BDA
BIOTHERAPY DEVELOPMENT ASSOCIATION

Different availability of new oncologic drugs in Europe - a medical oncologist perspective

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Our mission

BDA's mission is to provide a unique platform to interface academia, the industry and the regulatory authorities to improve the efficiency of drug development in oncology.

The non-profit BDA facilitates communication and partnerships between the following key parties

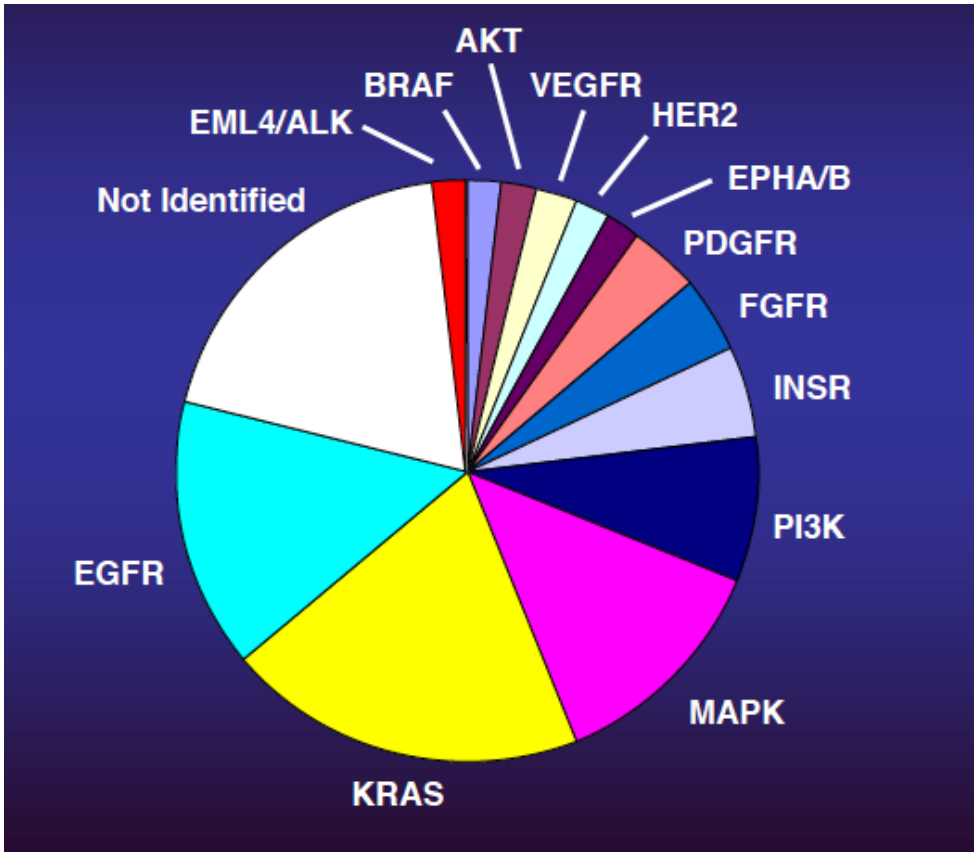
- **More than 800 anti-cancer drugs are in clinical development**
- **Success rates in bringing them to the market remain in the range of 5-8%**
- **A paradigm shift is required – a challenge for all parties involved**

Challenges for the pharmaceutical industry

- Development costs of a new drug are enormous
- Success rates in bringing them to the market remain in the range of 5-8%
- Number of blockbusters will go down (immunotherapy??)
- Biomarkers make frequent cancer types to rare disorders
- Patents are running out.
- Invest in rare cancer types?
- Input from academia is going down

A paradigm shift is required where all stakeholders are involved

Molecular redefinition & hypersegmentation of cancer: Somatic Mutations in Lung Adenocarcinoma N=188



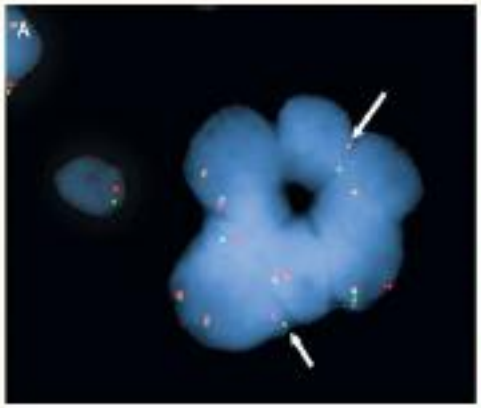
Modified from L Ding *et al.* Nature 455, 1069-1075 (2008)

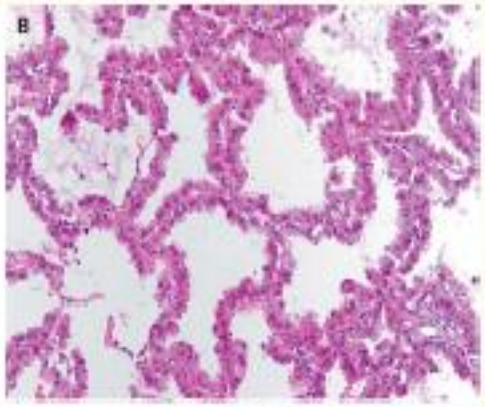
Case story:

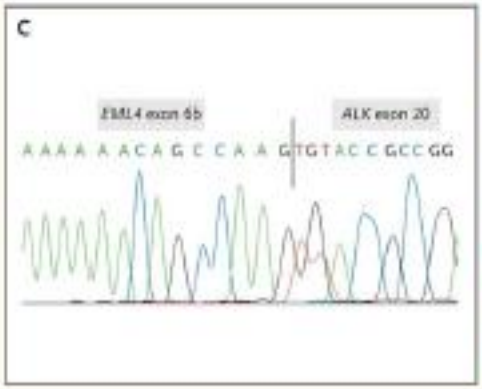
Lessons that can be learnt from the clinical development of drugs such as crizotinib

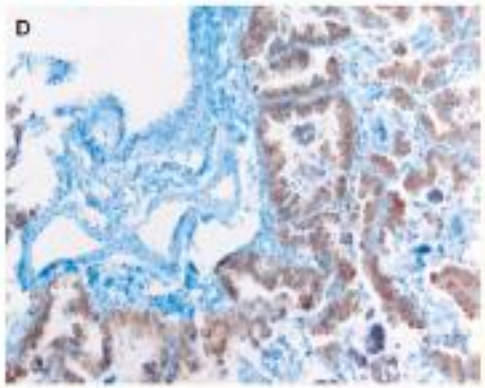
Crizotinib in metastatic NSCLC with ALK rearrangement

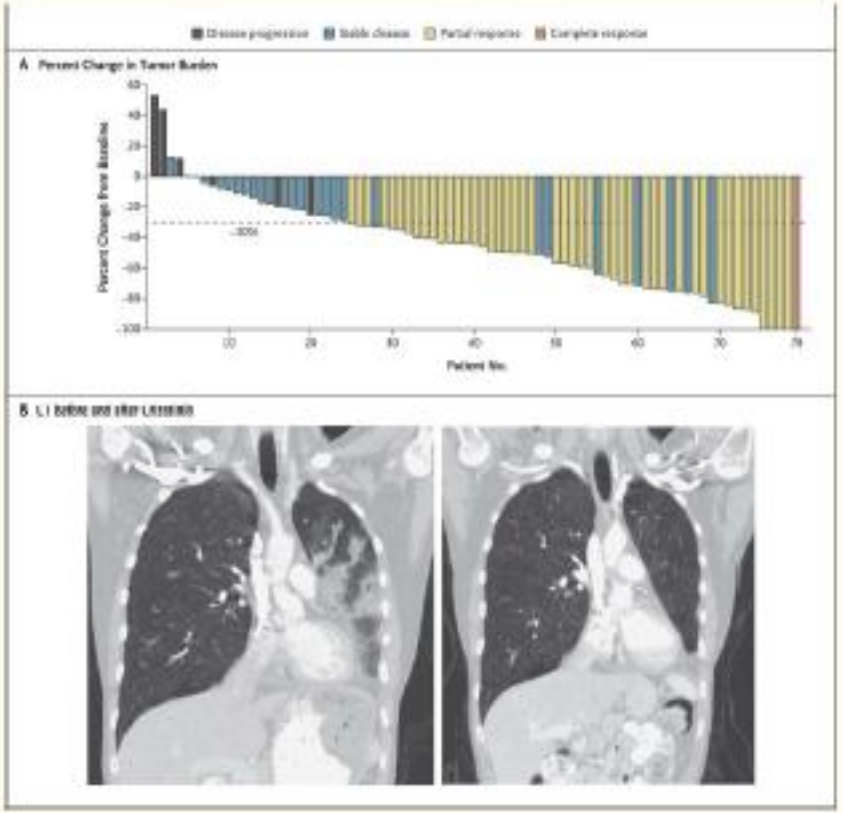
Incidence: 4-7% (mainly AdenoCa in nonsmokers)
n=82: RR 57% (1CR), SD 33%, 6-mths-PFS-Rate 72%











The NEW ENGLAND JOURNAL of MEDICINE

Kwak et., 2010

Many questions remain

- Do we always need to run large phase III trials in small but well-defined patient populations?
- What if a patient has got two or more mutations that can each be targeted with a drug?
- Targeted therapy makes frequent diseases to rare diseases
- Basically combinations are the only way to fight redundency
- Regulatory view? Payer´s view?

Currents System for Oncology Drug Appraisal

The current system for oncology drug appraisal is exceedingly complex.

- **Innovative medicinal products with oncology indications are within the mandatory scope of a centralized licensing procedure by an *European Regulatory Body (ERB).***

- **Such products are assessed in the EU by the *European Medicines Agency (EMA).* The decision of the EMA / European Commission to grant or refuse a marketing authorization is immediately binding for all member states.**

- **Decisions on pricing and reimbursement, in contrast, are the responsibility of HTA agencies and payers in individual member states, or even regions, and different HTA agencies may come to very different conclusions.**

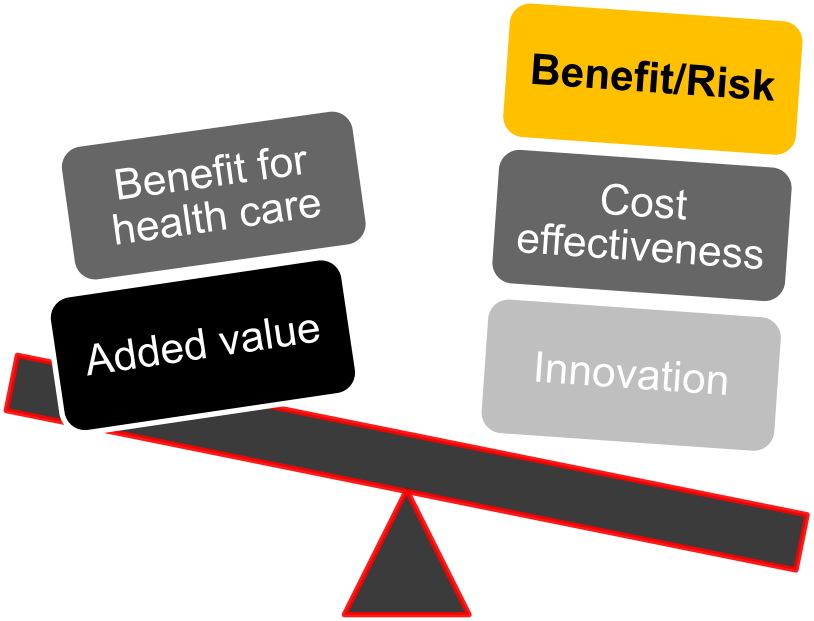
- **European citizens, therefore, do not have equal access to new oncology products.**

Developments in European Regulatory and HTA Management

EMA → Benefit : Risk

National HTAs

(Nice, HAS, IQWIG, GBA, etc)



Major pitfalls of the present system for oncology drug appraisal

ERBs and individual HTA agencies base their decisions on different types of clinical evidence and methodology.

- **An ERB focuses on risk–benefit assessments based on data from randomised controlled phase III (or phase-II) studies.**
- **The HTA agencies and payers base their decision on >30 different types of assessment as**
  - **Active controlled randomised studies, observational studies, cost-effectiveness calculations**
  - **The ERB's risk–benefit assessment or a new risk–benefit assessment**
  - **Innovation**
  - **Benefit-cost relation**
  - **Added value for market**
  - **The likely benefits to the healthcare system at a national level**
  - **Etc**

Some of the evidence considered often includes a repetition of assessment steps already carried out by EMA.

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Developments in European Regulatory and HTA Management

Centralized approval procedure by **EMA**
(risk/benefit)

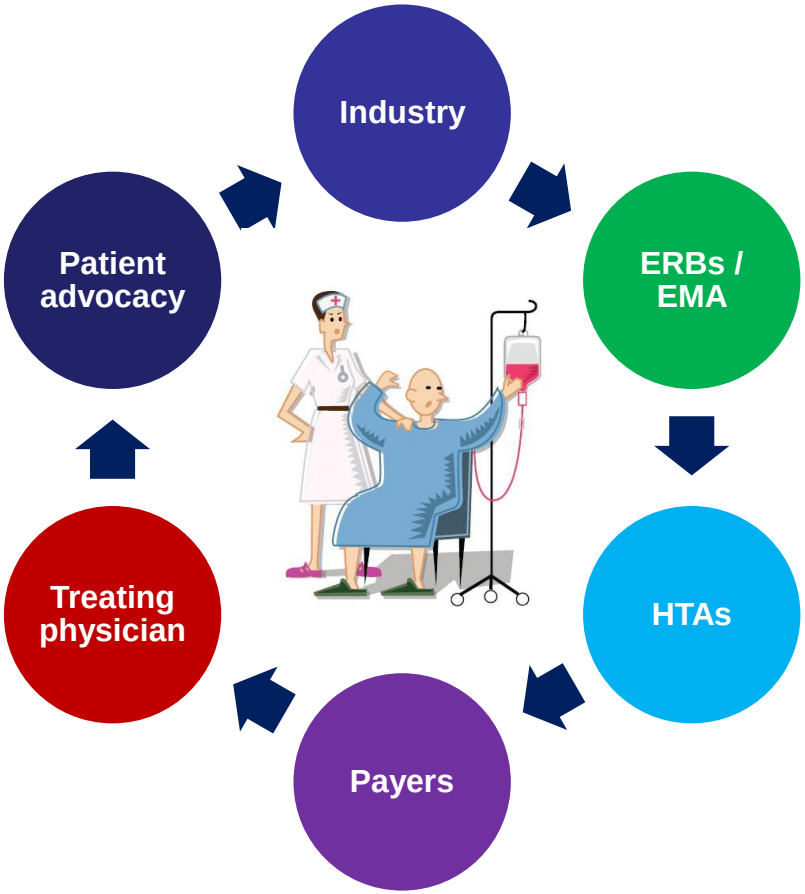
National HTAs (cost-effectiveness; risk/benefit, new risk/benefit assessment?, added value)

Pricing and Reimbursement on national basis (value for money)

Physician → Patient

Time from marketing authorisation (MAA) of a novel cancer drug until its availability for patients ranges from 104 days in Ireland to 517 days in Czech Republic.

Strong Collaboration and some mutual understanding between all stakeholders is required



The wish list of a medical oncologist…

- Ability to offer a high response rate: regression / control of the tumor that ultimately leads to
- Improved survival
- Low toxicity profile
- Tailored approach per patient
- (limited) off-label use („target expression in rare disorders“)
- Drive (also) academic drug development
- The opportunity to offer ALL suitable treatments to ALL patients provided there is a scientific rationale

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EVENT	VENUE	DATE	PROGRAMME OVERVIEW	MEETING CHAIRS
Preclinical/early clinical biomarker discovery	Brussels, Belgium	4-5 Oct. 2012	➢Evolving technologies ➢Criteria for selection of diagnostic and therapeutic targets ➢Monitoring primary and required resistance mechanisms ➢Impact of the immune response ➢Trial technique and design ➢Development of companion diagnostics	*Academia :* Leif Håkansson *Industry :* Kristen Hege *Regulators :* Bertil Jonsson
Harmonization of the approval process and reimbursement systems in Europe (Satellite meeting at ESMO Congress)	Vienna, Austria	29 Sept 2012	➢Different availability of new oncologic drugs in Europe (a medical oncologist 's perspective) ➢The need for better harmonization of the approval process (an industry perspective) ➢Approval procedures in Europe and USA – what are the future requirements ? ➢HTA in Europe – Activities towards harmonization	*Chair :* Lothar Bergmann *Co-Chair :* Francesco Pignatti
Present and future breast cancer management: bench to bedside and back	Vienna, Austria	29 -30 Nov 2012	➢Triple Negative Breast Cancer(s) ➢HER2/ErbB2 Positive Breast Cancer ➢Luminal Breast Cancers ➢Multi-targeted inhibitors vs. combination strategy ➢Novel strategies in neoadjuvant treatment	*Academia :* Christoph Zielinski *Industry:* Stefan Frings *Regulators :* Michel Marty
Immunotherapy workshop	TBC	Jan 2013	➢How to further improve efficacy ? ➢Definition of trial endpoints ➢Presurgical studies ➢Biomarker development ➢Regulatory hurdles	*Academia:* Samir Khleif *Industry:* Catherine Weil *Regulator :* Christian Schneider + FDA (TBC)
7th Alpine meeting	Innsbruck, Austria	March 2013	In preparation	TBC
4th BDA meeting on HTA	TBC	May 2013	➢Regulators view on the need for paradigm shift ➢Implications for drug development ➢HTA outcomes in different countries ➢How will changes impact oncologists ?	TBC

New oncology drugs – approval process and reimbursement systems in Europe, ESMO 2012