Personalised cancer care: a global perspective

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ESMO Madrid 2014

UICC global cancer control

SLACOM

E. Cazap disclosures

- *Leadership Position (no honoraria)* SLACOM, UICC, BHGI, NCI of Argentina
- *Consultant or Advisory Role* : Bayer; Schering Pharma
- *Honoraria :* Bayer; Bristol-Myers Squibb ; Fresenius ; Roche
- *Research Funding: Paid to Institution*: Poniard Pharmaceuticals ; Daiichi Sankyo Pharma ; Breast Cancer Research Foundation (BCRF)

Background

Introduction
Level of analysis

1. Global level
2. Regional /National level
3. Guidelines and recommendations from scientific societies
4. Clinical level (“personalized medicine”)

About this session (1)

- This is not a controversy between science and economy
- This is not an argument about the urgent need of more and better knowledge on the mechanisms and processes in the development of cancer

About this session (2)

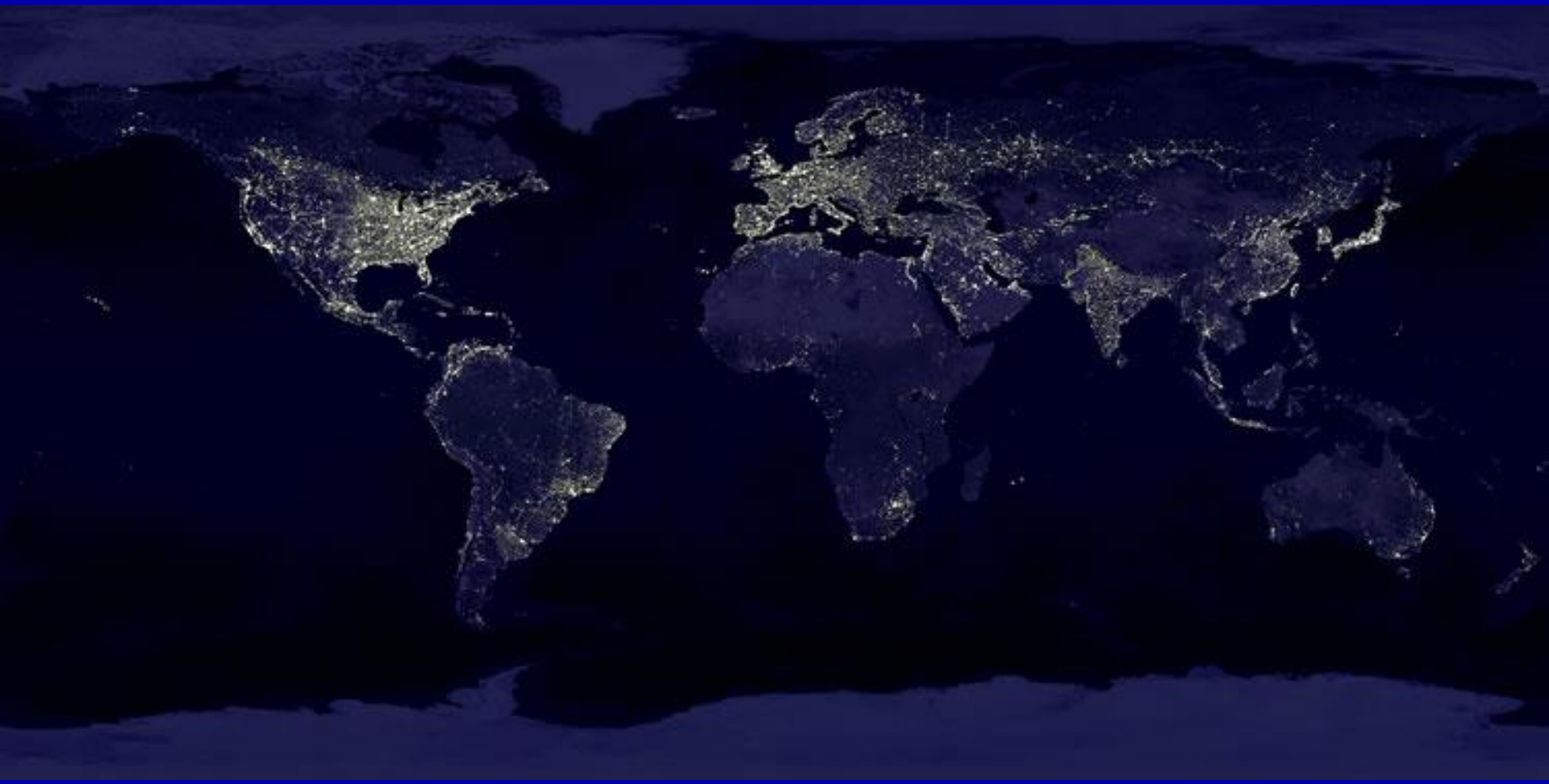
- This is a discussion about the best possible and more rational use of existing resources for cancer care and control
- Also an analysis for better strategies in cancer research
- Together with reflections on how to strategize and implement the existing available knowledge that today's only apply to 10 % of the world population.

What is global……

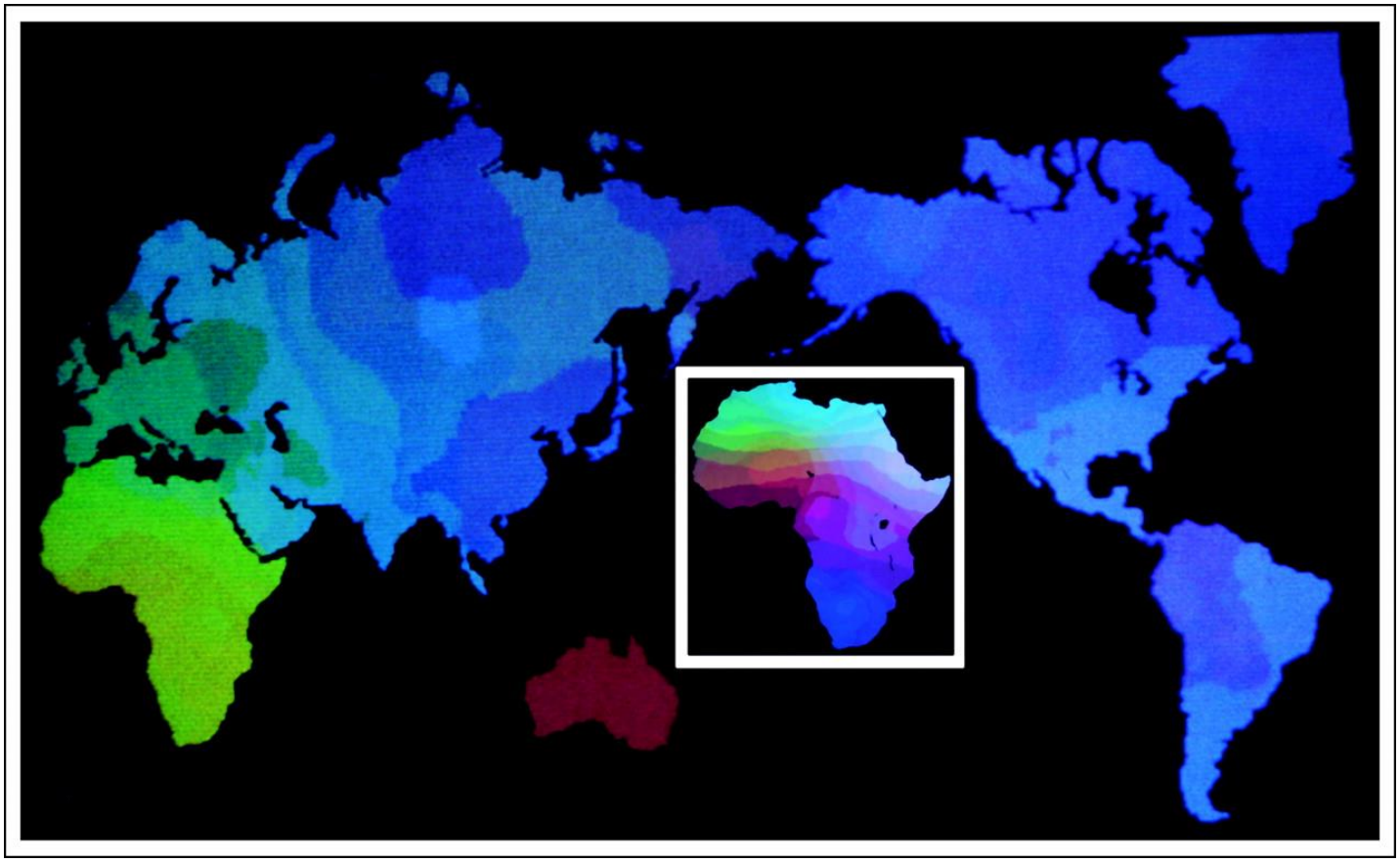
The real world

Brilliant Earth From Space

from: www. geology.com



Human genetic diversity is distributed in gradients among and within continents



Maitland, M. L. et al. J Clin Oncol; 24:2151-2157 2006

Global picture

- Today, cancer accounts for approximately one in every eight deaths globally (WHO, 2008)
- By 2030 more than 26 million incident cancer cases will occur each year – more than double the 12.4 million new cancer cases in 2008 (WHO, 2008)
- By 2050, it is projected that low-income countries alone will account for up to three-quarters of all cancer deaths (Cavalli, 2006).

Global picture (2)

- Today, an individual's odds of surviving cancer are strongly correlated with **where that person lives.**
- Whereas in the USA the five-year survival rate for patients with breast cancer is 84%, in The Gambia, breast cancer survival is just 12%

- Ref.Sankaranarayanan R et al., 2010

Titanic Passenger Survival Rates

Passenger Survival Rates by Class

- **First class** 325 / 202 (62%)
- **Second class** 285 / 118 (41%)
- **Third class** 706 / 178 (25%)

Totals 1,316 / 498 (38%)

Global picture (3)

- These gains in survival have not always been due to very expensive treatments
- Frequently, increased survival has been achieved due to cancer treatments that are relatively low cost such as generic drugs or radiotherapy machines.

Scientific and political perspectives

ESMO Position Paper

Annals of Oncology 25: 1673–1678, 2014
doi:10.1093/annonc/mdu217
Published online 20 June 2014

Delivering precision medicine in oncology today and in future—the promise and challenges of personalised cancer medicine: a position paper by the European Society for Medical Oncology (ESMO)

defining personalised cancer medicine

In its broadest sense, 'personalised medicine' is the tailoring of medical treatment to the characteristics of an individual patient and moves beyond the current approach of stratifying patients into treatment groups based on phenotypic biomarkers. Nowhere in medicine has the impact of personalised medicine been greater than in oncology. For scientists and oncologists, the term 'personalised medicine' is often used interchangeably with terms such as 'genomic medicine', 'precision medicine' and 'precision oncology'. These terms are used to describe the use of an individual patient's molecular information (including genomics and proteomics) to inform diagnosis, prognosis, treatment and prevention of cancer for that patient. As the transition from stratified cancer medicine to truly personalised cancer medicine intensifies, it is this definition that the ESMO Personalised Medicine Task Force prefers to use when describing personalised cancer medicine. But irrespective of the term used, the direction of travel is clear—precision diagnosis and treatment of cancer at the molecular level—and this change in paradigm has profound implications, from preclinical definition of mechanism of action to the development of molecular taxonomies of cancer, and from genome diagnostics to trial design.

from genomics to clinics—the context and history of personalised medicine

Although much of cancer biology is based on the central tenet that it is a genetic disease, caused by a clone of cells that expands in an unregulated fashion because of somatically acquired mutations, this view contributed little to cancer treatment until the 21st century. The targeting of *HER2* overexpression with the monoclonal antibody, trastuzumab, to improve outcome in metastatic breast cancer was the first example of targeted treatment [1]; but the paradigm of targeted interference of an oncogene with a specifically designed small molecular inhibitor is best exemplified by imatinib. The tyrosine kinase inhibitor imatinib, developed to target the *BCR-ABL* fusion gene, a consequence of the Philadelphia chromosome and pathognomonic of chronic myeloid leukaemia, transformed the care of patients, changing this aggressive, life-threatening disease to a manageable chronic disease [2]. Around the same time, the initiation of the Cancer Genome Project at the Wellcome Trust's Sanger Institute using exon Sanger sequencing quickly identified somatic mutations in the *BRAF* gene in the majority of malignant melanoma [3]. This opened a window into the biology of these tumours and provided the starting point for successful clinical translation, with the development of vemurafenib that specifically targets the underlying molecular lesion [4].

With the launch of large-scale cancer whole genome sequencing (WGS) projects such as the International Cancer Genome Consortium (ICGC) and The Cancer Genome Atlas (TCGA) expected to deliver a complete catalogue of genomic alterations in primary cancers and begin to elucidate the mutational patterns and influences across the natural history of cancers [5, 6], connecting recurrent genomic alterations to altered pathways and acquired cellular vulnerabilities will open the door to targeted therapies [6]. At the same time, elucidation of the mechanisms underlying the processes generating somatic mutations will lead to new insights into cancer causation and, potentially, new approaches to prevention [7].

oncology—at the frontline of utilising personalised medicine

Oncology is at the frontline of personalised medicine, moving beyond the previous model of giving cancer therapeutics based on trials of largely unselected patients beyond a simple phenotypic marker, to leading the way in utilising the molecular profile of an individual's cancer genome to optimise their disease management. At the centre is the patient, with personalised medicine offering the promise of delivering safe and efficacious cancer treatments that are targeted, biologically rational and avoid over- and under-treatment common with traditional chemotherapy, thus reducing toxicities associated with non-specific modes of action of chemotherapy. An intriguing example is the characterisation of germline variations in cancer patients that predict anthracycline-related cardiomyopathy and cisplatin-associated ototoxicity and now provide a mechanism for prospective identification of at-risk patients [8, 9].

The experiences of the oncology community in developing and delivering precision medicine are not unique and have parallels, more broadly, in other areas of medicine. For example the progress made in cystic fibrosis (CF) in developing treatments to correct the basic CF transmembrane conductance regulator protein has profoundly changed CF in a way that closely mirrors oncology, in particular the development of the novel drug, ivacaftor for molecularly distinct sub-types of CF when the mutational class is confirmed by companion diagnostic testing [10]. In addition, genomic sequencing is transforming the diagnosis

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ASCO vision

- "Although we have generated more effective therapies in the treatment of cancer through the knowledge we have gained in clinical trials**, we have not always focused as much attention on how to apply that knowledge to individual patients to realize the goal of personalized medicine.** I believe the best clinical results are achieved for each patient when the patient's personal values and goals are met. That is really what quality of care is all about: achieving outcomes that matter to patients"

Ref. Peter Yu, ASCO President, The ASCO Post September 1, 2014, Volume 5, Issue 14

ESMO and ASCO vision

- But, please take into account that both leader organizations are following criteria # 3: Guidelines and recommendations from scientific societies”

European Union

- Access to healthcare
- EU must act to address prohibitively high price of life-saving medicines
- **The European Parliament recently debated the issue of life-saving medicines and the excessively high pricing in certain member states**

The Greens | European Free Alliance
in the European Parliament

SLACOM

Reporting and Grading Financial Toxicity

Nandita Khera

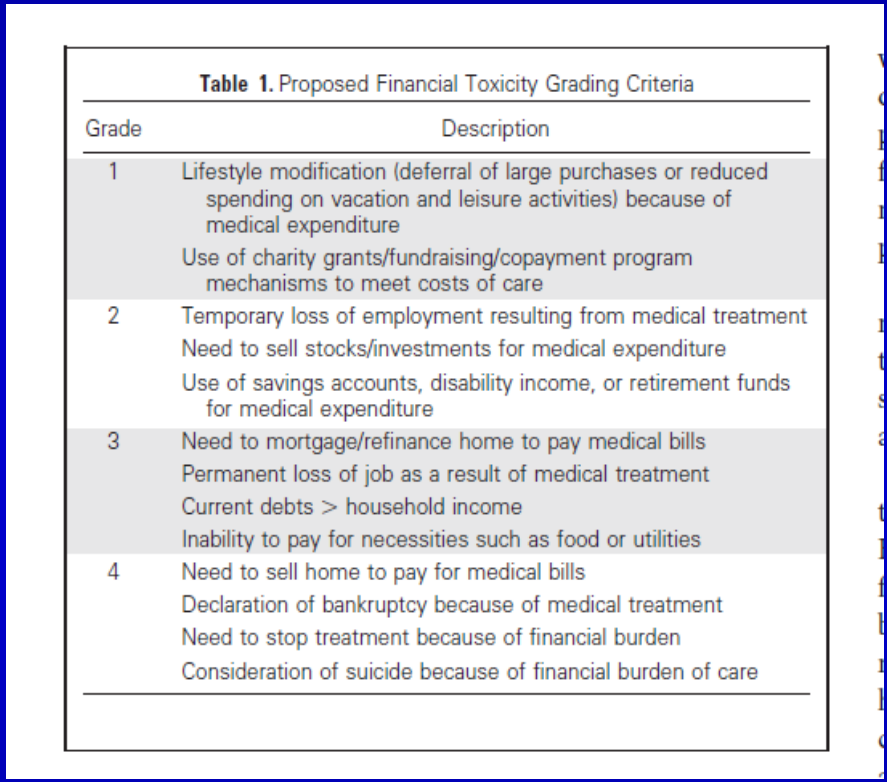


Table 1. Proposed Financial Toxicity Grading Criteria

Grade	Description
1	Lifestyle modification (deferral of large purchases or reduced spending on vacation and leisure activities) because of medical expenditure
	Use of charity grants/fundraising/copayment program mechanisms to meet costs of care
2	Temporary loss of employment resulting from medical treatment
	Need to sell stocks/investments for medical expenditure
	Use of savings accounts, disability income, or retirement funds for medical expenditure
3	Need to mortgage/refinance home to pay medical bills
	Permanent loss of job as a result of medical treatment
	Current debts > household income
	Inability to pay for necessities such as food or utilities
4	Need to sell home to pay for medical bills
	Declaration of bankruptcy because of medical treatment
	Need to stop treatment because of financial burden
	Consideration of suicide because of financial burden of care

Ref. Mayo Clinic, Phoenix, AZ. Published online ahead of print at www.jco.org on September 8, 2014.

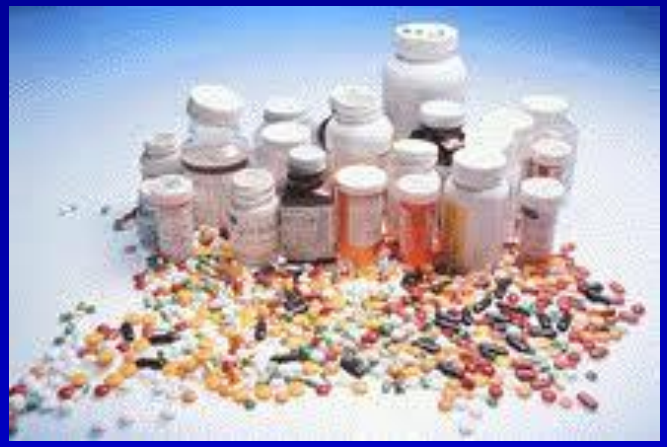
Financial Toxicity

- The # 1 reason for personal bankruptcy in the US is related to medical costs and disease.

Cancer Treatment

Cancer treatment

- Cancer is mostly treated using a combination of surgery, radiotherapy and drugs.
- Drugs are playing an increasingly important role in cancer management, however, many patients worldwide do not have access to the drugs they need.



Cancer Drugs: The Facts

Cancer Drugs: The Facts

- **In 2006 global pharmaceutical sales across all disease areas grew 7% to $643 billion**
- **87% of sales were in North America, Europe and Japan.**
- **It is estimated that the global pharmaceutical market will more than double in value to $1.3 trillion by 2020.**

Cancer Drugs: The Facts(2)

- **Sales of cancer drugs reached $34.6 billion in 2006 , a 20.5% increase in sales over the previous year.**
- **The global anticancer market was $70 billion in 2008.**
- **Cancer drug sales are now the second leading therapeutic class of sales after lipid regulators.**
- **Expenditure on cancer drugs account for between 10-20% of spending on cancer care and about 5% of total drugs expenditure.**

Some figures

- The 20 leading oncology brands generated global sales close to $50 billion in 2012

Ref: http://www.firstwordpharma.com/node/1132129

- **The cost of cancer drugs has more than doubled in the past decade. Of the 12 cancer drugs approved in 2012 by the FDA for cancer 11 were priced at more than $100,000 per patient per year.**

http://ecancer.org/journal/editorial/40-recycling-existing-drugs-for-cancer-therapy-delivering-low-cost-cancer-care.php

Cancer Drugs: The Facts(3)

- Innovative cancer drugs are developed with public and private investment in cancer research.
- The pharmaceutical industry spends between $6.5 – 8 billion per year on cancer research. Public investment in cancer research (ie. governmental and charitable) is at much lower levels
- The research and development of cancer drugs is mainly driven by commercial considerations rather than public health priorities.

Access to Cancer Drugs

World Health Organization

- The World Health Organization (WHO) estimates that nearly one third of the world's population does not have access to full and effective treatment with the medicines they need - this rises to over 50% in the poorest parts of the world.
- Even in highly developed countries access to some drugs and to the best available therapy is not guaranteed for everyone

Barriers to Access

- ***Drugs costs*: The high price of patent-protected cancer drugs makes them unaffordable for many countries. Patent enforcement by pharmaceutical companies in low-income countries can also inhibit access**
- ***Insufficient public funding of health*: Governments in some countries do not provide reimbursement for essential cancer drugs. This means that patients have to pay for drugs themselves**

Barriers to Access(2)

- ***Poor infrastructure:*** **M**any countries lack the facilities necessary to enable complex cancer drug regimens to be administered safely and effectively
- ***Irrational use of cancer drugs*** There is a dearth of adequately trained health professionals who are competent to prescribe and administer cancer drugs. In addition, many countries lack national evidence-based treatment guidelines to guide the rational selection of cancer drugs

Barriers to Access(3)

- ***Bureaucratic*** **policies:** In many countries worldwide national opiate policies are too restrictive which limits availability to morphine and other pain-relieving drugs. It is estimated that 80% of cancer patients who suffer severe pain have no access to opiates
- ***Counterfeit medicines*** In developed countries sales of counterfeit drugs represent less than 1% of the pharmaceutical market. This rises to 10-30% in parts of Asia and Latin America and up to 70% in some African countries

Overcoming barriers

- Some pharmaceutical companies have established drug donation programmes to address access problems in low-income countries. Although useful in the short-term these programmes are not a long-term solution to cancer drug access.
- WHO has developed a list of essential cancer medicines which is updated and revised biennially. This list is used to guide procurement of cancer drugs in many low- and middle-income countries.

WHO criteria

- WHO has previously produced recommendations on the essential drugs required for cancer therapy
- Over the last five years several new anti cancer drugs have been aggressively marketed.
- Most of these are costly and produce only limited benefits.

Ref. K. Sikora, Annals of Oncology, 1999

WHO criteria

- WHO divided currently available anti-cancer drugs into three priority groups (curable, increased curability-adjuvant- and prolong survival)
- Curable cancers and those cancers where the cost-benefit ratio clearly favours drug treatment can be managed appropriately with regimens based on only 1 7 drugs.

WHO criteria (cont.)

- All of these are available, at relatively low cost, as generic preparations.
- The wide availability of these drugs should be the first priority.

Table 3. Cancer drug priority list.

	Top 10 cancers	Category 1–2	Generic
Priority 1			
Bleomycin	+	+	+
Chlorambucil	+	+	+
Cisplatin	+	+	+
Cyclophosphamide	+	+	+
Doxorubicin	+	+	+
Etoposide	+	+	+
5-Fluorouracil	+	+	+
Methotrexate	+	+	+
Prednisolone	+	+	+
Procarbazine		+	+
Tamoxifen	+	+	+
Vincristine	+	+	+
Vinblastine	+	+	+
Cytarabine		+	+
Dactinomycin		+	+
Daunorubicin		+	+
6-Mercaptopurine		+	+

WHO drugs priority list 1 and 2

Table 1. Cancers grouped according to the effectiveness of chemotherapy and hormonal therapy.

Category 1, potentially curable even with systemic disease
- Germ-cell cancers
- Trophoblastic cancers
- Acute lymphoblastic leukaemia
- Acute myeloid leukaemia
- Acute promyelocytic leukaemia
- Hairy cell leukaemia
- Hodgkin's disease and non-Hodgkin's lymphoma

Category 2, adjuvant chemotherapy of established benefit in local disease
- Colo-rectal cancer (Dukes C)
- Breast cancer
- Ovarian cancer
- Osteosarcoma
- Ewing's sarcoma
- Neuroblastoma
- Retinoblastoma
- Soft tissue sarcoma
- Wilms' tumour

List of essential Medicines / Cancer Drugs Priority List

- Currently is under full review. Requested by UICC and Dana Farber , WHO decide to update the complete list of medications included in the list. ESMO, ASCO, NCCN International and others are collaborating in the task.

More cost effective options

- Modifying modes of administration
- Using shorter-but still effective-courses or doses
- Finding new combinations or indications of less expensive drugs
- The use of generics after testing bioequivalence

Ref.Elzawawy, 2009; Elzawawy, 2008,

UICC position

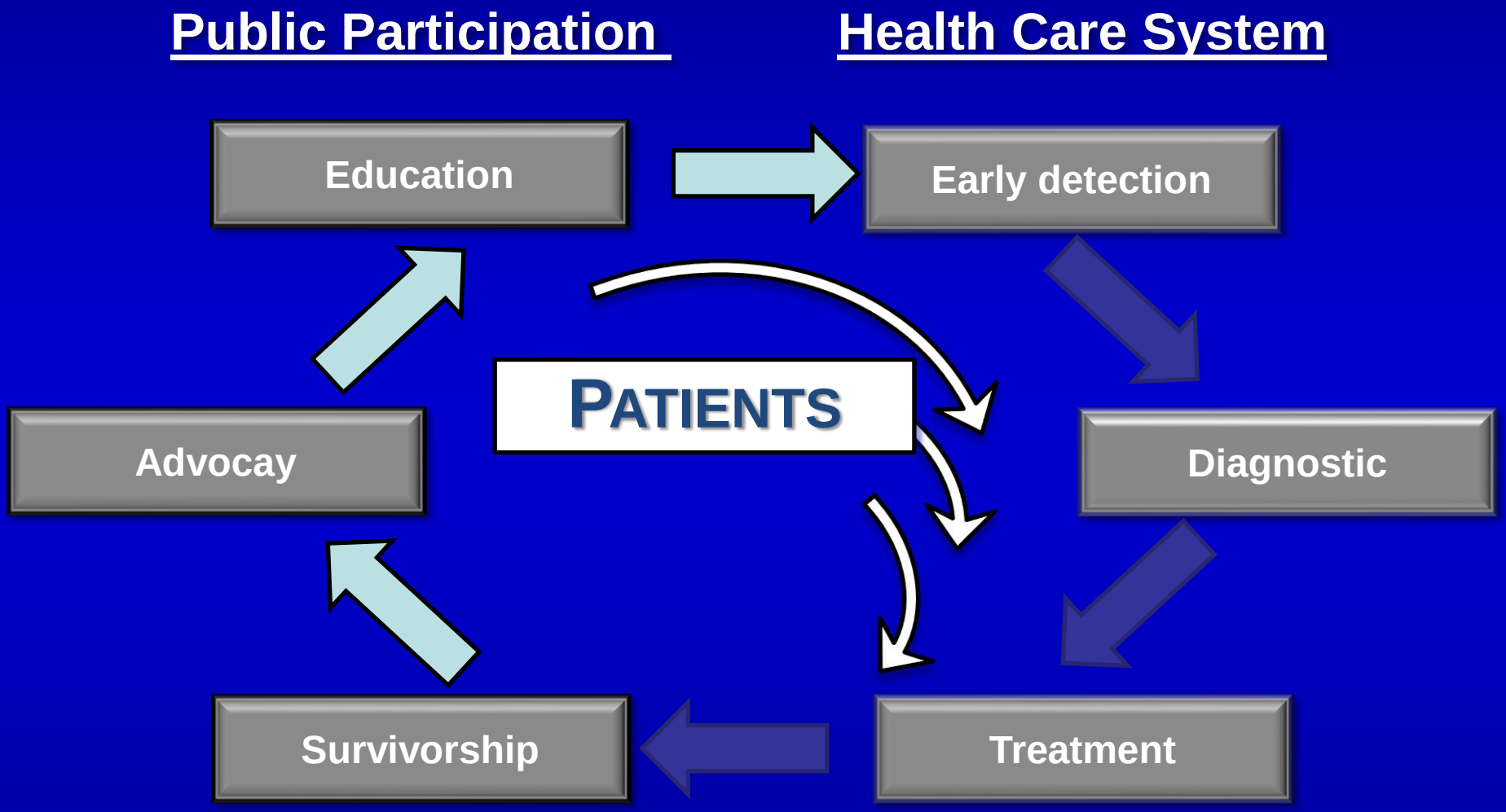
- **Worldwide access to the best possible cancer treatment, care and support is a top UICC priority. To deliver on its vision of a world where cancer is eliminated as a major life-threatening disease for future generations, UICC is committed to participate in building collaboration and cooperation to address barriers in access to cancer drugs worldwide.**

Ref. Position paper , Cost of cancer drugs, UICC

In conclusion

- Integrating innovative cancer medicines in the treatment of cancer should be considered according to resources and level of application
- Broad range of novel therapeutics in development
- Need to rationally develop strategies and possible combinations, economically feasible and accessible to different world populations

The patient-centric model



Reference : B. Anderson, BHGI

- **Every patient – regardless of where he or she is born – deserves an equal chance at a long life and good health (J.Seffrin, 2008).**

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Thank you very much for your attention!