S13. Challenges in Evaluating Molecular Markers as Surrogates for Cancer Prevention

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In studies of cancer prevention, biomarkers can be used as surrogates for two purposes: 1) as "surrogate outcomes" to assess efficacy of therapy; 2) as markers of diagnosis and prognosis. The purpose of this presentation is to discuss how, for both purposes, biomarkers may be studied in randomized controlled clinical trials (RCTs). Purpose #1 will be discussed briefly; it has been covered elsewhere in detail. Purpose #2 may be less familiar and will be discussed in more detail.

For cancer diagnosis, extraordinary claims have been made about biomarkers – e.g., Serum proteomics assays for ovarian cancer, and for other cancers, are ~100% sensitive and specific. Similarly, for predicting prognosis of cancer, RNA expression arrays for breast cancer have been said to be better than any available clinicopathological methods. Historically, however, the field of cancer marker research is characterized by strong initial claims that are not, in subsequent research, reproducible. That history provides lessons for understanding current research and for improving the process of conducting future research.

The presentation will discuss:

1. rules of evidence for evaluating markers for diagnosis and prognosis;
2. methods to study biomarkers using RCTs, in ways that may be more efficient and more reliable than other methods.

While molecular markers hold great promise for use in understanding diagnosis, prognosis, and response to therapy, that promise cannot be realized until we appreciate – and apply – appropriate "rules of evidence" to conduct and interpret research.