

Challenges associated with high prices of new cancer medicines; potential ways forward for CEE countries based on HTA principles

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neglected diseases**

1. Introduction

2. Considerations for new cancer medicines including designated orphan status

3. Conclusions

Cancer care is important. However, concerns with increasing costs to health systems

- Cancer is one of the most important NCDs - eventually affecting 1 in 3 of the population and a leading cause of death globally
- A number of factors are indisputable:
 - ❑ More can be done to diagnose and manage most types of cancer, including prevention
 - ❑ Cost of cancer care has risen appreciably in recent years and will continue to do so
 - ❑ Costs of new cancer medicines increased up to ten-fold during the past 10 years – despite often limited health gain
 - ❑ Ongoing debate whether increased spending on cancer care translates into improved patient outcomes – especially important given ever rising expenditures
- Worldwide costs of new cancer cases estimated at US\$286billion in 2009, with medical costs making up more than 50% of total expenditure and medicines approximately 25% of this

How much is life worth: Cetuximab, non-small cell lung cancer and the \$440bn question

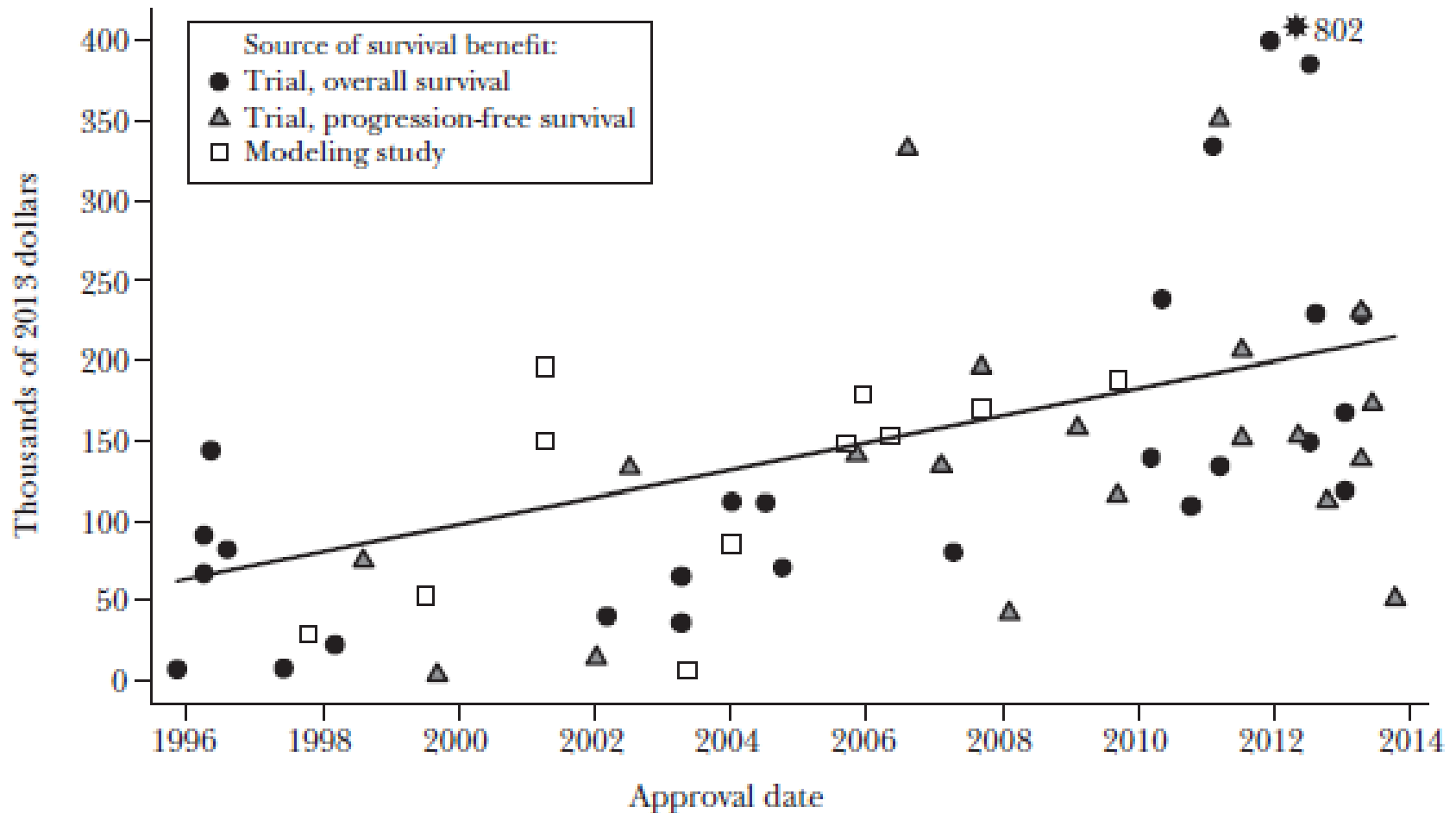
Drug and amount used until disease progression	Total medicine cost and estimated increase in survival
Cetuximab (6975mg)	<ul style="list-style-type: none"> ▪ \$80352 ▪ 1.2 months (NSCLC)
Bevacizumab (13200mg)	<ul style="list-style-type: none"> ▪ \$90816 ▪ 1.5 months (Metastatic breast cancer – not statistically significant)
Erlotinib (112 x 150mg tablets)	<ul style="list-style-type: none"> ▪ \$15752 ▪ 10 days (pancreatic cancer)
Sorafenib 682 x 200mg tablets)	<ul style="list-style-type: none"> ▪ \$34373 ▪ 2.7 months (renal cell carcinoma)

Increasing concerns with requested prices and the overall value of new cancer medicines

- Of the 12 drugs approved by the FDA for various cancers in 2012:
 - ❑ 9 were priced at more than US\$10,000/patient/ month
 - ❑ Only 3 prolonged survival, 2 by less than 2 months
- Of the 7 targeted therapies for renal cell carcinoma approved in the US between 2005 and 2012:
 - ❑ all improved progression-free survival (PFS) by typically 3 to 6 months
 - ❑ However, minimal or no impact on overall survival at a cost of US\$70,000 to US\$140,000/ patient annually

New cancer medicines averaging US\$207,000/ life year gained. Likely an underestimate as modelling and concerns between PFS and overall survival in solid tumours

Drug Price per Life Year Gained versus Drug Approval Date

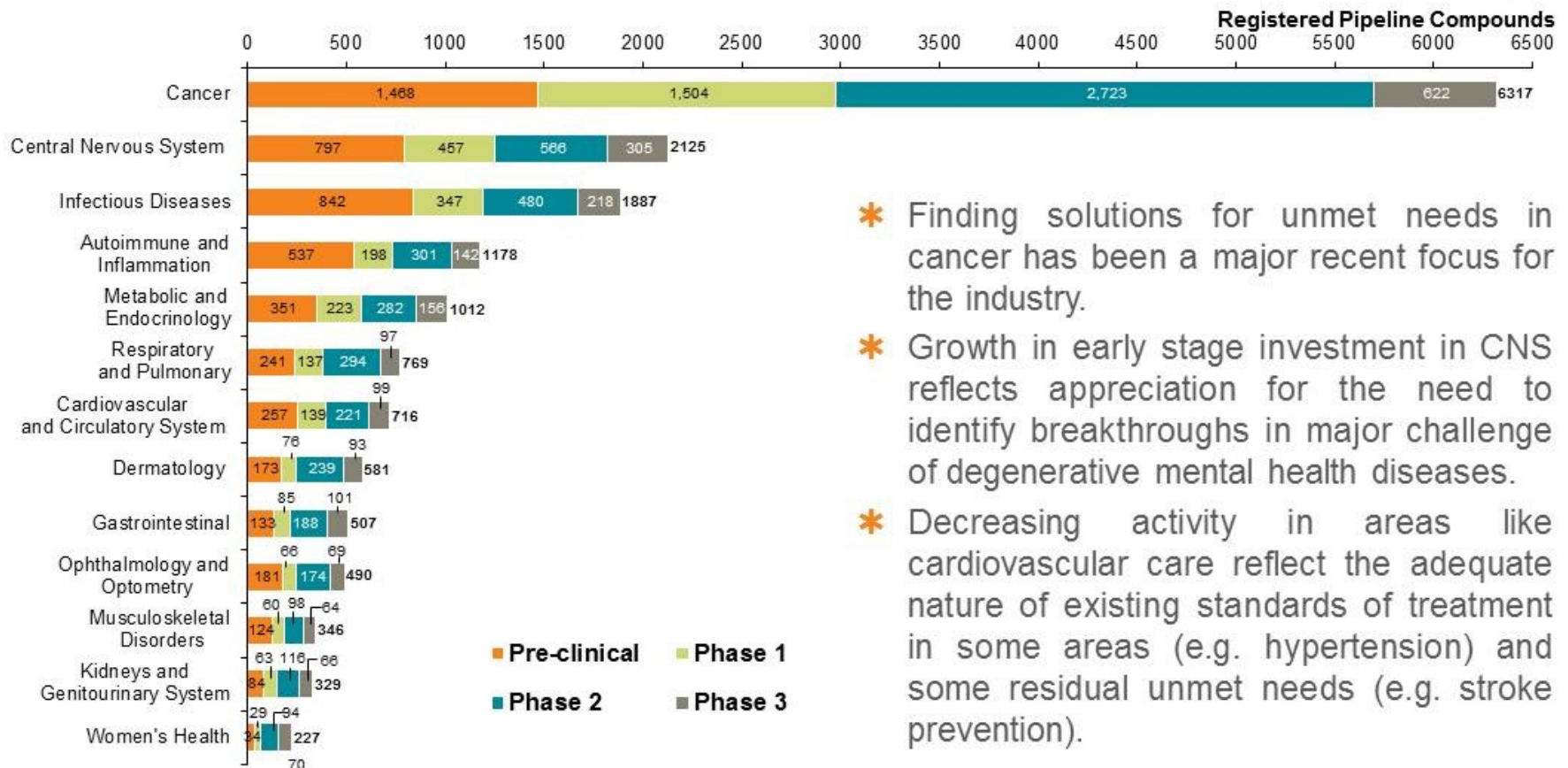


Cancer market is significant and will expand with new cancer medicines in development

- Within the pharmaceuticals market, anticancer medicines now rank first for global spending by therapeutic class: US\$91 billion in 2013 up from US\$71 billion in 2008
- The US market was US\$37 billion in 2013, of which one-third was spent on 10 patent-protected cancer medicines alone
- Anticancer drugs figure prominently in discussions with all key stakeholder groups and this will continue given the emotion surrounding these medicines as well as ever increasing prices
- The situation will become even more critical with over 6000 new cancer medicines in development – appreciably outstripping other disease areas

EFPIA believe over 16000 new medicines are in various stages of development to address current unmet need – greatest for cancer medicines

Registered Pipeline Compounds end of year 2011



- * Finding solutions for unmet needs in cancer has been a major recent focus for the industry.
- * Growth in early stage investment in CNS reflects appreciation for the need to identify breakthroughs in major challenge of degenerative mental health diseases.
- * Decreasing activity in areas like cardiovascular care reflect the adequate nature of existing standards of treatment in some areas (e.g. hypertension) and some residual unmet needs (e.g. stroke prevention).

There appears limited correlation between cancer spend and reduced mortality in reality

- De-Groot et al in a recent analysis found no correlation between number of deaths per 100,000 and cost/ person spent on cancer
- Furthermore, a decrease in survival can be related to accessibility, affordability or equity issues as well as factors such as life style
- Overall - the process of cancer delivery including prevention is complex and dynamic, with many potential approaches and increasingly involving shared decision making
- An optimal process of cancer care delivery consists of the use of new and existing diagnostic tests and treatment strategies of high quality and is effective, safe, patient centred, efficient and timely. Such a health system approach is highly recommended to all stakeholders

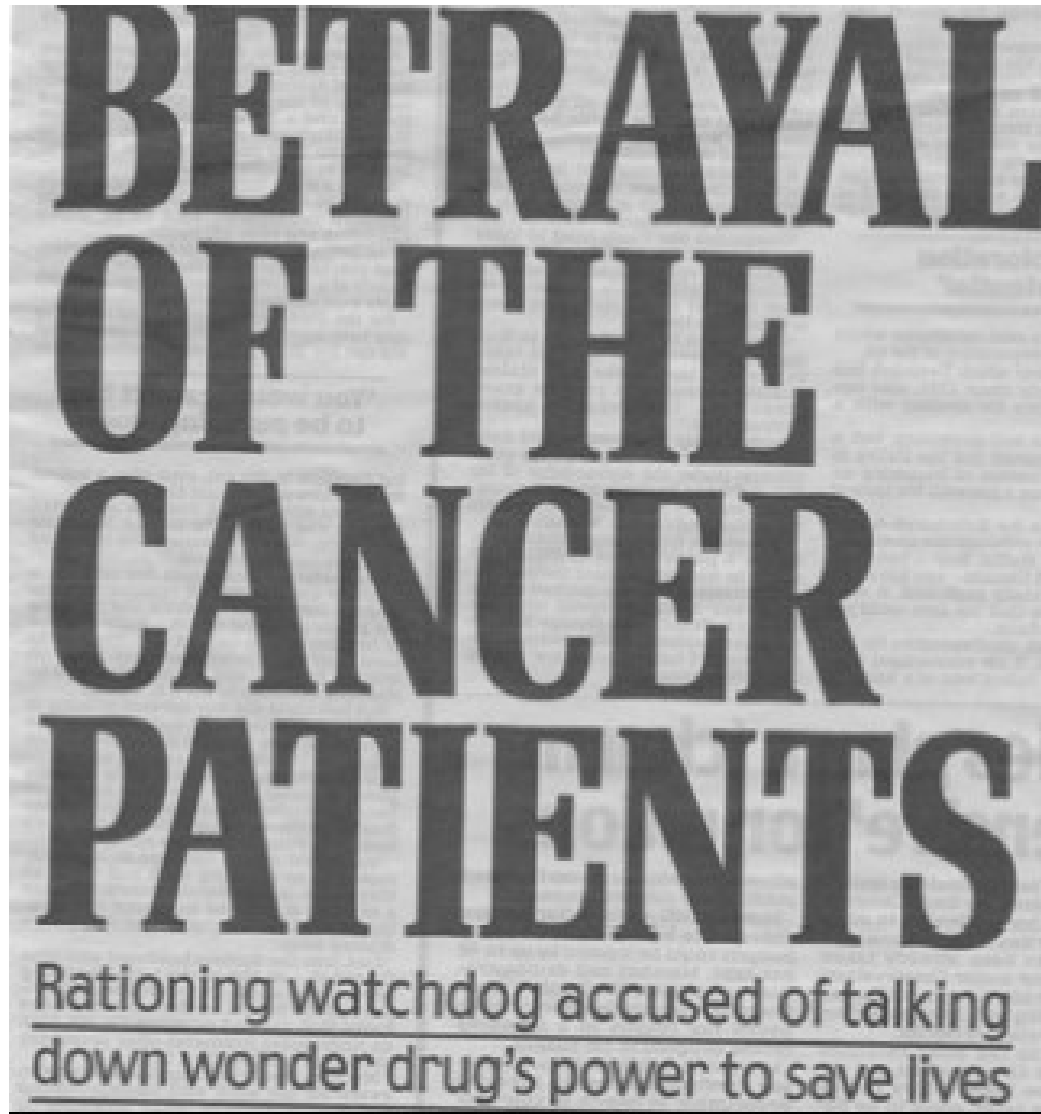
High prices of new cancer medicines is increasing the pressures on budgets, e.g. US

- Recent trends in insurance coverage place a heavy financial burden on patients, especially cancer, with their out-of-pocket share increasing to 20% to 30% of total costs
- This is assisted in 2014 by all new FDA approved cancer medicines priced above \$120,000/ patient/ year
- This results in patients in the US typically selling their assets to fund care – leading to care compromises
- These concerns have resulted in oncologists in the US recently pressurising companies to lower the price of their cancer medicines in the future - building on similar concerns among physicians treating patients with haematological cancers. In addition, calls for greater transparency in pricing in the US

Emotions have blurred the debate on prices of new cancer medicines. This needs to change

- The imperative to “save lives” or “beat cancer” — particularly where there’s vigorous public, professional and industry advocacy — can be so profound it overwhelms requirements that medicines should be efficacious and cost effective
- This tension between emotional and economic considerations has compromised decision making about the value of new cancer medicines
- Hope, fear and desperation, along with the unique characteristics of the cancer drug market, create a “perfect storm” that continues to drive up prices for cancer medicines
- Unless we talk about value, the increasing number of new cancer medicines at ever increasing costs ‘will become terminal for health systems’

All new cancer drugs are typically portrayed as 'cures' despite very limited health gain with most



The situation is similar for new treatments for orphan diseases with blurring of divides

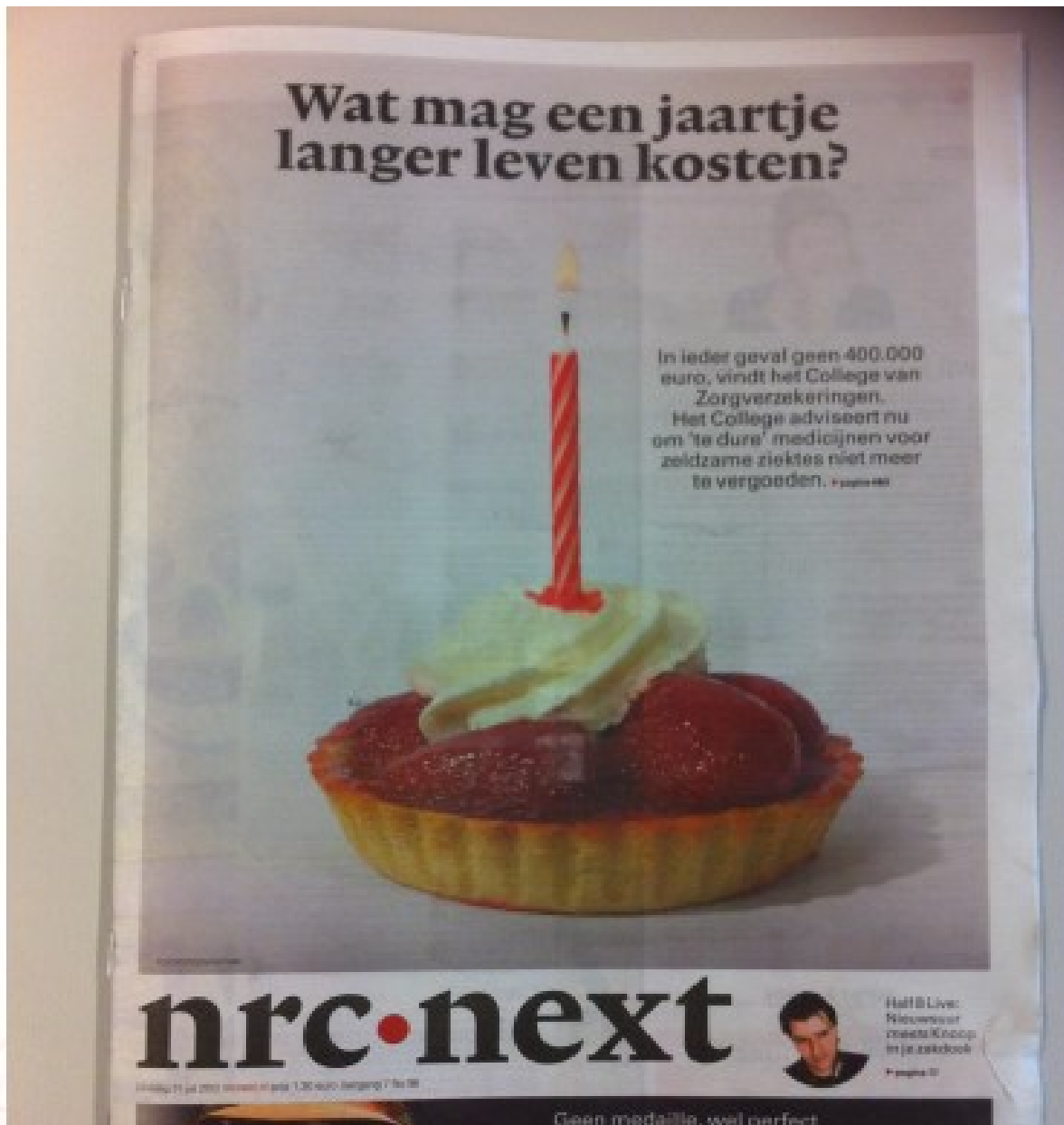
- There has also been an appreciable increase in the price of new medicines for orphan diseases (OMPs) in recent years, with emotion used to help ensure funding at high prices even when very limited health gain (as a result – a number achieving ‘blockbuster status’)
- The distinction between new cancer medicines and those for orphan diseases has become blurred in recent years, e.g. abiraterone was the only cancer drug approved by the FDA in 2011 without an orphan designation
- This has resulted in the proposed developments of new multicriteria decision matrices for new medicines for orphan diseases especially with low cost of goods (COG), e.g. COG of new medicines to treat patients with Hepatitis C as low as 1 – 2% of the selling price (higher for biological medicines)

The cost of new OMPs is growing and some now over US\$500k/patient/year – leading to blockbuster status (annual worldwide sales over US\$1billion/ year)

Orphan drug	Indication	Average annual cost/patient (US\$)
Teduglutide (GATTEX)	Short bowel syndrome	295,000
Imiglucerase (CEREZYME)	Type 1 Gaucher disease	300,000
Ivacaftor (KALYDECO)	Cystic fibrosis	325,000
Galsulfase (NAGLAZYME)	Mucopolysaccharidosis VI	441,000
Idursulfase (ELAPRASE)	Mucopolysaccharidosis I and II	475,000
Eculizumab (SOLIRIS)	Paroxysmal nocturnal hemoglobinuria	486,000- 500,000
C1 esterase inhibitor (CINRYZE)	Hereditary angioedema prophylaxis	487,000
Alglucosidase alfa (MYOZYME)	Pompe disease	575,000

Other examples of prices for new OMPs include:

- Naglazyme® (galsulfase) costing over €1 million per patient per year in France, Germany, Italy and Spain
- Lithuania - Galsulfase for the management of patients with mucopolysaccharidosis VI:
 - ❑ Currently funding all 10 patients in Lithuania with this treatment equates to 17% of the total in-patient budget for medicines and medical aids and 3% of the total reimbursed ambulatory care pharmaceutical expenditure
 - ❑ Considerable pressure on Ministry and Health Insurance to fund despite concerns with effectiveness
- Ivacaftor's at US\$294,000 (€220,000)/ patient/ year for life – resulting in a cost/ QALY of GB£285,000/ QALY (€360,000) to GB£1.077million/QALY (€1.36million) after an agreed discount. If this funding trend continues – new medicines for orphan diseases will also make health systems terminal



Pressure from the media in the Netherlands resulted in pressure on the MoH to ignore the advice of the reimbursement agency about funding enzyme replacement therapy for Fabry's disease (up to €3.3 million incremental cost / QALY) and up to €15million for alglucosidase alfa to treat Pompe's disease

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Potential approaches to improve the use of cancer medicines/ orphan medicines in future

- Inclusion of cancer medicines into essential medicines lists using robust methodologies (recent WHO list of essential medicines)
- Greater collaboration between authorities with setting minimum effectiveness levels for funding new higher priced cancer medicines
- Encouraging clinical trial designs to collect data relevant for all key stakeholder groups, e.g. improved overall survival
- Developing the Transparent Value Framework (TVF) for establishing funding/ pricing of new medicines for orphan diseases
- HTAs highlighting alternative treatment approaches with similar effectiveness but lower costs
- Increasing pro-activity among health authorities to optimise the use of new cancer medicines especially where budget and other issues. This builds on examples with other new medicines, e.g. dabigatran

Agreement of a minimum 3 months additional survival for funding new cancer medicines in UK

- Ferguson and clinical colleagues among the teaching hospitals in London, UK, in 2000 proposed the following when considering additional funding for new cancer medicines (versus current standards and costs):
 - ❑ Only new treatments rated A (Prolongation of median survival by > 9 months together with improvement in quality of life) or B (Prolongation of median survival by 3–6 months with improvement in quality of life) for effectiveness
 - ❑ Only those with data from at least one high-quality RCT and supporting non-randomized study data
- Otherwise no additional funding for new cancer medicines not fulfilling these strict criteria

Kantarjian and colleagues in the US also proposed overall survival as a key outcome

- A new cancer medicine that prolongs survival by more than 6 months or by more than one third of the life expectancy should be considered as extremely effective and should command a price in the range of US\$50,000 to US\$60,000/ patient/ year
- New cancer medicines that demonstrate “statistically significant” survival benefits of 2 months or prolong life by less than 15% should be considered to have minimal efficacy and be priced much lower, perhaps below \$30,000/ patient/ year
- New cancer medicines of intermediate effectiveness should be priced between these two ranges

ASCO also commented on improvements in survival as key for new cancer medicines

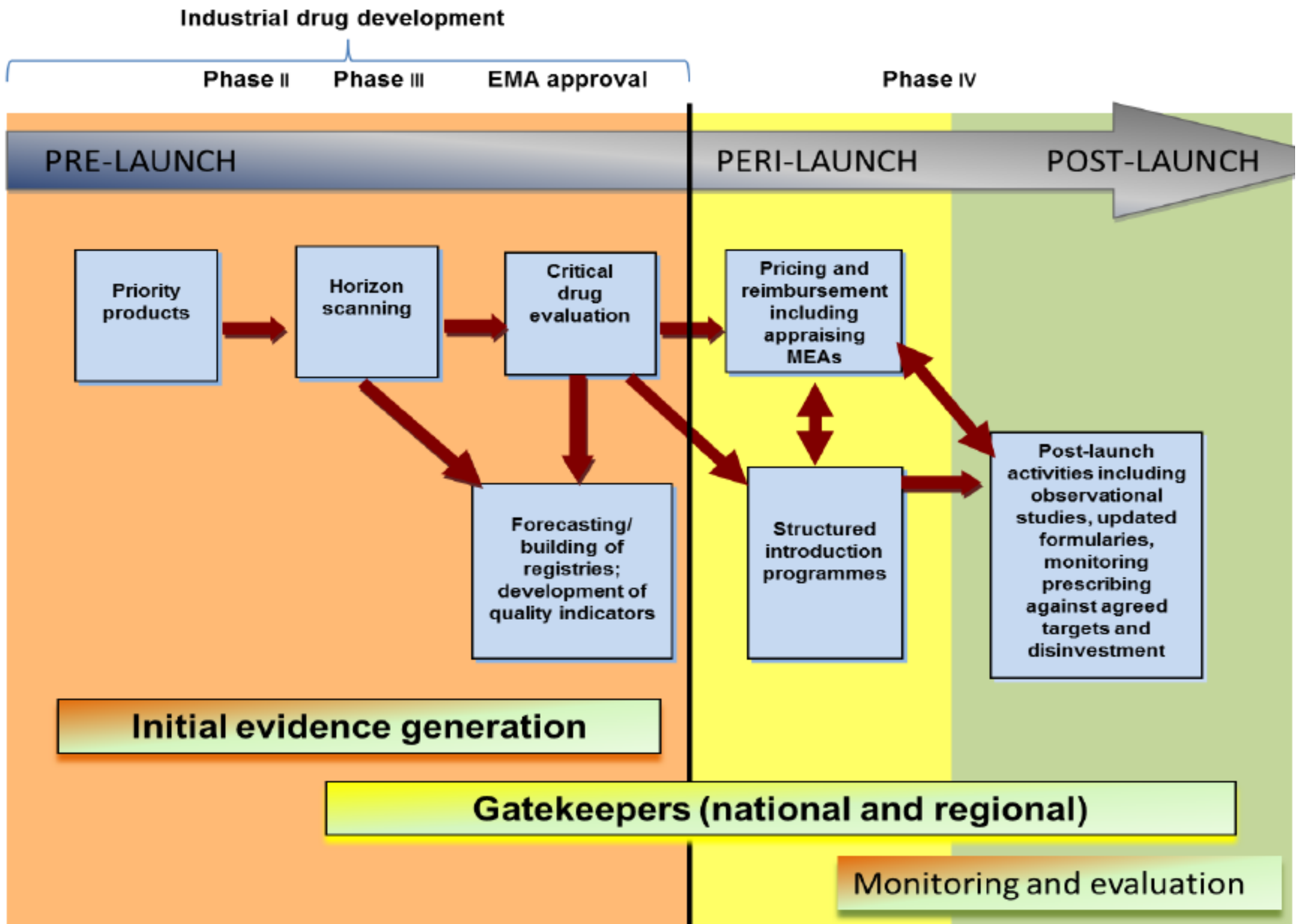
- ASCO in 2014 stated:
 - ❑ Overall survival (OS) should be considered the primary clinical end point of interest for new cancer medicines
 - ❑ An improvement in median OS within the range of 2.5 to 6 months, depending on the clinical context, is the minimum incremental improvement over standard therapy that would define a clinically meaningful beneficial outcome for new cancer medicines
 - ❑ New regimens that are substantially more toxic than current standards should also produce the greatest increments in OS to be considered as having achieved a clinically meaningful outcome

ESMO also recently defined minimum improvements for new cancer medicines

- ESMO again considered overall survival as a key outcome measure and defined the following as designating new cancer medicines as having meaningful benefits over existing standards:
 - Primary outcome OS:
 - ❑ Control < 12 months
 - ❑ HR 0.65 AND gain 3 months OR Increase in 2-year survival alone 10%
 - ❑ Control >12 months
 - ❑ HR 0.70 AND gain 5 months OR Increase in 3-year survival alone 10%

Key considerations for the authorities in Serbia for new cancer medicines should build on this

- Potential considerations for the funding of new cancer medicines in Serbia and other CEESTAHC countries include:
 - ❑ Minimum improvements in effectiveness (OS only) versus current standards – median of at least 3 to 6 months in overall survival
 - ❑ Potential ICER vs. current standards – maximum of 1.5 times GDP (Slovenia) or up to a maximum of €19,320/QALY (Slovakia)
 - ❑ No preferential consideration for new cancer medicines versus those for other disease areas (as seen currently in Poland – also applies to new medicines for orphan diseases)
 - ❑ Greater proactivity for 'optimising' the funding/ utilisation for new cancer medicines starting pre-launch



TVF was developed by key stakeholders as part of the MoCA-OMP project to provide guidance and is currently being tested

Criterion	Lower Degree	Medium Degree	High Degree
Available Alternatives/ Unmet Need, including non-pharmaceutical treatment options	yes, new medicine does not address unmet need	yes, but major unmet need still remains	no alternatives except best supportive care - new drug addresses major unmet need
(Relative) Effectiveness, Degree of Net Benefit (Clinical Improvement, QoL, etc. vs. side effects, societal impact, etc.) relative to alternatives, including no treatment.	incremental	major	curative
Response Rate (based on best available clinically relevant criteria)	<30%	30-60%	>60%
Degree of Certainty (Documentation)	promising but not well-documented	plausible	unequivocal

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In conclusion, regulations need to change for new cancer medicines (including orphans)

A number of initiatives can be introduced by CEESTAHC countries to optimise funding/ utilisation of new cancer medicines (including those designated as orphan status) - starting with the EML for cancer medicines. These include:

- More stringent criteria for valuing new cancer medicines to maintain the ideals of equitable and comprehensive healthcare given ever increasing requested prices – based on EBM/ HTA principals (similar for new medicines for orphan diseases)
- Not viewing cancer as a ‘special case’ - currently being exploited by Pharma Companies as seen by ever increasing requested prices (same for orphan diseases unless very rare – TVF - illustrated by Sanofi paying over US\$20billion for Genzyme in 2011)
- Seeking greater transparency in the pricing of new medicines – especially given their potential gross profitability
- Greater proactivity – starting pre-launch – to optimise use

Thank You

Any Questions!

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