III Foresight Training Course Gianni Benzi Foundation

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Rare Diseases Europe

About the course

- 1 – 4 September 2010, Krakow
- 65 participants
  - Regulators
  - Industry
  - 1 patient representative (=1.5%)
- All phases of the drug development process
- New EMA road map to 2015 as a guide for the programme sessions

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Course programme (highlights)

- Welcome Session: B/R in the perspective of the EU Road Map and National Agencies proposals
- Session 1 - Research, development and B/R ratio
- Session 2 - B/R assessment during the development
- Session 3 - R/B at the evaluation process
- Session 4 - Driving incentives by making a good application
- Session 5 - Take advice to be successful
- Session 6 - B/R Assessment after the MA
- Session 7 - B/R assessment and HTA

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From the EMA and its scientific committees

- EMA Road Map perspectives and contribution: A. Saint-Raymond
- EMA legal responsibility and role in B/R Assessment: T. Jablonski
- Paediatric Priority List: Kevin Connolly, PDCO
- PDCO Assessment of the B/R ratio: D. Brasseur, PDCO
- COMP Assessment of the B/R ratio: B. Dembowska-Baginska, COMP
- CHMP Assessment: M. Pirozynski
- The new EPAR including the CHMP evaluation process: I. Hudson, CHMP
- Optimisation of consultation process CHMP/SAGs: A. Saint-Raymond
- Procedure for PIP Approval: R. Ancuceanu, PDCO, CHMP
- Scientific advice and PA: preparation of the application: M. Pirozynski
- B/R in paediatric oncology: P. Paolucci, PDCO
- Success and failures in SA and PA: A. Saint-Raymond
- Risk Management Plans: D. Mentzer, PDCO
- B/R Assessment and off-label use in children: A. Ceci, PDCO
- National agencies experiences: R. Ancuceanu, PDCO

Patients who benefit, patients who take the risks

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EURORDIS

- Created 1997 to support the adoption of EU Orphan Drug Regulation
- Patient driven, largest pan-European patient organisation (PO)
- 434 members (POs)
- In 43 countries
- Covering > 4000 distinct rare diseases
- 25 staff
- Member of the COMP, PDCO, CAT, PCWP @ EMA and EU CERD @ DG Sanco

Main points

1. Benefit / risk: information better balanced. Why?
2. Benefit: easier to understand. How?
3. Risk: better perceived and quantified. How?
4. B / R evaluation: patients' to contribute.

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Main points

1. Benefit / risk: information better balanced. Why?

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Patients' doubts

- Shall I take my medicines today?
- Why am I taking it finally?
- Is it doing me any good?
- If only these side effects would not exist…
- Maybe I should stop for a few days to recover from side effect
- It may help, but will it cure?
- Advanced therapy they say, but I've no idea what this stuff is
- My brother receives a different treatment for the same disease, am I special?
- …

➲Are these questions answered in the package leaflet?

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Why do patients forget doses?

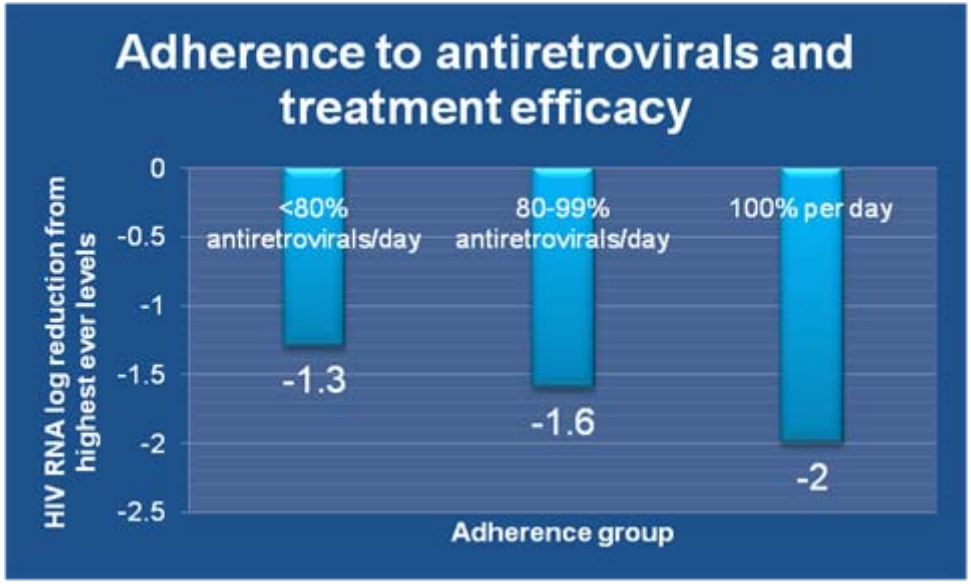
You need quite a good level of motivation to continue treatment

Gifford et al., JAIDS Journal of Acquired Immune Deficiency Syndromes, Vol. 23, No. 5, April 15, 2000

Benefit of better explaining the benefits

= higher motivation to take the drug (higher compliance)

= maximum treatment efficacy



Gifford et al., JAIDS Journal of Acquired Immune Deficiency Syndromes, Vol. 23, No. 5, April 15, 2000

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« Convenience » matters as much as intrinsec efficacy

Total pills per day	
2 pills per day	8.32
5 pills per day	3.03
10 pills per day	–2.40
16 pills per day	–6.23

1st

Dietary restrictions	
No food/water restrictions	5.92
Take with food	0.69
Take on an empty stomach	–2.36
Take 1.5 l of water each day	–0.33
Avoid taking with high fat meals	–2.60

2nd

Dosing Frequency	
All ARTs qd	7.59
All ARTs bid	4.91
One ART qd, the rest bid	0.12
One ART tid, the rest bid	–3.74

3rd

Pill Size	
Small size pills	5.18
Medium size pills	3.13
Large size pills	–2.52

4th

Combination Product	
ARTs as 1 pill	6.86
3 ARTs as 2 different pills	2.88
3 ARTs as 3 different pills	–0.10

5th

550 HIV patients treated for more than 3 months, self-questionnaire

J. Jordan, AIDS 2000, Oct 22-26;14(Suppl. 4); S51

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What patients and consumers recommend

Recommendation requiring a harmonised approach at EU level

- “in order to provide a good balance between information on benefits versus risks, the benefits of taking/using the medicine should be made more prominent and better explained in the PL”

EMEA/CPMP working group with patients’ organisations.
Outcomes of discussions: recommendations and proposals for action, April 2004

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Package leaflet

- X belongs to a group of antiviral medicines, also known as antiretrovirals, called nucleoside analogue reverse transcriptase inhibitors (NRTIs). These are used to treat Human Immunodeficiency Virus (HIV) infection.
- X is used in combination with other antiretroviral medicines for the treatment of HIV infection. It reduces HIV viral load, and keeps it at a low level. It also increases CD4 cell counts.
- CD4 cells are a type of white blood cell that play an important role in maintaining a healthy immune system to help fight infection.

EPAR summary for the public

- In one of the studies in adults, 77% of the patients taking X with A and B had viral loads below 400 copies/ml after 16 weeks (67 out of 87), compared with 38% of the adults taking A and B without X (33 out of 86).

What information does not say

- Since highly active antiretroviral (HAART) regimen were introduced, HIV related mortality declined by more than 90%
- Compared to pre-HAART era, where median time from infection to AIDS was 10-11 years, now it's beyond 20 years
- Life expectancy of treated PLWA now approaches life expectancy of uninfected people

A consensus between all

European Medicines Agency

London, 23 June 2009
Doc ref.: EMEA/40926/2009

Information on benefit-risk of medicines:
patients', consumers' and healthcare professionals' expectations

Information on medicines

- Always communicate benefits and risks together
- Clear information to help choose most appropriate treatment
- Clear description of benefits and risks, both qualitative and quantitative
- Factors which may influence a benefit or a risk in an individual should be clearly described

➲ Now in Agency's road map 2010-2015, Strategic Area 2

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Main points

2. Benefit: easier to understand. How?

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Communicating on benefits

More than just the indication:

- Why it is important to treat the disease
- Whether the treatment is for short term or chronic use
- Whether the medicine is curative or for control of symptoms
  - Which symptoms will be controlled and how long the effects will last
- Whether the effects will last after the medication is stopped
- Where the medicine is used to treat two or more discrete indications all should be succinctly described as above.
- Where to obtain more information on the condition

Beryl Keeley - MHRA Product Information & Advertising Unit

What information on the benefits?

WITHOUT BENEFIT INFORMATION

PRODUCT contains beclometasone propionate which is one of a group of medicines called corticosteroids.

These have an anti-inflammatory action and are used to treat asthma.

WITH BENEFIT INFORMATION

PRODUCT contains beclometasone propionate which is one of a group of medicines called corticosteroids, or "steroids".

Corticosteroids prevent attacks of asthma by reducing swelling of the air passages and are sometimes called "preventers".

You should take this medicine regularly every day even if your asthma is not troubling you.

Using PRODUCT can help prevent severe asthma attacks which sometimes need hospital treatment and if left untreated could even be life-threatening.

This medicine should not be used to treat a sudden asthma attack – it will not help. You will need to use a different inhaler ("reliever") to deal with these attacks.

Report of the Committee on Safety of Medicines, Working Group on Patient Information, UK

Main points

3. Risk: better perceived & quantified. How?

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Educating the public

hazardcards.com – accidents revisited. Danish School of Education, Aarhus University

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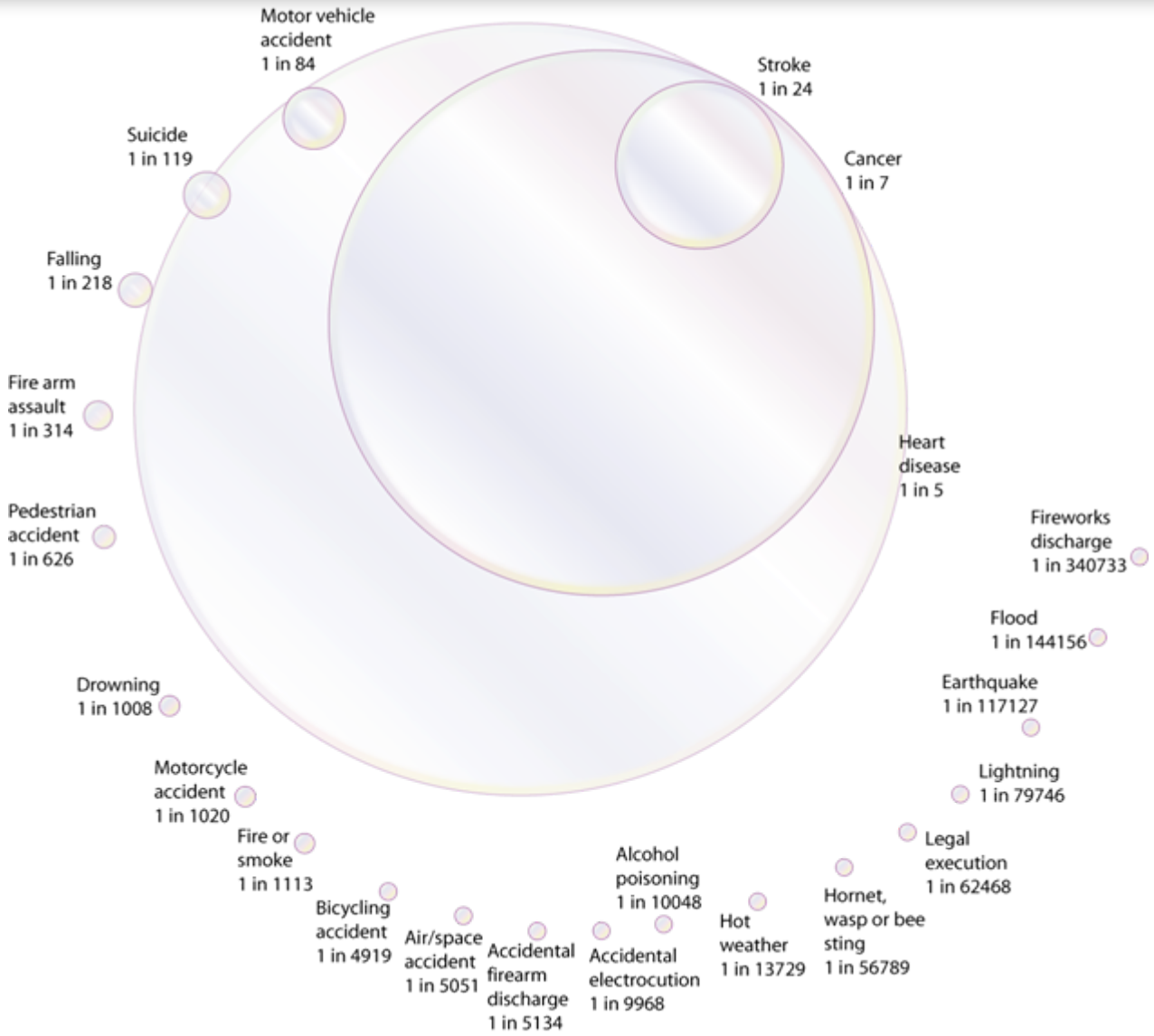
The public barely knows the risk scale



Other risks that public may learn about

Increasing frequency scale

5 Always happens

4

3

2 ← Adverse reaction with this product

1

0 Never happens

THE TORINO SCALE

Assessing Asteroid/Comet Impact Predictions

No Hazard	0	The likelihood of collision is zero, or is so low as to be effectively zero. Also applies to small objects such as meteors and bolides that burn up in the atmosphere as well as infrequent meteorite falls that rarely cause damage.
Normal	1	A routine discovery in which a pass near the Earth is predicted that poses no unusual level of danger. Current calculations show the chance of collision is extremely unlikely with no cause for public attention or public concern. New telescopic observations very likely will lead to re-assignment to Level 0.
Meriting Attention by Astronomers	2	A discovery, which may become routine with expanded searches, of an object making a somewhat close but not highly unusual pass near the Earth. While meriting attention by astronomers, there is no cause for public attention or public concern as an actual collision is very unlikely. New telescopic observations very likely will lead to re-assignment to Level 0.
	3	A close encounter, meriting attention by astronomers. Current calculations give a 1% or greater chance of collision capable of localized destruction. Most likely, new telescopic observations will lead to re-assignment to Level 0. Attention by the public and by public officials is merited if the encounter is less than a decade away.
	4	A close encounter, meriting attention by astronomers. Current calculations give a 1% or greater chance of collision capable of regional devastation. Most likely, new telescopic observations will lead to re-assignment to Level 0. Attention by the public and by public officials is merited if the encounter is less than a decade away.
Threatening	5	A close encounter posing a serious, but still uncertain threat of regional devastation. Critical attention by astronomers is needed to determine conclusively whether or not a collision will occur. If the encounter is less than a decade away, governmental contingency planning may be warranted.
	6	A close encounter by a large object posing a serious, but still uncertain threat of a global catastrophe. Critical attention by astronomers is needed to determine conclusively whether or not a collision will occur. If the encounter is less than three decades away, governmental contingency planning may be warranted.
	7	A very close encounter by a large object, which if occurring this century, poses an unprecedented but still uncertain threat of a global catastrophe. For such a threat in this century, international contingency planning is warranted, especially to determine urgently and conclusively whether or not a collision will occur.
Certain Collisions	8	A collision is certain, capable of causing localized destruction for an impact over land or possibly a tsunami if close offshore. Such events occur on average between once per 50 years and once per several 1000 years.
	9	A collision is certain, capable of causing unprecedented regional devastation for a land impact or the threat of a major tsunami for an ocean impact. Such events occur on average between once per 10,000 years and once per 100,000 years.
	10	A collision is certain, capable of causing a global climatic catastrophe that may threaten the future of civilization as we know it, whether impacting land or ocean. Such events occur on average once per 100,000 years, or less often.

Fig. 2. Public description for the Torino Scale, revised from Binzel (2000) to better describe the attention or response that is merited for each category.

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Package leaflet

4. POSSIBLE SIDE EFFECTS

Like all medicines, Revlimid can cause side effects, although not everybody gets them. The frequency of side effects is classified into the following categories:

Very common	Affects more than 1 user in 10
Common	Affects 1 to 10 users in 100
Uncommon	Affects 1 to 10 users in 1,000
Rare	Affects 1 to 10 users in 10,000
Not known	Cannot be estimated from the available data

It is important to note that Revlimid may reduce the number of white blood cells that fight infection and also the blood cells which help the blood to clot (platelets). Revlimid may also cause blood clots in the veins (thrombosis).
Therefore **you** must **tell** your **doctor** immediately if you experience:

- any fever, chills, sore throat, cough, mouth ulcers or any other symptoms of infection
- any bleeding or bruising in the absence of injury
- any chest or leg pain
- any shortness of breath

Very common side effects are given below. You should consult your doctor if you experience any of these:

- A fall in the number of white blood cells (the cells that fight infection), platelets (the cells that help the blood to clot, which may lead to bleeding disorders) and red blood cells (anaemia leading to tiredness and weakness)
- Constipation, diarrhoea, nausea, increase and decrease in weight, rash, sleep disturbance, muscle cramps and muscle weakness, tiredness, swelling of the peripheries.

Common side effects are given below. You should consult your doctor if you experience any of these:

- Infections of all types, fever and flu like symptoms
- Loss of appetite, retention of fluid, dehydration, raised blood sugar levels, changes to the calcium, potassium or magnesium in the blood
- Confusion, seeing or hearing things that do not exist (hallucinations), depression, aggression, agitation, mood changes, anxiety, nervousness, irritability
- Stroke, paralysis, fainting, memory disturbance, numbness, tingling or burning sensation to the skin, pains in hands or feet, dizziness, headache, tremor, sleepiness, taste disturbance or taste loss, giddiness
- Blurred or reduced vision, cataract, increased tear production
- Leg pain (which could be a symptom of thrombosis), increased blood pressure or a fall in blood pressure especially on standing (which may lead to dizziness or fainting when standing), flushing, chest pain or shortness of breath (which may be a symptom of blood clots in the lungs), irregular heart beat, palpitations
- Cough, hoarseness, hiccoughs, nosebleed
- Vomiting, indigestion, abdominal pain, abdominal swelling, sore inflamed mouth, dry mouth, excessive wind, blood in the stools
- Swelling of the face, dry skin, itching, redness of the skin, inflammation of the hair follicles, increased pigmentation of skin, increased sweating, hair loss, bruising
- Muscle, bone, back, limb or joint pains or weakness, general feeling of unwellness, generalised swelling
- Production of much more or much less urine than usual (which may be a symptom of kidney failure), passing blood in the urine
- Difficulty in obtaining an erection, breast enlargement, nipple pain, abnormal menstruation
- Chest pain spreading to the arms, neck, jaw, back or stomach, feeling sweaty and breathless, feeling sick or vomiting (which may be symptoms of a heart attack/myocardial infarction)

Uncommon side effects are given below. You should consult your doctor if you experience any of these:

- Swelling of lymph nodes
- Increased body hair, diabetes, gout, increased appetite, changes to blood chemistry including reduced blood protein (including the proteins that fight infection) and changes to blood phosphate, blood sodium, thyroid hormone and the hormone that controls salt and water absorption, thirst
- Changes to mental status or personality, abnormal dreams, loss of libido, panic attack, restlessness
- Voice disorder or voice loss, impaired concentration, impaired balance, movement difficulty, loss of sense of smell
- Loss of vision, swelling of eyelid, eye irritation and redness, dry eye , discharge from eye
- Deafness , ear pain or itching, ringing in the ear
- Collapse, circulatory problems, fast, slow or irregular heart beat, shortness of breath especially when lying down (which may be a symptoms of heart failure)
- Wheezing, increased throat secretions, dry throat, nasal or sinus congestion or pain, laryngitis
- Rapid swelling of the skin, especially on back of hands or feet, or of eyelids, lips, face, tongue or genitals
- Bleeding from bowels, stomach or gums, difficulty or pain on swallowing, haemorrhoids, inflammation, pain or ulceration of mouth, tongue or lips, toothache and coated tongue
- Yellowing of the skin (due to alteration in the function of the liver)
- Skin eruptions, skin cracking, flaking or discoloration, pressure sores, acne, sensitivity to sunlight
- Difficulty passing urine, passing urine more frequently
- Certain types of tumour of skin and brain

Rare side effects are given below. You should consult your doctor if you experience any of these:

- Serious allergic reaction that may begin as rash in one area but spread with extensive loss of skin over the whole body
- Tumour lysis syndrome - metabolic complications that can occur during treatment of cancer and sometimes even without treatment. These complications are caused by the break-down products of dying cancer cells and may include the following: changes to blood chemistry; high potassium, phosphorus, uric acid, and low calcium consequently leading to changes in kidney function, heart beat, seizures, and sometimes death

Side effects where the frequency is not known are given below. You should consult your doctor if you experience any of these:

- Sudden, or mild but worsening pain in the upper abdomen and/or back, which remains for a few days, possibly accompanied by nausea, vomiting, fever and a rapid pulse – these symptoms may be due to inflammation of the pancreas.
- Wheezing, shortness of breath or a dry cough, which may be symptoms caused by inflammation of the tissue in the lungs.

If any of the side effects gets serious, or if you notice any other side effects not listed in this leaflet, please tell your doctor or pharmacist.

A colour scale for ADRs

Revlimid® adverse reactions occurring more frequently than with placebo, based on the EPAR (table 12)		
Not severe grade 1	very common	Thrombocytopenia, muscle cramp, fatigue, asthenia, anaemia, tremor, dyspnoea, rash
	common	neutropenia, pneumonia
	uncommon	
	rare	
	very rare	
Moderately severe grade 2	very common	Thrombocytopenia, muscle cramp, fatigue, asthenia, anaemia, tremor, dyspnoea, rash
	common	neutropenia , pneumonia
	uncommon	
	rare	
	very rare	
Severe grade 3	very common	neutropenia, thrombocytopenia
	common	pulmonary embolism, deep vein thrombosis, anaemia, fatigue, asthenia, dyspnoea, pneumonia
	uncommon	muscle cramp, tremor, rash
	rare	
	very rare	
Extremely severe grade 4	very common	neutropenia, thrombocytopenia
	common	pulmonary embolism, deep vein thrombosis, anaemia, fatigue, asthenia, pneumonia
	uncommon	muscle cramp, tremor, dyspnoea, rash
	rare	
	very rare	
very common	affects more than 1 user in 10	
common	affects 1 to 10 users in 100	
uncommon	affects 1 to 10 users in 1 000	
rare	affects 1 to 10 users in 10 000	
very rare	affects less than 1 user in 10 000	
not known	frequency cannot be estimated from the available data	

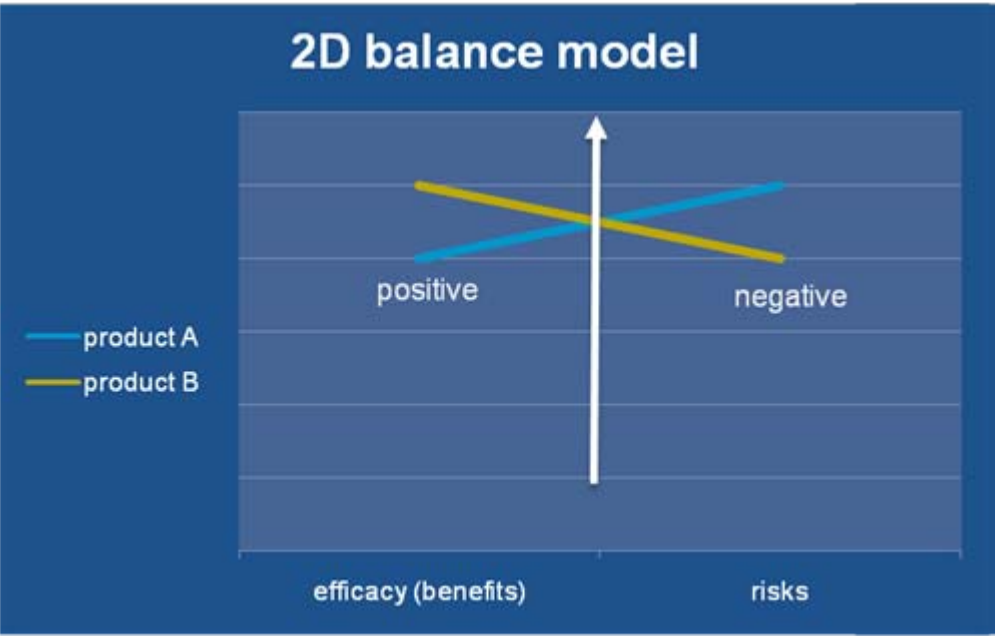
Packaging: colour codes could help

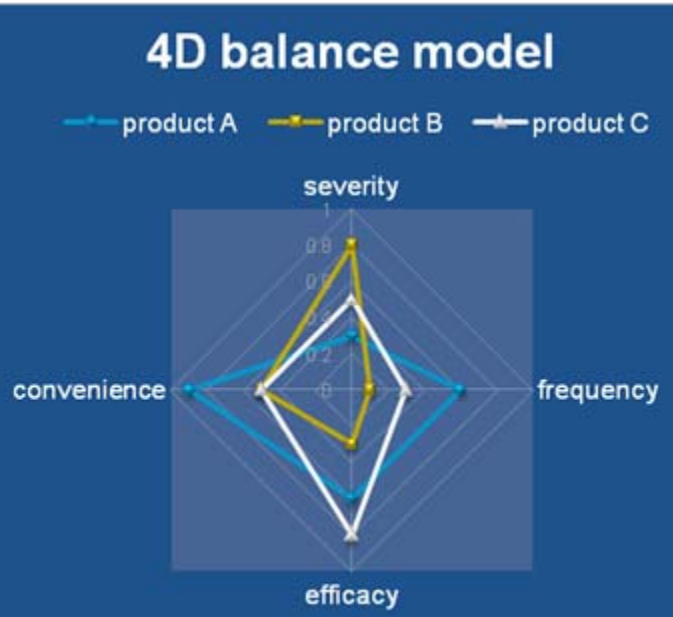
- If severe ADRs (e.g., CV events, death) have been reported and these ARDs are not part of the current labelling, the drug should be placed in this category.
- The drug would remain in this category while the regulatory bodies and/or the MAH are doing further investigation and evaluation of the data.

➲ Protect, IMI
WP5: Benefit-risk integration and representation

From John Mack, Pharma Marketing News 2005

More informative, more complex?





Aids progression risk

Risk at 3 years	*Viral load > 110 000 copies/ml*	*Viral load < 3000 copies/ml*
CD4 < 200/mm3	85% NNTb: 1 to 2	
CD4 > 750/mm3	30% NNTb: 3 to 4	0.25% NNTb: 400

Assuming treatment efficacy ≈ 90%

Adapted from Matthias Egger, Institut de médecine préventive et sociale, Université de Berne

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NNTH

estimate of absolute risk of cardiovascular disease in next 5 years for cases of HAART induced LD

Age at treatment start	*No HAART*	*HAART + LD*	*NNTH*	*NNTH in smokers*
30	0.5%	1.9%	71	40
50	3.6%	9.1%	18	13

Based on Framingham model

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Main points

4. B / R evaluation: patients' to contribute.

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Among other initiatives

- Direct patient reporting of positive and negative outcomes
- QofL scales, new graphic presentations
- Their representatives
  - CHMP discussions
  - Assessment of RMP: feasibility and acceptability
  - Definition of evaluation criteria (TREAT-NMD, Efficacy SAG for anti-HIV products…)
- CAVOD: see 3 September

Thank you.

HTA and patients' rights: assess versus access?

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A mother reports

- A Belgium mother reports 2 sons with the same rare diseases
- A new product is authorised
- The paediatrician prescribes the treatment for the 2 brothers, in line with the labelling and indication
- For one brother the prescription is accepted and the product reimbursed
- For the other, the treatment is not reimbursed as “patient not likely to respond”

Questions

- If likeliness to respond is only 20% or 10% or even less, and the disease is life-threatening
  - Any patient would like to give a try
  - Including each person in this room
- How can the mother explain to her child that he won't be treated?
  - That society considers the expense is worth for Paul but not for Mark?
- How can the two brothers look at each other?
- What does the term "indicated for" mean, finally?

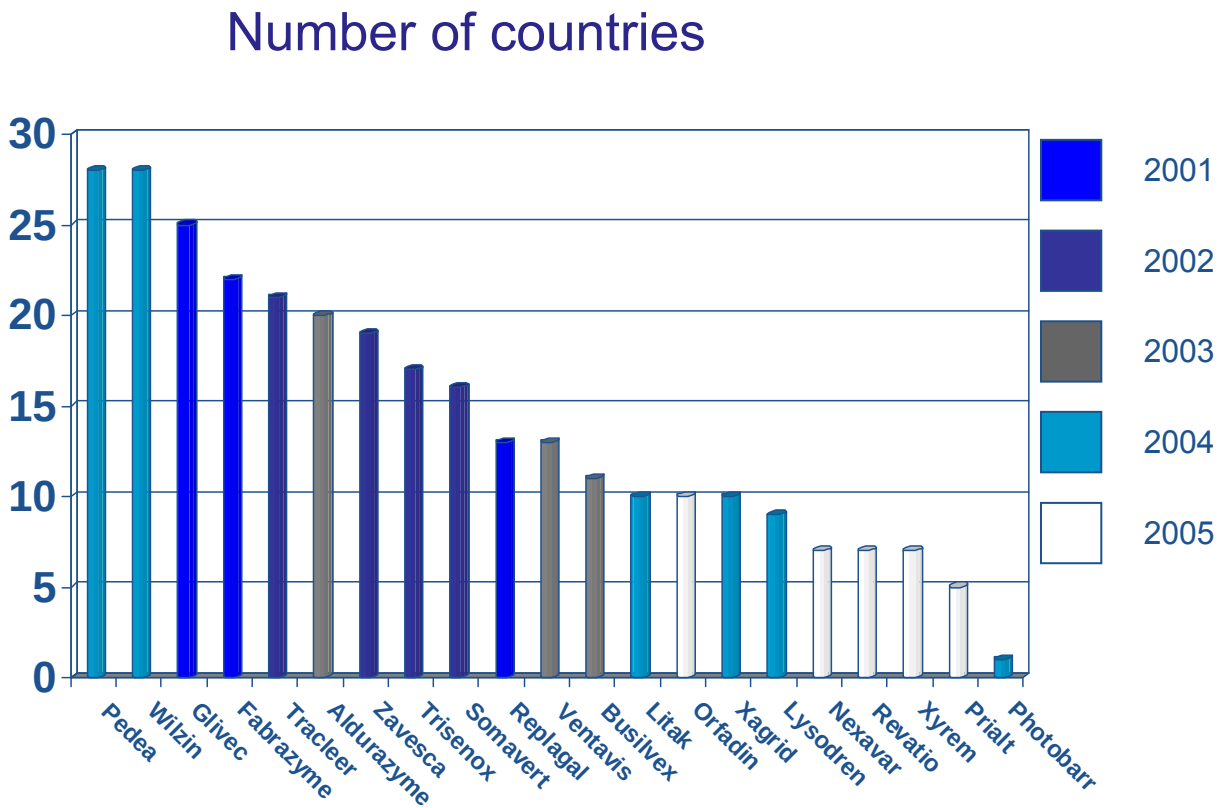
Today

- Reimbursement/availability decisions are often perceived as arbitrary ones
  - E.g. 20 000 - 30 000 £ per QALY gained (NICE)
- Patients hardly understand different conclusions from different agencies
  - “Authorised” by one agency
  - “Not worth the expense” by another agency
- Patients feel discriminated
  - within families
  - within and between countries

4th Eurordis Orphan Drugs availability survey 2007

2007: among 22 first authorised orphan drugs since Orphan Drug Regulation 2000 - 27 EU Member States

To be placed on the market in just one MS is enough for the legislation



E.g. Busilvex vs oral busulfan

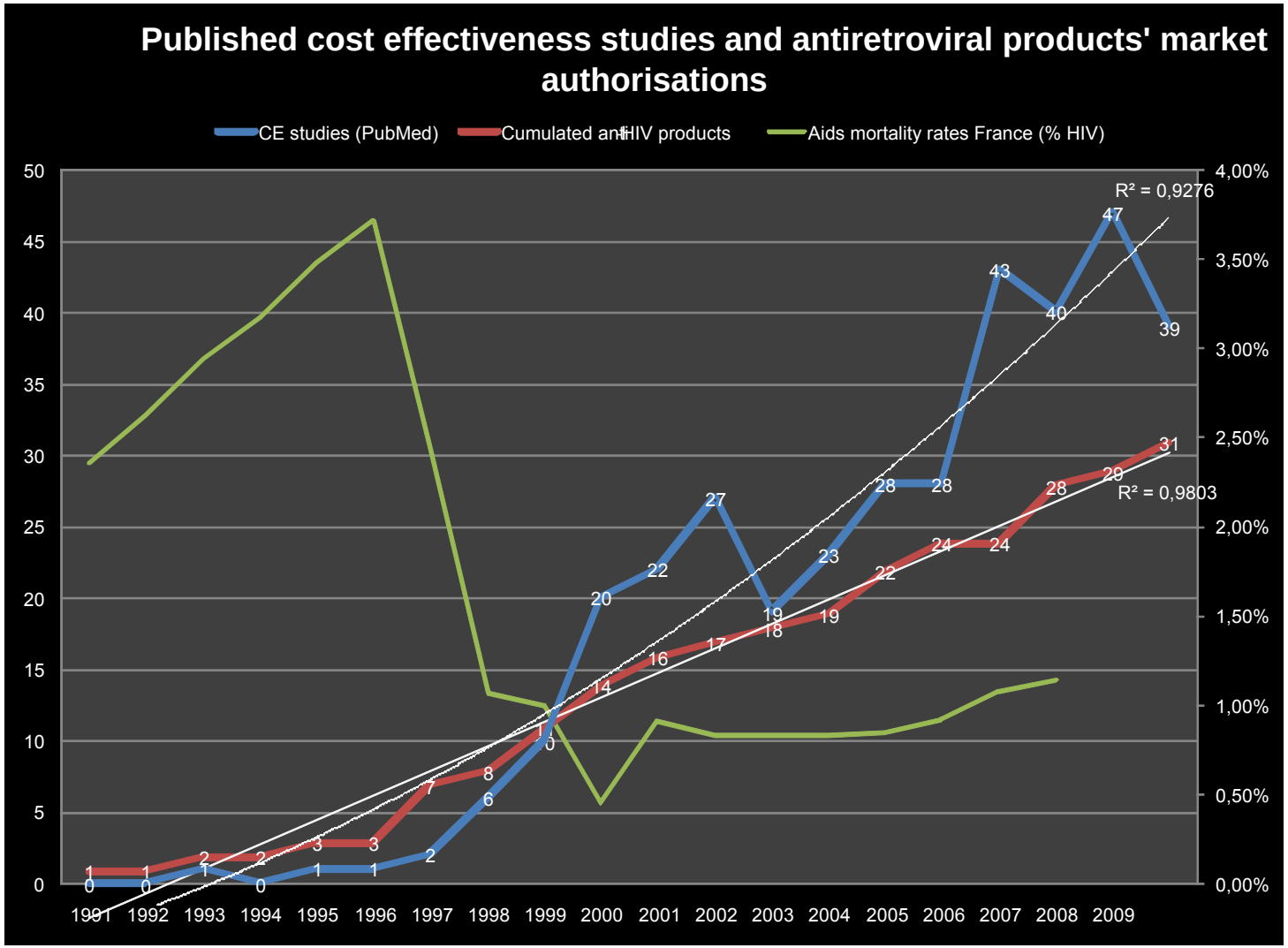
- Conditioning treatment prior to conventional haematopoietic progenitor cell transplantation
- Per os formulation (busulfan)
  - 560 pills needed (4 days), outpatient
  - Risk of life-threatening hepatic veno-occlusive disease
  - indicative cost 168 €
- Busilvex®
  - 2 hours infusion every 6 hours x 4 days, inpatient. 16 vials
  - lowers the risk of serious/life-threatening liver toxicity, graft rejection, and recurrent leukaemia (100-day survival rate significantly higher, Biol Blood Marrow Transplant. 2002)
  - indicative cost: 4480€ + 4 days inpatient stay ≈ 15 000 €

  →Not reimbursed/available in all MS

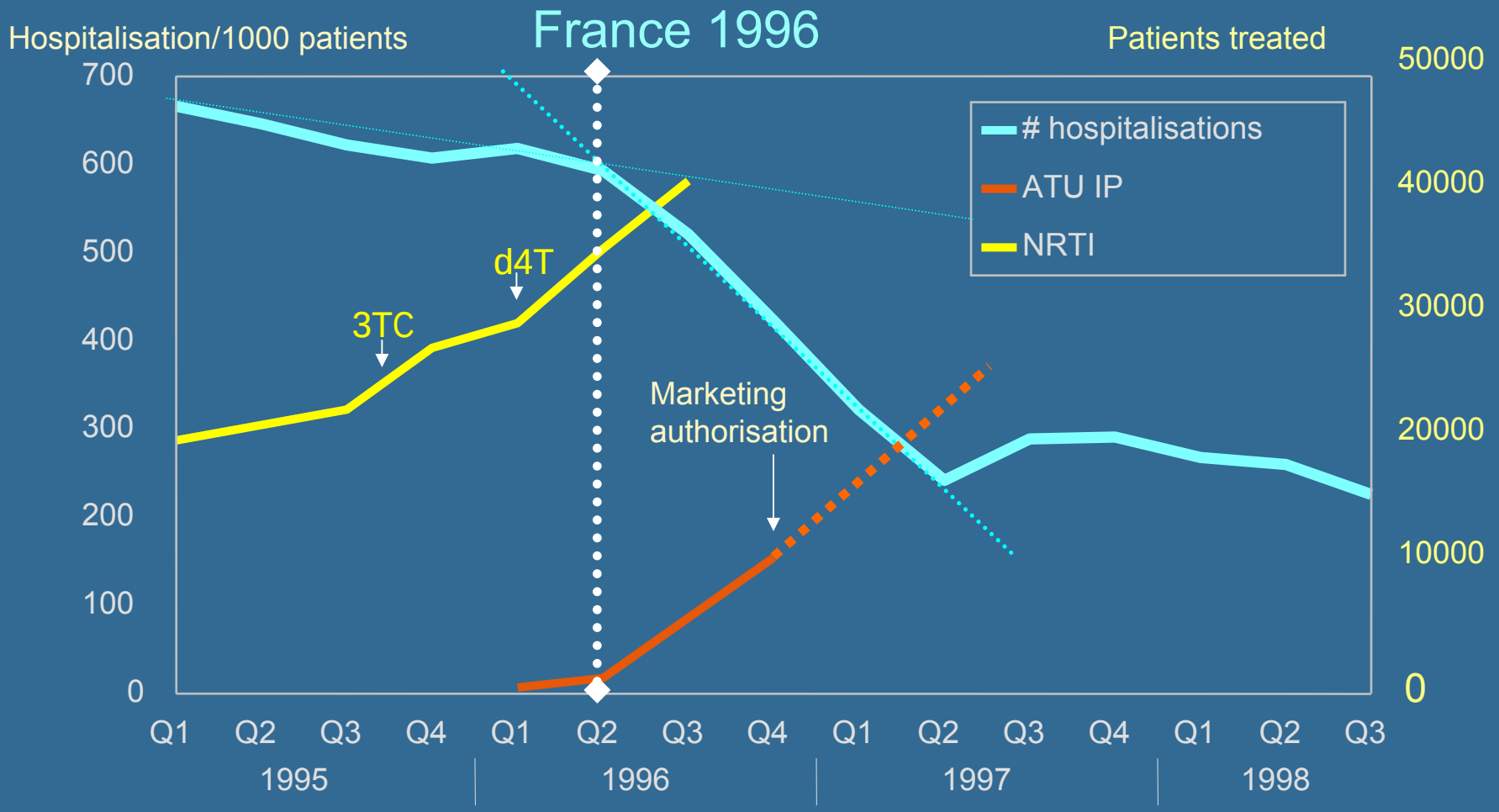
Consequence: patients do travel to save their lives

- European Court of Justice (12/07/2001, Geraets-Smits & Peerbooms)
  - Mr Peerbooms fell into a coma following a road accident on 10/12/1996
  - He was taken to hospital in the Netherlands and then transferred in a vegetative state to the University Clinic in Innsbruck in Austria on 22/02/1997
  - The Innsbruck clinic gave Mr Peerbooms special intensive therapy using neuro-stimulation
  - Mr Peerbooms came out of his coma and left the Innsbruck clinic on 20/06/1997
- authorisation to purchase treatment in other Member State cannot be refused where it appears that the treatment concerned is sufficiently tried and tested by international medical science
- authorisation can be refused on the ground of lack of medical necessity only if the same or equally effective treatment can be obtained without undue delay at an establishment having a contractual arrangement with the insured person's sickness insurance fund.

HIV drugs: a model

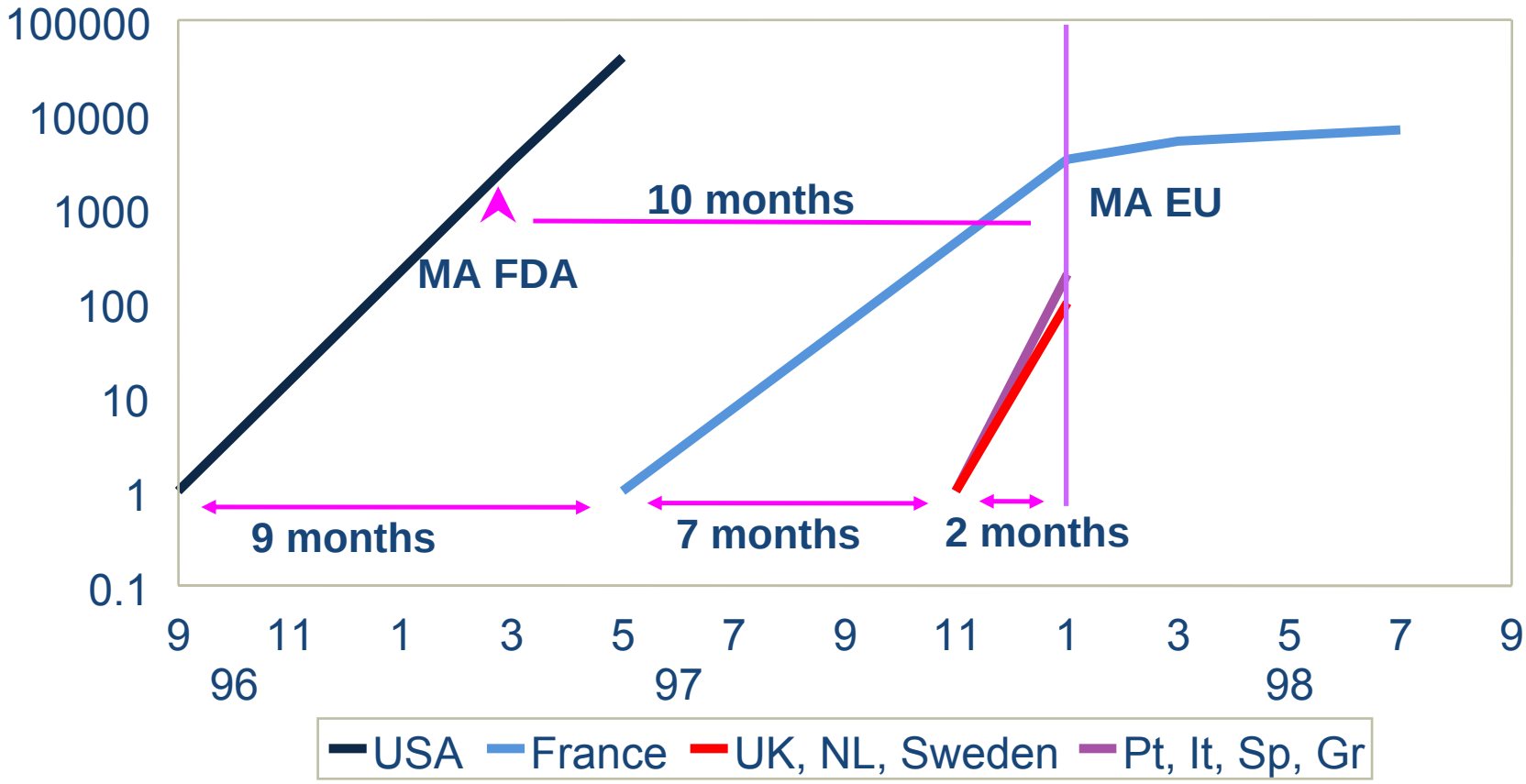


Compassionate use programmes deserve a HTA report



Sources: hospitalisations: DMI2 - Direction des hôpitaux - BEH n°44/96
patients treated in ATU: Roche, Abbott, MSD

ATU provide access earlier than in any other EU MS, e.g. nelfinavir



When to assess HTA?

England

- NICE timelines

1. Market authorisation
2. NICE appraisal (> 300 days)
3. If cost effective: NHS ok to purchase
4. Local hospitals decide to provide to their patients or not
5. Then access (long process), or not

➲ Budget containment orientated

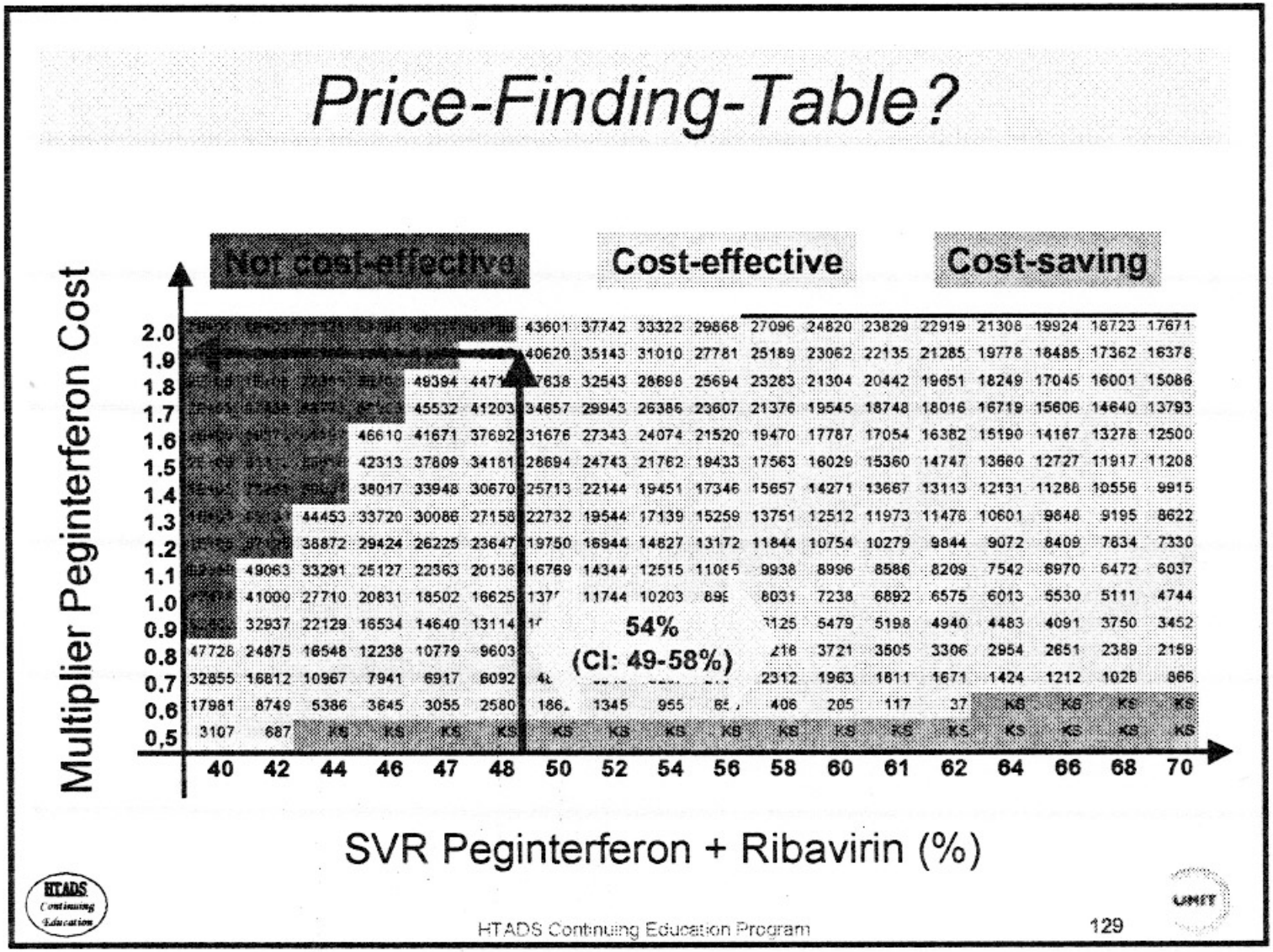
Germany

- IQWIG timelines

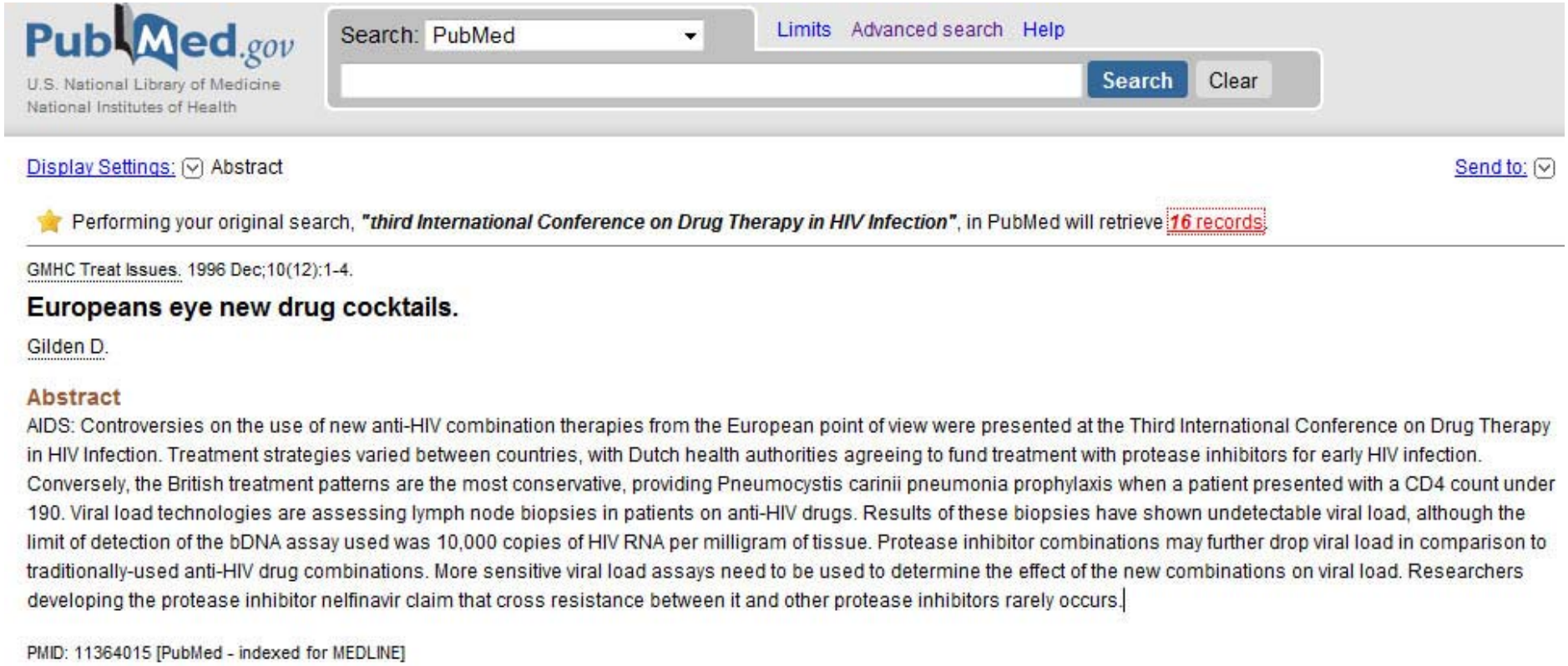
1. Market authorisation
2. Access granted, product purchased by health providers, and reimbursed
3. IQWIG appraisal
4. If not cost effective, results can be used to negotiate a price reduction until treatment/intervention becomes cost effective

➲ Patient and public health orientated

Efficiency frontier IQWIG



Treatment tourism: a must



PubMed.gov
U.S. National Library of Medicine
National Institutes of Health

Search: PubMed | Limits | Advanced search | Help

Search | Clear

Display Settings: Abstract | Send to:

Performing your original search, ***"third International Conference on Drug Therapy in HIV Infection"***, in PubMed will retrieve 16 records

GMHC Treat Issues. 1996 Dec;10(12):1-4.

Europeans eye new drug cocktails.

Gilden D.

Abstract

AIDS: Controversies on the use of new anti-HIV combination therapies from the European point of view were presented at the Third International Conference on Drug Therapy in HIV Infection. Treatment strategies varied between countries, with Dutch health authorities agreeing to fund treatment with protease inhibitors for early HIV infection. Conversely, the British treatment patterns are the most conservative, providing Pneumocystis carinii pneumonia prophylaxis when a patient presented with a CD4 count under 190. Viral load technologies are assessing lymph node biopsies in patients on anti-HIV drugs. Results of these biopsies have shown undetectable viral load, although the limit of detection of the bDNA assay used was 10,000 copies of HIV RNA per milligram of tissue. Protease inhibitor combinations may further drop viral load in comparison to traditionally-used anti-HIV drug combinations. More sensitive viral load assays need to be used to determine the effect of the new combinations on viral load. Researchers developing the protease inhibitor nelfinavir claim that cross resistance between it and other protease inhibitors rarely occurs.

PMID: 11364015 [PubMed - indexed for MEDLINE]

Do we need to prove the cost effectiveness to decide the purchase of products
-That can decrease HIV mortality by >90%
- When HIV lethality is 100%
Still, many EU Members States delayed access to HAART until cost effectiveness proven

EURORDIS

Utility: on who's view point?

(c) Health related quality of life	Quality of life weight		
	Base case	Lower limit	Upper limit
Health state			
Mild chronic hepatitis	0.95	0.90	1.00
Moderate chronic hepatitis	0.92	0.89	0.95
Compensated cirrhosis	0.89	0.82	0.92
Decompensated cirrhosis or hepatocellular carcinoma	0.81	0.76	0.87
Hepatocellular carcinoma	0.81	0.76	0.87
Liver transplantation	0.86	0.73	0.99
Death	0.00	0.00	0.00
Utility multiplier viral positive	0.98	0.93	1.00
Utility multiplier for interferon+ribavirin	0.95	0.92	0.98
Utility multiplier for peginterferon+ribavirin	0.90	0.84	0.96

Cost effectiveness of peginterferon α-2b plus ribavirin versus interferon α-2b plus ribavirin for initial treatment of chronic hepatitis C
U Siebert Gut 2003;52:425–432 - GEHMO Quality of Life Database

➲ Work with patient organisations to define patient outcomes

QofL questionnaire MPS1

A PILOT ASSESSMENT OF FOUR QUESTIONNAIRES FOR ASSESSING FUNCTIONAL STATUS AND QUALITY OF LIFE IN MUCOPOLYSACCHARIDOSIS TYPE I

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CONCLUSIONS

All four instruments seem appropriate for assessing disease burden in MPS I. The PEDI-MCAT's short time to complete and high correlation with the MPS-HAQ make it an attractive instrument for monitoring the functional status of MPS patients. The EQ-5D, while also a short instrument, may not be as suitable as the other scales for studies in MPS I.

Priority Setting between Groups

- Norwegian Government Commission 1987, ethical principals:

1. *Severity is of primary importance.*
2. *Everybody should have the same possibility to become as well as they can (= realise their health potential).*

These principles are not present in the QALY model itself. QALY is only on how big is the effect.

QALY don't qualify for severity

Table 1: Comparison of different treatment programs

Intervention	Utility 0 is dead and 1 is perfect health		Utility Gain (After – before)
	Before treatment	After treatment	
A	0.4	0.5	0.10
B	0.8	0.9	0.10
C	0.85	1.00	0.15
D	0.6	0.80	0.20

A and B: same net utility gain (0.10)
A: QofL improved by 25% / B: QofL improved by 12.5%

Report on NICE Citizens Council meeting
Quality Adjusted Life Years (QALYs) and the severity of illness
31 January – 2 February 2008

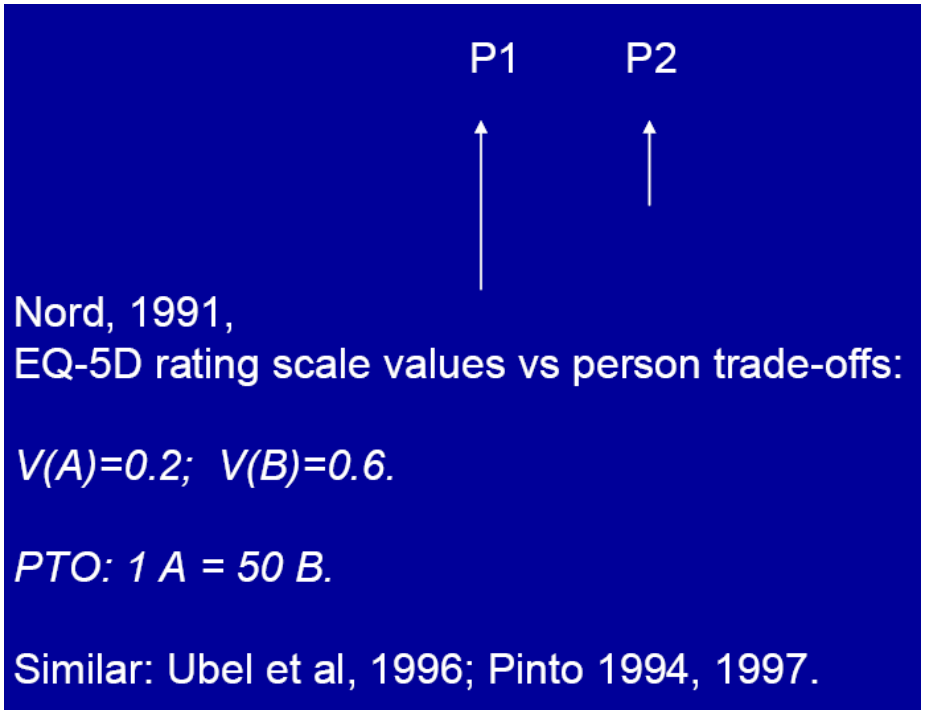
QALYs are only additive
Society may have other views

For B:
0.6 to 1= 0.4 gained
2 patients = 0.8 gained

For A:
0.2 to 1 = 0.8 gained
1 patient = 0.8 gained

The gain with A for 1 patient values the gain with B for 2 patients

Person Trade Off:
The gain with A for 1 patient values the gain with B for 50 patients



Erik Nord, Senior Adviser
Norwegian Institute of Public Health

Conclusion

A PROPOSAL & CHALLENGES

CAVOD

- EURORDIS, industry and academic leaders in the field of orphan drugs have developed a proposal
  - to the European Commission
  - To the European Medicines Agency
- for the establishment of a Working Party for European collaboration toward common scientific assessment of the clinical added value of orphan drugs

Objectives

- Currently, EMA's scientific committees rigorously assess orphan drugs during the review process
  - for marketing authorisation
  - for paediatric studies
  - and to maintain their orphan status.
- Orphan drugs sponsors are already required to show
  - that there is no existing satisfactory treatment
  - or that the new treatment offers a significant benefit over existing therapeutic interventions
- A simple document, made transparently available in a usable way to Member States
- An EMA Working Party would be able to bring together all the scientific evaluations into one useable document
- Member States would be able to coordinate their requests to the MAA, so as to define the minimum data set required to understand the place of the product in the therapeutic strategy

Challenges

- Patient's input in b/r evaluation @ CHMP
  - How to best participate in process?
  - CHMP (voting) members?
  - CHMP feedback: patients not systematically in favour of product (even when group is funded by the MAA)
- Patient's input in HTA decisions
  - How to best participate in process?
  - HTA bodies (voting) members?
  - Are we biased: if a product is authorised, won't we systematically be pleading for its reimbursement?