Orphan tumors definition and why selective targeted agents are of interest

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PATIENT CASES

Orphan Tumors – An ideal niche for selective targeted therapies

- Orphan tumors definition and why selective targeted agents are of interest : F Blackhall
- The role of RANK ligand inhibitor in giant cell tumors : J-Y Blay
- The role of mTOR inhibitors in astrocytoma-related to tuberous sclerosis : P Curatolo
- Hedgehog inhibitors in basal cell carcinomas : L Dirix
- Discussion

Disclosure slide

- Honoraria, research funding and advisory board roles for Pfizer and Astra-Zeneca

Orphan Tumors Definition

- Orphan : from the Greek *orphanos*, a child who has lost one parent or both, or an adult who has lost a child[1]
- MULTIPLE DEFINITIONS !...'neglected diseases'
- A suggested definition :

'A rare cancer for which orphan drug status might apply'

1Aronson JK. Rare diseases and orphan drugs. Br J Clin Pharmacol 2006

Rare Cancer : Definition ?

- In Europe
- Prevalence <50/100,000 (rare disease)
- [1]RARECARE (surveillance of rare cancers in Europe) working group : **incidence** <6/100,000 (corresponding to <30,000 new cases/year in Europe)
- In US <15 incident cases / 100, 000 per year

[1] Gatta et al. EJC 2011

The Rare Cancer Burden in Europe

- 186 rare cancers identified
- 22% of all new malignancies
- 24% of the total cancer prevalence
- Rare cancer survival is worse than common cancer 47% vs 65%
- 4 million people are living with a diagnosis of a rare cancer in EU27

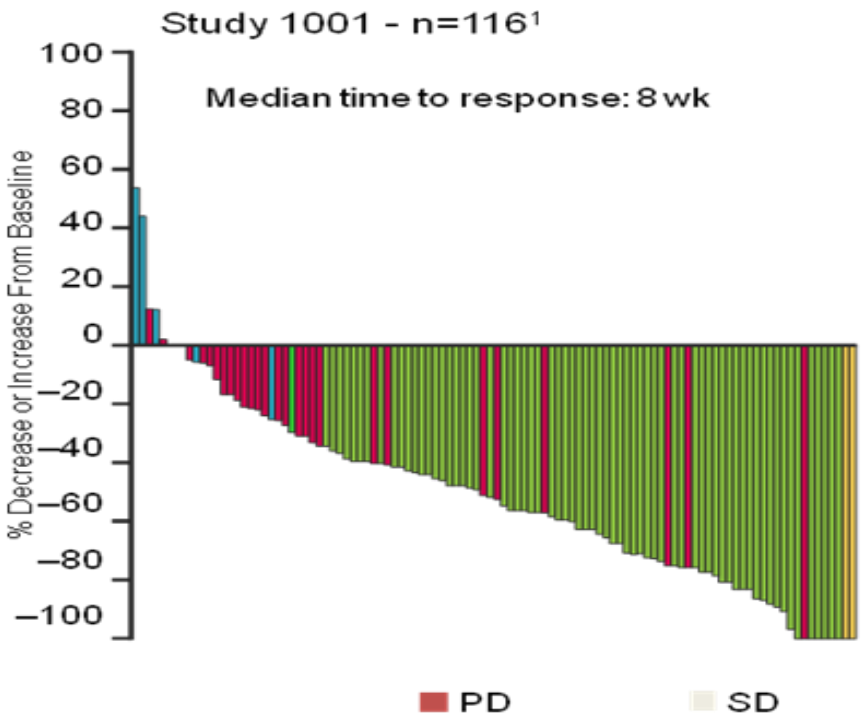
REF : Rare cancers are not so rare : The rare cancer burden in Europe Gatta et al, EJC 2011 The RARECARE working group

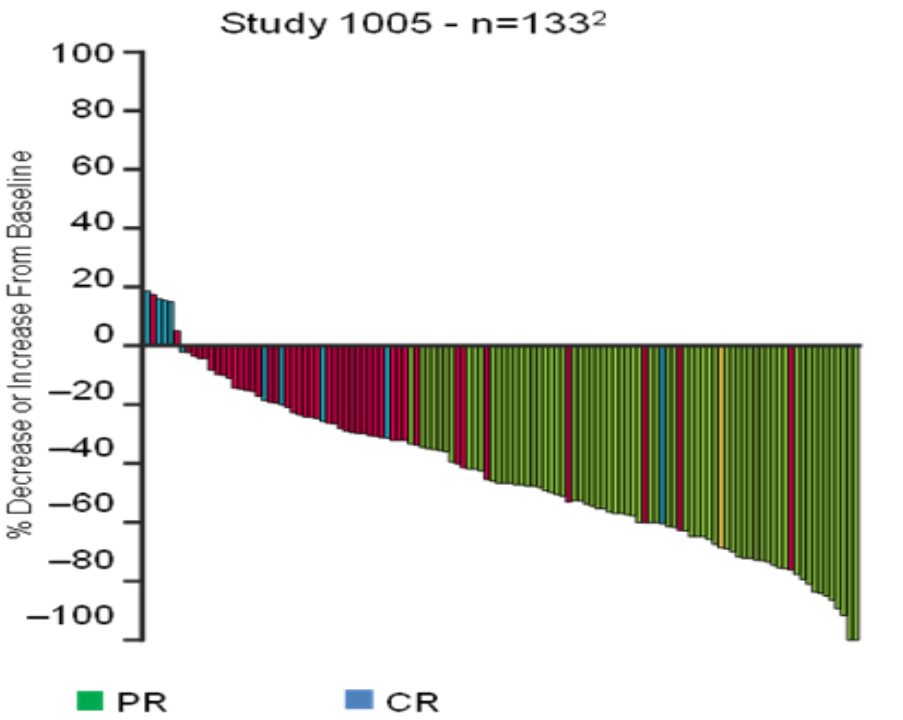
Selective targeted therapies are of interest to improve outcomes of rare cancers and because of the orphan drug approval process

- 30% of orphan drug approvals in US have been for oncology indications (since 2006)
- GIST – imatinib
- Rare molecularly defined subtypes of common cancers : eg EML4-ALK gene fusion in NSCLC

- ‘classical rare cancers and rare molecularly defined subtypes of common cancers’

FDA approval for Crizotinib in ALK+ NSCLC was based on Ph I & single arm Ph II data

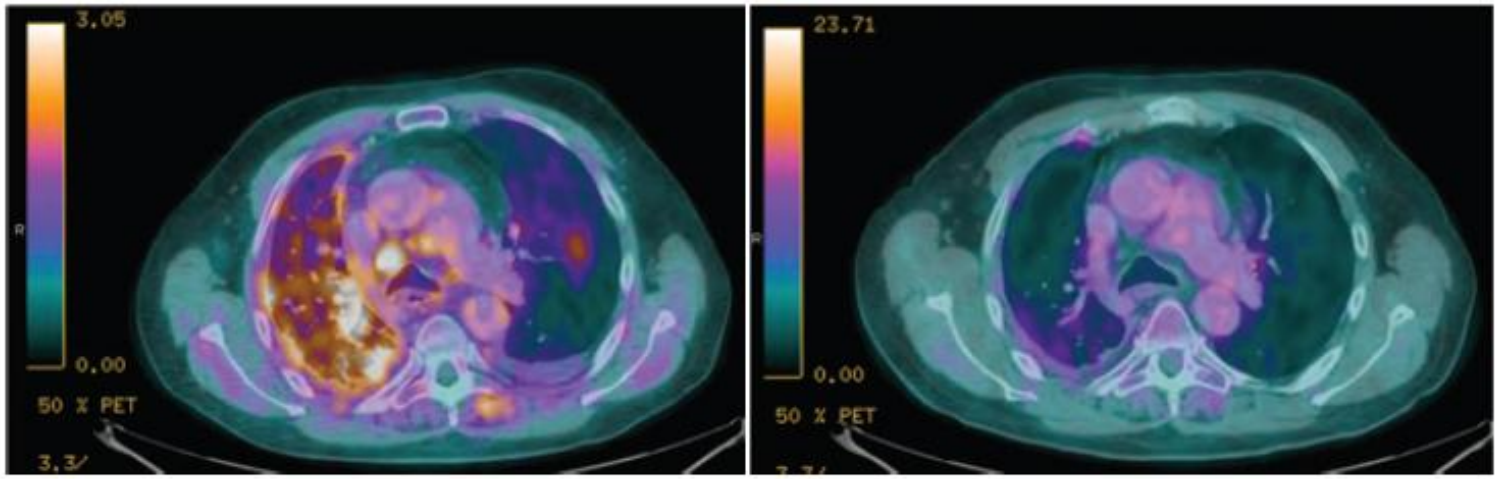




[1]Camidge DR, oral presentation at ASCO 2011; abstract 2501

[2]Riely GJ, oral presentation at WCLC 2011; abstract 1618

ROS-1 gene fusion & crizotinib



With 1.6 million new cases of lung cancer per year worldwide a prevalence of 1% to 2% for a molecular biomarker such as *ROS-1* corresponds to 12,000 to 27,000 patients per year

Davies KD, et al. *Clin Cancer Res.* 2012; 18(17):4570-4579.

European Medicines Agency : Procedure for orphan drug designation

I. **life-threatening or debilitating nature of the condition**

II. **MEDICAL PLAUSIBILITY of the proposed orphan indication**

(eg A rare molecular subtype of lung cancer ……. not lung cancer in left handed women)

I. **PREVALENCE in the EU not > 5 in 10,000 or**

II. **unlikely that marketing the medicinal product in the EU, without incentives, would generate sufficient return to justify the necessary investment**

III. **No satisfactory method of diagnosis, prevention or treatment, or if such a method exists, that the medicinal product will be of SIGNIFICANT BENEFIT to those affected by the condition**

Establishing the evidence base for successful orphan drug development - SIGNIFICANT BENEFIT -

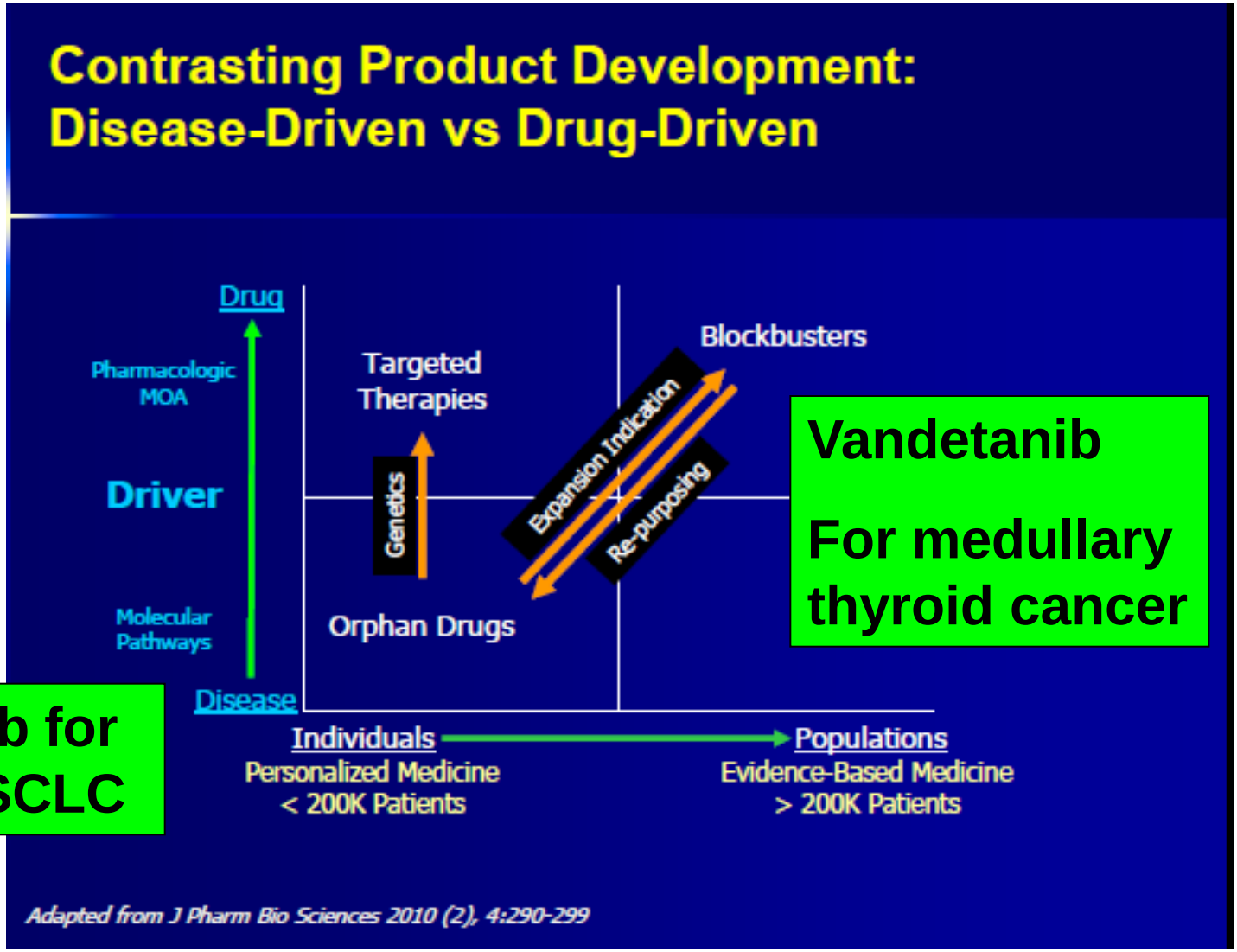
- Focus on effectiveness beyond traditional endpoints – quality, safety, efficacy
- Better and broader collection of relevant data

(retrospective data on prevalence, natural history, outcomes on standard therapies)

- Data collected all along the life cycle of the medicine on risks as well as benefits: compassionate use, real life studies (actual heterogeneous population and real life constraints beyond clinical trials), off label use
- Development of harmonised patient registries

Source : Yann Le Cam Chief Executive Officer, EURORDIS www.eurordis.org

Contrasting Product Development: Disease-Driven vs Drug-Driven



Vandetanib

For medullary thyroid cancer

Crizotinib for ALK+ NSCLC