



CHALLENGING THE EUROPE OF DISPARITIES IN CANCER

A FRAMEWORK FOR IMPROVED SURVIVAL AND BETTER QUALITY OF LIFE FOR EUROPEAN CANCER PATIENTS

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1. INTRODUCTION

The European Cancer Patient's Bill of Rights (BoR) was launched in the European Parliament on World Cancer Day 2014 and published simultaneously in the journals Lancet Oncology¹ and The Oncologist.² Developed by the European Cancer Concord(ECC), an equal partnership between patients, their advocates and cancer health professionals, the BoR is a "catalyst for change" which articulates the right of every European citizen

- to receive the most accurate information and be proactively involved in his /her care;
- to access optimal, timely and appropriate specialised care underpinned by research and innovation; and
- to receive this care within health systems that ensure improved outcomes, patient rehabilitation, improved Quality of Life (QoL) and affordable healthcare. 1,2

The European Cancer Patient Coalition (ECPC)³ is a key member of ECC and worked closely in partnership with ECC to launch the BoR. To strengthen the case for optimal and equitable patient care, ECPC launched the "Europe of Disparities in Cancer" initiative at the European Parliament in January 2015. The current document is the first output from this initiative. Through the Europe of Disparities in Cancer, European cancer patients demonstrate once more that they are not passive victims of health disparities but pro-active solution seekers.

2. A EUROPE OF DISPARITIES IN CANCER - THE EVIDENCE BASE

Cancer is a significant cause of morbidity and mortality in high, middle and low income nations across the world. In 17 out of 28 of EU countries, it has now overtaken cardiovascular disease as the leading cause of premature death. In Europe in 2012, there were 3.75 million (M) new cases of cancer, with 1.75M deaths; deaths; translating to three European patients dying every minute from this common disease. While this is a sobering statistic, even more revealing are the evident disparities between different European nations. EUROCARE 5 (the most recent analysis of cancer survival data across Europe) provides irrefutable evidence that cancer survival rates vary significantly between different European countries (Figure 1). Thus, for every Elsa in Sweden who has an 86% chance of survival following treatment for breast cancer, there is an Ilsa or Elze just across the Baltic Sea in Latvia or Lithuania, whose survival chances drop to 69% and 66% respectively; for every Luca in Italy with an almost 90% chance of being alive 5 years after a diagnosis of prostate cancer, there is a Luka a few kilometres away in Croatia whose 5 year survival chances have shrunk to 71%. Whether it be preventable (e.g. cervical cancer), curable (e.g. certain forms of breast cancer, childhood leukaemia), or poor prognosis (e.g. ovarian, pancreatic cancer), European inter-country variations in cancer survival rates are significant. 7-14

The situation in Eastern Europe is particularly challenging, with mortality rates for many cancers above the European average. In Poland for example, lung cancer mortality is 83% (EU Average 56.4%), 7,15 while in Romania, the mortality rate for cervical cancer is 14.2%, compared with an EU average of 3.7%. He are the compared with an EU average of 3.7%. are also challenges for Western/ Northern European nations. Studies such as the International Cancer Benchmarking Partnership (ICBP) have revealed that both United Kingdom (UK) and Denmark have significantly poorer survival rates, particularly for lung, colorectal and ovarian cancers, when investigated with comparator nations Australia, Canada, Norway and Sweden. 17 In addition to the significant disparities between European nations, regional intra-country variations are also evident, leading to differences in survival within individual countries. 18-20





3. THE ROLE OF CANCER INEQUALITIES IN THE EUROPE OF DISPARITIES

Inequalities are at the heart of many of these profound disparities that are experienced by European citizens. Key patient needs that must be addressed across Europe include a deficiency in accurate, up-to-date information that is patient-accessible;²¹ extreme variability in cancer screening services;^{22,23} unequal access to curative cancer treatments (surgery, radiation, medicines);²⁴⁻²⁶ fragmented cancer rehabilitation services;²⁷ poor governance, major organisational, structural and fiscal deficits in health planning 28-30 and the lack of a citizen-focussed European cancer survivorship plan.³¹ Additionally, in many Member States(MS), National Cancer Control Plans are lacking or are inadequately resourced, 32,33 underpinning both inter- and intra- country disparities in survival, quality of care and patient rehabilitation. Social and economic deprivation³⁴⁻³⁶ and the influence of recent austerity measures 26,37 further exacerbate many of these inequalities. For cancer patients to get the treatment that they both require and deserve, a multidisciplinary team (MDT) based strategy must be adopted for all MS,³⁸ providing a patient-centred approach that addresses all aspects of the cancer journey, with increasing emphasis on survivorship issues including psychosocial support and improved Quality of Life (QoL), delivered within a framework where patients' rights and views are respected and acted upon.

An important consideration for developing and implementing approaches that address the inequalities underpinning the Europe of Disparities in Cancer is the need for accurate and comprehensive cancer incidence/survival data. Capturing this data at an entire population level is critical. Data coverage across Europe is suboptimal, varying from 17 to 100% (average 50%), ³⁹ and must be improved and harmonised to inform future cancer policy.

3.1 CANCER HEALTH LITERACY

3.1.1 THE NEED FOR IMPROVED CANCER HEALTH LITERACY

Health literacy and awareness should underpin any modern cancer prevention/ care programme. For example, pancreatic cancer is the 4th most common cause of cancer death in Europe, ¹⁴ yet awareness is so low that it is often labelled a "forgotten cancer". 40 Public awareness of the potential advantages of screening are poor; >90% of men and women either overestimate or have no knowledge of the benefits of Prostate Specific Antigen (PSA) testing or mammography. 41 Many healthcare professionals fare little better, demonstrating limited appreciation of screening benefits.⁴² To enhance awareness, information on screening should be provided in an evidence-based transparent fashion. Germany has recently moved towards an "informed participatory decision-making" model; ⁴³ results of this citizen-focussed approach are eagerly awaited.

3.1.2 THE NEED FOR BETTER PATIENT-ADAPTED INFORMATION AND SUPPORT

Provision of appropriate information is critical to help patients navigate the entire trajectory of cancer care⁴⁴ and is increasingly relevant post treatment, as cancer survivors in Europe⁷ strive to live both with and beyond their disease. But in many cases, the quality of patient information provided is too complex and inaccessible to the average reader, 45 leading to increased inequalities. 46 Patient-adapted literature and online materials must be crafted with the input of patients, to ensure high levels of understanding and accessibility. Navigating the often complex systems that deliver cancer services can prove daunting to the cancer patient, particularly those





from lower socioeconomic/educational backgrounds,⁴⁷ leading to further disparities. The cancer patient navigator model, which is increasingly being embedded within the care pathway in the US^{48,49} is a promising intervention to address these inequalities, providing reliable and effective support for patients to utilise appropriate services throughout their cancer journey.

3.2 SCREENING AND EARLY DIAGNOSIS

3.2.1 THE NEED TO IMPROVE ACCESS TO CANCER SCREENING AND EARLY DETECTION

Appropriate cancer screening programmes and early detection methodologies can be important tools in ensuring an early and accurate cancer diagnosis and can be effective in reducing health disparities. The high mortality rate for cervical cancer in Romania is a direct consequence of its fragmented screening programme. Furthermore, the socio-economic status of the individual has a pivotal impact on his/her capacity and willingness to access appropriate screening services, emphasising a critical barrier to reducing cancer disparities.

The route to cancer diagnosis also has a significant influence on patient outcome - increased levels of initial presentation at hospital emergency departments are associated with higher short term mortality,⁵³ explaining at least in part the poorer survival rates identified by the ICBP in UK and Danish patients.¹⁷ Promoting early detection through public awareness campaigns⁵³ and delivering strategies that encourage early diagnosis⁵⁴ are key approaches that can improve survival, provided that they are linked to timely, appropriate and affordable treatment allowing patients to enter the cancer care pathway at an earlier stage of their disease, when their cancer can be more responsive to treatment.⁵⁵

3.3 ADDRESSING DISPARITIES IN CANCER CARE DELIVERY: ACCESS TO OPTIMAL CARE

3.3.1 ACCESS TO RADIOTHERAPY

Radiotherapy is an effective and frequently used approach in cancer management, in the curative setting, either alone or in combination with other approaches (surgery and chemotherapy), or in the palliative setting to improve symptoms and quality of life in patients with incurable cancers.

Across Europe, around half of all cancer patients should receive radiation therapy at some stage during the course of their disease. Radiotherapy plays a leading role in curing cancer and prolonging life, including for some of the commonest cancer killers in Europe (e.g. lung, colorectal, breast and prostate). However, despite being a significant part of our arsenal in combatting cancer, a large discrepancy exists between the actual and the optimal utilisation of radiation therapy in Europe. Sec. 18

Focusing on radiation oncology capacity, analyses conducted by the European Society for Radiotherapy and Oncology with the HERO project⁵⁹ (Health and Economics in Radiation Oncology); by the International Atomic Energy Agency; the International Agency for Research on Cancer and the International Prevention Research Institute, have revealed that there are significant deficits in Europe.⁶⁰ A similar picture emerges of a very heterogeneous map of Europe, when staffing levels or access to modern radiotherapy equipment are evaluated, thus translating into unequal access to cancer care for European patients. Thus, while a number of





European nations are well-served with state-of-the-art radiotherapy resources, there are deficiencies in many European countries (Figure 2). Emphasising the Europe-wide nature of the problem, these deficiencies are experienced not only in Southern and Eastern European countries (particularly Bulgaria, Macedonia and Romania), but also in some Western European countries such as Portugal and UK.⁶⁰ Lack of sufficient appropriately qualified manpower for optimal delivery of radiotherapy services exacerbates the problem.⁶¹ Fragmentation of radiotherapy services across Europe is leading to inequalities in access to this common forms of cancer care. ²⁵ In addition to the observed inequity in radiotherapy resources (staffing, state-of-the-art equipment and associated infrastructure) other barriers to optimal radiotherapy access and uptake include an insufficient awareness and positioning of radiation oncology in cancer care strategies and inadequate financing models. To facilitate access to state-of-the-art radiation oncology for all European citizens and ensure a patient-centred approach, embedding radiation oncology in NCPs is essential. ⁶²

3.3.2 ACCESS TO SURGERY

Surgery is a key component of multi-disciplinary cancer care and contributes significantly to improved survival.²⁴ However, variations in the quality of surgery delivered and unequal access to appropriate surgical interventions across Europe can lead to significant differences in cancer outcomes.⁶³ In breast cancer, a EUROCARE 4 study revealed that delivery of "standard-of-care" surgery ranged from 78% (France) to 9% (Estonia) and disparities were evident, even between countries with medium-to-high expenditure on health.⁶⁴ There were also significant disparities in relation to patient age – older patients received standard of care surgery much less than younger patients.⁶⁴ While introduction of European guidelines has improved surgical care, disparities still persist.⁶³ In colorectal cancer, where surgery is a significant component of the care plan, substantial disparities in surgical intervention between European countries were also evident, and have been linked to differences in survival.⁶⁵ Within-country disparities in surgical provision can also contribute to regional differences in overall survival.^{66,67}

Delivering surgical care in cancer centres where specialist surgical oncologists perform optimal numbers of procedures with appropriate complexity,⁶⁸ in an environment with access to other interventions (radiotherapy, chemotherapy) and appropriate support care, provides the best opportunity to ensure improved outcomes.⁶⁹ Establishing optimal benchmarking standards for surgical oncology at European level, through initiatives such as EURECCA(EUropean REgistry of Cancer Care),⁷⁰ will help reduce the current disparities experienced by cancer patients, while information sources such as the Italian Oncoguida⁷¹ provide patients with accurate activity data to aid in their choice of surgical centre and should act as a blueprint for other MS.

3.3.3 ACCESS TO CYTOTOXIC MEDICINES

While many cytotoxic medicines have been shown to be effective treatments for cancer patients, there are significant disparities in access across Europe. ^{26,72} Many life-preserving/ life-enhancing medicines are relatively inexpensive, yet cancer patients in many European countries are denied access to their positive benefits. ⁷² This is particularly ironic, given the significant contribution made by many European scientists and clinicians to the development of many of these medicines, and even more of a paradox when we consider that European patients have had considerable influence on validating their positive benefits, through participation in randomised clinical trials. While implementation of the EU Cross-Border Health Directive ⁷³ can improve patient's access to both medicines and other therapeutic interventions including radiotherapy and surgery,





long term solutions must ensure an optimal standard of diagnostic and therapeutic capacity in all European countries. Similarly, the recent decisions by Romania and Bulgaria (and in separate developments potentially by Belgium and the Netherlands, Romania and Bulgaria, Portugal, Greece) to undertake joint procurement agreements to access cancer medicines⁷⁴ are an encouraging development, but probably do not represent long term sustainable solutions.

3.3.4 SHORTAGES IN CANCER MEDICINES

A recent survey indicated that >50% of European hospital pharmacists have experienced significant shortages in access to life-preserving and life-sustaining cytotoxic regimens (ranging from 33% (Northern Europe) to 59% (Western and Southern Europe) and 65% (Eastern Europe)). 75 Pharmacists from individual countries such as the Netherlands (81%) also indicated significant shortages. Reasons for shortages are multifactorial. 76,77 They can include parallel trade, where medicines are bought in a MS where the agreed price is lower e.g. Romania, ⁷⁸ and resell at a discounted price in a MS where the agreed price is higher. Other major factors include production disruptions (often related to quality issues), demand spikes, quotas, globalisation of production, and unintended impacts from pricing policies (e.g. reduction in available suppliers). However, information on causes of medicines shortages is unfortunately not currently consistently collected and reported across Europe, making an accurate picture of the balance of causes difficult to determine. This should be addressed by a coordination and improvement of national information portals about shortages, including the product in shortage, the likely duration of shortage, reasons for the shortage and available alternatives. Many of the shortages occur for inexpensive injectable medicines. In Romania over the five year period from 2008 to 2013, over 25 cancer medicines (including Vinblastine, Bleomycin, Dacarbazine) from the World Health Organisation's recommended list of essential cancer medicines were either not available or in short supply; these shortages led to thousands of Romanian patients either being denied treatment, pursuing an incomplete treatment or being forced to arrange (and pay for) the purchase of the necessary medicines themselves from Western European countries. This was possible through a network of over 400 volunteers living or travelling in Western Europe who acquired and transported the medicines to Romania. 78 While the altruism demonstrated by these volunteers is laudable, it is unacceptable that such solutions have to be engineered by patients, families and friends to offset shortages caused by regulatory or business decisions and the lack of administrative capacity of the national authorities who should have tackled the issue.

3.3.5 ACCESS TO INNOVATIVE TREATMENT APPROACHES

Increased understanding of disease biology is fuelling a "personalised cancer medicine" revolution.⁷⁹ The finding that the *erbB2* gene was mutated in >20% of breast cancers for example, led to development of targeted anti-erb2 drugs that dramatically improved survival. ⁸⁰ However, providing these treatments in a timely fashion to European cancer patients is hampered by a pricing/ reimbursement approach that differs markedly between individual European countries, thus accentuating disparities in access to optimal cancer care.⁸¹ Innovative radiotherapy and surgical innovations must also be supported, particularly given their potential to deliver significant impact for the cancer patients.^{82,83}





3.3.6 DELAYS TO APPROVAL

While the EU has adopted a common procedure for granting market authorisation to cancer medicines through the European Medicines Agency (EMA), pricing and reimbursement decisions reside with national governments/agencies. Agency (EMA), pricing and reimbursement that specifies a 180-day limit post EMA authorisation for national implementation, as adherence/compliance with this deadline is extremely variable. Thus, for a drug like transtuzumab, which targets the ERB2 receptor and has led to a new standard of care for this aggressive breast cancer, there are marked differences in time to approval/reimbursement across EU members (Figure 3). For metastatic disease for example, variations within Western Europe were significant; while countries like Germany, the Netherlands and Spain had rapid approvals, in the UK (+564 days), Belgium (+1160 days) and Denmark (+1891 days), delays were significant. Disparities were even more pronounced in Eastern Europe, with all countries bar the Czech Republic exceeding the 180 day limit, while for certain countries (e.g. Hungary (+2713 days), Romania (+2878 days), Slovakia (+3686 days) and Latvia (+4660 days), delays were even more striking and were associated with concomitant reductions in breast cancer survival.

3.3.7 HEALTH TECHNOLOGY ASSESSMENT (HTA)

The two-stage process for registration of new therapeutics, involving both EMA approval and in many countries a HTA, allied to the pricing/ reimbursement issues outlined above, can lead to significant differences in time-to-access for new therapeutic interventions. HTA approaches Europe-wide, through collaborative networks such as the EUropean network for Health Technology Assessment (EUnetHTA), s9,90 is necessary to close the gap in access to new diagnostics/ therapeutics. A harmonised HTA Relative Effectiveness Assessment has the potential to reduce workload, create efficiencies and underpin speedier patient access to life preserving treatments.

3.4 CANCER SURVIVORSHIP AND PATIENT REHABILITATION

Medical advances have contributed to improved survival rates for many cancers. Over 10M European cancer patients are now living with and beyond their disease, demonstrating that it is possible to return to a normal life. However, a new challenge has arisen – identifying and addressing the patients' cancer rehabilitation needs. The end of cancer treatment does not signal the end of cancer care. In this survivorship phase, all aspects of the individual's wellbeing must be considered, not only long-term physical effects of treatment, but also psychological, social and economic needs. Cancer's long-term impact must be addressed, through the delivery of integrated cancer survivorship care plans. Highlighting the challenge, a survey by the *Associazione Italiana di Oncologia Medica (AIOM)* indicated significant organisational, communication and implementation gaps, including lack of interdisciplinary shared structures and infrequent communication between oncologists and primary care physicians, while a survivorship care plan following discharge was implemented by <10% of oncologists. Development of an EU-wide cancer survivorship policy would represent a significant step forward for the European cancer patient.

A 2nd disparity that surviving cancer patients must endure is discrimination in relation to employment and other societal issues including insurance, mortgage approval and social re-integration. ⁹⁴ Employment challenges can be significant. Almost 50% of cancer patients will receive a cancer diagnosis at some stage





during their working life.⁹⁵ Employment practices for cancer patients vary widely across Europe and often do not consider job preservation approaches that acknowledge patients' residual work capacity.⁹⁶ Many cancer survivors are at risk for loss of employment, which can lead to significant financial, social and QoL burdens. The European Cancer and Work Network (CANWON) has brought together stakeholders and researchers from 19 European countries to address these issues⁹⁷ while the European Organisation for Research and Treatment of Cancer (EORTC), through its EORTC Survivorship Task Force⁹⁸ has also prioritised cancer survivorship and employment.

3.5. CANCER CONTROL AT MEMBER STATE LEVEL

While the European Commission (EC) has demonstrated a degree of commitment to improving cancer outcomes through its support for initiatives such as EPAAC (European Partnership for Action Against Cancer), and CanCon (Joint Action on Cancer Control), and EUROCHIP (European Cancer Health Indicator Project), and European Cancer Health Indicator Project Project Project Project Project Project Project Pr

As indicated above, policy recommendations from EPAAC or CanCon are not binding at European MS level. There is an urgent need for such policy recommendations to be implemented within national health systems. In contrast, the European Centre for Disease Control (ECDC), ¹⁰² established in 2005, identifies, assesses and communicates current and emerging threats to human health posed by infectious diseases and has significant influence on EU Policy in this area. Without diminishing ECDC's fundamental importance, communicable diseases account for ~1% of all deaths in Europe. Cancer, as the leading cause of premature death in >50% of European countries, ⁷ merits a dedicated European agency whose main mission would be to develop authoritative scientific opinions and recommend clear achievable targets for MS to reduce cancer inequalities, therefore crystallising the collaborative activities of EPAAC, CanCon, etc. into a pan-European agency. The EC's recently formed Expert Group on Cancer Control could be an appropriate incubator to kick-start the establishment of a European Centre for Cancer Control.

3.6 THE COST OF CANCER

The economic burden of cancer across the EU is significant, with an annual cost estimated at €126 billion (B) in 2009, ¹⁰⁴ of which less than half (€51B) involved direct healthcare costs. While the average healthcare costs for cancer equated to €102 per EU citizen, there were significant disparities, ranging from €16 per person (Bulgaria) to €184 per person (Luxembourg). While this wide inter-country variation in cancer health budgets does underpin some of the inequalities highlighted in this article, increased spend does not always equate with improved patient care e.g. healthcare costs per prostate cancer case in Hungary (€30,273), Romania (€33,938) and Slovakia (€34,474) are over twice the EU average and yet are not reflected in superior outcomes for prostate cancer patients in those countries. ¹⁰⁴ However, the effects of recent austerity measures on the health of the European citizen ^{26,37,105,106} will undoubtedly have a negative effect on cancer outcomes. A recent Department of Health-imposed reduction in pre-symptomatic checks for breast, uterine and prostate cancers in Greece, ¹⁰⁷ whose use of screening services is already lower than that recommended by the EU Council, ¹⁰⁸ is

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expected to lead to an increase in cancer incidence. The societal burden of cancer is also significant, reflected in EU productivity losses due to early death (€42·6B) or lost working days (€9.43B). Analysis of GLOBOCAN figures from 30 European countries confirmed the significant lost productivity costs due to premature cancer-related mortality. 109

4. POLICY RECOMMENDATIONS

We have highlighted the significant challenges that European cancer patients are experiencing and the health and socioeconomic inequalities that underpin this Europe of Disparities in Cancer. In order to address these issues that impact so negatively on European cancer patients every day, we propose a series of policy recommendations:

Cancer Control

- o Establish a European Centre for Cancer Control
- o Implement the relevant policy recommendations produced by EPAAC and CanCon

• Cancer Registries

 Develop mechanisms to promote increased registration of cancer incidence, prevalence and mortality across Member States

Multidisciplinary Teams(MDT)

o Promote patient-centred MDT cancer care delivery as the Standard of Care

Cancer Health Literacy

- Make cancer health literacy a patient—enabled European public health priority
- Develop European cancer patient navigation pilot projects

Screening and Early Diagnosis

 Remove educational and socio-economic barriers for European citizens in accessing cancer screening programmes

Access to optimal care

- Issue guidelines on optimal radiotherapy capacity(equipment/manpower) in Europe
- Provide patients with accurate surgical oncology activity data to allow informed decision-making on choice of accredited hospital/cancer centre
- o Identify and catalogue cancer medicine shortages to inform future healthcare policies
- Facilitate access to life-preserving and life-enhancing therapeutic interventions through a harmonised European Health Technology Assessment (HTA)

Cancer Survivorship and patient rehabilitation

- o Develop an integrative EU Cancer Survivorship Plan
- o Protect cancer survivors from employment discrimination

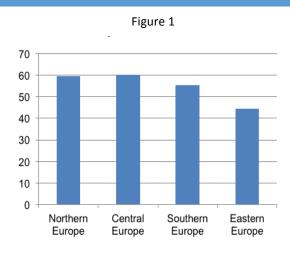
5. CONCLUSION

Cancer knows no geographical boundaries. Neither do cancer disparities, which as demonstrated here, are universal across Europe, from Aarhus to Athens, from Bonn to Bratislava. As Vytenis Andriukaitis, European Commissioner for Health & Food Safety recently stated "Europe needs a plan for action to define how it should invest in health for all", 111 reflecting a refreshing philosophy of the potential for enshrining health issues within EU treaties. Cancer is a growing health and socio-economic challenge in Europe. 30 The increasing age of our population will underpin a substantial rise in cancer incidence, 112-114 such that, by 2050, a European citizen will die from cancer every 10 seconds. With the disparities that we continue to face, both between countries and



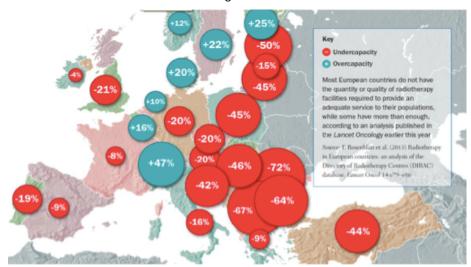


within countries, this may translate to a cancer death in certain parts of Europe every 5 seconds. We need to act NOW.



Survival rate for colorectal cancer in Europe (%). Data adapted from De Angelis R, Sant M, Coleman MP, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE--5-a population-based study. Lancet Oncol. 2014 Jan;15 (1):23-34.

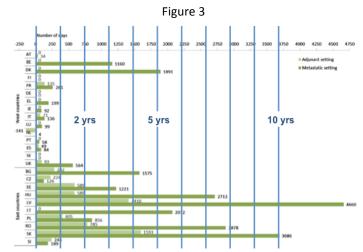








Radiotherapy capacity in Europe – Number of Linacs machines per 1 million inhabitants. Data adapted from Rosenblatt E, Izewska J, Anacak Y, Pynda Y, Scalliet P, Boniol M, Autier P. Radiotherapy capacity in European countries: an analysis of the Directory of Radiotherapy Centres (DIRAC) database. Lancet Oncol. 2013 Feb;14(2):e79-86



Timeframe for reimbursement of trastuzumab in Europe. Data adapted from Ades F, Senterre C, Zardavas D, de Azambuja E, Popescu R, Parent F, Piccart M. An exploratory analysis of the factors leading to delays in cancer drug reimbursement in the European Union: the trastuzumab case. Eur J Cancer. 2014 Dec;50(18):3089-97.





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