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Best Practices and Emerging Trends for Market Access to Personalized Medicine in the EU and US

3rd Annual Health Economics & Personalized Medicine Symposium
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By Iain Miller, Ph.D.
EPEMED Board Member and Editorial Committee member, Market Access Project
Member, Technology Appraisal Committee, NICE
Founder Healthcare Strategies Group

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Overview

- Context - Market Access
  - Powerful macro drivers and lots of recent progress
    - e.g. accelerated timelines for BRAF / ALK inhibitors, MiSeq approval, NGS Actionable Genome Consortium (US)
  - But, wide heterogeneity exists in global practice and rapid access to high quality companion* tests
    - e.g. slow global penetrance of “high value” tests, regional access disparities across EU, variable quality

- Presentation’s objectives
  - High level overview of EPEMED/La Charité European Access study
  - Identify EU pathways / best practices & selected recommendations for enhancing access to companion products
  - Review two case studies
  - Highlight some US comparators from recent review article (*source: Healthcare Strategies Group*)

** NGS baseline testing not considered here*

EPEMED / Charite EU Patient Access Study 2014

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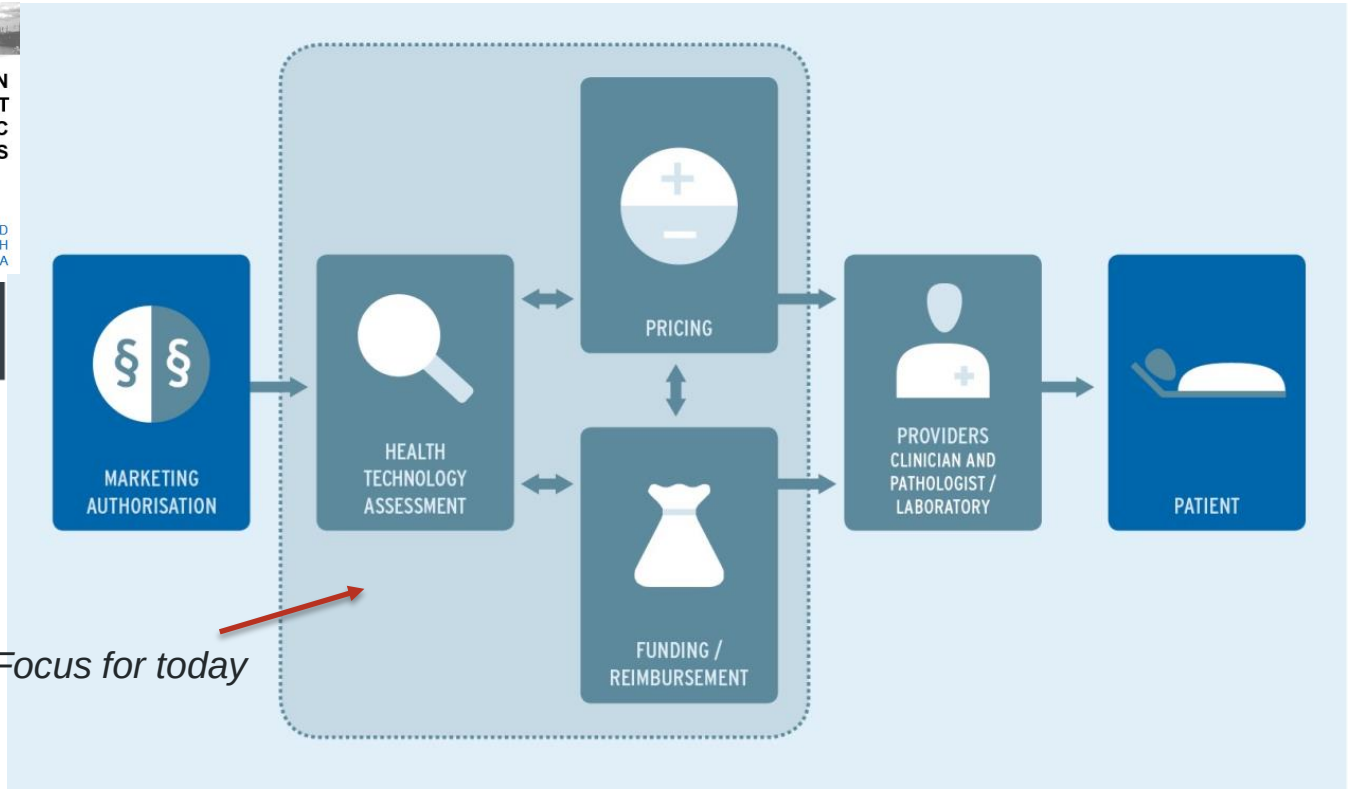

Methodology: Charite review of relevant publications and (30) exploratory interviews with EU expert stakeholders, oversight by EPEMED Steering Committee

Outputs: EU-5 Environmental Analysis, recommendations for improved patient access

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(Illustrative) Motivation for EPEMED Study High Variability in EU HTA Criteria

Country	Clinical Effectiveness	QOL	Cost Effectiveness	Cost / QALY	Budget Impact
US	Very Important	Not considered	Informative	Informative	Not considered
FRA	Very Important	Informative	Informative	Informative	Very Important
GER	Very Important	Important	Important	Important	Important
UK	Very Important	Important	Very Important	Mandatory	Important
ITA	Very Important	Informative	Informative	Informative	Very Important
SPA	Very Important	Very Important	Important	Important	Very Important

- Wide inter- and intra-national HTA variation
- EU-coordinated trans-EU body set up in 2009 (EUnetHTA) to attempt to harmonize, replacement by 2015 with permanent body
- Wide HTA variation even within countries (e.g. within the UK, NICE and the Scottish Medicines consortium differed by 4x in Iressa value assessment)

Rx frameworks (illustrative). Highlighted red criteria are of key importance.

Different HTA criteria → Different Coverage Decisions, Nationally and Locally

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Environmental Analysis, UK*

- Clinical Commissioning Groups (CCGs) established in 2013 under the new Health and Social Care Act
- Diagnostic technologies may be reviewed centrally by the National Institute for Health and Care Excellence (NICE)* and/or regionally by individual CCGs
- Novel CDx tests may be reviewed under Diagnostic Assessment Program (DAP) or Technology Appraisals process (with drugs)
- Reviews typically take 50+ weeks
- The NICE review focus is clinical and cost effectiveness utilizing an Incremental Cost Effectiveness Ratio threshold of £30k/QALY
- NICE guidance not binding for diagnostics
- If drugs not funded by NICE, may be funded under Cancer Drugs Fund

** Disclosure – Iain Miller sits on NICE Technology Appraisal Committee C, which reviews drug / companion tests*

Environmental Analysis, Germany

- Manufacturers submit dossier on benefit assessment to the Federal Joint Committee (G-BA) when a new product is launched
- G-BA sometimes seeks HTA support from the Institute for Quality and Economic Efficiency in Healthcare (IQWiG)
- Inclusion of CDx in the fee schedule (EBM) if *test is mandatory on drug label*
- If testing not mandatory on label, a separate evaluation by G-BA/out-patient committee will occur *(can take 3+ years for review and inclusion in EBM)*
- *Inpatient* testing is provided under DRG, though funding gaps exist:
  - For high cost/innovative procedures the (slow) NUB process is used
  - *As with out-patient testing, cover is mandatory if the test required on label*

Environmental Analysis, France

- Within Health Authority Sante (HAS), 2 separate committees are responsible for conducting Health Technology Assessments
  - Transparency Commission for Rx
  - The device and technology committee (CNEDiMTS) for Dx

- In 2004 the Institute National du Cancer (INCa) was created. Responsible for providing infrastructure and budget for early nationwide access to innovative CDx testing in oncology

- INCa provided € 2.5 M for KRAS testing in 2010, € 2 M for ALK, some pharma subsidies

- Environment in transition - CDx Funding gradually shifting from INCa to the Ministry of Health (MIGAC funds)

Environmental Analysis, Italy

- Separate review of drugs and diagnostics. Drugs reviewed centrally by AIFA, Dx regionally, sometimes with central coordination
- Individual Hospital Drug CPTO Committees review clinical requests for CDx reimbursement in local formulary, potentially resulting in local NTPA codes
- Funding of CDx may be limited by capacity of local providers to absorb new fee codes
- Most inpatient CDx tests ultimately appear on same DRG as drugs, but high local variability in timeline and pricing.
- Ultimate inclusion in outpatient and inpatient formularies (NTPA and NTPO resp)

Environmental Analysis, Spain

- The health ministries in the 17 autonomous communities (Communidades Autónomas – CA + 2 cities) are responsible for delivery and organization of their health services
- Budget-based system, cost-containment health reforms in 2012 and 2013
- New technologies are assessed via a mix of national (Agencia de Evaluación de Tecnologías Sanitarías – AETS) and regional HTAs
- CDx products often first sponsored by pharma or at local level (eg. EGFR)
- National/regional HTAs consider incremental effectiveness. The designation of *required use* of test on drug label will favor positive review. In the future, UK-like NICE model may be adopted

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Selected Observations and Recommendations from Charite / EPEMED analysis (CDx only)

Observation	Recommendation	Exemplar (if any)
Lack of regulatory direction on which CDx test to use	EMA specification of minimum validation criteria	
High variability in QA across environment	Mandatory use of accreditation / External Quality Assessment	
Separate national & regional (Rx-Dx) HTA bodies / processes	Coordinated national review	
De-coupled funding, temporal gaps	Link between CDx/Rx funding, interim funding provisions	 
Few innovative Managed Entry schemes	Performance based, early access funding	

Full EU Market Access Report Publication on Epemed website, Nov 2014

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Case Study: Country-Specific Scenarios for Lung Cancer Testing (EGFR / ALK)

Country	Status	Observation
	EGFR initially pharma funded, now NHS funded. ALK pharma funded.	Temporary funding/access gap for EGFR. Structural funding gap for ALK
	EGFR and ALK both funded and available via INCa network	Good availability and rapid uptake; indirect pharma sponsorship for ALK
	EGFR funded and ALK funding pending under SHI funds	Good availability under mandatory funding model for required tests, though gaps in DRG setting
	EGFR initially pharma funded, now NHS funded. ALK funded under NHS via generic codes.	Some funding and access delays, especially in DRG setting
	EGFR pharma funded, ALK NHS funded since Dec 13 launch	Some funding and access delays

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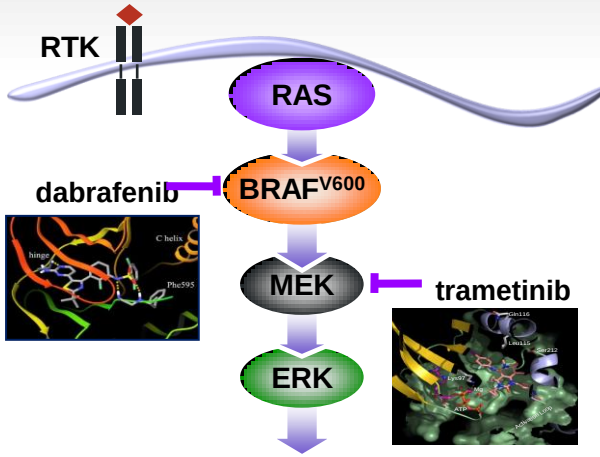
Market Access Case Study: GSK / Biomerieux Development of BRAF Tests

Sign CDx agreement	• On NOV 2009 GSK signed an agreement with **BioMerieux** for the development of a CDx for BRAF
FDA approval	• On MAY 2013 both the GSK drug and the **BioMerieux** CDx were approved by the FDA
Increasing market access	• On SEP 2014 GSK signed an agreement with **GE Healthcare** to enhance market access and quality of the CDx
Scaling up CDx	• On SEP 2014 GSK and PFIZER signed an interim agreement with **ThermoFisher** for the co-development of CDx on NGS platform



Opportunities:

CDx for indications with low % of incidence

Increase knowledge and set of data

Create platform to enhance market access

GSK and partners sponsor new complementary business models (service-based in new geographies with GE) and platforms (NGS with Life/Thermo)

** Slide based on materials kindly provided by Pablo Jordan of GSK*

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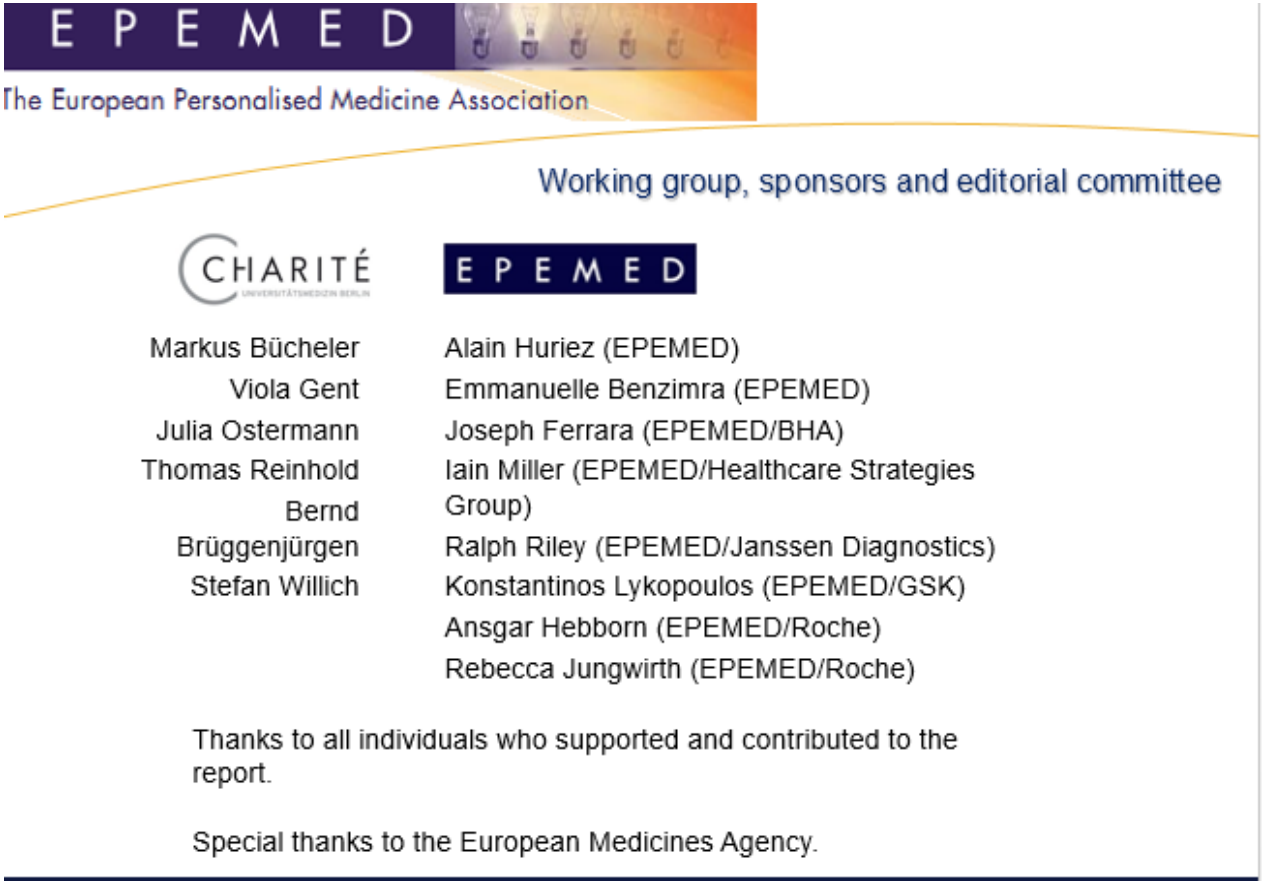
Some Emerging US & Global Best Practices*

- **Regulatory.** Relaxation of onerous US clinical validation criteria in scenarios where community-generated evidence and/or or baseline testing deemed adequate
  - Ivacaftor (CF) 2012 approval without PMA CDx for G551D mutation
  - Analytical validation focus of FDA review for Illumina 2013 MiSeq approval for CF
  - Analytical validation of 6/21 EGFR mutations in 2013 Qiagen EGFR assay approval
- **Quality.** CAP requirement (2007/2013) for participation in EQA schemes for Her-2 testing
- **Evidentiary**. New NGS-guided multi-arm adaptive study designs
  - Cancer Research UK Lung Matrix Study- 14 medicines from 2 sponsors (AZ/Pfizer)
  - LungMAP trial - 5 sponsors/medicines (Amgen, Genentech, Pfizer, AZ, MedImmune)
- **Reimbursement / Access**. Preferential reimbursement and early access models
  - CMS contractor Palmetto's 50%+ premium for use of FDA approved Braf tests
  - CMS Coverage With Evidence Development (15 active programs)
- **Business model innovation**. Emergence of nontraditional business models (eg. CF Foundation $75M funding for Ivacaftor, FIND funding for GeneExpert, precompetitive NGS consortium), Actionable Genome Consortium (US),

* *Miller, 2014, Current Pharmacogenomics and Personalized Medicine* (CPPM)

Thank You for Listening !

Acknowledgement to EPEMED / Charite EU Market Access team for EU analysis:



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Konstantinos Lykopoulos (EPEMED/GSK)
Ansgar Hebborn (EPEMED/Roche)
Rebecca Jungwirth (EPEMED/Roche)

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