



Incorporating Translational Science

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5/11/17

Presentation Objectives

- Definitions
- The review process
- Strategies for success

Important Terms

Analytical Validity

Clinical Validity

Clinical Utility

= fit for intended use

Clinical Utility

- Using the test improves patient care in some meaningful way

OR

- The outcomes related to a test result are so strongly positive or negative that that the result becomes clinically actionable

OR

- The test is accurate and fills an otherwise unmet need

Important Terms

Integral Biomarker

Integrated Biomarker

Correlative Biomarker

Integral Biomarker

- The purpose of the trial is to test the biomarker
OR
- Biomarker status defines the treatment arm
OR
- Biomarker status defines the analysis plan

Integral Biomarker: Strategy

- Assumes or tests clinical utility
- Requires pre-defined assay and thresholds
- Null hypothesis might not be tested
- Will be reviewed by the NCI Disease Committee & CTEP
- Will usually require review by the FDA as an IVD
- Expense of the biomarker is part of the cost of the trial

Integral Biomarker: Comments

- This is an “all in” setting that requires a very strong clinical rationale that is based on strong data and/or strong need with some data
- If the translational study fails it is “all over” because it is very difficult to reconstruct what went wrong
- Higher probability of NCI support grant (BIQSFP), but that hardly justifies the “social promotion” of a biomarker that is not essential to the conduct of the trial

Integrated Biomarker

- The biomarker will be formally tested in the entire trial
- Biomarker status not essential to the conduct of the trial

Integrated Biomarker: Strategy

- Can be better way to test clinical validity or clinical utility
- Requires robust statistical plan
- Appropriate justification for collection of biomaterials from all subjects in the trial (\$?)
- Not reviewed by NCI Disease Committee with protocol
- Reviewed by CTEP
- Not relevant to the FDA

Integral Biomarker: Comments

- This is probably the best approach for biomarkers that would become diagnostic tests if successful in the trial
- The null hypothesis is tested
- If the translational study fails it is very easy to determine what happened, and other biomarkers can be fairly tested
- Reasonable probability of NCI support grant (BIQSFP), and strong chance of other grant support

Correlative Science

- Nonessential translational studies
- Can be described or outlined in the protocol

Correlative Biomarker: Strategy

- Can evaluate clinical validity or clinical utility
- NCI Disease Committee cannot review with the protocol
- Try to include in the protocol – primary use
- Prefer to use generic translational objectives
- Reviewed by CTEP, but they can delete them
- Can justify optional banking of biomaterials from the trial for future use – prospective biopsies unlikely to be approved

Correlative Biomarker: Secondary Use Concept

- Evaluation of materials from a completed clinical trial
- Can evaluate clinical validity or clinical utility
- Reviewed by Cancer Biomarkers Correlative Science Committee & CTEP/NCI
- Recommend submitting through the Alliance TRP
- Analysis and statistical plan is critically important
- Results are highly respected as “Level IB”

Conclusion

- Translational science objectives should intelligently address questions that relate to the clinical trial
 - Analytical validity
 - Clinical validity
 - Clinical utility
- The review is rigorous
- Exploratory-only proposals are usually rejected
- Balance specific goals for diagnostic development with research using high-throughput technology
- TRP can help you