EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Breakout session 2

Science and Data

Moderators

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Context

Can different stakeholders work together to improve the efficiency of evidence generation?

Does each party understand enough about the needs and responsibilities of other stakeholders to identify where synergies and compromises can be made?

Issues re Science and Data (recognising need for efficiency)

1. Choosing populations and comparators
2. Choosing endpoints (clinical outcomes, QoL/PROs)
3. Duration of follow-up (controlled and uncontrolled)
4. Standards for data collection, analysis and reporting
5. Which data from the drug development programme will be needed for the economic modelling (and what other data are needed)?
6. Is there any reason for methodological principles to differ?
7. Other issues?

1. Choosing target population and choice of comparator

Challenges

Population – Regulators focus on the trials and the population that has been tested, HTA seeks to identify those who benefit most and what is added value compared to BSC

Should we increase heterogeneity to improve external validity? It increases noise and it's unclear whether it will be helpful for HTA given they need long-term data and there will be challenges to do meta-analysis as population will be different to that used previously

Off-label drugs? Need to provide a treatment, so used as comparator (BSC), but regulators can't assess benefit-risk (so how do you make an HTA comparison) – **Need to think outside box**

Comparators – regulatory chooses one comparator for comparative efficacy

2. Choosing endpoints (QoL/PROs)

Is there a regulatory acceptance of disease specific PROs? Variation in approach to PROs that are not fully validated

Concern about number of PROs that patients are being asked to complete – need for mapping?

Recognise complexity in collecting data for PROs (require nurse support, but still lots of missing data) – But these are really important for patients and they understand the need for disease specific ones more.

Think about the capacity of the patient as well – hand held devices…

2. Choosing endpoints (clinical outcomes, effect size)

HTA needs lots of outcomes… can we be more specific to increase efficiency?

Some HTA Agencies don't accept PFS as a "patient relevant outcome" and this "really harms patients",
But is this really about "patient needs" or is it about efficacy signal

Challenge is that some patient relevant outcomes take many years to collect

What is a clinically relevant effect vs what is relevant for the patient?

How will HTA guidelines be developed to show how evidence on the outcomes can be gathered, recognising the possible use of meta-analysis?

3. Duration of follow-up (controlled and uncontrolled)

HTA would like to see longer trials for effectiveness, not just for safety (but often directed to switch patients by DSMB)

Difference between how long can you keep someone on a DB RCT vs longer term follow-up (but methodological advances can help)

US is talking about Big Data (from providers) to understand therapeutic value of a product in practice, what data are available in our systems in Europe?

Frequency of assessment is important as well

Clinical data + other data to build models

4. Standards for data collection, analysis and reporting (and methodological endpoints)

Going beyond classical data gathering to create validated data that are suitable for regulatory and HTA purposes requires standardisation and could be a major burden,
HTAs would probably be flexible

Analysis planning – understand it needs to be different for regulators and HTA. Trying to plan but data (and indication) evolves. For HTA more estimation than hypothesis generation. What is needed for HTA?

It all depends on the claim – if it's premium efficacy, premium price (this cannot depend on surrogates, short term data etc)

It must be affordable

4. Standards for data collection, analysis and reporting (and methodological endpoints)

Need improved standardisation of data to allow comparisons across trials

Increase academic capacity

Need glossary to help increase understanding

5. If you had experience with getting data for an economic model, what did you get from the clinical trial programme and what was a challenge?

Try to identify data gaps in economic model early in drug development programme, but trying not to unduly increase data burden

Scientific Advice worked really well in Phase I to drive economic modelling and literature searching.

Even when you have the outcome, you may not have sufficient follow-up, eg overall survival. Models can get really complex.

Can HTA Agencies help optimize drug development to identify what they don't value.

Has VoI, EVPI been used in Scientific Advice? Yes.

6. Is there any reason for methodological principles to differ?

For sub-groups are we asking different questions? Regulators looking for consistency of effect. HTA looking at who benefits most.

We could create guidelines for the areas that are similar and have additional regulatory or HTA specific guidance for the areas that are different.

(Need a conditional approval process for HTA where there is high unmet need)