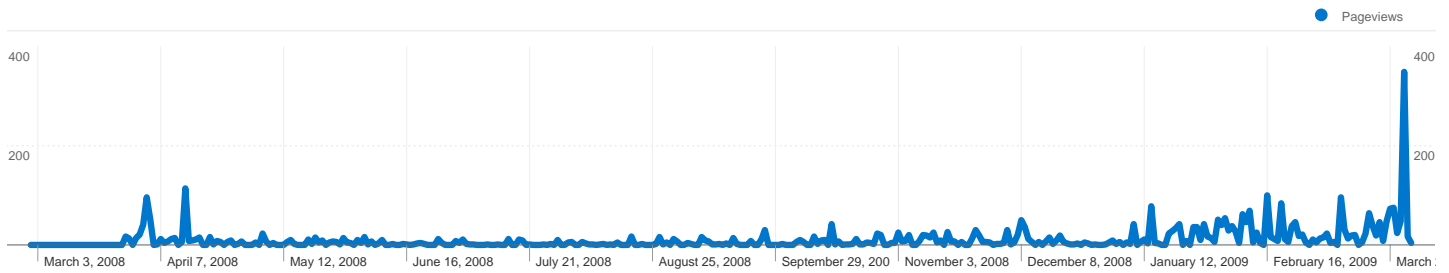
Sources	Visits	% visits	Keywords	Visits	% visits
(direct) ((none))	524	52.40%	rarecare	163	46.57%
google (organic)	328	32.80%	www.rarecare.eu	40	11.43%
ec.europa.eu (referral)	59	5.90%	rarecare project	19	5.43%
eurocare.it (referral)	20	2.00%	rarecare.eu	12	3.43%
yahoo (organic)	13	1.30%	rarecare eu	10	2.86%




## 1,000 visits came from 44 countries/territories


### Site Usage


<b>Visits</b> <b>1,000</b> % of Site Total: <b>100.00%</b>	<b>Pages/Visit</b> <b>4.14</b> Site Avg: <b>4.14</b> (0.00%)	<b>Avg. Time on Site</b> <b>00:03:32</b> Site Avg: <b>00:03:32</b> (0.00%)	<b>% New Visits</b> <b>53.90%</b> Site Avg: <b>53.90%</b> (0.00%)	<b>Bounce Rate</b> <b>29.80%</b> Site Avg: <b>29.80%</b> (0.00%)		
Country/Territory		Visits	Pages/Visit	Avg. Time on Site	% New Visits	Bounce Rate
Italy		211	3.39	00:02:55	35.55%	26.54%
United Kingdom		189	6.46	00:06:07	49.74%	32.80%
Netherlands		101	4.51	00:02:11	44.55%	26.73%
Spain		66	3.74	00:02:39	53.03%	27.27%
Poland		58	3.60	00:02:39	27.59%	24.14%
United States		56	1.91	00:01:53	80.36%	57.14%
Belgium		56	4.77	00:04:55	64.29%	17.86%
Switzerland		50	3.02	00:02:11	62.00%	24.00%
Germany		34	3.62	00:02:26	76.47%	32.35%
France		32	4.41	00:04:26	81.25%	21.88%



Pages on this site were viewed a total of 4,142 times

 4,142 Pageviews

 2,605 Unique Views

 29.80% Bounce Rate

## Top Content

Pages	Pageviews	% Pageviews
/activities/activities.asp	764	18.45%
/aims/aims.asp	731	17.65%
/	663	16.01%
/default.asp	593	14.32%
/rarecancers/rarecancers.asp	557	13.45%

## Appendix 5 List of rare tumour entities, rare disease entities and rare tumour families

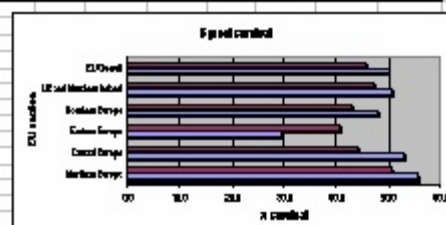
A sample of the list of rare tumours is included below. The list remains subject to revision, but can be considered virtually final. This version can be provided in full on request.

Layer	Tumour	Rate	Patients
1	<b>EPITHELIAL TUMOURS OF THE NASAL CAVITY and SINUSES</b>	0.471	3,060
2	<b>Squamous cell carcinoma and variants of the Nasal Cavity and Sinuses</b>	0.37	2,615
3	Squamous carcinoma	0.24	1,708
3	Verrucous carcinoma	0.01	35
3	Squamous cell carcinoma spindle cell	0	6
3	Papillary squamous cell carcinoma	0	8
3	Basaloid carcinoma	0	10
3	Adenosquamous carcinoma	0	13
3	Squamous cell carcinoma, adenoid	0	3
3	Basaloid squamous cell carcinoma	0	0
3	Spindle cell carcinoma	0	0
2	<b>Lymphoepithelial carcinoma of the Nasal Cavity and Sinuses</b>	0	12
2	<b>Undifferentiated carcinoma of the Nasal Cavity and Sinuses</b>	0.015	106
2	<b>Intestinal type adenocarcinoma the Nasal Cavity and Sinuses</b>	0.002	16
1	<b>EPITHELIAL TUMOURS OF THE NASOPHARYNX</b>	0.446	3,171
2	<b>Squamous cell carcinoma and variants of the Nasopharynx</b>	0.32	2,288
3	Squamous carcinoma	0.162	1,156
3	Squamous cell carcinoma nonkeratinizing, NOS	0.02	144
3	Squamous cell carcinoma keratinizing, NOS	0.016	111
3	Papillary squamous cell carcinoma	0.001	7
3	Basaloid squamous cell carcinoma	0	0
3	Squamous cell carcinoma, adenoid	0	1
3	Lymphoepithelial carcinoma	0.057	405
3	Undifferentiated carcinoma	0.064	457

## Appendix 6 Layout of tables for results

EPITHELIAL TUM OF THE NASAL CAVITY AND SINUSES									
	Incidence			Prevalence			Mortality		
	rate	Lower CI	Upper CI	rate	Lower CI	Upper CI	rate	Lower CI	Upper CI
Expected cases x year in EU									
Crude rate - Total	0,45	0,43	0,48	2,46	2,36	2,61			
Sex									
men	0,69	0,67	0,62	3,07	2,99	3,29			
women	0,31	0,29	0,33	1,88	1,73	2,04			
Age									
0-14	0	0	0	0	0	0,03			
15-24	0,01	0,01	0,02	0,01	0	0,08			
25-64	0,33	0,31	0,35	1,69	1,55	1,84			
65+	1,69	1,61	1,76	9,49	8,9	10,12			
region*									
North	0,32	0,29	0,36	2,63	2,37	2,91			
Centre	0,37	0,35	0,4	2,2	1,96	2,47			
East	0,38	0,31	0,46	1,78	1,27	2,37			
South	0,38	0,35	0,41	4,01	3,52	4,59			
UK-Ireland	0,36	0,34	0,38	2,56	2,06	2,45			
Overall EU	0,36	0,36	0,39	2,49	2,36	2,61			
GDP level*									
Low GDP 0-20000	0,35	0,31	0,4	1,76	1,27	2,37			
Middle GDP 20000-25000	0,35	0,34	0,37	2,55	2,39	2,71			
High GDP >25000	0,38	0,36	0,42	2,4	2,18	2,69			
TNEH level*									
TNEH low 0-1300	0,35	0,31	0,4	1,76	1,27	2,37			
TNEH middle >1301-2250	0,36	0,34	0,37	2,46	2,32	2,6			
TNEH high >2250	0,36	0,36	0,38	2,63	2,44	3,26			

EPITHELIAL TUM OF THE NASAL CAVITY AND SINUSES									
Period 2016-2018									
Sex	Period 2016-2018						Period 2016-2018		
	Observed			Relative			Observed	Relative	Coldest of Europe
Age	survival	Lower CI	Upper CI	survival	Lower CI	Upper CI	survival	Lower CI	Upper CI
1y	71,1	68,5	73,7	72,2	70,3	74,1	72,2	70,3	74,1
2y	67,7	65,0	70,4	67,8	65,8	69,8	67,8	65,8	69,8
3y	64,3	61,5	67,1	64,3	62,3	66,3	64,3	62,3	66,3
4y	60,9	57,9	63,9	60,9	58,9	62,9	60,9	58,9	62,9
5y	57,5	54,5	60,5	57,5	55,5	59,5	57,5	55,5	59,5
Significant survival by EU region	Period 2016-2018						Period 2016-2018		
Region	survival	Lower CI	Upper CI	survival	Lower CI	Upper CI	survival	Lower CI	Upper CI
Northern Europe	65,1	62,1	68,1	65,1	63,1	67,1	65,1	63,1	67,1
Central Europe	62,1	59,1	65,1	62,1	60,1	64,1	62,1	60,1	64,1
Eastern Europe	59,1	56,1	62,1	59,1	57,1	61,1	59,1	57,1	61,1
Southern Europe	67,1	64,1	70,1	67,1	65,1	69,1	67,1	65,1	69,1
UK and Northern Ireland	60,1	57,1	63,1	60,1	58,1	62,1	60,1	58,1	62,1
EU Overall	58,1	55,1	61,1	58,1	56,1	60,1	58,1	56,1	60,1



## **Appendix 7 Data Quality Working Group - participating cancer registries and scientists**

Estonia - Margit Magi

France (Côte d'Or) - Jean Faivre, Anne-Marie Bouvier, Valerie Jooste

Ireland - Sandra Deady

Italy (Varese) - Giovanna Tagliabue, Paolo Contiero

Malta - Kathleen England

Netherlands (Amsterdam) - Otto Visser

Netherlands (North Netherlands) - Renée Otter

Netherlands (Twente) - Sabine Siesling

Poland (Kielce ) - Ryszard Mezyk

Poland (Silesia) - Jerzy Slowinski

Slovenia - Maja Primic-Žakelj

Spain (Granada) - Carmen Martinez-Garcia

Sweden - Jan Adolfsson, Mats Lambe

Switzerland (Geneva) - Massimo Usel



## **Appendix 8 Rare tumours most affected by data quality problems - short-list**

Mesothelioma

Liver angiosarcoma

Sarcomas

Tumours of the oral cavity

Central nervous system (CNS) tumours

Germ-cell tumours

Leukaemias

Endocrine tumours