TUMORI RARI

Documento di posizione

A cura di Novartis Oncology

PREMESSA

Novartis, leader mondiale nell'area della salute, è fortemente impegnata nella ricerca e nello sviluppo di farmaci per curare le malattie, ridurre il carico delle sofferenze e migliorare la qualità di vita delle persone. Da sempre orientata allo sviluppo di farmaci che rispondano a esigenze terapeutiche ancora non soddisfatte, la ricerca di Novartis Oncology è sempre più impegnata nell'area delle **malattie rare** ed in particolare in ambito di **tumori rari.** Attraverso il suo costante orientamento all'innovazione e il suo approccio responsabile alle esigenze della salute, Novartis Oncology è oggi una realtà consolidata di riferimento nella ricerca e sviluppo dei tumori rari.

Nell'ambito delle malattie rare, i tumori rari costituiscono una famiglia eterogenea di patologie che, sulla base di un progetto di ricerca dell'Unione Europea, denominato RARECARE, sono state classificate in una lista di 186 neoplasie aventi un'incidenza non superiore alla soglia dei 6 casi su 100.000 all'anno[1].

Pur essendo rari nell'incidenza, nell'insieme tuttavia i tumori rari rappresentano circa il 25-30% di tutte le neoplasie nell'Unione Europea, con oltre 500.000 nuove diagnosi ogni anno in Europa e in Italia almeno 67.000[2], riguardando circa 450.000 persone in totale[2].

Tra i tumori rari più conosciuti si possono citare alcune neoplasie ematologiche (alcune forme di leucemie e linfomi) dell'età pediatrica (il retinoblastoma), i tumori solidi dell'adulto (come i sarcomi, il tumore gastrointestinale stromale o GIST e i tumori neuroendocrini).

Si tratta di patologie per lo più non adeguatamente conosciute e classificate, per le quali spesso non vi sono delle cure specifiche. Ai tumori rari è inoltre frequentemente associata una serie di difficoltà e problematiche, che coinvolgono tanto il percorso diagnostico-terapeutico della persona malata, quanto l'impatto sull'efficienza del Sistema Sanitario.

Queste le **principali criticità** che i pazienti con tumore raro devono affrontare:

- **difficoltà ad accedere** a un centro di riferimento per una diagnosi clinica e patologica certa e tempestiva, e ad essere assistiti con approccio multidisciplinare;
- **limitata disponibilità di terapie efficaci**, che si collega alla difficoltà nello sviluppo di trial clinici, dovuto al numero esiguo di pazienti e alla potenziale carenza d'interesse nello sviluppo di nuove terapie;
- **decorso rapido della patologia,** essendo malattie oncologiche: la variabile tempo rappresenta una delle problematiche maggiori legate ai tumori rari.

I tumori rari comportano infatti difficoltà aggiuntive rispetto ai tumori frequenti. La minore frequenza determina una minore disponibilità di expertise super-specialistica nel territorio e una minore numerosità delle casistiche cliniche, in particolare dei pazienti candidati a studi clinici prospettici. Ne derivano rischi di disomogeneità nella qualità di cura sulla popolazione e un difetto di "evidenza". Per quanto sopra, **la sopravvivenza a 5 anni per i pazienti con tumore raro risulta essere inferiore rispetto ai pazienti affetti da tumori di incidenza frequente (51% vs 69% [2])**

Occorre quindi dotarsi di nuovi strumenti specifici, sia normativi che scientifici, se si vuole evitare la discriminazione nell'accesso alle cure dei pazienti affetti da tumori rari, anche con particolare riferimento ai nuovi farmaci che oggi si rendono disponibili e che spesso trovano proprio nei tumori rari dei potenziali bersagli sensibili.

Sul versante terapeutico, sono qualificati come orfani[3], i medicinali indicati per

- una condizione clinica rara (definita da una prevalenza di non più di 5 soggetti ogni 10.000 individui, calcolata a livello dell'Unione Europea),
- cronicamente debilitante o che mette in pericolo la vita ,
- per la quale non sono disponibili trattamenti validi o, se sono già disponibili dei trattamenti, il nuovo farmaco deve rappresentare un beneficio clinico significativo.

L'Unione Europea prevede una serie di facilitazioni per lo sviluppo dei farmaci orfani, essenzialmente rappresentate da incentivi alle aziende farmaceutiche che sviluppino nuovi farmaci in malattie rare, cioè in malattie a basso mercato e dunque a limitato vantaggio economico.

Tuttavia, il problema attuale dei nuovi farmaci nell'Unione Europea è sempre più rappresentato dal divario fra approvazione regolatoria centralizzata (da parte dell'EMA, l'agenzia regolatoria europea), rimborsabilità a livello nazionale e reale disponibilità a livello regionale. In Italia ciò è causa di gravi ritardi di mesi o anche anni, all'accesso a

terapie per malattie in cui, più che per altre, fondamentale è la variabile tempo: trattandosi infatti di neoplasie, quindi patologie dal decorso rapido e ingravescente, frequentemente a fare la differenza è un pronto accesso alle terapie, spesso orfane, che man mano vengono rese disponibili dalle aziende farmaceutiche.

PROPOSTE

Il tema delle malattie rare ed in particolare dei tumori rari sta molto a cuore a Novartis Oncology, che auspica di poter offrire il proprio contributo alla Commissione su ricerca e sviluppo di farmaci per le malattie e tumori rari ed in particolare desidera portare all'attenzione del legislatore tre aspetti importanti per i pazienti e le loro famiglie:

- la creazione ed il riconoscimento istituzionale di un elenco di tumori rari
- la creazione di una rete sul territorio nazionale tra i centri oncologici con expertise nell'ambito tumori rari, finalizzata al miglioramento della diagnosi, ricerca e cura dei pazienti.
- l'agevolazione e l'omogeneità di accesso per i pazienti con tumori rari e farmaci orfani, al fine di garantire tempestività ed equità di accesso su tutto il territorio nazionale.

A. Creazione e riconoscimento istituzionale di un elenco di tumori rari secondo la Lista di RARECARE

In Italia è in uso un Elenco delle Malattie Rare, che fu istituito ai sensi del Decreto Ministeriale 279/2001 ("Regolamento di istituzione della rete nazionale delle malattie rare e di esenzione dalla partecipazione al costo delle relative prestazioni sanitarie"), che attua il Decreto legislativo 29 aprile 1998, n. 124.

Questo **elenco esclude sostanzialmente i tumori.** Infatti, la sezione n. 2, sui tumori, include solo due tumori pediatrici (tumore di Wilms e retinoblastoma), una neoplasia come la linfangioleiomiomatosi, quattro condizioni predisponenti (m. di Cronkite-Canada, s. di Gardner, poliposi familiare e neurofibromatosi).

Risulta quindi fondamentale ufficializzare una lista ad hoc di tumori rari, che potrebbe essere assunta come uno strumento operativo ragionevole per l'introduzione di nuove misure regolatorie e normative.

Il progetto europeo di ricerca "RARECARE", finanziato nell'ambito del Framework Project 7 dell'Unione Europea, ha proposto una definizione di rarità basata su una soglia di incidenza a 6/100.000/anno. Questo è stato il risultato di un processo di consenso nella

comunità europea degli oncologi. Ne è derivata una "lista" dei tumori rari, recentemente pubblicata[1], disponibile sul sito web del progetto[4] e che alleghiamo.

L'ufficializzazione della lista permetterebbe all'Italia di avere un criterio di riferimento unico ed omogeneo, riconosciuto a livello europeo, utile a scopi concreti quali:

- la selezione delle condizioni da includere in bandi di ricerca sulle malattie rare
- la creazione di reti nazionali
- l'identificazione di misure mirate a permettere l'accesso alle cure tempestivo e uniforme sul territorio italiano.

B. Creazione di una rete sul territorio nazionale tra i centri oncologici con expertise nell'ambito tumori rari, finalizzata al miglioramento della diagnosi, ricerca e cura dei pazienti.

Come per le malattie rare, non è immediato anche per il paziente affetto da tumore raro identificare e accedere a un centro con expertise nella diagnosi, cura e follow up di tale patologia. Come per le altre forme tumorali, anche per le neoplasie rare è fondamentale la tempestività della diagnosi: la possibilità del controllo della malattia dipende dalle caratteristiche biologiche del tumore, cioè dall'aggressività delle cellule tumorali, ma anche da una corretta diagnosi clinica precoce, unitamente a precisa diagnosi istologica e molecolare e da un'accurata valutazione dell'estensione della malattia mediante esami clinici e strumentali (cosiddetta "stadiazione"). **Per il paziente affetto da un tumore raro, spesso la diagnosi giunge in ritardo, a causa della aspecificità dei sintomi** che non orientano in maniera univoca e inequivocabile. Di frequente si ritiene utile richiedere una second opinion.

La gestione clinica dei tumori rari richiede spesso, tra l'altro, **approcci multidisciplinari** e ciò comporta che professionalità e competenze, siano non omogeneamente distribuite sul territorio nazionale e a volte non presenti in un unico centro clinico. Di qui il problema, anch'esso comune alle malattie rare, della **frammentazione territoriale, dell'assistenza** e **della migrazione sanitaria** in ambito nazionale e internazionale, con conseguenti **costi sociali elevati.**

- Per ridurre gli infrequenti errori diagnostici e di gestione, sarebbe auspicabile che il paziente fosse tempestivamente indirizzato a un centro specializzato.
- La qualità di cura verrebbe ulteriormente garantita facilitando il riferimento dei pazienti a centri di eccellenza e creando reti geografiche collaborative, che rendano disponibile l'expertise dei centri di eccellenza anche al di fuori di essi.

In Italia le reti oncologiche ed ematologiche regionali e la Rete Tumori Rari (quest'ultima limitatamente ai tumori rari solidi dell'adulto) cercano di affrontare in questo modo le problematiche del riferimento elettivo dei pazienti e della condivisione dell'expertise clinico disponibile, tali realtà sono tuttavia disomogenee da punto di vista geografico.
Si rende necessario quindi, in analogia con quanto in essere per le malattie rare, la creazione di una rete nazionale di centri di riferimento per i tumori rari, condivisa tra le Regioni attraverso accordi interegionali.

C. Agevolazione ed omogeneità di accesso per i pazienti con tumori rari e farmaci orfani, al fine di garantire tempestività ed equità di accesso su tutto il territorio nazionale.

L'accesso alla terapia farmacologica, anche se autorizzata a livello centrale dall'AIFA, ad oggi non è affatto né scontata né omogenea sul territorio nazionale, spesso a causa di mere considerazioni di contenimento dei costi da parte delle strutture coinvolte e dei prontuari implementati a livello locale (regionali, provinciali e ospedalieri). Il tempo che decorre dall'Autorizzazione all'Immissione in Commercio(AIC) sancita da AIFA alla effettiva erogazione del farmaco a livello locale, è molto diverso tra regione e regione e può arrivare anche a una differenza di molti mesi (anche 12-18 mesi). Questo comporta situazioni gravemente discriminatorie tra pazienti che vivono in Regioni differenti, con una "variabile tempo" che è fondamentale nella gestione di queste patologie. Inoltre, considerata la rarità della patologia, spesso il paziente non ha a disposizione alternative terapeutiche, essendo il farmaco in approvazione spesso orfano.
Al fine di evitare discriminazioni d'accesso ai farmaci orfani andrebbe quindi considerata la possibilità di intervenire per ridurre alcuni fattori di distorsione collegati ai sistemi di rimborsabilità e accesso dei farmaci.
L'utilizzo di farmaci orfani, rimborsati dal Servizio Sanitario Nazionale, è comunque oggi monitorato e controllato tramite i Registri AIFA, che ne assicurano l'uso razionale e l'impiego solo nei pazienti che possono trarne beneficio, raccogliendo inoltre i dati reali di sicurezza ed efficacia.
Inoltre, delegando la presa in carico del paziente affetto da tumore raro ai soli presidi accreditati per quella specifica patologia, si garantirebbe l'appropriatezza diagnostica e prescrittiva.
Andrebbe considerato un percorso accelerato e omogeneo tra le varie regioni italiane d'inserimento dei farmaci orfani, secondo la definizione EMA: una soluzione potrebbe

essere **prevedere l'immediata disponibilità a carico del SSN dei farmaci orfani in concomitanza con la pubblicazione in Gazzetta Ufficiale del decreto di AIC, in attesa dell'inserimento nei prontuari regionali o ospedalieri** (PTOR-PTO), eliminando così gli ostacoli tra la diagnosi, il piano terapeutico e l'accesso alla terapia.

CONCLUSIONI

Il riconoscimento ufficiale di una lista di tumori rari è un presupposto doveroso, per consentire un avanzamento sensibile nell'erogazione della qualità di cura e della presa in carico dei pazienti affetti da tali patologie.

A fronte di un elenco finalmente riconosciuto dei tumori rari, sarebbero possibili finalmente dei provvedimenti specifici attesi da tempo: la creazione di una rete nazionale per tumori rari e misure per l'accesso omogeneo e tempestivo su tutto il territorio nazionale per i farmaci orfani per la cura dei tumori rari garantirebbero razionalità, equità e appropriatezza all'accesso alle cure.

NOTE

1 Gatta G. et al.; European Journal Cancer 2011;47:2493

2 Dati Associazione Italiana dei Registri TUMori - AIRTUM), XIV Riunione Aprile 2010

3 Articolo 9 del Regolamento CE 141/2000

4 www.rarecare.eu – http://www.rarecare.eu/rarecancers/rarecancers.asp

EUROPEAN JOURNAL OF CANCER 47 (2011) 2493–2511

Available at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.ejconline.com

Rare cancers are not so rare: The rare cancer burden in Europe

Gemma Gatta [a,*], *Jan Maarten van der Zwan* [b], *Paolo G. Casali* [c], *Sabine Siesling* [b], *Angelo Paolo Dei Tos* [d], *Ian Kunkler* [e], *Renée Otter* [b], *Lisa Licitra* [f], *Sandra Mallone* [g], *Andrea Tavilla* [g], *Annalisa Trama* [a], *Riccardo Capocaccia* [g], *The RARECARE working group*

[a] *Department of Preventive and Predictive Medicine, Fondazione IRCSS, Istituto Nazionale dei Tumori, Via Venezian 1, 20133 Milan, Italy*
[b] *North East Netherlands Cancer Registry, Comprehensive Cancer Centre North East, P.O. Box 330, 9700 AH Groningen, The Netherlands*
[c] *Department of Cancer Medicine, Fondazione IRCSS, Istituto Nazionale dei Tumori, Via Venezian 1, 20133 Milan, Italy*
[d] *Department of Pathology, General Hospital of Treviso, Via Borgo Cavalli 42, 31100 Treviso, Italy*
[e] *Department of Clinical Oncology, Western General Hospital, Crewe Road South, Edinburgh EH4 2XU, UK*
[f] *Head and Neck Cancer Medical Oncology Unit, Fondazione IRCSS, Istituto Nazionale dei Tumori, Via Venezian 1, 20133 Milan, Italy*
[g] *Department of Cancer Epidemiology, Istituto Superiore di Sanità, Viale Regina Elena 299, Rome, Italy*

ARTICLE INFO

Keywords:
Rare cancers
Cancer registries
Incidence
Prevalence
Survival

ABSTRACT

Purpose: Epidemiologic information on rare cancers is scarce. The project Surveillance of Rare Cancers in Europe (RARECARE) provides estimates of the incidence, prevalence and survival of rare cancers in Europe based on a new and comprehensive list of these diseases.
Materials and methods: RARECARE analysed population-based cancer registry (CR) data on European patients diagnosed from 1988 to 2002, with vital status information available up to 31st December 2003 (latest date for which most CRs had verified data). The mean population covered was about 162,000,000. Cancer incidence and survival rates for 1995–2002 and prevalence at 1st January 2003 were estimated.
Results: Based on the RARECARE definition (incidence <6/100,000/year), the estimated annual incidence rate of all rare cancers in Europe was about 108 per 100,000, corresponding to 541,000 new diagnoses annually or 22% of all cancer diagnoses. Five-year relative survival was on average worse for rare cancers (47%) than common cancers (65%). About 4,300,000 patients are living today in the European Union with a diagnosis of a rare cancer, 24% of the total cancer prevalence.
Conclusion: Our estimates of the rare cancer burden in Europe provide the first indication of the size of the public health problem due to these diseases and constitute a useful base for further research. Centres of excellence for rare cancers or groups of rare cancers could provide the necessary organisational structure and critical mass for carrying out clinical trials and developing alternative approaches to clinical experimentation for these cancers.

1. Introduction

There is no internationally agreed definition of rare cancers. In Europe rare diseases are often defined as those with a prevalence of <50/100,000.[1] In the US, the Orphan Drug Act defined rare diseases as those affecting <200,000 persons.[2] However, a recent analysis of rare cancers in the US employed the definition of <15 incident cases per 100,000 per year.[3]

* *Corresponding author:* Address: Evaluative Epidemiology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1, 20133 Milan, Italy. Tel.: +39 02 23903518; fax: +39 02 23903522.
E-mail address: gemma.gatta@istitutotumori.mi.it (G. Gatta).
0959-8049/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ejca.2011.08.008

A major problem with rare cancers is that their overall burden on society has not been adequately estimated, although they are thought to constitute a major public health problem.[4–6] Rare cancers are often inadequately diagnosed and treated[4] in relation both to lack of knowledge and lack of clinical expertise. Improving the quality of care for these cancers is a public health priority. One way of doing this would be to use a similar approach to that used for rare childhood cancers: concentrate treatment at specialised centres, and recruit most patients diagnosed to clinical trials.[5] However this requires a huge organisational effort; and for the rarest cancers it will always be impossible to recruit sufficient patients to perform standard clinical trials. Thus new approaches to obtaining evidence on treatment efficacy need to be developed.[6]

The project Surveillance of Rare Cancers in Europe (RARECARE) collected data on cancers from 89 population-based cancer registries (CRs) in 21 European countries, making it possible to study the epidemiology of these cancers as a whole in a large and heterogeneous population. Working from this database and the literature, a RARECARE working group produced a new list of cancers and developed a new definition of rare cancers (http://www.rarecare.eu).

This paper delineates the burden of these cancers in Europe, providing estimates of the incidence, prevalence and survival of rare cancers diagnosed from 1988 to 2002, based on the RARECARE definition and list.

2. Materials and methods

RARECARE gathered data on cancer patients diagnosed from 1978 to 2002 and archived in population-based CRs, all of which had vital status information available up to at least 31st December 2003. For 11 countries, the CRs covered the entire national population (Austria, Iceland, Ireland, Malta, Norway, Slovakia, Slovenia, Sweden, Northern Ireland, Scotland and Wales); the other countries do not have national cancer registration and were represented by regional CRs covering variable proportions of their national populations. The mean population covered, over the period 1995–1999, was about 162,000,000, corresponding to 39% of the population of countries participating in RARECARE and 32% of the European Union (EU27) population.

Systematic data checks were performed to detect errors, inconsistencies or unusual combinations of site, morphology, sex and age at diagnosis.[7,8] Only a negligible proportion (0.14%) of cases had major errors and had to be excluded.[7] RARECARE collected data from 89 CRs; however the present paper considered data from 76 CRs, excluding CRs which did not classify cancers according to the third edition of the International Classification of Diseases for Oncology (ICD-O-3),[9] and also those which collected data on childhood cancers only.

2.1. Incidence

The incidence analysis only considered cases incident in the more recent 1995–2002 period. Specialised CRs and some non-specialised CRs, with information available only for some anatomical sites were excluded. This criterion implied restricting the incidence analyses to 4,048,903 cases from 64 CRs.

Incidence rates were estimated as the number of new cases occurring in 1995–2002 divided by the total person-years in the general population (male and female) in each CR area, over the same period. The expected number of new cases per year in EU27 in 2008 was also estimated, assuming that incidence rates in Europe were same as those in the RARECARE sample.

2.2. Prevalence

CRs that started up recently do not have records of longer-term cancer survivors diagnosed before start up, resulting in underestimation of prevalence. To estimate prevalence, we therefore used data from CRs able to provide cases for the relatively long period 1988–2002; only 22 CRs fulfilled this condition. We calculated the number of prevalent cancers in 2008 and prevalence per 100,000 at the index date of 1st January 2003. The counting method,[10] based on CR incidence and follow-up data, was applied to CR data from 1988 to 2002. The completeness index method[11] was used to estimate the complete prevalence and involved adding the estimated surviving cases diagnosed prior to 1988 to those counted in 1988–2002. The total number of prevalent cases in the EU27 in 2008 was estimated assuming the same prevalence as in the RARECARE sample. Overall, 4,302,067 cancer cases were used to produce the prevalence estimates.

2.3. Survival

Data from all 76 CRs (including specialised registries) were used to produce survival estimates. We used the cohort approach[12] to estimate survival for patients diagnosed in 1995–1999 and followed-up until at least the end of 2003, enabling estimation of 5-year survival. A total 2,708,344 cases were used for the analysis. We estimated relative survival[12], the ratio of observed survival to the expected survival in the general population of the same age and sex, to correct for deaths from causes other than the cancer under investigation.

2.4. List of cancers and definition of rare cancers

The present analyses are based on the new list of cancer types provided by RARECARE. The list was produced by a group of pathologists, haematologists, clinicians and epidemiologists and emerged after a consultation process during which the developing list and its rationale were available at http://www.rarecare.eu. The list, endorsed by major European cancer organisations, is organised into three tiers as exemplified in Table 1. The bottom tier corresponds to the WHO names of individual cancer entities (http://www.iarc.fr/en/publications/pdfs-online/pat-gen/) and their corresponding ICD-O-3[9] codes. Bottom tier entities were grouped into categories (middle tier) considered to require similar clinical management and research. Middle tier entities were grouped into general categories (top tier) considered to involve the same clinical expertise and patient referral structure.

Table 1 – The three-tier structure of the RARECARE list of cancers illustrated for epithelial cancers of the anal canal.

TIER	NAME
Top	EPITHELIAL TUMOURS OF ANAL CANAL
Middle	**Squamous cell carcinoma and variants of anal canal**
Bottom	Verrucous carcinoma
Bottom	Undifferentiated carcinoma
Bottom	Basaloid carcinoma
Middle	**Adenocarcinoma and variants of anal canal**
Bottom	Mucinous adenocarcinoma
Middle	**Paget disease of anal canal**

RARECARE defined rare cancers as those with an incidence of <6/100,000/year, corresponding to <30,000 new cases/year in Europe. A total of 186 cancers were rare according to this definition. The list of the rare and common cancers defined by RARECARE is available at the RARECARE web site and in Table 2 which shows the top and middle tiers only. Table 2 also shows the estimates of crude annual incidence, complete prevalence and 5-year survival, together with the expected number of new cases per year and prevalent cases in the EU27 in 2008.

3. Results

Table 3 shows quality indicators for the data on rare and common cancers diagnosed from 1995 to 2002 and archived by the 76 CRs considered in the study. The overall proportion of death-certificate only (DCO) cases was 3%, with only six CRs having more than 5% DCOs. The overall proportion of cases discovered at autopsy was 0.5%. A high proportion of cases (86% overall) was verified microscopically (MV). Follow-up was complete for most CRs, with follow-up censored before 5 years for only 1.2% of cases overall, with only two CRs having high proportions of cases not followed-up after 2002.

Two other data quality indicators, pertinent to the accuracy of diagnoses and completeness of incidence for rare cancers, are the proportion of cases with not otherwise specified (NOS) morphology codes (M8000–8001) and the proportion of cases with poorly defined topography (codes C260, C268, C269, C390, C398, C399, C559, C579, C639, C689, C729, C759–C765, C767–C768). The former was 8.2% overall and varied markedly across CRs. The latter did not exceed 2% and was <1% overall and for almost all CRs.

3.1. *Incidence*

RARECARE estimated that about 2,511,000 persons were diagnosed with cancer in the EU27 each year from 1995 to 2002 (Table 4). The annual EU27 incidence rate of all rare cancers was about 108 per 100,000 corresponding to 541,000 new diagnoses annually or 22% of all cancer diagnoses.

Fig. 1a shows the distribution of cancer types, as defined by RARECARE, according to incidence rate. Fig. 1b shows the estimated number of new cancer diagnoses in the EU27 each year, again according to incidence rate. About 74% of rare cancers had an annual incidence rate of <0.5/100,000. However, this plethora of cancers accounted for only 70,000 (3%) of the 2.5 million cancers diagnosed each year. Another 17 cancer types, with incidence 0.5–1/100,000, accounted for 49,000 new diagnoses each year in EU27, while the 31 cancer types with incidence >1–6/100,000, accounted for 422,000 new cases/year. Seventeen common cancers accounted for the remaining cases.

Fig. 2 shows age-specific incidence rates by age class for rare and common cancers. Patients with rare cancers were on average younger than those with common cancers. Essentially all childhood cancers and most cancers (sarcomas and lymphomas) in persons up to 39 years were rare. From age 40 on, the common cancers (breast, prostate, colon, rectum and lung) became increasingly prominent. Average age at diagnosis was 60 years for rare cancers and 67 for common cancers.

Table 4 shows incidence and prevalence rates of rare and common cancers by site. Rare cancers constituted 72% of incident haematological malignancies, 55% of incident female genital tract cancers, 21% of incident respiratory cancers and 15% of incident digestive tract cancers. Rare cancers were <10% of incident cancers at other sites. The proportions of rare and common cancers (columns 6 and 10) do not sum to 100% for each cancer site, since some cancers could not be classified as rare or common because of unspecified morphology. The proportion of unclassifiable cancers varied with site, being highest (30%) for respiratory tract cancers and lowest (2%) for skin cancers.

3.2. *Prevalence*

We estimated that 4,300,000 people were alive in the EU27 with a previous diagnosis of a rare cancer, 24% of the total cancer prevalence. Almost all cancers considered rare according to RARECARE are also rare according to the commonly adopted prevalence criterion in Europe[1] of <50/100,000. Only squamous cell carcinoma of the uterine cervix and thyroid carcinoma are rare according to the incidence (RARECARE) criterion and 'common' according to the prevalence criterion. Six cancers are common according to the incidence criterion and rare according to the prevalence criterion. These are stomach adenocarcinoma, pancreatic adenocarcinoma, lung adenocarcinoma, lung squamous cell carcinoma, poorly differentiated endocrine carcinomas of lung and the group other non-Hodgkin mature B cell lymphomas. The explanation is that these are poor prognosis cancers which hence have low prevalence, even though incidence is relatively high.

3.3. *Relative survival*

Rare cancers had, on average, worse relative survival than common cancers. For patients with rare cancers diagnosed in 1995–1999, 1, 3 and 5-year relative survival was 68%, 52% and 47%, respectively; the corresponding figures for patients with common cancers were 80%, 69% and 65% (Fig. 3). Fig. 3 shows that survival differences between rare and common cancers were small 1 year after diagnosis but survival for rare cancers declined more markedly thereafter, consistent with the idea that treatments for rare cancers are less effective than those for common cancers, and suggesting that later

Table 2 – RARECARE estimates of incidence, survival and prevalence of cancers for EU27, together with expected number of new cases per year and prevalent cases in EU27.

Rare (R) or common (C) (middle tier only)	Tier	Top tier (upper case) and middle tier (lower case) tumour categories	Crude incidence per 100,000 per year	Standard error incidence	Expected new cases per year	Observed 5-year survival (%)	Relative 5-year survival (%)	Standard error relative survival (%)	Complete prevalence per 100,000	Standard error complete prevalence	Prevalent Cases
	1	EPITHELIAL TUMOURS OF NASAL CAVITY AND SINUSES	0.44	0.01	2198	39.3	48.3	1.3	2.92	0.08	14,492
R	2	Squamous cell carcinoma with variants of nasal cavity and sinuses	0.31	0.01	1545	40.2	49.2	1.5	2.10	0.07	10,416
R	2	Lymphoepithelial carcinoma of nasal cavity and sinuses	0.00	0.00	12	28.6	31.0	13.1	0.01	0.01	72
R	2	Undifferentiated carcinoma of nasal cavity and sinuses	0.02	0.00	86	27.5	32.4	6.0	0.13	0.02	665
R	2	Intestinal type adenocarcinoma of nasal cavity and sinuses	0.00	0.00	12	43.0	50.1	14.6	0.02	0.01	123
	1	EPITHELIAL TUMOURS OF NASOPHARYNX	0.44	0.01	2205	44.1	49.1	1.1	2.94	0.09	14,637
R	2	Squamous cell carcinoma with variants of nasopharynx	0.33	0.01	1626	44.4	49.2	1.3	2.20	0.07	10,966
R	2	Papillary adenocarcinoma of nasopharynx	0.00	0.00	4	57.1	58.8	23.8	0.01	0.00	29
	1	EPITHELIAL TUMOURS OF MAJOR SALIVARY GLANDS AND SALIVARY-GLAND TYPE TUMOURS	1.31	0.01	6501	54.2	64.8	0.7	13.08	0.18	65,063
R	2	Epithelial tumours of major salivary glands	0.73	0.01	3624	53.7	64.6	1.0	7.90	0.14	39,290
R	2	Salivary gland type tumours of head and neck	0.43	0.01	2134	60.3	69.1	1.2	4.53	0.11	22,553
	1	EPITHELIAL TUMOURS OF HYPOPHARYNX AND LARYNX	6.26	0.03	31,138	46.9	54.8	0.3	39.98	0.33	198,863
R	2	Squamous cell carcinoma with variants of hypopharynx	1.19	0.01	5905	21.6	24.6	0.6	3.47	0.09	17,293
R	2	Squamous cell carcinoma with variants of larynx	4.64	0.02	23,082	54.5	63.7	0.4	34.39	0.28	171,098
	1	EPITHELIAL TUMOURS OF OROPHARYNX	2.75	0.02	13,667	33.1	37.1	0.4	13.04	0.18	64,877
R	2	Squamous cell carcinoma with variants of oropharynx	2.58	0.02	12,858	33.3	37.2	0.5	12.52	0.18	62,254
	1	EPITHELIAL TUMOURS OF ORAL CAVITY AND LIP	4.79	0.02	23,828	49.0	59.1	0.4	34.07	0.35	169,507
R	2	Squamous cell carcinoma with variants of oral cavity	3.28	0.02	16,337	41.3	48.2	0.4	19.34	0.25	96,196
R	2	Squamous cell carcinoma with variants of lip	1.22	0.01	6093	70.1	91.7	0.7	12.79	0.18	63,621
	1	EPITHELIAL TUMOURS OF OESOPHAGUS	7.51	0.03	37,379	8.4	10.6	0.2	12.11	0.16	60,221

R	2	Squamous cell carcinoma with variants of oesophagus	3.40	0.02	16,927	8.7	10.7	0.3	5.42	0.10	26,953
R	2	Adenocarcinoma with variants of oesophagus	2.85	0.02	14,182	9.1	11.7	0.3	5.55	0.10	27,625
R	2	Salivary gland type tumours of oesophagus	0.01	0.00	29	8.1	9.6	5.3	0.01	0.00	36
R	2	Undifferentiated carcinoma of oesophagus	0.07	0.00	367	5.6	7.3	1.5	0.08	0.01	390
	1	EPITHELIAL TUMOURS OF STOMACH	18.62	0.05	92,649	16.4	21.6	0.2	49.17	0.32	244,582
C	2	Adenocarcinoma with variants of stomach	15.23	0.04	75,772	17.8	23.1	0.2	45.90	0.31	228,325
R	2	Squamous cell carcinoma with variants of stomach	0.13	0.00	646	11.3	14.2	1.5	0.24	0.02	1193
R	2	Salivary gland-type tumours of stomach	0.01	0.00	25	16.9	20.6	7.8	0.02	0.01	118
R	2	Undifferentiated carcinoma of stomach	0.17	0.00	838	10.1	13.2	1.3	0.33	0.02	1633
	1	EPITHELIAL TUMOURS OF SMALL INTESTINE	0.72	0.01	3595	20.4	25.3	0.8	2.67	0.08	13,276
R	2	Adenocarcinoma with variants of small intestine	0.57	0.01	2823	21.1	25.8	0.9	2.21	0.07	10,983
R	2	Squamous cell carcinoma with variants of small intestine	0.01	0.00	30	18.2	21.4	7.9	0.03	0.01	125
	1	EPITHELIAL TUMOURS OF COLON	42.64	0.07	212,093	41.3	53.2	0.1	251.08	1.08	1,248,973
C	2	Adenocarcinoma with variants of colon	37.21	0.07	185,092	44.5	56.3	0.1	241.06	0.99	1,199,156
R	2	Squamous cell carcinoma with variants of colon	0.02	0.00	104	25.0	31.9	5.2	0.09	0.01	440
	1	EPITHELIAL TUMOURS OF RECTUM	17.11	0.05	85,133	41.6	52.5	0.2	110.89	0.73	551,594
C	2	Adenocarcinoma with variants of rectum	15.52	0.04	77,205	43.5	54.3	0.2	105.49	0.68	524,771
R	2	Squamous cell carcinoma with variants of rectum	0.07	0.00	368	41.4	50.4	3.0	0.67	0.04	3323
R	2	Basaloid carcinoma of rectum	0.01	0.00	74	42.6	51.1	6.6	0.06	0.01	307
	1	EPITHELIAL TUMOURS OF ANAL CANAL	1.09	0.01	5427	45.2	55.4	0.8	8.16	0.14	40,589
R	2	Squamous cell carcinoma with variants of anal canal	0.73	0.01	3634	51.6	61.4	1.0	6.84	0.13	29,266
R	2	Adenocarcinoma with variants of anal canal	0.26	0.01	1276	32.3	42.0	1.7	1.07	0.05	5333
R	2	Paget's disease of anal canal	0.00	0.00	20	47.8	59.9	13.0	0.02	0.01	4750
	1	EPITHELIAL TUMOURS OF PANCREAS	11.79	0.04	58,639	2.9	3.7	0.1	8.30	0.12	41,268
C	2	Adenocarcinoma with variants of pancreas	7.59	0.03	37,758	2.7	3.4	0.1	6.27	0.11	31,178
R	2	Squamous cell carcinoma with variants of pancreas	0.03	0.00	129	8.0	9.7	2.9	0.05	0.01	242
R	2	Acinar cell carcinoma of pancreas	0.02	0.00	108	18.4	21.4	4.3	0.06	0.01	281
R	2	Mucinous cystadenocarcinoma of pancreas	0.01	0.00	40	32.7	36.5	8.9	0.04	0.01	200
R	2	Intraductal papillary mucinous carcinoma invasive of pancreas	0.00	0.00	3	NE	NE	NE	0.01	0.00	29
R	2	Solid pseudopapillary carcinoma of pancreas	0.00	0.00	4	66.7	70.7	28.9	0.00	0.00	18
R	2	Serous cystadenocarcinoma of pancreas	0.00	0.00	1	100.0	102.2	0.0	0.00	0.00	0
R	2	Carcinoma with osteoclast-like giant cells of pancreas	0	NE	NE	NE	NE	NE	0	NE	0
	1	EPITHELIAL TUMOURS OF LIVER AND INTRA-HEPATIC BILE TRACT (IBT)	6.19	0.03	30,802	7.0	8.7	0.2	5.62	0.10	27,957

(continued on next page)

Table 2 – (continued)

Rare (R) or common (C) (middle tier only)	Tier	Top tier (upper case) and middle tier (lower case) tumour categories	Crude incidence per 100,000 per year	Standard error incidence	Expected new cases per year	Observed 5-year survival (%)	Relative 5-year survival (%)	Standard error relative survival (%)	Complete prevalence per 100,000	Standard error complete prevalence	Prevalent Cases
R	2	Hepatocellular carcinoma of liver and IBT	3.09	0.02	15,352	9.6	11.6	0.3	3.66	0.08	18,186
R	2	Cholangiocarcinoma of IBT	0.84	0.01	4167	4.3	5.5	0.4	0.74	0.03	3675
R	2	Adenocarcinoma with variants of liver and IBT	0.21	0.01	1027	4.4	5.3	0.8	0.19	0.02	951
R	2	Undifferentiated carcinoma of liver and IBT	0.02	0.00	81	3.0	3.6	2.5	0.01	0.00	45
R	2	Squamous cell carcinoma with variants of liver and IBT	0.01	0.00	57	7.7	9.6	4.6	0.02	0.01	80
R	2	Bile duct cystadenocarcinoma of IBT	0.00	0.00	9	11.1	12.1	11.4	0.00	0.00	11
	1	EPITHELIAL TUMOURS OF GALLBLADDER AND EXTRAHEPATIC BILIARY TRACT (EBT)	4.37	0.02	21,763	9.7	12.6	0.3	6.83	0.11	33,974
R	2	Adenocarcinoma with variants of gallbladder and EBT	2.62	0.02	13,038	12.1	15.0	0.3	5.37	0.10	26,702
R	2	Squamous cell carcinoma of gallbladder and EBT	0.04	0.00	180	9.8	12.3	2.7	0.05	0.01	227
	1	EPITHELIAL TUMOUR OF TRACHEA	0.13	0.00	670	10.1	12.1	1.4	0.28	0.02	1396
R	2	Squamous cell carcinoma with variants of trachea	0.08	0.00	408	7.2	8.5	1.4	0.12	0.01	602
R	2	Adenocarcinoma with variants of trachea	0.01	0.00	67	6.6	7.6	3.3	0.02	0.01	119
R	2	Salivary gland type tumours of trachea	0.01	0.00	48	50.9	55.2	7.7	0.11	0.02	523
	1	EPITHELIAL TUMOUR OF LUNG	55.93	0.08	278,226	8.5	10.6	0.1	85.00	0.44	422,831
C	2	Squamous cell carcinoma with variants of lung	13.49	0.04	67,125	10.9	13.4	0.1	25.35	0.23	126,097
C	2	Adenocarcinoma with variants of lung	10.29	0.04	51,193	11.8	13.9	0.2	22.14	0.22	110,140
R	2	Large cell carcinoma of lung	4.01	0.02	19,936	10.2	12.3	0.3	6.83	0.12	33,969
R	2	Well differentiated endocrine carcinoma of lung	0.63	0.01	3148	53.0	58.7	1.0	6.96	0.18	34,627
C	2	Poorly differentiated endocrine carcinoma of lung	7.68	0.03	38,221	3.9	4.6	0.1	8.43	0.13	41,925
R	2	Bronchiolo-alveolar carcinoma of lung	0.68	0.01	3383	26.5	31.1	0.9	2.42	0.07	12,066
R	2	Salivary gland type tumours of lung	0.04	0.00	220	38.5	43.4	3.6	0.30	0.03	1505
R	2	Sarcomatoid carcinoma of lung	0.14	0.00	697	13.4	15.9	1.5	0.32	0.02	1621
R	2	Undifferentiated carcinoma of lung	0.98	0.01	4887	5.6	6.6	0.4	1.27	0.05	6328
	1	EPITHELIAL TUMOURS OF THYMUS	0.17	0.00	829	52.6	57.7	1.9	1.40	0.06	6962
R	2	Malignant thymoma	0.14	0.00	680	55.7	60.9	2.0	1.22	0.06	6055
R	2	Squamous cell carcinoma of thymus	0.00	0.00	23	40.0	44.6	10.9	0.02	0.01	119
R	2	Undifferentiated carcinoma of thymus	0.00	0.00	12	16.7	18.2	11.8	0.00	0.00	16

R	2	Lymphoepithelial carcinoma of thymus	0.00	0.00	4	66.7	67.6	27.6	0.01	0.01	60
R	2	Adenocarcinoma with variants of thymus	0.00	0.00	10	31.0	32.8	15.5	0.01	0.00	40
	1	EPITHELIAL TUMOURS OF BREAST	63.85	0.09	317,621	71.4	80.6	0.1	697.23	6.27	3,468,450
C	2	Invasive ductal carcinoma of breast	40.32	0.07	200,559	75.9	83.5	0.1	441.33	4.02	2,195,417
C	2	Invasive lobular carcinoma of breast	7.18	0.03	35,742	77.5	86.0	0.2	78.54	1.01	390,709
R	2	Mammary Paget's disease of breast	0.51	0.01	2544	71.3	83.0	1.0	6.10	0.14	30,348
R	2	Special types of adenocarcinoma of breast	3.55	0.02	17,682	84.5	95.4	0.3	46.91	0.65	233,346
R	2	Metaplastic carcinoma of breast	0.06	0.00	303	57.2	65.7	3.4	0.56	0.04	2800
R	2	Salivary gland type tumours of breast	0.05	0.00	262	77.3	85.4	2.7	0.49	0.04	2443
R	2	Epithelial tumour of male breast	0.47	0.02	2338	60.3	77.1	1.3	3.52	0.18	17,536
	1	EPITHELIAL TUMOURS OF CORPUS UTERI	10.40	0.04	51,743	69.5	79.5	0.2	133.11	0.61	662,186
C	2	Adenocarcinoma with variants of corpus uteri	9.53	0.03	47,393	71.7	81.3	0.2	126.65	0.61	630,048
R	2	Squamous cell carcinoma with variants of corpus uteri	0.12	0.00	581	46.2	53.5	2.3	0.95	0.05	4721
R	2	Adenoid cystic carcinoma of corpus uteri	0.00	0.00	7	70.0	74.5	15.4	0.29	0.05	1445
R	2	Transitional cell carcinoma of corpus uteri	0.00	0.00	1	NE	NE	NE	0.01	0.00	31
	1	EPITHELIAL TUMOURS OF CERVIX UTERI	6.08	0.03	30,227	62.0	66.7	0.3	106.46	0.66	529,610
R	2	Squamous cell carcinoma with variants of cervix uteri	4.28	0.02	21,295	62.9	67.4	0.3	76.24	0.56	379,273
R	2	Adenocarcinoma with variants of cervix uteri	1.01	0.01	5023	62.3	66.8	0.7	15.59	0.24	77,548
R	2	Undifferentiated carcinoma of cervix uteri	0.03	0.00	125	30.2	34.4	4.6	0.32	0.03	1589
	1	MIXED EPITHELIAL AND MESENCHYMAL TUMOURS OF UTERUS	0.44	0.01	2213	31.4	37.3	1.2	2.59	0.08	12,888
R	2	Mixed epithelial and mesenchymal tumours of uterus	0.44	0.01	2213	31.4	37.3	1.2	2.59	0.08	0
	1	EPITHELIAL TUMOURS OF OVARY AND FALLOPIAN TUBE	9.39	0.03	46,735	33.0	37.7	0.3	59.78	0.44	297,397
R	2	Adenocarcinoma with variants of ovary	5.97	0.03	29,692	33.0	36.9	0.3	39.13	0.37	194,668
R	2	Mucinous adenocarcinoma of ovary	0.85	0.01	4206	52.5	58.1	0.8	9.55	0.18	47,536
R	2	Clear cell adenocarcinoma of ovary	0.32	0.01	1611	50.0	53.9	1.3	2.55	0.08	12,691
R	2	Adenocarcinoma with variants of fallopian tube	0.26	0.01	1316	42.5	47.8	1.5	1.99	0.07	9866
	1	NON-EPITHELIAL TUMOURS OF OVARY	0.43	0.01	2153	57.9	62.6	1.1	6.69	0.17	33,286
R	2	Mixed epithelial/mesenchymal tumours of ovary	0.16	0.00	775	15.9	18.2	1.5	0.49	0.03	2461
R	2	Sex cord tumours of ovary	0.13	0.00	670	76.1	82.7	1.7	1.85	0.08	9224
R	2	Malignant/Immature teratomas of ovary	0.07	0.00	337	80.5	83.3	2.1	1.50	0.09	7481
R	2	Germ cell tumour of ovary	0.07	0.00	371	83.5	84.3	1.8	2.23	0.16	11,128
	1	EPITHELIAL TUMOURS OF VULVA AND VAGINA	1.91	0.02	9517	47.0	60.9	0.7	15.34	0.18	76,299
R	2	Squamous cell carcinoma with variants of vulva and vagina	1.50	0.01	7480	46.4	59.6	0.7	12.42	0.17	61,791
R	2	Adenocarcinoma with variants of vulva and vagina	0.08	0.00	383	35.5	43.2	2.9	0.52	0.03	2610
R	2	Paget's disease of vulva and vagina	0.05	0.00	249	77.5	97.8	3.2	0.47	0.04	2338
R	2	Undifferentiated carcinoma of vulva and vagina	0.01	0.00	40	26.3	31.5	8.0	0.05	0.01	235
	1	TROPHOBLASTIC TUMOUR OF PLACENTA	0.02	0.00	119	89.6	90.0	2.7	0.86	0.12	4275
R	2	Choriocarcinoma of placenta	0.02	0.00	119	89.6	90.0	2.7	0.86	0.12	3886
	1	EPITHELIAL TUMOURS OF PROSTATE	47.89	0.08	238,222	54.2	74.4	0.1	303.98	1.42	1,512,168

(*continued on next page*)

Table 2 – (continued)

Rare (R) or common (C) (middle tier only)	Tier	Top tier (upper case) and middle tier (lower case) tumour categories	Crude incidence per 100,000 per year	Standard error incidence	Expected new cases per year	Observed 5-year survival (%)	Relative 5-year survival (%)	Standard error relative survival (%)	Complete prevalence per 100,000	Standard error complete prevalence	Prevalent Cases
C	2	Adenocarcinoma with variants of prostate	40.51	0.07	201,518	58.8	78.8	0.2	278.96	1.36	1,387,707
R	2	Squamous cell carcinoma with variants of prostate	0.11	0.00	562	33.4	45.1	2.7	0.75	0.04	3753
R	2	Infiltrating duct carcinoma of prostate	0.47	0.01	2335	59.3	77.3	1.5	4.50	0.09	22,403
R	2	Transitional cell carcinoma of prostate	0.06	0.00	320	33.2	48.5	3.6	0.29	0.02	1459
R	2	Salivary gland type tumours of prostate	0.00	0.00	8	36.4	50.0	19.9	0.01	0.00	36
	1	TESTICULAR AND PARATESTICULEAR CANCERS	3.15	0.02	15,679	93.0	94.8	0.2	87.77	0.75	436,638
R	2	Paratesticular adenocarcinoma with variants	0.00	0.00	7	66.7	81.4	23.5	0.01	0.00	60
R	2	Non-seminomatous testicular cancer	1.21	0.01	6031	92.4	93.3	0.3	33.53	0.60	166,788
R	2	Seminomatous testicular cancer	1.71	0.01	8518	95.5	97.4	0.2	46.01	0.58	288,900
R	2	Spermatocytic seminoma	0.03	0.00	137	90.6	100.5	2.8	0.75	0.05	3731
R	2	Teratoma with malignant transformation	0.00	0.00	7	59.2	62.4	19.3	0.04	0.01	199
R	2	Testicular sex cord cancer	0.02	0.00	109	77.6	83.7	4.8	0.44	0.04	2207
	1	EPITHELIAL TUMOURS OF PENIS	0.62	0.01	3101	56.7	71.7	1.1	5.54	0.11	27,557
R	2	Squamous cell carcinoma with variants of penis	0.57	0.01	2851	58.1	72.8	1.1	5.03	0.10	25,045
R	2	Adenocarcinoma with variants of penis	0.00	0.00	25	35.8	51.9	13.7	0.03	0.01	140
	1	EPITHELIAL TUMOURS OF KIDNEY	10.55	0.04	52,472	47.6	56.6	0.3	72.81	0.45	362,188
C	2	Renal cell carcinoma with variants	8.35	0.03	41,521	54.9	63.6	0.3	67.18	0.44	334,179
R	2	Squamous cell carcinoma spindle cell type of kidney	0.01	0.00	35	6.5	7.9	5.4	0.01	0.01	73
R	2	Squamous cell carcinoma with variants of kidney	0.04	0.00	175	10.3	12.4	2.7	0.06	0.01	306
	1	EPITHELIAL TUMOURS OF PELVIS, URETER AND URETHRA	1.58	0.01	7870	42.8	53.5	0.7	10.96	0.15	54,515
R	2	Transitional cell carcinoma of pelvis, ureter and urethra	1.37	0.01	6805	45.1	56.0	0.7	9.85	0.15	49,030
R	2	Squamous cell carcinoma with variants of pelvis, ureter and urethra	0.05	0.00	254	25.8	32.1	3.3	0.21	0.02	1043
R	2	Adenocarcinoma with variants of pelvis, ureter and urethra	0.04	0.00	185	40.2	48.2	4.5	0.20	0.02	1025
R	2	Salivary gland-type tumours of pelvis, ureter and urethra	0.00	0.00	1	0.0	0.0	0.0	0.00	0.00	8

	1	EPITHELIAL TUMOURS OF BLADDER	20.11	0.05	100,031	50.0	65.6	0.2	148.17	0.58	737,090
C	2	Transitional cell carcinoma of bladder	17.41	0.05	86,610	52.7	68.5	0.2	134.96	0.56	671,365
R	2	Squamous cell carcinoma with variants of bladder	0.43	0.01	2120	25.2	33.6	1.2	1.75	0.06	8711
R	2	Adenocarcinoma with variants of bladder	0.29	0.01	1425	31.9	40.3	1.5	1.38	0.05	6862
R	2	Salivary gland type tumours of bladder	0.00	0.00	6	50.0	66.3	23.4	0.00	0.00	20
	1	EPITHELIAL TUMOURS OF EYE AND ADNEXA	0.04	0.00	177	66.5	85.0	4.3	0.35	0.04	1741
R	2	Squamous cell carcinoma with variants of eye and adnexa	0.02	0.00	119	66.9	88.5	5.3	0.18	0.02	895
R	2	Adenocarcinoma with variants of eye and adnexa	0.01	0.00	32	62.9	74.3	10.1	0.07	0.02	348
	1	EPITHELIAL TUMOURS OF MIDDLE EAR	0.03	0.00	151	34.5	41.9	4.5	0.23	0.02	1122
R	2	Squamous cell carcinoma with variants of middle ear	0.02	0.00	111	26.1	32.2	4.8	0.14	0.02	709
R	2	Adenocarcinoma with variants of middle ear	0.00	0.00	18	79.1	90.2	10.6	0.04	0.01	213
	1	MALIGNANT MESOTHELIOMA	1.90	0.02	9437	4.5	5.5	0.3	2.38	0.07	11,841
R	2	Mesothelioma of pleura and pericardium	1.60	0.01	7964	4.0	4.9	0.3	1.97	0.06	9824
R	2	Mesothelioma of peritoneum and tunica vaginalis	0.12	0.00	617	9.8	11.4	1.4	0.22	0.02	1072
	1	MALIGNANT SKIN MELANOMA	12.41	0.04	61,752	74.5	84.3	0.2	202.32	0.91	1,006,430
C	2	Malignant skin melanoma	12.41	0.04	61,752	74.5	84.3	0.2	202.32	0.91	1,006,430
	1	MALIGNANT MELANOMA OF MUCOSA	0.26	0.01	1293	32.1	40.6	1.8	1.51	0.06	7485
R	2	Malignant melanoma of mucosa	0.26	0.01	1293	32.1	40.6	1.8	1.51	0.06	7485
	1	MALIGNANT MELANOMA OF UVEA	0.51	0.01	2533	59.4	68.9	1.6	5.97	0.13	29,676
R	2	Malignant melanoma of uvea	0.51	0.01	2533	59.4	68.9	1.6	5.97	0.13	29,676
	1	EPITHELIAL TUMOURS OF SKIN	48.58	0.08	241,674	74.1	97.8	0.1	554.33	1.13	2,757,555
C	2	Basal cell carcinoma of skin	32.05	0.06	159,410	79.8	100.8	0.1	389.91	1.05	1,939,620
C	2	Squamous cell carcinoma with variants of skin	16.39	0.05	81,554	63.5	91.6	0.3	152.86	0.65	760,420
	1	ADNEXAL CARCINOMA OF SKIN	0.28	0.01	1378	64.3	87.1	1.8	2.67	0.08	13,304
R	2	Adnexal carcinoma of skin	0.28	0.01	1378	64.3	87.1	1.8	2.67	0.08	13,304
	1	EMBRYONAL NEOPLASMS	0.34	0.01	1713	76.4	76.8	1.0	7.96	0.41	39,580
R	2	Neuroblastoma and ganglioneuroblastoma	0.12	0.00	603	59.7	59.9	1.9	1.58	0.12	7862
R	2	Nephroblastoma	0.14	0.00	705	85.6	86.0	1.3	3.65	0.26	18,145
R	2	Retinoblastoma	0.05	0.00	268	97.1	97.4	1.0	1.05	0.06	5200
R	2	Hepatoblastoma	0.02	0.00	112	61.6	62.4	4.3	0.54	0.15	2692
R	2	Pulmonary blastoma	0.00	0.00	21	43.2	44.8	11.6	0.12	0.05	614
R	2	Pancreatoblastoma	0.00	0.00	4	100.0	100.2	0.0	NE	NE	NE
	1	EXTRAGONADAL GERM CELL TUMOURS	0.13	0.00	630	68.1	69.5	1.9	3.40	0.15	17,027
R	2	Extragonadal malignant/immature teratomas	0.04	0.00	207	64.0	65.5	3.3	0.91	0.09	4549
R	2	Extragonadal germ cell tumours	0.09	0.00	423	70.1	71.4	2.2	2.51	0.25	12,478
	1	SOFT TISSUE SARCOMA	4.74	0.02	23,574	48.6	55.8	0.4	46.86	0.40	233,097
R	2	Soft tissue sarcoma of head and neck	0.29	0.01	1431	51.5	64.7	1.6	2.94	0.10	14,628
R	2	Soft tissue sarcoma of limbs	1.03	0.01	5124	57.5	67.1	0.8	11.63	0.20	57,837
R	2	Soft tissue sarcoma of superficial trunk	0.46	0.01	2307	40.8	47.5	1.2	4.02	0.12	20,003
R	2	Soft tissue sarcoma of mediastinum	0.03	0.00	129	19.9	22.2	3.8	0.10	0.02	503

(continued on next page)

Table 2 – (*continued*)

Rare (R) or common (C) (middle tier only)	Tier	Top tier (upper case) and middle tier (lower case) tumour categories	Crude incidence per 100,000 per year	Standard error incidence	Expected new cases per year	Observed 5-year survival (%)	Relative 5 year survival (%)	Standard error relative survival (%)	Complete prevalence per 100,000	Standard error complete prevalence	Prevalent Cases
R	2	Soft tissue sarcoma of heart	0.01	0.00	74	12.6	13.1	3.9	0.05	0.01	248
R	2	Soft tissue sarcoma of breast	0.19	0.00	927	71.7	78.5	1.6	2.21	0.08	10,994
R	2	Soft tissue sarcoma of uterus	0.50	0.01	2466	46.8	50.6	1.1	4.88	0.13	24,295
R	2	Other soft tissue sarcomas of genitourinary tract	0.24	0.01	1185	41.2	47.6	1.6	2.16	0.09	10,746
R	2	Soft tissue sarcoma of viscera	0.51	0.01	2517	34.2	40.1	1.1	2.64	0.08	13,145
R	2	Soft tissue sarcoma of paratestis	0.03	0.00	162	71.8	87.1	4.1	0.30	0.03	1511
R	2	Soft tissue sarcoma of retroperitoneum and peritoneum	0.29	0.01	1419	32.2	37.1	1.4	1.24	0.05	6192
R	2	Soft tissue sarcoma of pelvis	0.01	0.00	71	30.8	35.6	6.0	0.08	0.02	391
R	2	Soft tissue sarcoma of skin	0.31	0.01	1524	82.0	92.3	1.1	4.54	0.15	22,582
R	2	Soft tissue sarcoma of paraorbit	0.01	0.00	33	60.6	65.7	9.2	0.23	0.04	1166
R	2	Soft tissue sarcoma of brain and other parts of nervous system	0.19	0.00	947	51.2	56.0	1.8	2.12	0.08	10,527
R	2	Embryonal rhabdomyosarcoma of soft tissue	0.06	0.00	305	66.6	67.4	2.6	1.67	0.23	8307
R	2	Alveolar rhabdomyosarcoma of soft tissue	0.03	0.00	161	40.6	41.7	3.9	0.20	0.02	984
R	2	Ewing's family tumours of soft tissue	0.05	0.00	263	43.6	44.9	3.2	0.55	0.03	2713
	1	BONE SARCOMA	0.80	0.01	4003	56.6	60.6	0.8	9.29	0.18	46,193
R	2	Osteogenic sarcoma	0.23	0.01	1135	52.3	54.6	1.5	3.17	0.12	15,834
R	2	Chondrogenic sarcomas	0.24	0.01	1215	67.1	73.9	1.4	3.55	0.11	17,691
R	2	Notochordal sarcomas, chordoma	0.04	0.00	218	57.4	64.5	3.8	0.42	0.03	1959
R	2	Vascular sarcomas	0.00	0.00	16	25.0	28.0	10.8	0.02	0.01	88
R	2	Ewing's family of tumours	0.13	0.00	647	49.7	50.0	1.9	2.33	0.19	11,381
R	2	Epithelial tumours, adamantinoma	0.01	0.00	43	74.0	83.9	7.4	0.11	0.02	576
R	2	Other high grade sarcomas (fibrosarcoma, malignant fibrous histiocytoma)	0.02	0.00	90	46.7	52.5	5.5	0.16	0.02	783
	1	GASTROINTESTINAL STROMAL SARCOMA	0.07	0.00	331	60.4	70.3	4.3	§	§	§
R	2	Gastrointestinal stromal sarcoma	0.07	0.00	331	60.4	70.3	4.3	§	§	§
	1	KAPOSI SARCOMA	0.34	0.01	1716	54.6	63.8	1.3	2.11	0.09	10,516
R	2	Kaposi sarcoma	0.34	0.01	1716	54.6	63.8	1.3	2.11	0.09	10,516
	1	NEUROENDOCRINE TUMOURS	2.53	0.02	12,587	43.0	50.7	0.5	20.10	0.25	100,003
R	2	Well differentiated endocrine tumours, carcinoid	0.37	0.01	1828	27.6	32.2	1.3	1.57	0.06	7791
R	2	Well differentiated endocrine tumours, atypical carcinoid	0.00	0.00	4	100.0	101.8	0.0	0.01	0.00	35
R	2	Poorly differentiated endocrine carcinoma (lung small cell carcinoma and skin excluded)	0.52	0.01	2596	10.4	12.8	0.7	1.34	0.06	6679

R	2	Mixed endocrine–exocrine carcinoma	0.00	0.00	11	30.0	34.8	16.8	0.02	0.01	96
R	2	Endocrine carcinoma of thyroid gland	0.22	0.01	1084	74.7	80.5	1.4	3.25	0.11	16,164
R	2	Well differentiated not functioning endocrine carcinoma of pancreas and digestive tract	1.26	0.01	6244	55.6	64.3	0.7	12.80	0.20	63,691
R	2	Well differentiated functioning endocrine carcinoma of pancreas and digestive tract	0.02	0.00	122	45.5	50.4	4.8	0.21	0.02	1070
R	2	Endocrine carcinoma of skin	0.13	0.00	667	39.1	57.6	3.0	0.86	0.04	4273
	1	CARCINOMA OF ENDOCRINE ORGANS	4.13	0.02	20,563	77.9	84.4	0.3	65.82	0.50	327,441
R	2	Carcinomas of pituitary gland	0.04	0.00	206	57.3	67.9	4.0	0.87	0.06	4334
R	2	Carcinomas of thyroid gland (medullary carcinoma included)	3.65	0.02	18,137	81.7	88.1	0.3	61.68	0.50	306,808
R	2	Carcinomas of parathyroid gland	0.02	0.00	109	65.2	73.5	5.2	0.28	0.03	1418
R	2	Carcinoma of adrenal gland	0.18	0.00	902	36.0	39.3	1.7	1.15	0.06	5698
	1	GLIAL TUMOURS OF CENTRAL NERVOUS SYSTEM (CNS)	5.35	0.03	26,610	18.4	20.0	0.3	26.29	0.41	130,764
R	2	Astrocytic tumours of CNS	4.80	0.02	23,859	13.7	15.1	0.2	20.42	0.37	101,593
R	2	Oligodendroglial tumours of CNS	0.35	0.01	1759	51.8	54.0	1.2	2.65	0.09	13,187
R	2	Ependymal tumours of CNS	0.20	0.00	992	68.8	71.3	1.5	3.85	0.14	19,125
	1	NON-GLIAL TUMOURS OF CNS AND PINEAL GLAND	0.22	0.01	1116	52.5	53.0	1.5	4.73	0.24	23,569
R	2	Embryonal tumours of CNS	0.22	0.01	1085	52.6	53.1	1.5	4.31	0.23	21,470
R	2	Choroid plexus carcinoma of CNS	0.01	0.00	31	45.5	46.9	10.5	0.35	0.06	1735
	1	MALIGNANT MENINGIOMAS	0.15	0.00	756	54.2	61.7	2.0	1.75	0.07	8699
R	2	Malignant meningiomas	0.15	0.00	756	54.2	61.7	2.0	1.75	0.07	8699
	1	GLIAL TUMOURS OF CRANIAL AND PERIPHERAL NERVES, AUTONOMIC NERVOUS SYSTEM	0.01	0.00	51	83.4	86.5	5.2	0.41	0.06	2030
R	2	Astrocytic tumours of cranial and peripheral nerves, autonomic nervous system	0.00	0.00	25	66.7	68.7	9.3	0.16	0.04	820
R	2	Ependymal tumours of cranial and peripheral nerves and autonomic nervous system	0.01	0.00	26	100.0	104.4	0.0	0.10	0.02	473
	1	NON-GLIAL TUMOURS OF CRANIAL AND PERIPHERAL NERVES, AUTONOMIC NERVOUS SYSTEM AND PARAGANGLIA	0.10	0.00	488	60.4	63.9	2.3	1.18	0.07	5896
R	2	Embryonal tumours of cranial and peripheral nerves, autonomic nervous system	0.07	0.00	365	64.3	67.6	2.6	0.87	0.06	4366
R	2	Paraganglioma	0.02	0.00	124	47.0	51.0	5.2	0.27	0.03	1345
	1	LYMPHOID DISEASES	29.09	0.06	144,707	45.9	55.2	0.2	229.39	1.13	1,141,118
R	2	Hodgkin lymphoma	2.44	0.02	12,158	77.9	82.3	0.4	46.89	0.46	233,280
R	2	Precursor B/T lymphoblastic leukaemia/lymphoblastic lymphoma (and Burkitt leukaemia/lymphoma)	1.45	0.01	7216	56.3	58.9	0.6	26.79	0.50	133,279
R	2	T cutaneous lymphoma (Mycosis fungoides, Sezary syndrome)	0.52	0.01	2562	67.9	80.4	1.1	5.18	0.10	25,753

(*continued on next page*)

Table 2 – (continued)

Rare (R) or common (C) (middle tier only)	Tier	Top tier (upper case) and middle tier (lower case) tumour categories	Crude incidence per 100,000 per year	Standard error incidence	Expected new cases per year	Observed 5-year survival (%)	Relative 5-year survival (%)	Standard error relative survival (%)	Complete prevalence per 100,000	Standard error complete prevalence	Prevalent Cases
R	2	Other T cell lymphomas and NK cell neoplasms	0.47	0.01	2351	37.6	43.2	1.2	2.83	0.08	14,082
R	2	Diffuse and follicular B lymphoma	4.91	0.02	24,413	48.5	56.7	0.4	31.04	0.50	154,392
R	2	Hairy cell leukaemia	0.29	0.01	1434	78.4	89.7	1.2	3.12	0.09	15,521
R	2	Plasmacytoma/multiple myeloma (and heavy chain diseases)	5.86	0.03	29,139	25.9	32.8	0.3	22.59	0.50	112,380
C	2	Other non-Hodgkin, mature B cell lymphoma	6.22	0.03	30,963	51.1	65.1	0.4	40.96	0.50	203,735
	1	ACUTE MYELOID LEUKAEMIA AND RELATED PRECURSOR NEOPLASMS	3.69	0.02	18,376	16.3	19.8	0.3	10.98	0.17	54,619
R	2	Acute promyelocytic leukaemia (AML with t(15;17) with variants)	0.11	0.00	547	56.7	61.2	2.2	0.65	0.04	3219
R	2	Acute myeloid leukaemia	3.39	0.02	16,868	15.0	18.2	0.3	10.75	0.19	53,486
	1	MYELOPROLIFERATIVE NEOPLASMS	3.07	0.02	15,269	48.7	59.8	0.5	20.34	0.43	101,158
R	2	Chronic myeloid leukaemia	1.25	0.01	6212	34.6	41.7	0.7	5.63	0.12	28,002
R	2	Other myeloproliferative neoplasms	1.81	0.01	8980	58.6	73.0	0.6	17.13	0.22	85,215
R	2	Mast cell tumour	0.02	0.00	76	66.8	71.7	5.8	0.20	0.03	982
	1	MYELODYSPLASTIC SYNDROME AND MYELODYSPLASTIC/-MYELOPROLIFERATIVE DISEASES	1.79	0.01	8907	23.5	34.7	0.7	5.64	0.12	28,078
R	2	Myelodysplastic syndrome with 5q syndrome	0.00	0.00	2	NE	NE	NE	NE	NE	NE
R	2	Other myelodysplastic syndrome	1.50	0.01	7460	25.0	37.2	0.8	5.02	0.12	24,958
R	2	Chronic myelomonocytic leukaemia	0.29	0.01	1432	15.7	22.6	1.4	0.69	0.04	3442
R	2	Atypical chronic myeloid leukaemia BCR/ABL negative	0.00	0.00	4	0	0	0	0.00	0.00	19
	1	HISTIOCYTIC AND DENDRITIC CELL NEOPLASMS	0.05	0.00	243	68.7	71.6	3.0	1.06	0.07	5264
R	2	Histiocytic and dendritic cell neoplasms	0.05	0.00	243	68.7	71.6	3.0	1.06	0.07	5264

NE = not estimated.
§ = this entity definition is too recent for prevalence estimation.

stage at diagnosis is not a factor in the poorer survival for rare cancers.

Fig. 4 shows 5-year relative survival for rare and common cancers by age class. For patients 0–39 years – most of whose cancers were rare – survival did not differ between common and rare cancers. The survival disadvantage of having a rare cancer increased from –17% at 40–59 years to –30% at 75–99 years. In the oldest age group, survival for rare cancers was almost half that of common cancers. From Fig. 4 it is evident that 5-year survival was similarly high for both rare and common cancers in children and young adults (up to 39 years) but that 5-year survival for rare cancers fell increasingly behind that of common cancers as age of diagnosis increased. Most cancers in children and young adults were rare (Fig. 2) and usually of embryonal or haematological types for which effective treatments are available. In older patients, most of the rare cancers were rare epithelial forms, for which therapies are not so effective as for the rare paediatric cancers.

Five-year relative survival was ≥50% for most rare cancers (Table 2) but was poor (<20%) for cancers of liver, gallbladder and trachea, as well as mesothelioma, acute myeloid leukaemia and glioma. Survival was also poor for some rare cancers belonging to common categories (squamous cell cancer of kidney, and some rare histotypes of lung, pancreatic, oesophagus and stomach cancers). Highest 5-year survival (>90%) was for testicular cancers (except epithelial testicular cancers), pancreatoblastoma, retinoblastoma, Paget's disease of vulva and vagina, soft tissue skin cancers, special types of breast adenocarcinoma and middle ear adenocarcinoma.

4. Discussion

4.1. *Data quality*

The data were derived from the largest available database on rare cancers itself obtained from European CRs. The major indicators of data quality (Table 3) indicate a high quality dataset.[7]

For rare cancers, the most likely quality problem is lack of specificity of morphology codes making it impossible to assign such cases to a specific (rare) cancer entity, resulting in underestimation of the true incidence and prevalence of such entities (although they still contribute to *overall* incidence and prevalence estimates). Nine percent of RARECARE cases had missing morphology specification (codes M8000 or M8001) and could be assigned to a 'top tier' (Table 1) cancer category but not to middle (more specific) tiers. This is well illustrated for epithelial tumours of oesophagus, liver and intra-hepatic bile tract, and ovary: for these top tier categories (Table 2), the incidence was greater than the sum of incidences of the specific rare (middle tier) subcategories and the difference is due to NOS cases.

In addition, the incidence of a few entities, including gastrointestinal stromal tumours and several haematological malignancies, is almost certainly underestimated because they were newly erected during the study period (specific morphological codes introduced for the first time only with ICD-O-3) and would not have been recognised by many pathologists at that time.

Unspecified morphology can be due to genuine difficulty in assigning a specific morphological category or because inadequate documentation was supplied to the CR when the case was registered. The latter is registration bias and results in incidence and prevalence underestimation. To assess the extent of registration bias, RARECARE reviewed the original data (mainly pathologic reports) of a selected sample (about 18,000 cases) of eight rare cancers (for details see RARECARE web site). Briefly, the great majority of NOS morphology cases were confirmed as NOS. The few NOS cases that changed to a more specific diagnosis generally increased the incidence of the more common cancer forms. For example, 11% of the oral cavity epithelial cancers were reclassified from NOS to more specific diagnoses: 8% were reclassified as squamous cell carcinoma (commoner) and only 3% as adenocarcinoma (rarer). This finding suggests that the problem with poorly specified morphology cases is mainly one of difficulty in reaching a precise diagnosis, not registration bias.

4.2. *How representative are our EU27 estimates?*

In providing rare cancer burden estimates, we assumed that the population covered by our CRs was representative of the population of the EU27 as a whole. It is important to assess to what extent this assumption may be true. For rare cancers, this is not possible because morphology information (essential for identifying a rare cancer) is not available in published incidence estimates. For common cancers the assumption of representativity can be tested by comparison of our incidence estimates with those of GLOBOCAN, considered the best available.[13] We found that RARECARE incidence rates for major cancers (lung 56.2, colorectal 61, breast 64, all sites 454) were closely similar to those of GLOBOCAN for EU27 (lung 56.5, colorectal 61.2, breast 59.8, all sites 450.6), suggesting that the RARECARE population is as representative of the EU27 population as the population covered by GLOBOCAN.

4.3. *RARECARE definition of rare cancers*

We used a new incidence-based criterion for defining rare cancers. In Europe[1] rare cancers are often defined according to the prevalence criterion of <50/100,000, in the same way as rare diseases in general. However, prevalence has shortcomings as a measure of cancer rarity since some cancers with low incidence but good survival will fall into the common category as good survival pushes up prevalence; examples are squamous cell carcinoma of the uterine cervix and thyroid carcinoma. Similarly, some commonly-occurring diseases for which survival is poor are considered rare because poor survival pushes prevalence down. Examples are adenocarcinoma of stomach and lung and squamous cell carcinoma of lung (Table 2). These considerations suggest that incidence is better for defining rare cancers, and is also in harmony with the sub-acute clinical course of most rare cancers; whereas most rare non-neoplastic diseases have a chronic course so prevalence is a better measure.

The RARECARE rarity threshold at <6/100,000 might be considered too high. However, if the lower threshold of <3/100,000/year were adopted, glial tumours, epithelial cancers of the oral cavity and lip, epithelial cancers of gallbladder

Table 3 – Data quality indicators and other characteristics of malignant cancers diagnosed in European cancer registries 1995–2002 and included in the analyses.

Country	Registry	Number of malignant cancers	Data quality indicators					
			Death certificate only (%)	Autopsy (%)	Microscopic verification (%)	Cases 1995–1998 censored before 5 years (%)	Morphology code NOS[b] (%)	Topography code NOS[b] (%)
Austria	Austria	304,493	8.9	0.0	85.2	5.9	10.1	0.6
Belgium	Flanders	144,715	0.0	0.2	89.8	0.0	7.3	0.5
France	Bas Rhin	13,113	0.0	0.0	95.8	3.3	3.9	0.2
	Calvados	5695	0.0	0.0	98.1	6.1	2.5	0.3
	Calvados digestive	2801	0.0	0.0	87.0	4.4	10.5	0.3
	Côte d'Or digestive	4376	0.0	0.0	82.8	0.5	17.5	0.2
	Côte d'Or haematol.	1884	0.0	0.0	100.0	7.2	0.0	0.5
	Doubs	5742	0.0	0.0	95.8	2.1	3.2	0.3
	Haut Rhin	9073	0.0	0.0	96.4	5.8	2.9	0.1
	Hérault	10,505	0.0	0.0	0.0	6.4	1.5	0.1
	Isère	12,526	0.0	0.0	94.1	4.6	4.1	0.1
	Loire Atlantique	3746	0.0	0.0	100.0	6.8	0.0	0.0
	Manche	6267	0.0	0.0	96.5	2.7	3.4	0.3
	Marne and Ardennes	168	0.0	0.0	100.0	3.6	0.0	0.0
	Somme	6481	0.0	0.0	94.2	6.6	5.5	0.8
	Tarn	4935	0.0	0.0	93.8	2.0	5.9	1.3
Germany	Saarland	54,132	3.9	0.0	91.8	5.8	8.0	0.5
Iceland	Iceland	8854	0.1	1.4	96.6	0.0	3.5	0.0
Ireland	Ireland	156,529	2.0	0.3	86.7	0.0	11.0	0.7
Italy	Alto Adige	18,676	0.7	0.0	89.5	0.0	9.2	0.5
	Biella	11,770	1.3	0.4	87.0	0.0	12.5	0.3
	Ferrara	23,740	1.1	0.0	88.1	0.4	9.7	0.6
	Firenze	66,097	0.9	0.1	80.4	0.4	17.7	0.8
	Friuli V.G.	78,882	0.6	1.9	91.0	0.3	9.8	2.1
	Genova	44,207	1.8	0.0	81.4	0.0	16.6	0.9
	Macerata	10,396	1.3	0.0	87.4	0.2	13.1	0.6
	Modena	34,947	0.5	0.0	88.6	0.4	11.8	0.5
	Napoli	8145	3.9	0.0	73.0	1.9	17.6	1.4
	Palermo	581	2.2	0.0	92.6	0.0	7.2	0.0
	Parma	23,836	1.0	0.0	86.0	0.3	13.1	0.7
	Ragusa	10,687	1.9	0.8	80.9	0.1	24.6	0.6
	Reggio Emilia	22,152	0.2	0.0	88.1	0.0	13.8	0.5
	Romagna	60,667	2.4	0.0	87.9	0.1	12.3	0.5
	Salerno	26,917	2.5	0.0	77.5	4.0	23.7	1.1
	Sassari	18,084	2.9	0.2	84.4	0.0	16.4	0.7
	Trento	17,788	2.0	0.0	85.0	0.3	27.8	3.8
	Umbria	45,221	0.7	0.0	84.0	0.1	12.6	0.6
	Varese	24,728	1.1	0.0	89.0	11.5	10.8	0.4
	Veneto	84,528	1.5	0.2	87.5	0.8	13.7	1.7

Malta	Malta	9848	1.9	0.1	87.6	0.0	12.9	0.7
Norway	Norway	197,240	1.0	0.4	93.1	0.1	6.7	0.6
Poland	Cracow	24,545	1.1	0.1	75.2	2.9	27.2	1.2
	Kielce	34,123	0.0	0.0	80.2	0.0	21.7	1.0
	Warsaw	50,238	3.4	0.0	80.2	0.2	19.1	0.8
Portugal	South Portugal	32,917	0.0	0.0	93.9	0.0	7.2	0.4
Slovakia	Slovakia	128,686	12.8	1.5	81.8	0.5	17.9	1.6
Slovenia	Slovenia	56,632	1.6	1.1	90.8	0.1	9.6	0.7
Spain	Albacete	1941	4.7	0.0	89.3	0.3	11.9	0.0
	Basque Country	44,809	4.2	0.0	86.3	0.1	11.4	0.7
	Castillon	1608	4.7	0.0	95.0	0.0	5.4	0.0
	Girona	19,936	3.8	0.1	87.7	0.1	12.8	0.6
	Granada	7298	2.1	0.1	89.3	0.0	10.8	0.0
	Murcia	14,068	3.5	0.1	88.0	2.5	11.1	1.0
	Navarra	15,381	2.2	0.6	90.9	0.6	7.6	0.4
	Tarragona	12,412	4.8	0.0	86.4	0.1	13.3	0.7
Sweden	Sweden	347,616	0.0	2.2	98.2	0.1	2.6	1.3
Switzerland	Basel	13,654	0.0	4.3	99.0	3.8	0.2	0.0
	Geneva	16,775	0.5	1.1	92.6	1.7	6.2	0.7
	Grisons	2788	0.7	0.5	91.9	2.4	6.3	0.0
	St. Gallen	16,588	0.7	1.2	92.8	0.5	4.4	0.4
	Ticino	10,784	3.0	0.3	91.4	0.6	6.8	1.4
	Valais	4533	1.5	0.4	91.2	2.4	8.2	0.9
	Zurich	777	0.3	3.9	97.3	2.7	2.2	0.0
Netherlands	Amsterdam	95,439	0.0	0.5	95.7	0.6	4.2	0.1
	Eindhoven	27,985	0.0	0.0	95.7	0.1	4.1	0.2
	North Netherlands	58,508	0.0	1.0	94.7	0.0	5.3	0.2
	Twente	41,217	0.0	0.7	95.1	0.1	5.1	0.3
UK England	East Anglia	131,829	0.5	0.9	86.4	10.1	0.6	0.3
	Northern and Yorkshire	265,499	1.1	0.4	86.8	0.0	3.9	0.3
	Oxford	85,848	0.8	0.4	88.8	0.0	0.4	0.5
	South Western	168,672	7.8	0.1	70.2	0.0	10.6	1.3
	Trent	109,768	7.3	0.0	74.0	0.0	2.4	0.8
	West Midlands	190,726	5.1	1.1	81.9	0.0	4.2	0.4
UK North Ireland	Northern Ireland	69,558	1.2	0.4	83.4	0.0	16.7	0.6
UK Scotland	Scotland	263,710	0.9	0.1	86.4	0.0	5.8	0.5
UK Wales[a]	Wales	120,606	12.7	0.0	51.0	0.0	6.3	0.8
RARECARE		4,082,646	3.0	0.5	85.9	1.2	8.2	0.7

[a] MV status not ascertainable for all cases from Wales CR.

[b] Morphology codes NOS (Not otherwise specified) are M8000–8001; topography codes NOS are C260, C268, C269, C390, C398, C399, C559, C579, C639, C689, C729, C759-C765 and C767–C768.

Table 4 – RARECARE estimates of incidence and prevalence for rare and common cancers by site in EU27.

		Crude incidence per 100,000 per year	Standard error	Estimated incident cases in EU27 per year	Incidence distribution (%)	Prevalence per 100,000	Standard error	Estimated prevalent cases in EU27 per year	Prevalence distribution (%)
Rare	Digestive tract	17.5	0.1	87,280	15	50.9	0.4	254,473	11
Common	Digestive tract	75.7	0.1	378,507	67	399.3	1.2	1,996,625	84
All	Digestive tract	113.7	0.1	568,548	100	476.0	1.4	2,380,246	100
Rare	Respiratory tract	13.6	0.0	68,147	21	60.0	0.4	300,193	46
Common	Respiratory tract	31.5	0.1	157,445	49	56.0	0.3	279,942	43
All	Respiratory tract	63.9	0.1	319,349	100	129.7	0.6	648,321	100
Rare	Skin	1.5	0.0	7649	2	14.8	0.3	73,849	2
Common	Skin	60.8	0.1	304,186	96	744.9	1.5	3,724,477	96
All	Skin	63.2	0.1	316,171	100	779.9	1.5	3,899,301	100
Rare	Breast	4.4	0.0	22,041	7	60.2	0.7	300,759	9
Common	Breast	47.5	0.1	237,529	74	519.9	4.1	2,599,432	74
All	Breast	64.1	0.1	320,548	100	700.2	6.3	3,500,906	100
Rare	Female genital tract	16.1	0.0	80,699	55	176.2	0.8	880,922	53
Common	Female genital tract	9.5	0.0	47,639	32	126.7	0.6	633,280	38
All	Female genital tract	29.5	0.1	147,433	100	331.8	1.1	1,658,891	100
Rare	Male genital tract	4.4	0.0	21,872	8	93.1	0.8	465,363	23
Common	Male genital tract	40.6	0.1	202,766	78	279.4	1.4	1,396,883	70
All	Male genital tract	51.9	0.1	259,642	100	399.5	1.6	1,997,563	100
Rare	Urinary system	2.6	0.0	12,740	8	18.3	0.4	91,683	8
Common	Urinary system	25.8	0.1	128,798	78	202.1	0.7	1,010,735	85
All	Urinary system	33.0	0.1	164,983	100	237.7	0.8	1,188,660	100
Rare	Haematopoietic system	15.9	0.0	79,409	72	90.1	0.7	450,444	70
Common	Haematopoietic system	4.8	0.0	24,091	22	32.3	0.3	161,618	25
All	Haematopoietic system	22.0	0.1	109,738	100	129.5	0.7	647,596	100
Rare	All sites	108.3	0.1	541,296	22	859.5	2.2	4,297,365	24
Common	All sites	297.4	0.2	1,486,956	59	2368.3	4.8	11,841,483	66
All	All sites	502.1	0.3	2,510,662	100	3566.4	7.2	17,831,883	100

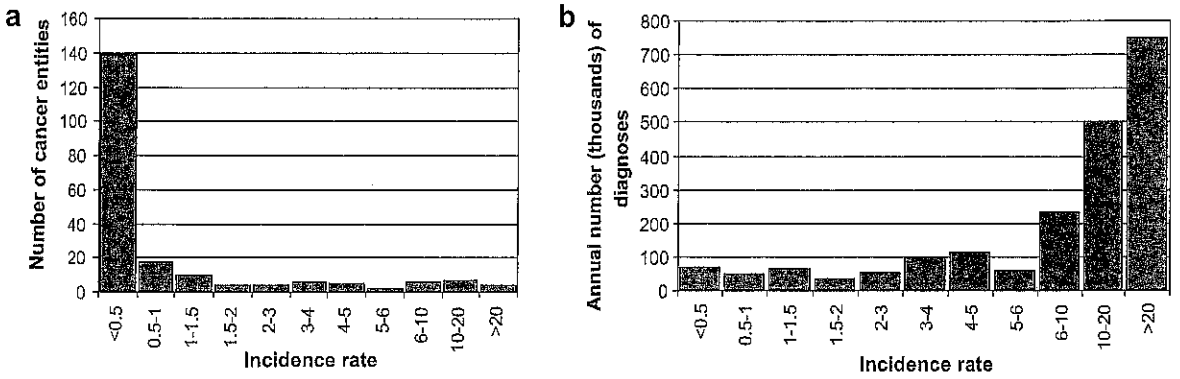


Fig. 1 – Distribution of number of cancer types (1a) and annual number of diagnoses (1b) in EU27 according to categories of incidence rate.

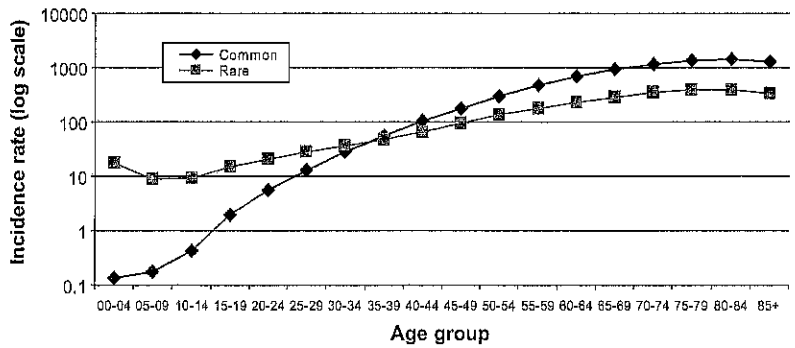


Fig. 2 – RARECARE estimates of age-specific incidence rates for rare and common cancers in EU 27.

and extrahepatic biliary tract, soft tissue sarcomas, tumours of testis and paratestis, carcinomas endocrine organs, myeloproliferative neoplasms and acute myeloid leukaemia, would all be excluded. Yet these forms are often inadequately diagnosed and treated in relation both to lack of knowledge and lack of clinical expertise, and clinical trials are rarely performed. They are all diseases that are best treated in specialised centres.[14] Thus the <6/100,000 threshold includes several forms with the problems typically present in rare cancers.

4.4. *Survival*

Overall, rare cancer survival was worse than common cancer survival. Relative survival was lower at 1 year and continued to diverge up to 3 years, while the gap remained constant from 3 to 5 years after diagnosis. However in children and adolescents – among whom rare cancers are more common than common cancers – survival was similar to that of the common cancers. Advances in treatment as a result of clinical trials have markedly improved prognoses for many childhood cancers over the last 30–40 years.[15] Perhaps this lesson can be applied to rare cancers in adults; however it is unclear why survival for rare cancers is low in adults. Possibilities include factors inherent in the diseases, and

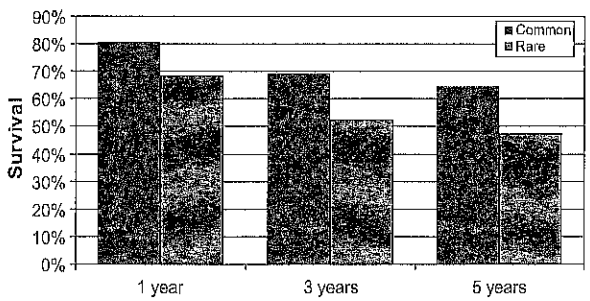


Fig. 3 – RARECARE estimates of relative survival for rare and common cancers in EU27 by year since diagnosis.

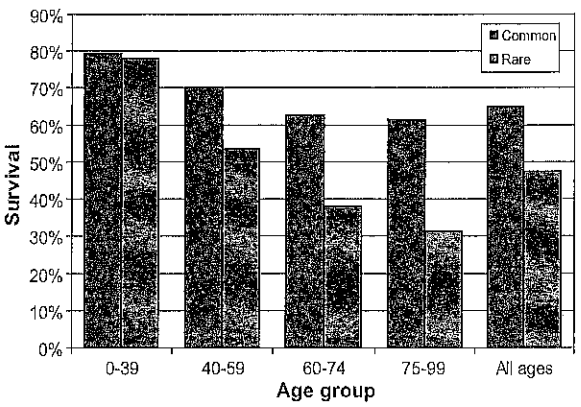


Fig. 4 – RARECARE estimates of relative survival for rare and common cancers in EU27 by age group.

inadequacies of care or treatment, including delayed diagnosis, lack of effective therapies or lack of evidence-based treatment guidelines.

4.5. *Prevalence*

Since the definition of rare diseases is based on prevalence and the EU directive on orphan drugs[16] provides incentives to foster research and development of orphan drugs for rare diseases, the availability of prevalence data for rare cancers should facilitate application of the EU orphan drug directive. If the existing European definition of rare diseases were used (prevalence <50/100,000), rare cancers would be 24% of total cancer prevalence as estimated by RARECARE.

5. Concluding remarks

We have at last put numbers to a problem long known to exist. Our estimates indicate that 22% of all cancers diagnosed in the EU27 each year are rare. In absolute terms, this is slightly more than half a million new rare cancer cases each year, while 4,300,000 rare cancers are prevalent in the population. It is noteworthy that 30% of Europeans with a rare cancer have one of the particularly rare forms that affect <1/100,000 (Fig. 1) and this is important, because low incidence is a major obstacle to conducting clinical trails to develop effective treatments.[6] One way to overcome this obstacle would be to establish centres of excellence for rare cancers and international collaborative groups to network centres across the EU to thereby achieve necessary organisational structure, critical mass and patients for carrying out clinical trials, developing alternative study designs and methodological approaches to clinical experimentation and improving accuracy and standardisation of staging procedures for rare cancers. RARECARE (http://www.rarecare.eu) will continue to encourage initiatives to put these cancers on the map.

The RARECARE working group consists of:

Austria: M. Hackl (Austrian National Cancer Registry); Belgium: E. Van Eycken; D. Schrijvers (Ziekenhuisnetwerk Antwerpen, ZNA – Hospital Network), H. Sundseth, Jan Geissler (European Cancer Patient Coalition), S. Marreaud (European Organisation for Research and Treatment of Cancer), R. Audisio (European Society of Surgical Oncology); Estonia: M. Mägi (Estonian Cancer Registry); France: G. Hedelin, M. Velten (Bas-Rhin Cancer Registry); G. Launoy (Calvados Digestive Cancer Registry); A.V. Guizard (Calvados General Cancer Registry); A.M. Bouvier (Côte d'Or Digestive Cancer Registry); M. Maynadié, (Côte d'Or Haematological Malignancies Registry); M. Mercier (Doubs Cancer Registry); A. Buemi (Haut-Rhin Cancer Registry); B. Tretarre (Hérault Cancer Registry); M. Colonna (Isère Cancer Registry); F. Molinié (Loire Atlantique Breast and Colon Cancer Registry); B. Lacour, (Manche Cancer Registry); C. Schvartz (Marne and Ardennes Thyroid Cancer Registry); O. Ganry (Somme Cancer Registry); P. Grosclaude (Tarn Cancer Registry); E. Benhamou, M. Grossgoupil (Institute Gustave Roussy), I.R. Coquard, J.P. Droz (Centre Léon Bérard), S. Baconnier (Connective tissue cancer network – CONTICANET); Germany: B. Holleczek (Saarland Cancer Registry); M. Wartenberg (Global GIST Network), R. Hehlmann (European LeukemiaNet); Iceland: L. Tryggvadottir (Icelandic Cancer Registry); Ireland: S. Deady (National Cancer Registry of Ireland); Italy: F. Bellù (Alto Adige Cancer Registry); S. Ferretti (Ferrara Cancer Registry); D. Serraino (Friuli Venezia Giulia Cancer Registry); M. Vercelli (Liguria Cancer Registry c/o IST/UNIGE, Genoa); S. Vitarelli (Macerata Province Cancer Registry); C. Cirilli (Modena Cancer Registry); M. Fusco (Napoli Cancer Registry); A. Traina (Palermo Breast Cancer Registry); M. Michiara (Parma Cancer Registry); A. Giacomin (Piedmont Cancer Registry, Province of Biella); G. Pastore (Childhood Cancer Registry of Piedmont-CPO); R. Tumino (Cancer Registry and Histopathology Unit, 'M.P. Arezzo' Civic Hospital, Ragusa); L. Mangone (Reggio Emilia Cancer Registry); F. Falcini (Romagna Cancer Registry); G. Senatore (Salerno Cancer Registry), M. Budroni (Sassari Cancer Registry); S. Piffer (Trento Cancer Registry); E. Crocetti (Tuscan Cancer Registry); F. La Rosa, (Umbria Cancer Registry); P. Contiero (Varese Cancer Registry); P. Zambon (Veneto Cancer Registry); F. Berrino, P.G. Casali, G. Gatta, A. Gronchi, L. Licitra, S. Sowe, A. Trama (Fondazione IRCCS Istituto Nazionale dei Tumori); R. Capocaccia, R. De Angelis, S. Mallone, A. Tavilla (Centro Nazionale di Epidemiologia, Istituto Superiore di Sanità); A.P. Dei Tos (Local Health Unit No. 9, Region of Veneto), A.A. Brandes (Medical Oncology Department, Local Health Unit, Bologna); Malta: K. England (Malta National Cancer Registry); Norway: F. Langmark (Cancer Registry of Norway); Poland: J. Rachtan (Cracow Cancer Registry); R. Mezyk (Kielce Cancer Registry); M. Zwierko (Warsaw Cancer Registry); M. Bielska-Lasota (National Institute of Public Health – National Institute of Hygiene, Warsaw); J. Slowinski (Department of Neurosurgery in Sosnowiec, Medical University of Silesia); Portugal: A. Miranda (Southern Portugal Cancer Registry); Slovakia: Ch. Safaei Diba (National Cancer Registry of Slovakia); Slovenia: M. Primic-Zakelj (Cancer Registry of Slovenia); Spain: A. Mateos (Albacete Cancer Registry); I. Izarzugaza (Basque Country Cancer Registry); R. Marcos-Gragera (Girona Cancer Registry); M.J. Sánchez (Granada Cancer Registry); C. Navarro (Murcia Cancer Registry); Eva Ardanaz (Navarra Cancer Registry); J. Galceran (Tarragona Cancer Registry); J.A. Virizuela-Echaburu (Hospital Universitario Virgen Macarena, Sevilla); C. Martinez-Garcia, J.M. Melchor (Escuela Andaluza de Salud Pública), A. Cervantes (University of Valencia); Sweden: Jan Adolfsson (Stockholm-Gotland Cancer Registry); M. Lambe (Uppsala Regional Cancer Registry), T.R. Möller (Lund University Hospital); Ulrik Ringborg (Karolinska Institute); Switzerland: G. Jundt (Basel Cancer Registry); M. Usel (Geneva Cancer Registry); H. Frick (Grisons Cancer Registry); S.M. Ess (St. Gallen Cancer Registry); A. Bordoni (Ticino Cancer Registry); I. Konzelmann (Valais Cancer Registry); S. Dehler (Zurich Cancer Registry); J.M. Lutz (National Institute for Cancer Epidemiology and Registration); The Netherlands: O. Visser (Amsterdam Cancer Registry); R. Otter, S. Siesling, J.M. van der Zwan (Comprehensive Cancer Centre the Netherlands); J.W.W. Coebergh (Eindhoven Cancer Registry), H. Schouten (University of Maastricht); UK-England: D.C. Greenberg (Eastern Cancer Registration and Information Centre); J. Wilkinson (Northern and Yorkshire Cancer Registry); M. Roche (Oxford Cancer Intelligence Unit); J. Verne (South-West Cancer Intelligence Service); D. Meechan (Trent

Cancer Registry); G. Lawrence (West-Midlands Cancer Intelligence Unit); M.P. Coleman (London School of Hygiene and Tropical Medicine), J. Mackay (University College of London); UK-Northern Ireland: A. Gavin (Northern Ireland Cancer Registry); UK-Scotland: D.H. Brewster (Scottish Cancer Registry); I. Kunkler (University of Edinburgh); UK-Wales: J. Steward (Welsh Cancer Intelligence & Surveillance Unit).

Conflict of interest statement

The authors declare no conflicts of interest. The funding sources had no role in study design, data collection, data analysis, data interpretation, writing this paper or the decision to submit for publication.

Acknowledgements

This research was supported by the European Commission through the Executive Agency for Health and Consumers (Grant No. 2006113) and the Programma Italia-USA Malattie Rare (Grant No. 526D/42). We thank Don Ward for help with the English and Samba Sowe for editorial support.

REFERENCES

1. European parliament and council of the European communities. Decision no. 1295/1999/EC of the European parliament and of the council of 29 April 1999 adopting a programme of community action on rare diseases within the framework for action in the field of public health (1999–2003); 1999.
2. Available from: http://www.fda.gov/orphan/oda.htm [accessed 11.12.09].
3. Greenlee RT, Goodman MT, Lynch CF, et al. The occurrence of rare cancers in US adults, 1995–2004. *Public Health Rep* 2010;125(1):28–43.
4. No Authors listed. Very rare cancers – a problem neglected. Lancet Oncol 2001;2(4):189.
5. Pritchard-Jones K, Kaatsch P, Steliarova-Foucher E, Stiller CA, Coebergh JW. Cancer in children and adolescents in Europe: developments over 20 years and future challenges. *Eur J Cancer* 2006;42:2183–90.
6. Tan SB, Dear KB, Bruzzi P, et al. Strategy for randomised clinical trials in rare cancers. *BMJ* 2003;327:47–9.
7. De Angelis R, Francisci S, Baili P, et al. The EUROCARE-4 database on cancer survival in Europe: data standardization, quality control and methods of statistical analysis. *Eur J Cancer* 2009;45:909–30.
8. Ferlay J, Burkhard C, Whelan S, et al. Check and conversion programs for Cancer Registries. Lyon, France: International Agency for Research on Cancer, Technical Report No. 42; 2005. Available from: http://www.iacr.com.fr/TR42.htm.
9. Percy C, Fritz A, Jack A, et al. *International classification of diseases for the oncology (ICD-O)*. 3rd ed. World Health Organisation; 2000.
10. Capocaccia R, Colonna M, Corazziari I, et al. Measuring cancer prevalence in Europe: the EUROPREVAL Project. *Ann Oncol* 2002;13:831–9.
11. Capocaccia R, De Angelis R. Estimating the completeness of prevalence based on cancer registry data. *Stat Med* 1997;16:425–40.
12. Hakulinen T. Cancer survival corrected for heterogeneity in patient withdrawal. *Biometrics* 1982;38:933–42.
13. Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002 Cancer Incidence, Mortality and Prevalence Worldwide IARC CancerBase No. 5, version 2.0. Lyon: IARCPress; 2004.
14. Available from: http://www.rarecancers.eu [accessed 19.04.11].
15. Terracini B, Coebergh JW, Gatta G, et al. Childhood cancer survival in Europe: an overview. *Eur J Cancer* 2001;37:810–6.
16. Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products. Official Journal of the European Communities, 22.1.2000.

I Tumori Rari e Novartis Oncology

Luigi Boano, General Manager Novartis Oncology Italia
Gianluca Fincato, Direttore Medico Novartis Oncology Italia

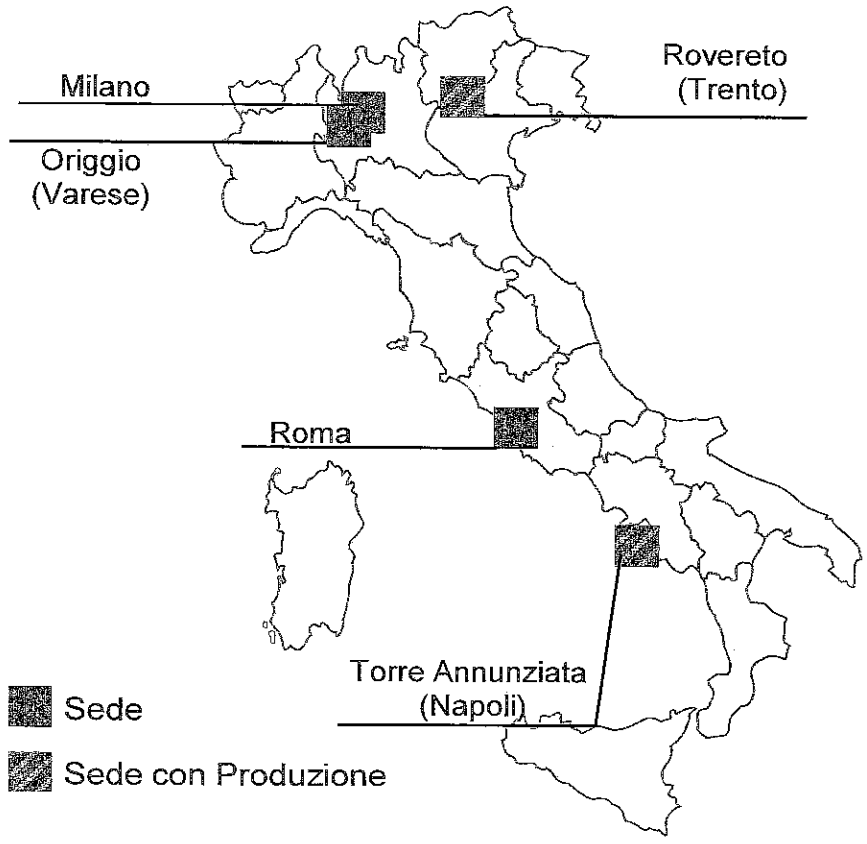
Audizione alla XII Commissione, Camera dei Deputati
Roma, 20 Aprile 2015

NOVARTIS

Novartis in Italia

- Una presenza strategica in Italia dal 1911

Novartis in Italia – 2014	
Fatturato	**1.700 milioni** di euro
Esportazioni	**473 milioni** di euro (17,4% del fatturato)
Investimenti	**221 milioni di euro** in attività **di Ricerca &Sviluppo**, pari al **18%** degli investimenti totali in R&S del settore farmaceutico **72 milioni di euro** specificamente in ricerca clinica, coinvolgendo **527 centri** e **17.555 pazienti** 2015-2017: **pianificati ulteriori investimenti** in Italia per oltre **€200 milioni**



NOVARTIS

All'interno di Novartis Italia opera la divisione Novartis Oncology

- Novartis Oncology nasce nel 2000
- Creata per sviluppare **terapie innovative per i pazienti** in campo oncologico, ematologico ed endocrinologico
- **Pioniere delle *Target Therapy***
- Leader in onco-ematologia
- Organizzata in 3 aree:

Oncologia solida | *Ematologia* | *Malattie Rare*

Ricerca mirata su Malattie Rare e <u>Tumori Rari</u>: ruolo importante di Novartis in Italia e nel mondo

NOVARTIS

Il *Paziente* con Tumore Raro presenta caratteristiche diverse da quello con Malattia Rara per natura della patologia

Natura delle patologie

Malattie Rare

- Patologie gravi, spesso ereditarie
- Patologie croniche, nella maggior parte dei casi a lunga sopravvivenza
- Bassa prevalenza (≤ 50 / 100.000)
- Totale: circa 50.000 nuovi casi/anno in Italia(1)

Tumori Rari

- Patologie neoplastiche (onco-ematologiche)
- Patologie spesso a breve sopravvivenza (*circa il 50% dei pazienti affetti da Tumore Raro non sopravvive a 5 anni dalla diagnosi*)
- Bassa incidenza (≤ 6 / 100.000)
- Totale: circa 67.000 nuovi casi/anno in Italia(2)

Entrambe patologie neglette

Fonti: (1) Piano Nazionale Malattie Rare 2013-16 (2) AIRTUM, Associazione Italiana Registro Tumori

NOVARTIS

Il 76% delle indicazioni dei nostri prodotti è rivolto a ***pazienti*** con Patologie Rare

Tumori «Big Killer»

- Tumore della mammella
- Tumore renale
- Tumore al polmone
- Melanoma

Tumori Rari

- Tumori neuroendocrini (NET)
- Sarcoma dei Tessuti molli
- Tumori Stromali-Gastro Intestinali (GIST)
- Dermatofibro Sarcoma Protuberans

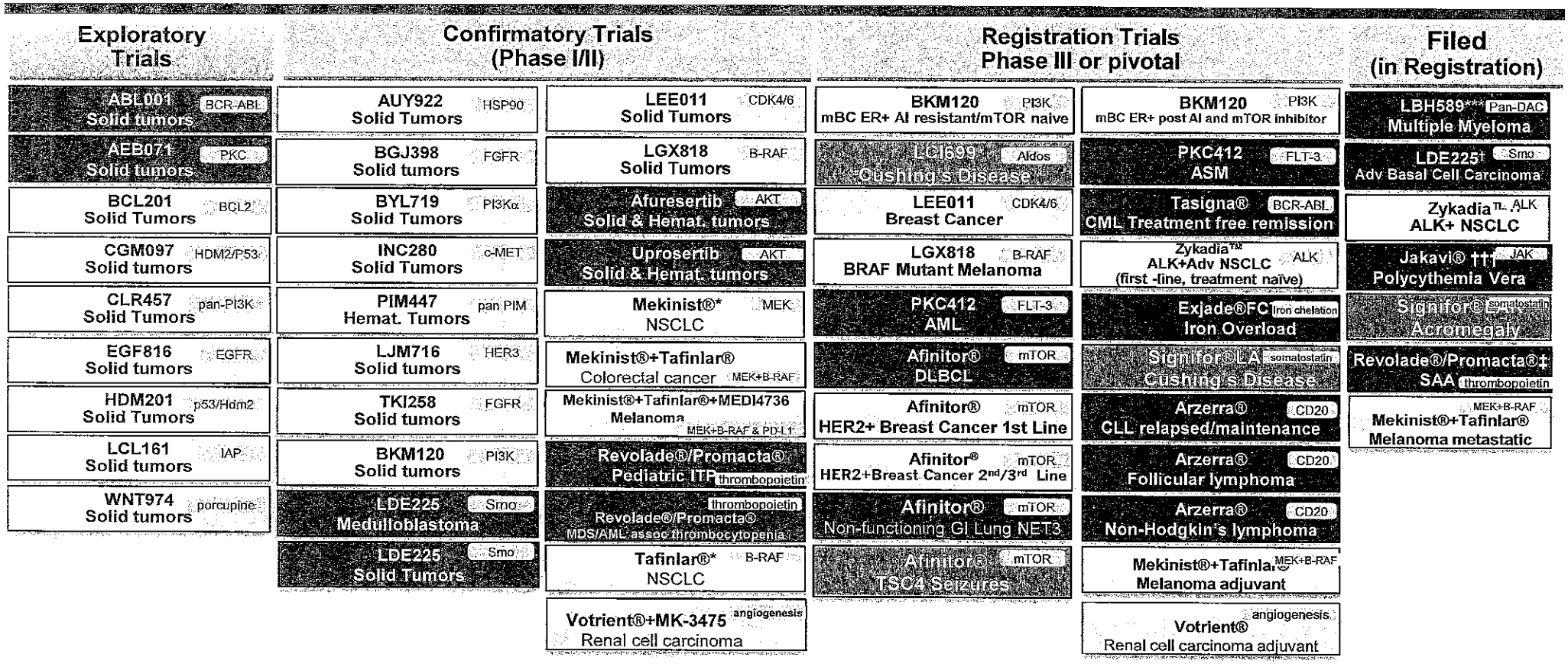
- Leucemia Mieloide Cronica
- Sindromi Mielodisplastiche
- Malattie Mieloproliferative
- Trombocitopenia Immune
- Leucemia Linfatica Cronica

Malattie Rare

- Talassemia
- Acromegalia
- Sindrome di Cushing
- Sclerosi Tuberosa

NOVARTIS

Anche tra i prodotti in sviluppo Malattie Rare e Tumori Rari hanno un ruolo importante



Target
Tumori "Big Killer"
Tumori Rari
Malattie Rare

* Ph III registration trial is planned
** Exjade® FCT was submitted in the US Q2 2014
*** LBH589 was filed in the US and the EU - Q2 2014
† LDE225 was filed in the EU - Q2 2014, submitted in the US Q3 2014
†† Zykadia™ (ceritinib) was approved in the US April 29, 2014
††† Jakavi® was filed in the EU Q2 2014, submitted in Japan Q3 2014
‡ Approved in the US – August 26, 2014

NOVARTIS

Le necessità del ***paziente*** con Tumore Raro

Corretta Diagnosi

- **Centri specializzati**
- **Approccio multidisciplinare**

Conoscenza

- **Creare reti tra centri specializzati**

Disponibilità delle terapie

- **Aumentare la ricerca**

Necessità comuni tra Malattie Rare e Tumori Rari

Fattore tempo

- **Tempestività nella diagnosi**
- **Rapidità di accesso a farmaci innovativi**

Necessità specifica dei Tumori Rari

NOVARTIS

Esempio: diagnosi e monitoraggio dei pazienti con leucemia, in partnership con la comunità scientifica

fondazione GIMEMA onlus
per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche FRANCO MANDELLI

+

NOVARTIS ONCOLOGY

labnet
Network tra laboratori di biologia molecolare

Rete di laboratori standardizzati per la diagnostica integrata

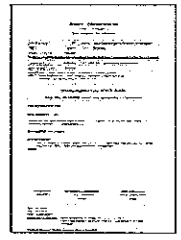
Totale Laboratori standardizzati: 54
Tot centri afferenti: 164

Come funziona?

1) **Il centro spedisce il campione**

2) **Il lab analizza con tecniche standardizzate**

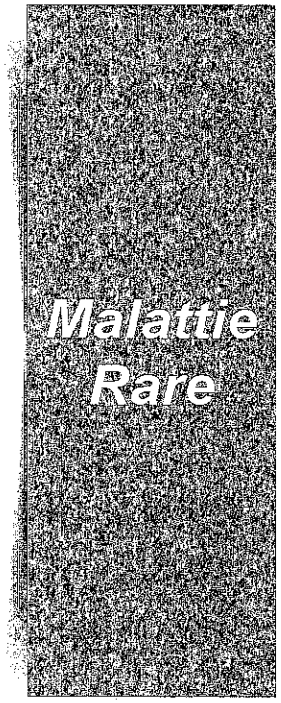
3) **Il centro visualizza il risultato**



4) **Il lab spedisce al centro il risultato dell'analisi**

Il ***Paziente*** con Malattia Rara ha una chiara identificazione dalla legge e dal SSN

Forme di tutela riconosciute



- Elenco delle Malattie Rare
- Rete nazionale per la prevenzione, sorveglianza, diagnosi e cura delle Malattie Rare
- Registro nazionale di pazienti (*Istituto Superiore di Sanità*)
- Esenzione per diagnosi, monitoraggio e assistenza

(D.M. n.279/ 2001)

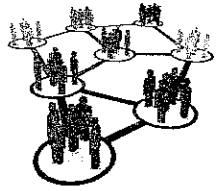
- Piano Nazionale per le Malattie Rare (*n.2013/16*)

NOVARTIS

Pazienti* con Tumori Rari**: considerazioni finali per migliorare la gestione del ***paziente

Creazione e riconoscimento istituzionale di un **elenco di tumori rari**, recependo l'elenco Europeo (RARECARE[1])

La creazione di **reti sul territorio nazionale** tra i centri oncologici specializzati sui vari tumori rari
=> miglioramento della diagnosi, ricerca e cura per i pazienti



Favorire l'**accesso** dei farmaci per i Tumori Rari
=> garantire tempestività ed equità di accesso su tutto il territorio nazionale

(1) *Gatta G. et al.; European Journal Cancer 2011;47:2493*

NOVARTIS

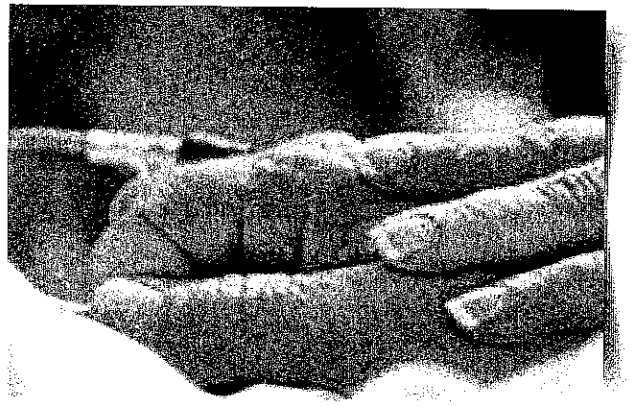
Novartis Oncology continuerà il proprio ***impegno in ricerca e sviluppo di farmaci per Malattie e Tumori Rari***

NOVARTIS

Back-up

Esiste una lista dei Tumori Rari definita a livello Europeo grazie al progetto *RARECARE*

1. **L'Unione Europea** ha finanziato e supportato un **progetto di ricerca "RARECARE"**, coordinato dall'Istituto Nazionale dei Tumori. Da questo è derivato un **consenso nella comunità** europea **degli oncologi e una "lista" dei Tumori Rari**(1)



2. In continuità con questo progetto, l'iniziativa **"RARECARE*Net*"** mira a **sviluppare maggiori conoscenze** sui tumori rari e identificare i criteri di **definizione dei Centri di Eccellenza** (CE) dove curare i tumori rari e diffondere le informazioni sui CE (elenco)

(1) *Gatta G. et al.; European Journal Cancer 2011;47:2493*

NOVARTIS