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R CANCERS EUROPE



European Society for Medical Oncology



FONDAZIONE IRCCS
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DEI TUMORI





Rare Tumours in Europe

CHALLENGES AND SOLUTIONS

6 November 2008 - Brussels

11:15 –13:15 PARALLEL BREAKOUT SESSIONS INCLUDING WORKING LUNCH

Workshop I

Rare tumours: Methodological and Regulatory Challenges

Chair: *Paolo Casali, ESMO* - Co-Chair: *Jan Lillemark, Swedish Medicines Agency*

The orphan drugs approval process - *Filippo De Braud, European Institute of Oncology*

Current guidelines on efficacy assessment in the EU - *Iordanis Gravanis, EMEA*

Strategies for rare tumours in medical statistics - *Paolo Bruzzi, National Institute for Cancer Research of Genoa*

A parliamentary perspective - *Jolanta Dickute, MEP*

Discussion

Workshop II

Rare tumours: Organisational Challenges

Chair: *Jean-Yves Blay, Conticonet* - Co-Chair: *Bertram Wiedenman, Charité University Hospital Berlin*

The challenge of rare tumours treatment in the EU - *Peter Hohenberger, University of Heidelberg*

The role of patient advocacy groups - *Jan Gelssier, European Cancer Patient Coalition*

Developing networks in hematology - *Rüdiger Hehlmann, Leukemia Network*

Examples of overcoming the barriers - *Thor Alvegard, Scandinavian Sarcoma Group & Markus Wartenberg, Sarcoma Patients EuroNet*

Discussion

Workshop III

Rare tumours: Patient Access Challenges

Chair: *Kathy Redmond, Cancer World* - Co-Chair: *Flaminia Macchia, Eurardis*

Challenges and barriers: An overview - *Yann Le Cam, Eurardis*

Living with a rare tumour: a patient story - *Ella Pybus, Meningioma UK*

Discussion



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Recommendations Addressing Regulatory Barriers in Rare Cancer Care

We:

1. Acknowledge that while the process for establishing the efficacy of new medicines is in principle the same for all cancers, the strength of the evidence – intended as level and quality of evidence and statistical precision – that is achievable in common cancers is difficult to achieve in rare conditions and, therefore, a higher degree of uncertainty should be accepted for regulatory as well as clinically informed decision-making.





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11.

Encourage clinical studies in rare cancers that would provide data that supports rational, **patient-shared, clinical decision-making**, whilst acknowledging this as an essential means **to overcome uncertainty** surrounding patients' immediate clinical needs.



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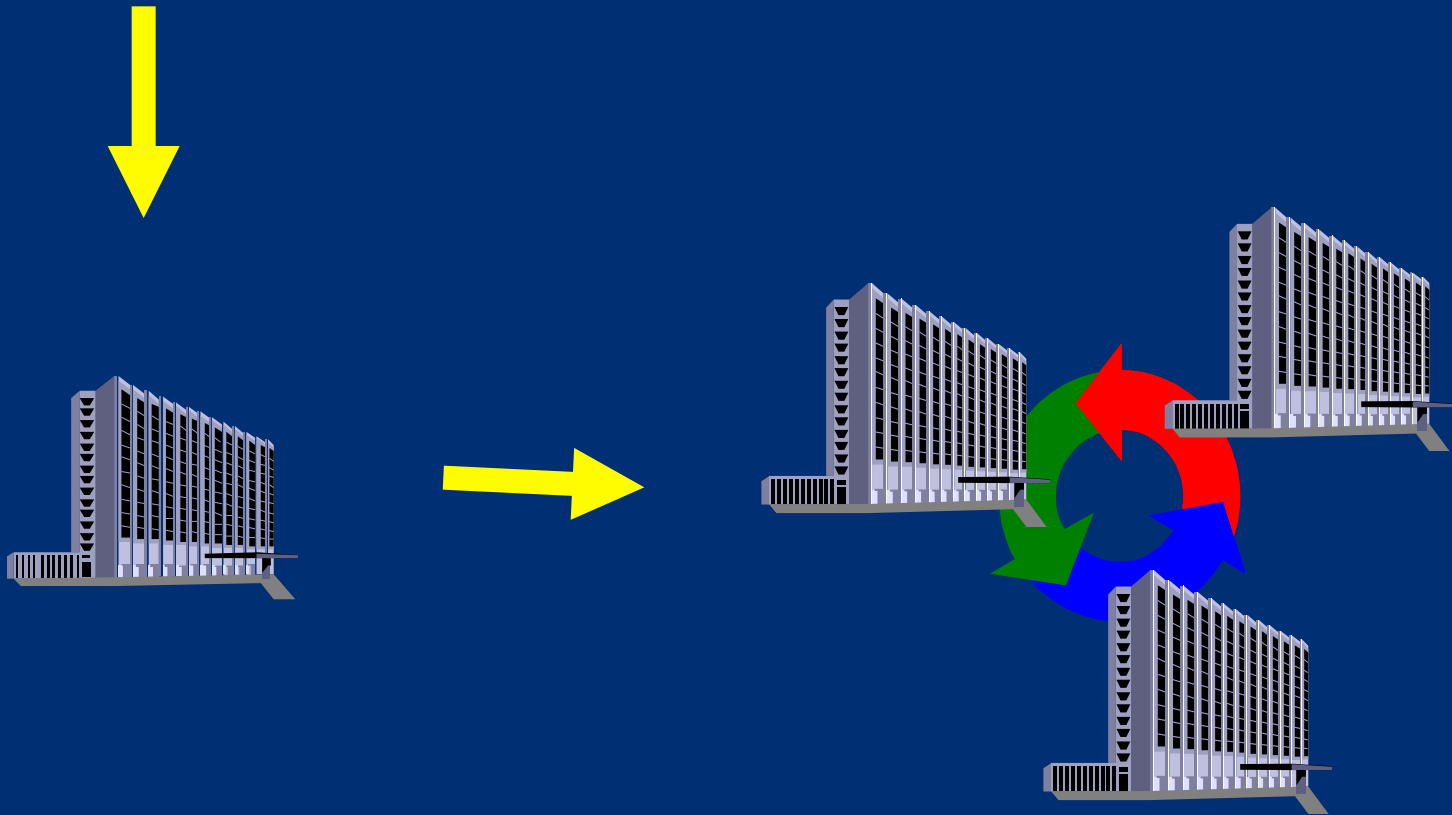
17.

Call for increased integration of local, national and European centres of expertise into European **reference networks**, based on specific criteria as set out in the Commission's proposed Directive on the application of patients' rights in cross-border healthcare , in order to provide the necessary sound organisational structures for more efficient clinical research and early transfer of research data into clinical practice, thus improving the clinical management of rare cancers.

From the reference center...



...to the Reference network



Reference center



- **expertise**
- **multidisciplinarity**
- **research**

- **health migration**
- **implicit rationing**
- **failures in routine care**



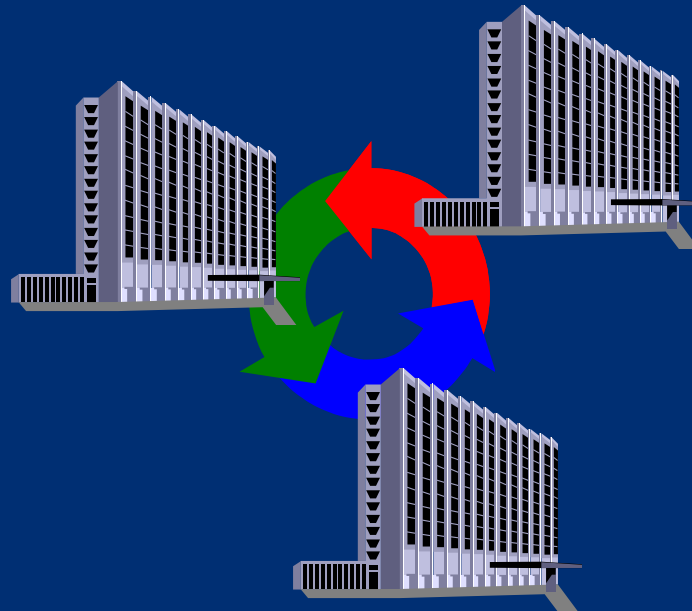
Reference network

- **expertise**
- **multidisciplinary**
- **research**

- **health migration**
- **implicit rationing**
- **failures in routine care**



Collaborative networks



Extra medical time!





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7.

Call upon the research community to consider using a **Bayesian approach for the design of clinical trials** whenever well-powered randomised trials are not feasible due to the low incidence of the cancer entity and granted that sufficient information is available on the specific disease entity to empower such statistics (e.g. other clinical studies, biological evidence, analogies with more frequent diseases, the natural history of the disease, etc.). A mechanism for consensus development for definition of prior probability distributions should be devised.

PHILOSOPHICAL TRANSACTIONS:



LII. *An Essay towards solving a Problem in the Doctrine of Chances. By the late Rev. Mr. Bayes, F. R. S. communicated by Mr. Price, in a Letter to John Canton, A. M. F. R. S.*

Dear Sir,

Read Dec. 23,
1763.

I Now send you an essay which I have found among the papers of our deceased friend Mr. Bayes, and which, in my opinion, has great merit, and well deserves to be preserved. Experimental philosophy, you will find, is nearly interested in the subject of it; and on this account there seems to be particular reason for thinking that a communication of it to the Royal Society cannot be improper.

Mr. Bayes & Mr. Price. Phil Trans 1763;53:370

The Bayes theorem...

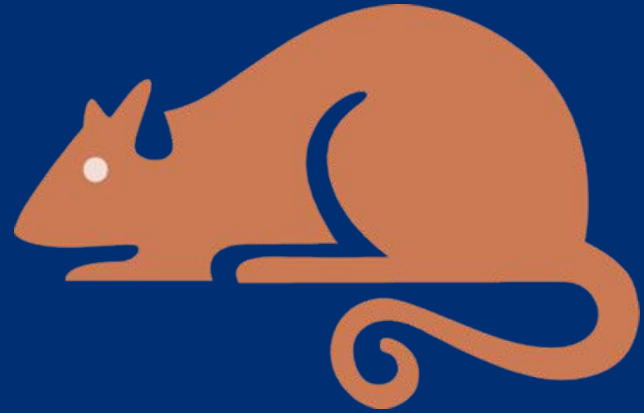


$$P[A|B] = P[A] \times \frac{P[B|A]}{P[B]}$$

Mr. Bayes & Mr. Price. Phil Trans 1763;53:370



The preclinical rationale



Prior probability



R
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Rare cancers – more common than most people think

- **clinical decision-making**
- **methods to combine evidence**
- **new study designs**
- **surrogate end points**
- **organization of studies**

European Rare Cancer Research Network

Let's join forces to beat rare cancers



Joining Forces for Action
Against Rare Cancers

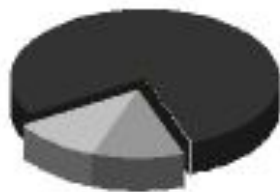
Rare cancers are not so rare: The rare cancer burden in Europe

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

Table 1 Data quality indicators and other characteristics of malignant cancers diagnosed in European cancer registries 1995-2001 and included in the analyses.

Country	Registry	Number of malignant cancers	Data quality indicators				
			Death certificate only (%)	Accuracy (%)	Missing/unclassified (%)	Cancer 1989-1990 associated before system (%)	Morphology code ICD-O (%)
Austria	Austria	395,495	9.9	9.0	81.3	5.9	92.1
Belgium	Flanders	194,713	0.0	0.3	89.8	0.0	7.9
France	Bas Rhin	15,313	0.0	0.0	91.8	3.3	5.9
	Calvados	5991	0.0	0.0	88.1	6.1	0.5
	Calvados-Eparges	2881	0.0	0.0	87.0	4.4	80.0
	Cher (20th Department)	4376	0.0	0.0	81.9	0.5	0.5
	Cher (20th Department)	1884	0.0	0.0	100.0	7.2	0.0
	Creuse	1762	0.0	0.0	92.9	0.1	0.5
	Haute Rhin	3073	0.0	0.0	96.4	5.9	0.1
	Mayenne	10,001	0.0	0.0	8.0	4.9	0.1
	Mayenne	12,326	0.0	0.0	94.1	8.6	0.1
	Lot-et-Garonne	2769	0.0	0.0	100.0	0.0	0.0
	Mayenne	6367	0.0	0.0	90.3	2.7	0.0
	Mayenne and Andrennes	188	0.0	0.0	100.0	1.6	0.0
	Mayenne	1481	0.0	0.0	94.2	0.6	0.0
	Tarn	4070	0.0	0.0	93.9	0.0	1.1
Germany	Saxony	54,032	9.9	0.0	91.9	5.9	0.0
Ireland	Ireland	8954	0.1	1.4	96.6	0.0	1.1
Ireland	Ireland	150,339	0.0	0.0	96.7	0.0	0.0
Italy	Abruzzo	14,094	0.7	0.0	89.9	0.0	0.0
	Basilicata	17,170	1.1	0.4	87.0	0.0	0.0
	Basilicata	23,760	0.1	0.0	98.1	0.4	0.7
	Basilicata	60,987	0.0	0.1	80.9	0.4	0.7
	Friuli-V.G.	76,887	0.0	1.9	91.0	0.1	0.0
	Liguria	94,337	0.0	0.0	91.9	0.0	0.0
	Liguria	10,584	0.1	0.0	87.4	0.0	0.0
	Liguria	60,987	0.1	0.0	90.0	0.4	0.0
	Liguria	60,987	0.1	0.0	91.0	1.9	0.4
	Liguria	540	0.0	0.0	90.0	0.0	0.0
	Liguria	23,339	0.0	0.0	90.0	0.0	0.0
	Liguria	10,987	0.0	0.0	80.9	0.1	0.0
	Liguria-Trento	21,012	0.0	0.0	90.1	0.0	0.0
	Liguria	60,987	0.0	0.0	87.0	0.1	0.0
Spain	Madrid	10,917	0.0	0.0	71.9	0.0	0.0
	Madrid	10,984	0.0	0.0	94.9	0.0	0.0
	Madrid	17,769	0.0	0.0	95.0	0.0	0.0
	Madrid	40,011	0.7	0.0	94.0	0.1	0.0
	Madrid	19,709	0.0	0.0	89.0	0.0	0.0
	Madrid	94,019	1.1	0.0	87.0	0.0	0.0

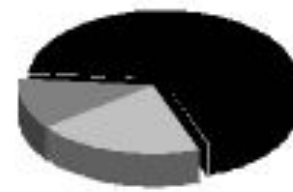
Incidence <6/100,000/y



Incidence <15/100,000/y

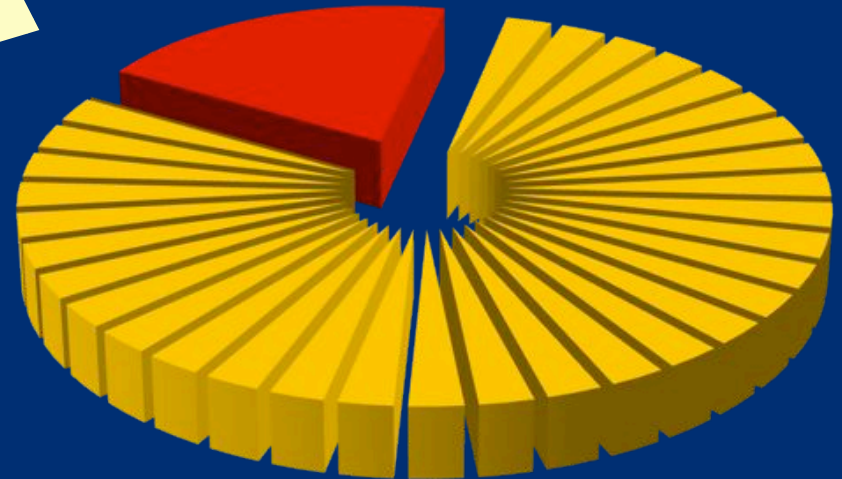
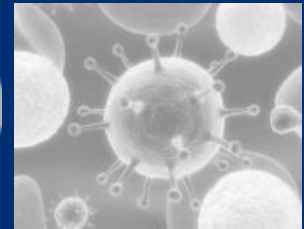
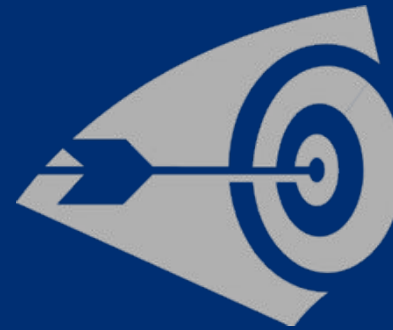


Prevalence <50/100,000



«Families» of rare cancers

- **NON CUTANEOUS MELANOMA**
- **SKIN - Rare**
- **THORACIC - Rare**
- **UROGENITAL - Rare**
- **FEMALE GENITAL - Rare**
- **MALE GENITAL**
- **NEUROENDOCRINE**
- **ENDOCRINE ORGAN**
- **CNS**
- **SARCOMAS**
- **DIGESTIVE - Rare**
- **HEAD & NECK – Rare**
- **HEMATOLOGICAL - Rare**
- **PEDIATRIC**



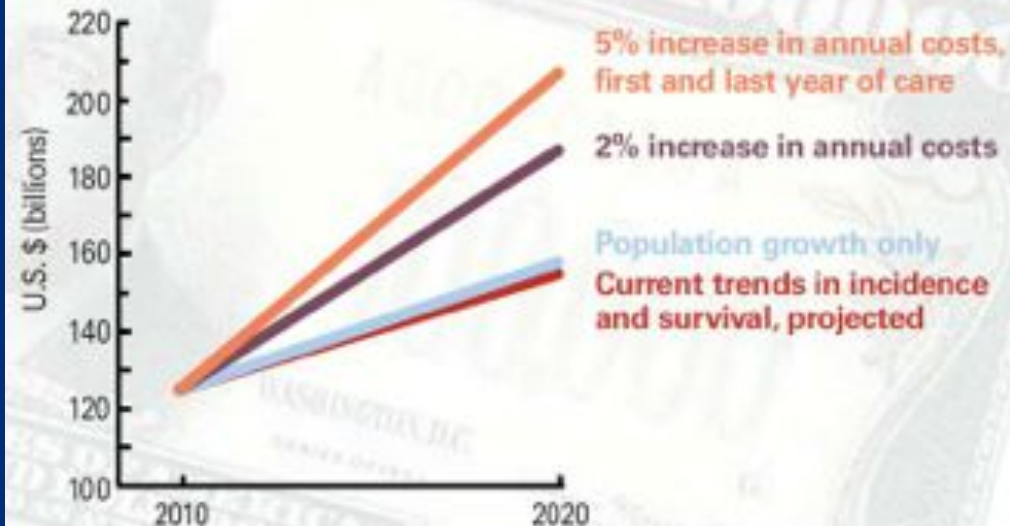
OPINION

Personalized medicine in oncology: the future is now

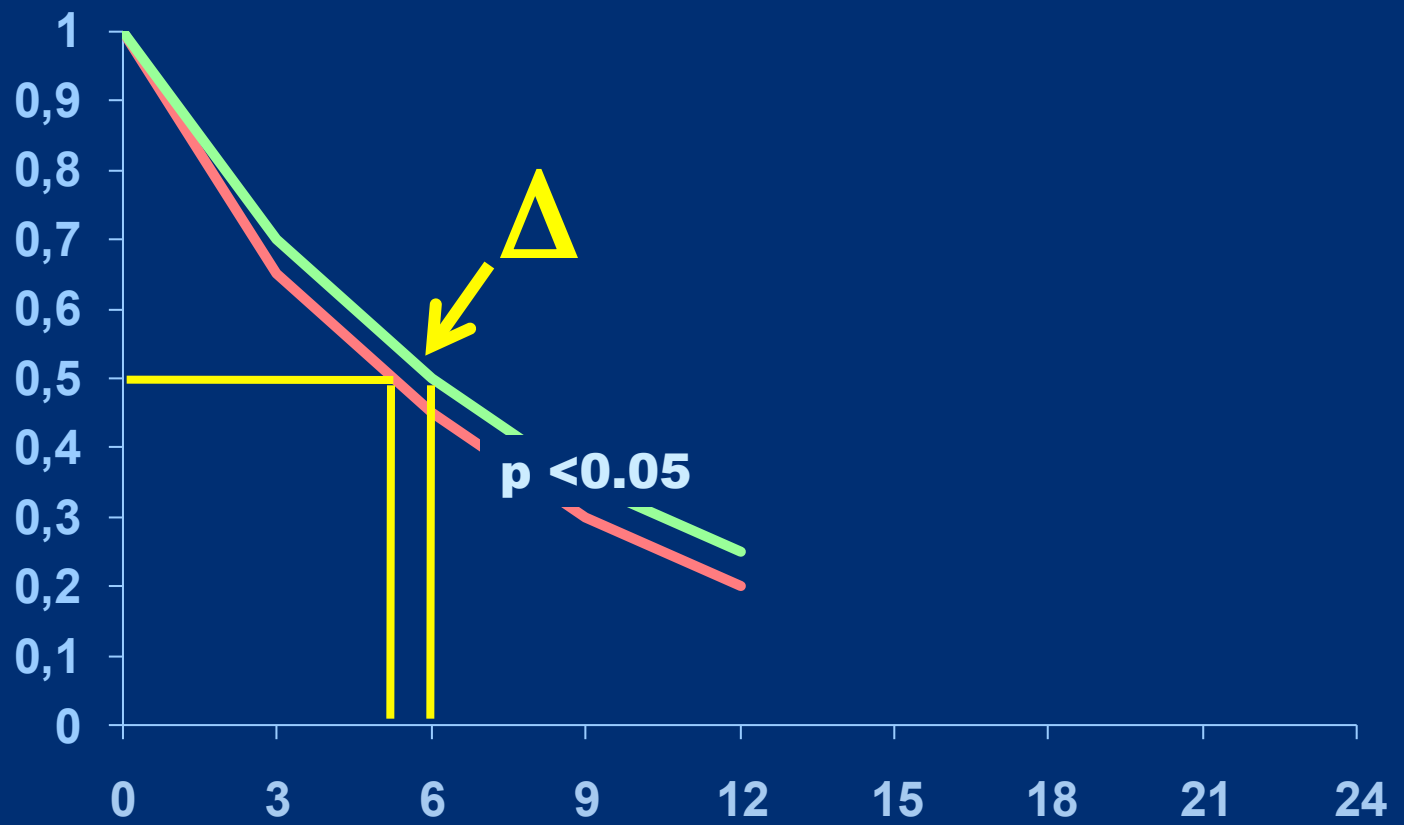
Richard L. Schilsky

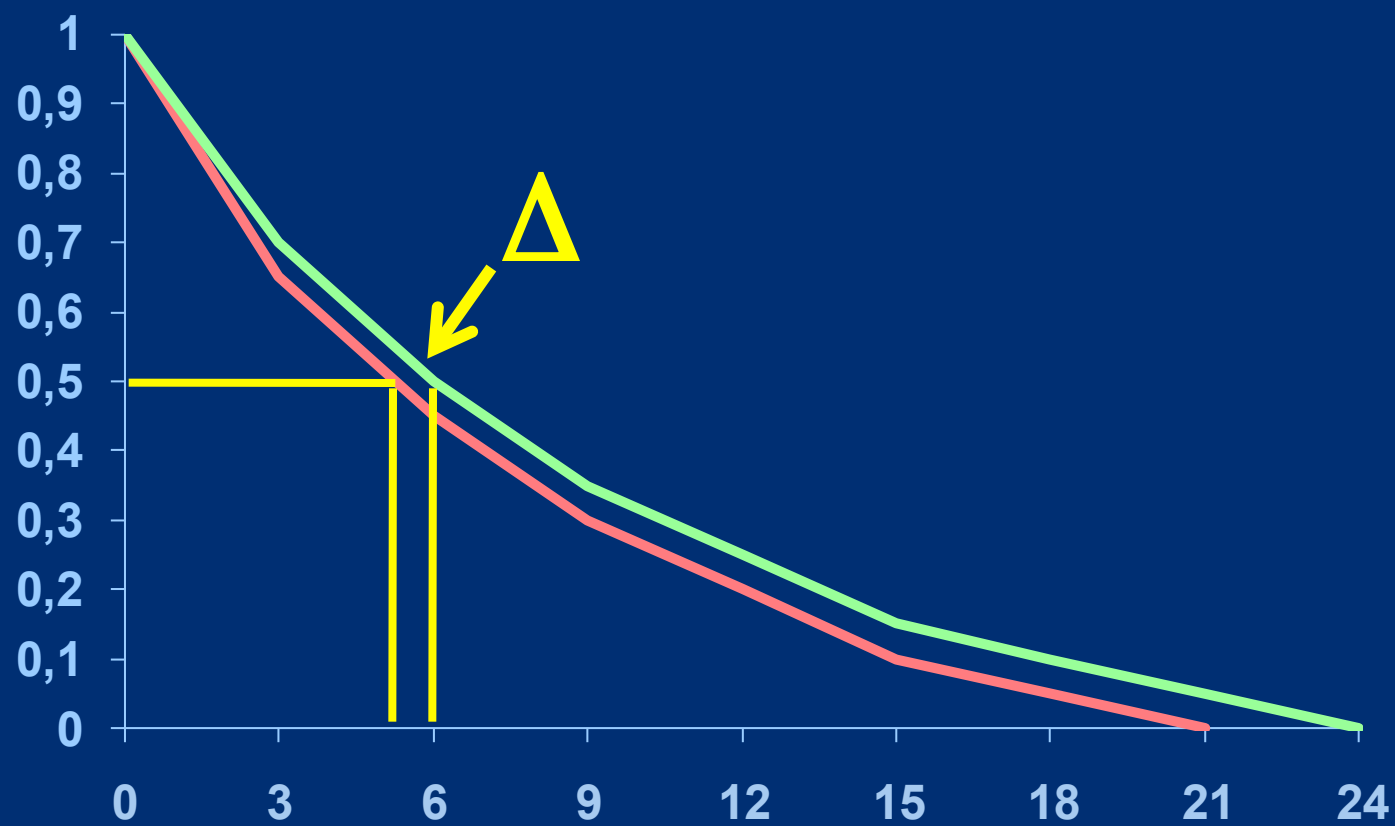
Abstract | Cancer chemotherapy is in evolution from non-specific cytotoxic drugs that damage both tumour and normal cells to more specific agents and immunotherapy approaches. Targeted agents are directed at unique molecular features of cancer cells, and immunotherapeutics modulate the tumour immune response; both approaches aim to produce greater effectiveness with less toxicity. The development and use of such agents in biomarker-defined populations enables a more personalized approach to cancer treatment than previously possible and has the potential to reduce the cost of cancer care.

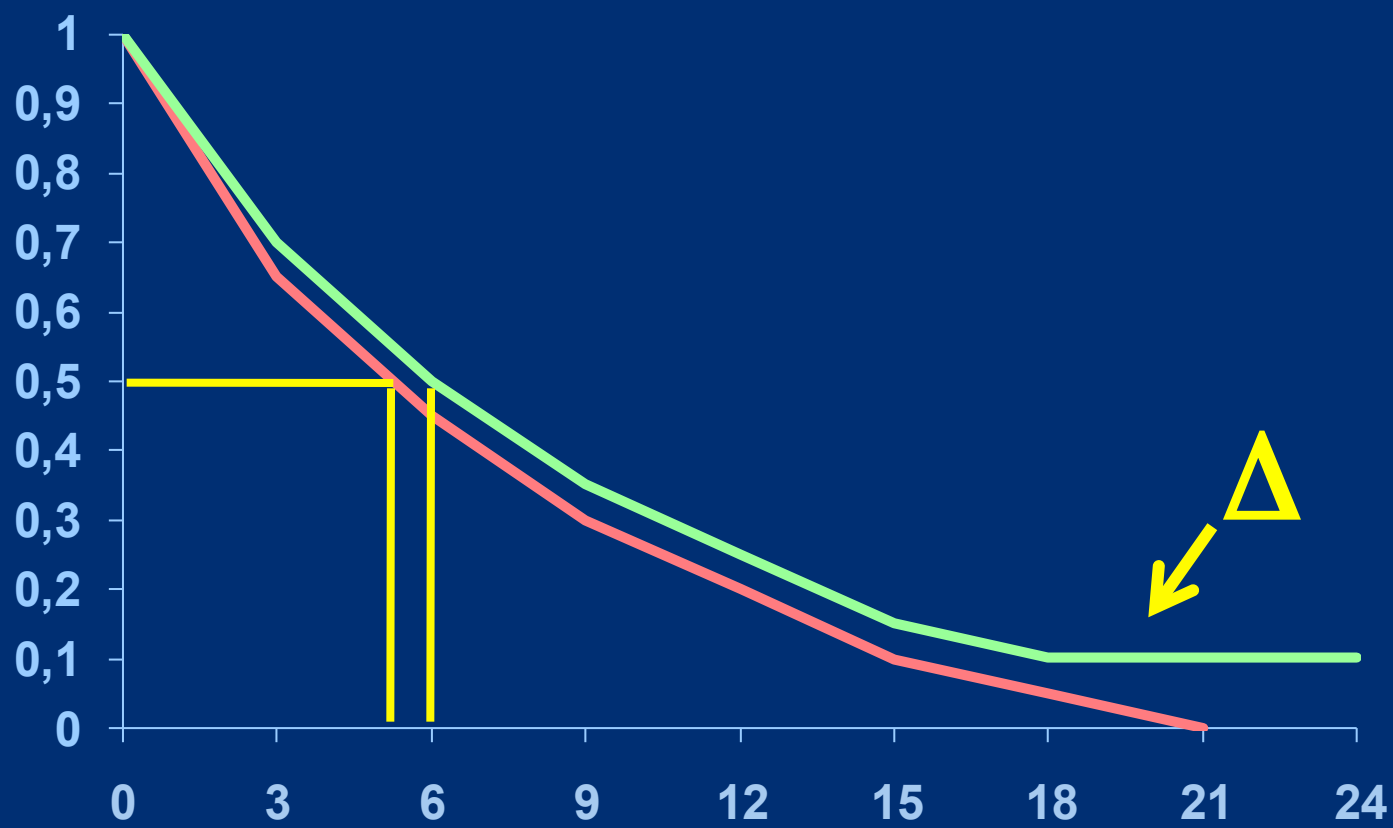
PROJECTED COSTS OF TOTAL U.S. CANCER CARE, 2010-20

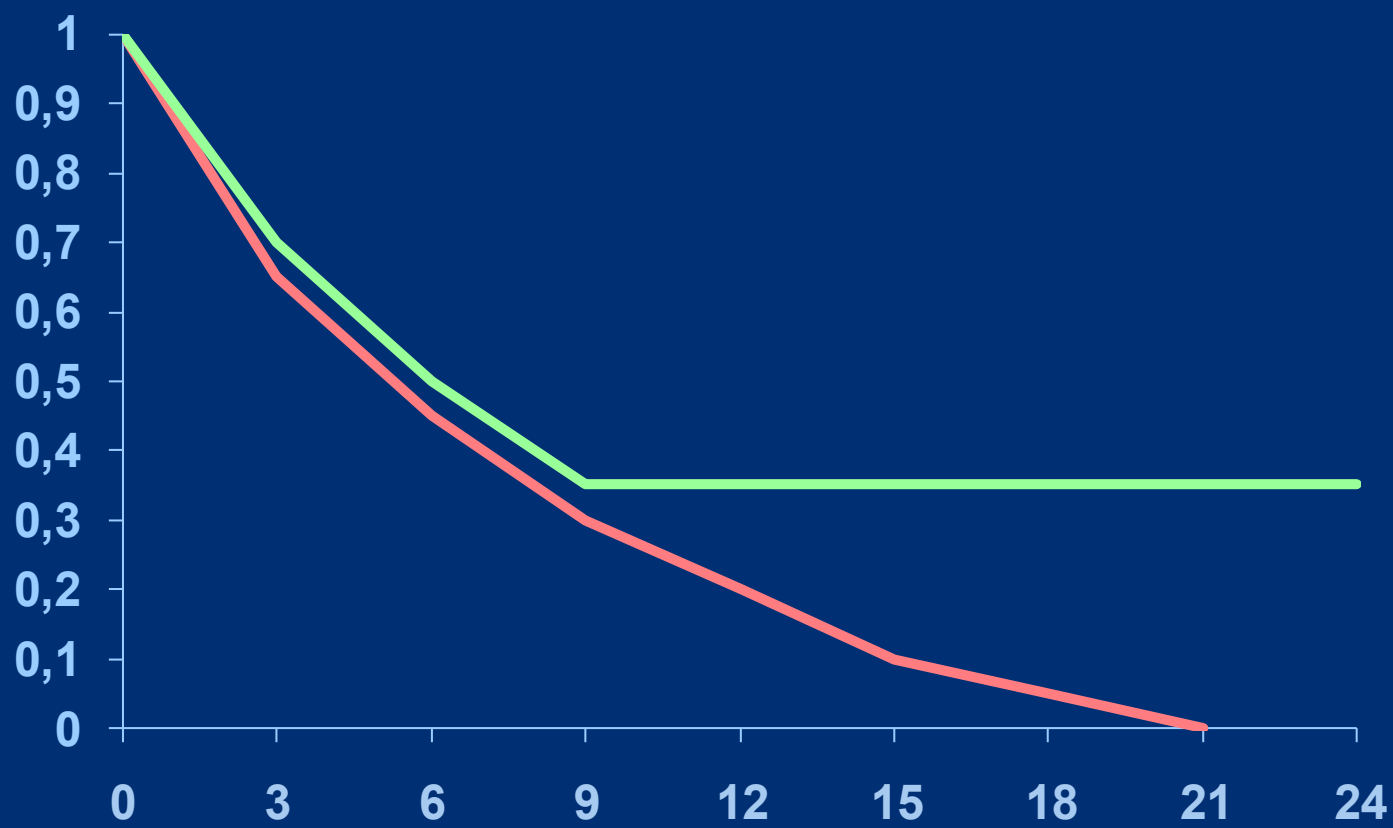


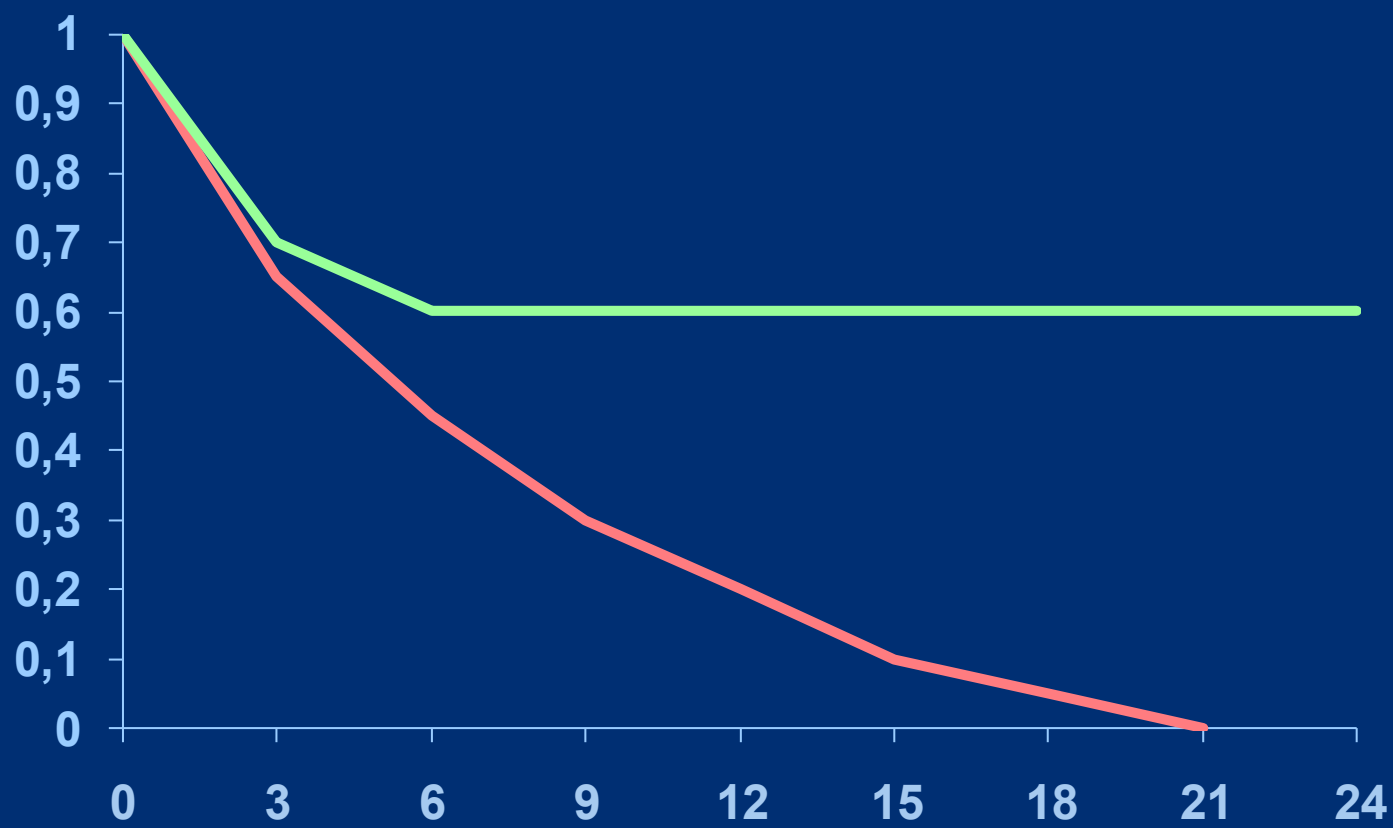
Malakoff D, Science 2011;331:1545













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