Development and Reimbursement in the PHC era: Industry Perspective

Todd Riehl, PharmD, BCOP
Global Development Team Leader BFAST Program
Associate Clinical Science Director, Genentech, South San Francisco

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Evolution in Personalised Healthcare (PHC)

Science and technology are evolving fast and are shifting boundaries of what is possible in medical research and patient care

Pre-PHC

RCT Required

One drug fits all

PHC Today

RCT Feasible

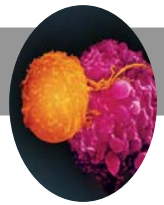
One patient segment, one biomarker, one drug

PHC Future

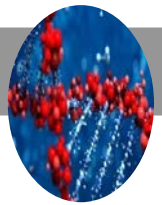
RCT Not Always Feasible

Single patient, comprehensive profile, individualised treatment

Deeper understanding of disease biology



New therapeutic modalities



Comprehensive diagnostics

Big data & advanced analytics

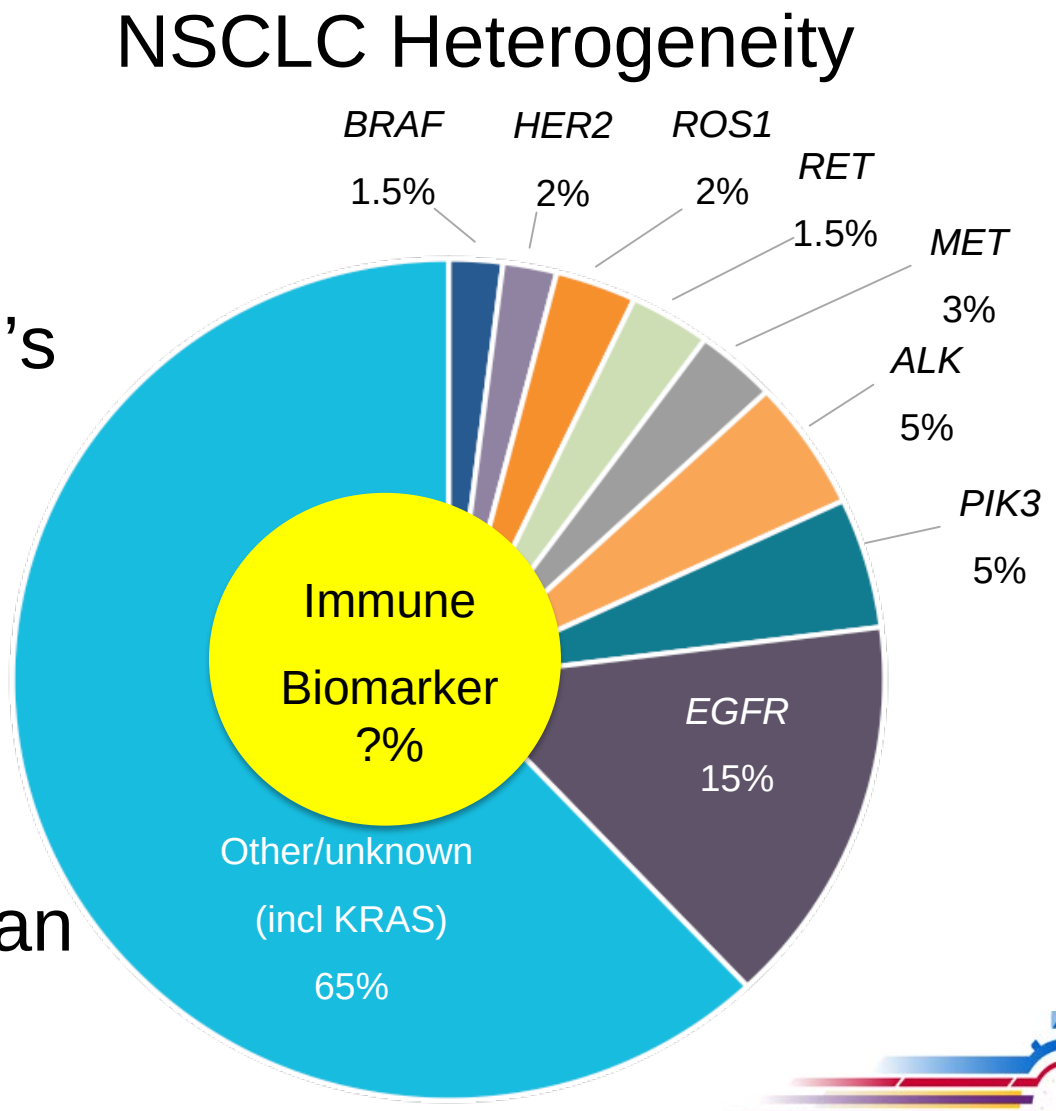
Clinical Decision Support (CDS) tools

Disruptive technologies prioritised as key drivers of evolution in PHC

Key trends/technologies driving evolution in PHC

Heterogeneity of cancer includes many Biomarker driven subsets

- Next step in PHC is directly addressing cause of each person's cancer
- Requires appropriate diagnostic selection
- More homogeneous, smaller populations can lead to improved outcomes



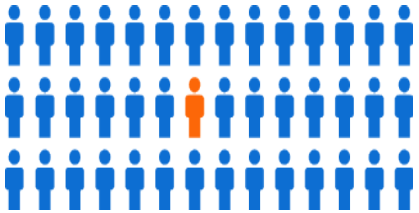
Genomically Driven Trials: Model of Efficiency?

Basket Trials:

Umbrella Trials:

Rare Mutation Population Example

PHC Future



Single patient, comprehensive profile, individualised treatment

- ROS-1 NSCLC (Prevalence 1.5% of NSCLC):
  - Crizotinib US FDA and EMA Full Approval
  - Single arm trial (n=50-53)
    - ~80% 2L+ NSCLC with prior platinum chemo, 14% 1L NSCLC
    - ORR 66% (95% CI 51-79%) by IRC[1]
      - ORR 72% (95% CI 58-84%) by investigator
    - mDOR 18.3 mos (95% CI 12.7-NR) by IRC
    - Safety profile was generally consistent with ALK+ NSCLC experience
    - Companion DX (none available at approval)
      - PMC for further validation and approval of CDx in US (importance of patient selection)

- Recent EMA sponsored symposium: single arm trials in rare populations
  - HA, academia, industry, payers, and patient advocates
  - desiring to find ways to advance drug development for patients

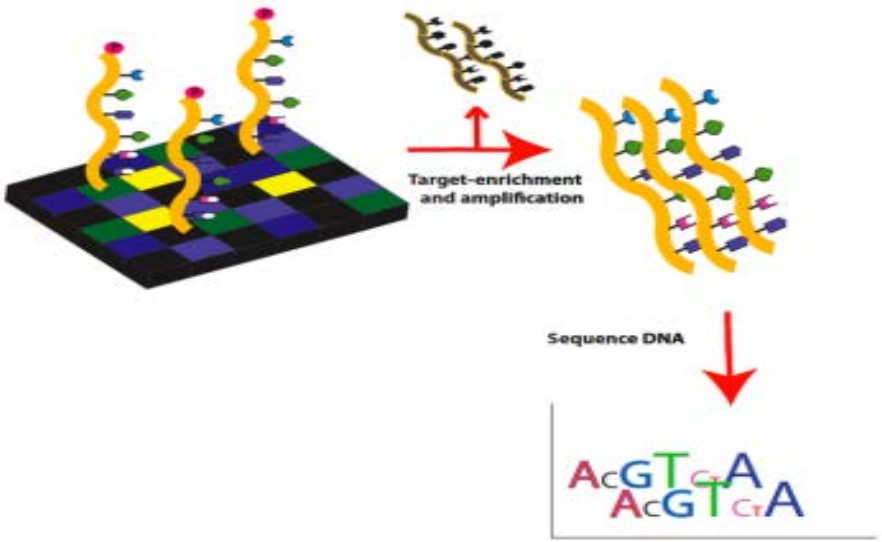
Germany: “No Added Benefit”
France: ASMR V

1. Xalkori US prescribing information

Importance of Consistent Diagnostics

Diagnostic Selection in the PHC-era

- Diagnostic panels allow for testing of more biomarkers simultaneously
- Blood-based diagnostics can expand access to all patients
  - Easy (
  - Can d ase, but requires shedd
  - Retes HC treatment
  - Blood ance earlier



Multiplex Panel

Diagnostic Selection in the PHC-era

		Condition (as determined by "Gold standard")		
		Condition Positive	Condition Negative	
Test Outcome	Test Outcome Positive	**True Positive**	**False Positive** (Type I error)	**Positive predictive value** = Σ True Positive / Σ Test Outcome Positive
	Test Outcome Negative	**False Negative** (Type II error)	**True Negative**	Negative predictive value = Σ True Negative / Σ Test Outcome Negative
		Sensitivity = Σ True Positive / Σ Condition Positive	Specificity = Σ True Negative / Σ Condition Negative	

- Accuracy and consistency is paramount
  - Specificity and Sensitivity (PPV and NPV)
  - Selecting the patient population accurately ensures outcomes
  - Do we need more regulation/enforcement of which tests are appropriate for patient selection?

Industry Proposals for PHC-era Reimbursement

Consideration for Combination Development

Payer (HTA) concerns

- Payers are in a challenging position
  - Desire to get truly innovative therapies to patients as quickly as possible
  - Limited and restricted budgets
  - Need for as much assurance as practical that they are investing limited budget wisely
    - Evidence is key, preferably compared to the standard of care
    - Single arm trials do not provide the level of assurance that they are seeking
    - Consistent and growing concerns that they will be assessing a greater proportion of new targeted products with less evidence in the future
- There needs to be a consistent and agreed-upon approach that will meet payer needs for evidence while still addressing the challenges of rare populations and ethical/timing/practical considerations of rare mutations

What is needed? …a new solution?

- Collaboration within industry, academia, HA, and HTAs and Patient advocate groups
  - Rare populations do not allow for feasibility of randomized clinical trials
  - Starting premises of molecularly-driven populations warrant confidence in single arm trial data successes
  - Keys will be consistent patient selection via validated diagnostic testing and appropriately targeted drugs

- Agreement on approach to providing appropriate amount of data
  - How many patients can be reasonably enrolled at various prevalence levels?
  - Use of RWD to provide an appropriate SOC historical control acceptable
    - Need to try to match populations as closely as possible
    - Need to better characterize natural history of disease
  - Longer follow-up is more feasible alternative to finding/enrolling more patients

Data Support of Reimbursement for PHC

- Traditional Randomized Ph 3 trials where possible (agree on threshold?)
  - Threshold accounts for prevalence and time constraints
- Appropriate diagnostic selection of patients (CDx or accurate equiv) whenever possible (suitable, effective biomarker)
- Single Arm trials for rare populations
  - With population-based RWD to define natural course of disease (how population fairs with standard treatment)
  - RWD confirmation of efficacy outcomes post-approval
  - HR QOL data to supplement traditional endpoints (ORR, DoR, PFS, OS)
  - Consider novel endpoints

Reimbursement Models for PHC

- Indication-based pricing (based on level of evidence)
  - May need to apply different evidence requirements based on prevalence
- Conditional approval and pricing (with opportunity to adjust pricing with RWD confirmation)
- Risk/Cost sharing arrangements
- Other options?
  - Lead to access for patients to the best drugs and outcomes
  - Help assure that limited funds for healthcare are gaining the best returns for spend

Summary

- Randomized clinical trials are not obsolete
  - Still serve to minimize uncertainty in more common populations

- Rare populations require a different approach
  - Embrace the scientific advances that decrease uncertainty
  - Accept the limitations and risks of the approach
  - Achieve common agreement of a new standard premise
    - Establish new reimbursement approaches
    - Establish new required data standards
  - Collaborate to ensure patient access to the most effective treatments

Doing now what patients need next

Working together to make PHC

A reality for all patients