


Speaker

Third Plenary Session


Heterogeneity in the Cost-effectiveness of Medical Interventions: The Challenge of Matching Patients to Appropriate Care



Greg Rossi, PhD
 Vice President, Payer Evidence
 AstraZeneca
 Macclesfield, Cheshire, UK

Personalised Healthcare and HTA
“Laminar or Turbulent flow”

ISPOR 2011
 G. Rossi Ph.D.
 V.P. Payer Evidence | AstraZeneca



Legal Disclaimer

The information presented here is intended to facilitate debate and is not meant to be promotional in any fashion.

Laminar Flow and Turbulent Flow


Navier-Stokes Equation

$$\rho \frac{Dv}{Dt} = -\nabla p + \nabla \cdot T + f.$$

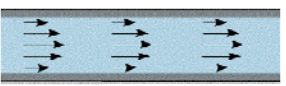
Acceleration
Stress

Pressure
Sum of body forces

Turbulent flow



Laminar flow



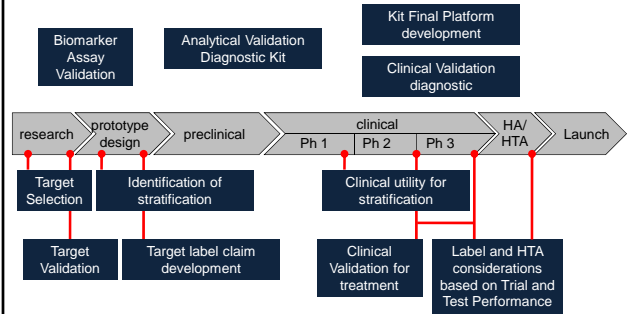
Topics for Today's Discussion

Accelerating assessment and coverage of high value PHC based health technologies

- ▶ **Pressure | Managing Uncertainty**
- ▶ **Stress | Test Performance Requirements in HTA**
- ▶ **Sum of Body Forces | Alignment of Dx and Tx P&R Processes**

Ideal Co-development of Drug and Diagnostic

However, many times, confirmatory biomarker information will emerge after initial phase 3 program



EGFR mAbs for treatment of refractory mCRC

Post hoc analyses consistently indicated no effect in patients with tumors harboring Kras mutations

Kras status	Overall Survival			
	Wildtype		Mutant	
Treatment	Erbix	Control	Erbix	Control
Median (months)	9.5	4.8	4.5	4.6
HR	0.55		0.98	
P value	<0.0001		0.89	

Erbix and Vectibix US labels:

- Retrospective, subset analyses of metastatic or advanced colorectal cancer trials have not shown a treatment benefit for Erbix [Vectibix] in patients whose tumors had KRAS mutations in codon 12 or 13.

P13 Imclone/BMS briefing book for ODAC 2008: Study NCIC CO.17

Trastuzumab in mGC

Access varies according to region based on acceptability of different subset analyses of the TOGA trial

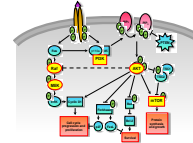
	Definition of „Herceptin eligible,, (% of GC cases)	Overall Survival (Months)		ICERs (cost/QALY) considered by NICE
		Overall control arm (XP/FP)	Herceptin-containing arm	
FDA label	IHC3+ or FISH+ (~22%)	11.1	13.8	n/a
EU label	IHC3+ or IHC2+/FISH (~16%)	11.8	16	GBP 63k-72k
Final NICE guidance	IHC3+ only (~11%)	12.3	17.9 months*	GBP 45k-50k

Stress | Test Performance Requirements in HTA

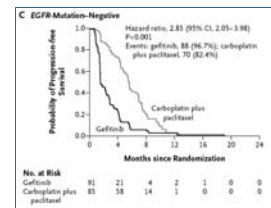
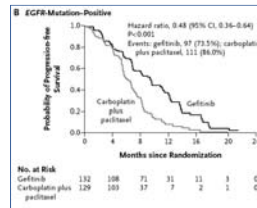
PHC



The case of EGFR TKIs in advanced NSCLC



THE NEW ENGLAND JOURNAL OF MEDICINE
 Published online first
 Gefitinib or Carboplatin-Paclitaxel in Platinum Administration



NICE and PBAC

Assessment for Iressa raised questions regarding the companion diagnostic test

PBAC:

•“A minimal performance of eligible tests should be specified in terms of analytical validity, in order to minimise both false positives and false negatives. **The sensitivity and specificity of the EGFR tests affects the cost-effectiveness and these aspects are the subject of an ongoing assessment by the Medical Services Advisory Committee (MSAC).**”

•“The PBAC therefore **rejected** the submission on the basis of unacceptably high and uncertain cost-effectiveness. **The main uncertainties related to the prevalence of EGFR M+ in unselected Australian NSCLC patients, EGFR testing performance and cost, . . .**”

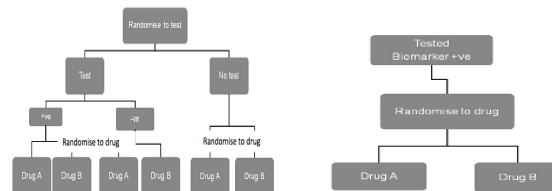
Australian 2010 Draft for Consultation Document

The draft specified over 70 specific questions regarding HTA for cost-dependent technologies

Evidence Development Strategies

Level 1:
Double Randomised Trial

Level 3:
Randomised trial of drug only (with the eligibility of all subjects determined by test result)



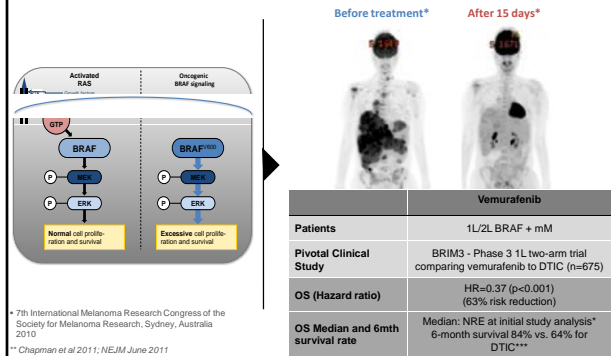
Sum of Body Forces | Alignment of Dx and Tx P&R Processes

PHC



Braf v600 mutation status and its role in new treatment options for metastatic Melanoma

Clinical data demonstrate significant improvements in survival for vemurafenib, a selective inhibitor of Braf V600



Summary of Final Mutation for 132 cobas BRAF positive patients Enrolled on BRIM-2 Study

~20% of appropriate patients may have been excluded if Sanger method used for screening

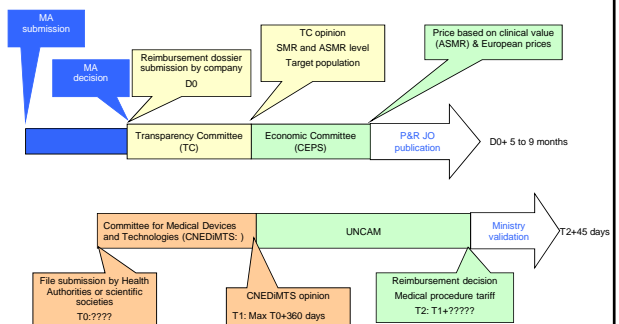
		Sanger Sequencing Results				
		V600E	V600K	Wild Type	Invalid	Total
Cobas® BRAF	Mutation Detected	97 (73.5%)	9 (6.8%)	11 (8.3%)	15 (11.4%)	132

Post Discordant Result analysis


		Sanger + 454 Sequencing Results				
		V600E	V600K	Wild Type	Invalid	Total
Cobas® BRAF	Mutation Detected	122 (92.4%)	10 (7.6%)	0	0	132

Reimbursement coordination Rx-Dx challenge due to P&R processes

Example: France



Conclusion

PHC 

Optimizing “right side” variables can “accelerate” PHC towards its lofty promise....



- Save & Improve Lives
- Save Pharma
- Save Healthcare Budgets

 **ISPOR** www.ispor.org *Speaker*

Third Plenary Session
Heterogeneity in the Cost-effectiveness of Medical Interventions: The Challenge of Matching Patients to Appropriate Care



Greg Rossi, PhD
 Vice President, Payer Evidence
 AstraZeneca
 Macclesfield, Cheshire, UK