International Guidance for Drug Trials from HTA groups and Payers

Sean Tunis MD, MSc
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Panel Agenda

- Overview of Green Park Collaborative - Tunis
- HTAi policy forum on reg/payers – Henshall
- Scientific advice at NICE - Longson
- Scientific advice at HAS / Tapestry – Meyer
- EUnetHTA JA1 and JA2 - Kristensen
- Pharma Industry perspectives - Hebborn
- Questions / Discussion

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Off-label Uses of Oncology Drugs

- Systematic review of off-label use of oncology
  - several thousand trials, 400+ pages
- "Because of the paucity of high quality evidence, the data available – though voluminous – may have little meaning or value for informing clinical practice"

The Evidence Paradox

- 18,000+ RCTs published each year
- Tens of thousands of other clinical studies
- Systematic reviews intended to inform clinical and health policy decisions routinely conclude that evidence is inadequate

Decision-Maker Guided Methods

- Gaps in evidence should be reduced with greater engagement of decision makers (patients, clinicians, payers) in:
  - Identifying critical gaps in knowledge
  - Provide guidance for design of future trials that address recurring deficiencies in evidence

ACP Clinical Guideline on AD (2008)

- 5 drugs approved by FDA for dementia based on significant improvement in cognitive function
- Evidence for clinical recommendations “weak”
- No convincing comparative studies
- Most outcomes in trials not used in routine clinical practice….and “not clinically important”
- Follow-up too short: generally less than 1 year.

NICE review of psoriasis

- Regulatory studies report extent and severity of body surface area affected by plaques
- Patients stated that face and joint involvement had biggest impact on QoL
- NICE appraisal committee questioned relevance of the standard outcomes
- Might justify addition of secondary endpoint to future trials
  - Or validation of face/joint severity measure

Effectiveness Guidance Documents

- Payers, HTA groups, clinicians and patients could provide useful guidance on trial design
- Specific to individual conditions / technologies
- Targeted to product developers, clinical researchers
- Analogous to FDA-guidance
- Build on existing regulatory guidance; add what is determined to be missing
- Result could be more efficient, predictable clinical development to meet regulator/payer needs

EGD Development Process

- Systematic reviews help to identify recurring concerns with existing evidence
- CMTP consults with experts / stakeholders to generate initial draft recommendations
- Technical working group refines draft recs
- Expert - stakeholder methods symposium to explore key issues identify by TWG
- Revised recs circulated for public comment
- Final methods recommendations posted

CMTP Guidance on PROs in Oncology Trials

- Recommends specific PROs for oncology drug trials
- Also proposes standard timing and process for collecting PRO data
- TWG includes oncologists, trialists, PRO experts, industry, patient rep, payer rep
- Intended to be complementary to FDA PRO guidance
- Hope to increase frequency, quality, relevance and comparability of PRO information in oncology trials

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Example: PROs in off-label studies of oncology drugs

- Include the following 14 patient-reported symptoms ("core symptom set") in all research designs for post-market cancer clinical trials: anorexia, anxiety, constipation, depression, diarrhea, dyspnea, fatigue, insomnia, mucositis-oral, nausea, pain, sensory neuropathy, rash, and vomiting.

Green Park Collaborative

- First meeting in London 17 March 2011
- Meeting purpose
  - **….to identify the steps needed to produce technology-specific guidance documents with recommendations for the design of clinical studies that address the information needs of payers and HTA bodies from a number of different countries.**

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Organizations Represented

- HAS (France)
- PBAC (Australia)
- CADTH (Canada)
- NICE (UK)
- Kaiser (USA)
- Ingenix / United (USA)
- HTAi
- EUnetHTA
- EMA
- Patient Engagement ISG
- Roche
- Pfizer
- ICER (USA)
- CMTP (USA)
- Sheffield University
- CMS

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GPC Progress / Next Steps

- Developing partnership with HTAi to co-chair steering group
- Confirming/inviting individuals & organizations with interest in continued participation
- Preparing draft of guidance development process from London mtg notes
- Selected dementia drugs as likely pilot topic and partial funding obtained
- Follow-up mtg of steering group Oct 2011

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Contact Info

- sean.tunis@cmtpnet.org
- www.cmtpnet.org
- 410 547 2687 x120 (W)
- 410 963 8876 (M)

Improving Interactions: Goals

- Speed patient access to valuable products
- Remove unnecessary barriers to successful development and appropriate market access for innovative products
- Give manufacturers greater clarity about what evidence is required by which bodies and when
- Improve alignment of the timing and logistics of processes where appropriate
- Align methodological guidance and data requirements for establishing safety, efficacy, effectiveness, and comparative efficacy and effectiveness in so far as necessary and possible, and to be clear why requirements differ when they do
- Give patients and the public better understanding of the reasons for decisions by regulators and coverage bodies, especially where these differ

HTAi 2011 Policy Forum Recommendations on HTA-payer-regulatory alignment

1. Build on current work to develop **joint scientific advice** from regulatory/HTA/coverage bodies **for manufacturers** on the design of pre-market evaluations (e.g., phase II/III trials) for **specific products**, expanding to more products, more jurisdictions, and to phase IV study design

2. Develop **joint scientific advice** from regulatory/HTA/ coverage bodies **for industry** on the design of pre- and post-market evaluations (e.g., phase II/III/IV studies) for **specific conditions**, including such matters as appropriate comparators, outcome measures, study populations and subgroups

   - **These might be initiated in a particular region of the world, with the ultimate aim of developing internationally recognized guidance (allowing for the regional variations on specific issues) if possible**