Bayesian and adaptive trial methods: What it means to payers

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Agenda

• Current healthcare environment
• Payer perceptions of traditional clinical trial design
• Payer awareness and familiarity with adaptive and Bayesian methods
• Potential impact of adaptive and Bayesian methods on access/reimbursement decision making
• Need for regulatory endorsement
• Recommendations

1. Payers are struggling under increasing budgetary pressures and, as a result, introducing new hurdles to gain market access

- Financial/budgetary constraints
- Aging population
- Rising drug costs

2. Greater expectations have led to payers increasingly demanding more data and applying more scrutiny when evaluating drugs

- Comparative effectiveness
- CER assessment by private insurers
- Fewer products receiving high scores of clinical improvement in France
- New legislative reforms in Germany that require proof of incremental benefit and introduction of efficacy frontier

3. Payers' main criticisms about traditional clinical trials are largely based around lack of comparative and real world data

- Placebo-controlled studies should be the exception rather than the rule.
- Usual double blind placebo controlled is far from the real world.

4. Payers are largely unaware of adaptive and Bayesian methods and therefore do not immediately recognize their potential value

- National level payers are more familiar with terminology and methodology than regional or local level payers
- Those who are familiar with these methodologies are statisticians by training
- NICE uses Bayesian analysis but no use of it was reported in other markets

Concerns with current clinical trial design

- Placebo
- Real-world relevance
- Duration (too short)
- Surrogate markers

Payer Reported Familiarity with Adaptive and Bayesian Methodology

- Of 26 payers interviewed for this presentation, only 3 have a good understanding of familiarity with the terms "adaptive" and "Bayesian"
- Familiarity with adaptive design is greater than with Bayesian analysis
- National level payers are more familiar with terminology and methodology than regional or local level payers
- Those who are familiar with these methodologies are statisticians by training
- There are few statisticians on P&T committees
- NICE uses Bayesian analysis but no use of it was reported in other markets
The benefits associated with adaptive and Bayesian approaches resonate well with payers:

- Key attributes associated with Bayesian and adaptive approaches to clinical trial design resonate well with payers.
- Payers most value the real-world applicability and use of biomarkers, as they help provide certainty in outcomes (benefit to the patient and the payer).
- The idea of dose tailoring is important to payers, however, there is little basis for payers to reward this.
- Quicker trials are seen as more of an interest to the manufacturer than to payers.

However, payers are likely to question results based on these methods given their unfamiliarity with the approaches:

- Risk:
  - Suspicion of bias
  - Rejection of analysis
  - Too complex (not enough internal experts/statisticians)
  - Delays in formulary decisions
  - Restricted coverage/reimbursement

Careful application to the payer population will be essential for success:

- "It has to be a very compelling set of personalized medicine prescribing. It’s going to be more difficult and more errors are likely to occur." - US Payer

By appropriately targeting patient groups, manufacturers enhance the value of their product.

While the regulatory support in the US seems positive, the EMEA has been more reserved in its opinion:

Current EU Regulatory Environment

- EMEA: The Guideline on Clinical Trials in Small Populations recognizes that Bayesian methods may be administered, but results may be based if methods are improperly selected.

European payers will discount the value of outcomes derived from adaptive and Bayesian methodologies if the EMEA does not take a clearer position on validity of these approaches.

Adaptive and Bayesian methodologies offer opportunities to both manufacturers and payers:

- Adaptive and Bayesian methodologies are purported to bring manufacturers meaningful benefits.
- Faster clinical trials
- Potential to enhance the value of a product while better meeting payer needs by identifying those patients who benefit most
- "Real world" outcomes are likely to better enable payers to make appropriate funding decisions.
- However, this will likely be primarily at the national level in the EU given the lack of statistical knowledge at the regional and local levels.
- US payers could use data to develop management controls that would more specifically regulate therapies to individual patients, but many are sceptical of the likelihood of implementation.

Payers’ belief in and acceptance of adaptive and Bayesian methods hinges upon regulatory endorsement:

Payer Response

- FSA: The Critical Path Initiative is the FDA’s national strategy to drive innovation in the scientific process. Includes both adaptive and Bayesian approaches.
- FDA, Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials – Feb. 2010
  - The FDA has been largely supportive of adaptive and Bayesian approaches; this positive nod will greatly influence private care providers.

To further strengthen payer acceptability of adaptive and Bayesian methodologies, payer education is needed:

- Transparency in assumptions and methodological approach.
- Publication of results in peer-reviewed journals.
- Comparison of post-hoc Bayesian analysis of PII data vs. real-world outcomes.
- Have Bayesian analysis conducted or reviewed by an independent party.

* "Would have to compare a trial design like that to more traditional structure - but anything that gives enhanced results is going to be beneficial in terms of providing us with more data to manage products." - US Payer
* "The only way to make this acceptable is to do both approaches and to encourage the acceptance of [Bayesian methodology] by title. Compare both kinds of trials and demonstrate that the new one gives more precise information." - French Payer (SMC)
* "The most convincing thing would be for payers to use the real-world decisions they made and show how the results would be different." - UK Payer (SMC)
Before investing in adaptive and Bayesian methods, prepare and educate the market to recognize and reward its value.

Payer acceptance of adaptive clinical trials and Bayesian Analysis and their willingness to reward their use with market access primarily depends on building broader regulatory acceptance of and familiarity with these methodologies.

- Support Educational Efforts
- Build Support from Independent and Influential Parties
- Work With Payers to Identify Most Appropriate Therapy Areas