Using health data for innovative trial designs

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www.vermilion-lifesciences.co.uk
Why is this important?

- Medicines development is risky, time and cost intensive
- Pipeline failures increase cost of development and cost of medicines
- High medicine costs reduce patient access and benefit
- The $2.6bn problem

- Curative Hepatitis C therapy
  - 12 week course
  - $84,000 / €51,000 - €41,000

- Alternate week lipid lowering MAb
  - Lifetime treatment
  - $14,100 pa / €7,000 – €8,000

- Malignant melanoma IgG4 PD-1 Checkpoint inhibitor
  - Every 3 weeks
  - $150,000 pa / ~£69,000 pa

- Squaring the circle of affordability, cost effectiveness and uptake vs risk, investment prioritisation and need for return
Regulatory Requirements

• Regulatory hurdles to protect public
  – Safety scares increase desire for certainty, study duration and exposure
  – RCT seen as the gold standard
  – Poorly relevant to reimbursement needs or real life clinical practice

• New models provides opportunity to capitalise on new data
  – MAPPs / 21\textsuperscript{st} Century Cures / Conditional approval
  – Change the paradigm of ‘RCT Studies – Approval - Widespread use’

• Improve on RCTs with a new methodology?
  – Faster, less costly, more relevant while protecting public health
  – Develop real world utility assessment
  – Build on observational studies: the ‘poor relation’ of RCTs
Health Data - measures of patient value

- mHealth devices capture relevant patient data in clinical trials
- Involving patients in design and data parameters

Collection: Active input with passive measures
Integration: Correlate labs with other inputs
Endurance: Reducing loss to follow up. Active reminders and passive collection

Use 2 fingers to alternately tap as fast as you can for 20 seconds.
Total Taps
101

mPower helps decipher Parkinson’s disease.
Keeping tabs to keep diabetes in check.

The Dana-Farber School of Public Health, Penn Medicine and Sage Bionetworks
View in the US App Store

To see how your activity levels correlate to symptoms, you need to input data on a regular and frequent basis. Your iPhone enables this while you’re on the go — daily or even hourly.
Health Data – Design benefits

• Identify patient populations in databases
  – Traditional approach for RCTs
    • Prevalence and incidence
    • Geographic distribution
    • Feasibility and selection criteria
  – Disruptive approach
    • Wider cohort for more representative population
    • Improve patient measures to improve participation (RWD)
    • Broaden comparator evaluation
    • Improved IMP management
Health Data – Comparator and IMP benefits

• Cluster randomisation to investigational product
  – Open label or single blind geographic cohorts

• Matched case control
  – Standard of care = placebo
  – Standard of care plus competitor = comparative effectiveness
  – New comparator flexibility

• Disruptive Benefits (Front / Middle / Back)
  – Substantial time & cost savings (IMP / patient accrual)
  – Simultaneously generate data for regulatory approval and reimbursement

• Real time data feeds for ongoing viability assessment
  • In existing or sponsor constructed databases depending on parameters
Health Data – Ongoing indicative value assessment

• Target Product Profile
  – Regulatory efficacy and safety parameters
  – Patient QoL and benefit measures

• Indicative prediction to assess net value
  – Efficacy benefits vs safety / tolerability penalties
  – Weighted patient relevant measures
  – Construct value : response curves for each parameter
  – Fit value curve to price models to estimate cost effectiveness
  – Set individual and net thresholds for progression or termination in TPP

• Value indicators become development decision factor
  – Knowledge of likely acceptable price for sponsor / payer
  – Ability to analyse in real time and investigate stratification if needed
Hypothetical Value Indicator Scale
Impact value apportioned to each data scale

-2500 -2000 -1500 -1000 -500 0 500 1000 1500 2000

Placebo 5mg 10mg 15mg

HbA1c FPG Pain Activity score Steps (000) Heart failure Net Value Score
Health Data - Adaptive design, analysis, stratification

- Real time analyses against TPP thresholds
  - Review safety, efficacy and value
    - Extend benefit:risk to concept of benefit:risk:value
  - Earlier identification of thresholds for approval & value
    - Earlier go/no-go decisions increases portfolio efficiency to file fast
    - Earlier identification of futility to fail fast
  - Adaptive designs with stratification opportunities
    - Improve benefit:risk and benefit:risk:value
  - Streamlined regulatory review with a more parallel reimbursement process
    - Phased, or adaptive approval with ongoing study conduct and data updates
    - Control of clinical use and ongoing database monitoring

- Lower investment to approval and earlier return on investment
Data is an enabler. People make it work

• Need scientific validity to establish PoC and dose range in Phase II

• Establish ‘end of Phase II’ dialogue and stakeholder partnership
  – Agree value parameters, thresholds, development and analysis plans

• Earlier, threshold-based, decision points
  – File fast or fail fast

• Phased approvals
  – Improved robustness of cost effectiveness data

• Earlier uptake
  – Study continuation and ongoing monitoring to outcomes

• Incremental indications / expanded populations
  – Sequential filing and uptake as part of ongoing lifecycle plan

• Lower initial price?
  – Adaptive pricing reflecting strength of data?

• Partnership and predictability
From: Reengineering Medicines Development. ABPI & Vermilion Life Sciences. March 2015

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People will make it work

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