

**Publicly Funded
Clinical Trials in the
Era of Comparative
Effectiveness
Research**

Richard L. Schilsky, M.D.
Professor and Chief
Section of Hematology-Oncology
University of Chicago
Deputy Director, Comprehensive
Cancer Center

**Goals of Therapeutic
Clinical Trials**

Commercial
Sponsor

Public
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Drug
Registration

Optimize
Treatment

Goals of Therapeutic Clinical Trials

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| Expand Market Share | Create New Knowledge |
| Create Shareholder Value | Improve Public Health |

Why Publicly Funded Trials are Important

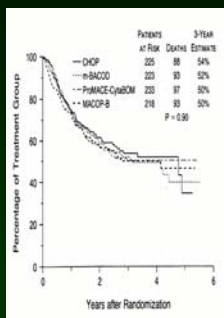
- Compare the effectiveness of various treatment options
- Combine/compare drugs developed by different sponsors
- Develop therapies for rare diseases
- Address optimal dosing
- Test multi-modality therapies such as radiation therapy in combination with drugs

Why Publicly Funded Trials are Important

- Identify patient and tumor subsets most likely to benefit from interventions
- Study screening and prevention strategies
- Focus on survivorship and quality of life
- Publish negative results
- Assess cost and cost-effectiveness
- Provide "gold standard" databases for registry studies

Comparing Efficacy

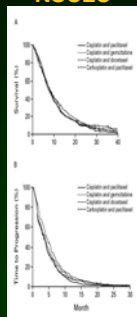
SWOG Comparison of Lymphoma Treatments



Fisher B et al. N Engl J Med 1993;328:1002-1006



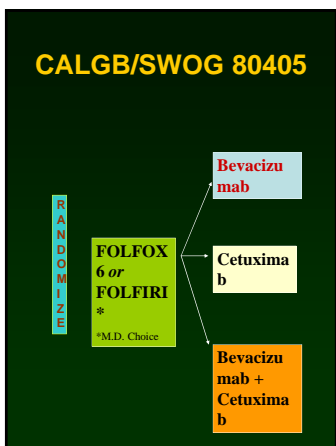
ECOG Comparison of 4 Chemotherapy Regimens for NSCLC

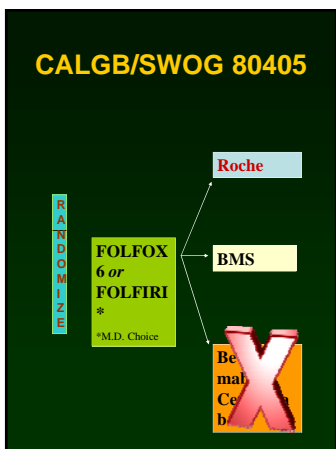


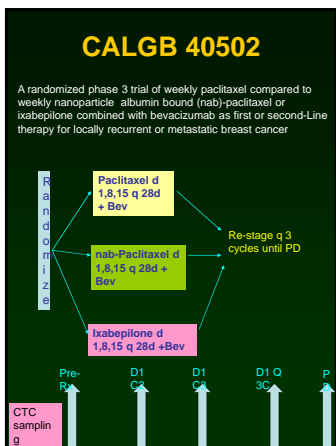
Schiller J et al. N Engl J Med 2002;346:124-132

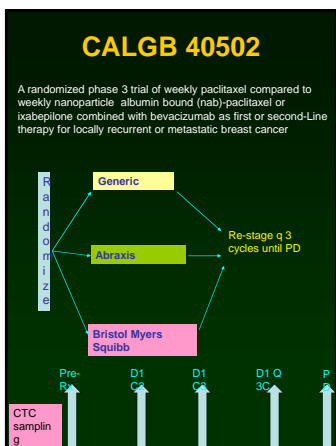


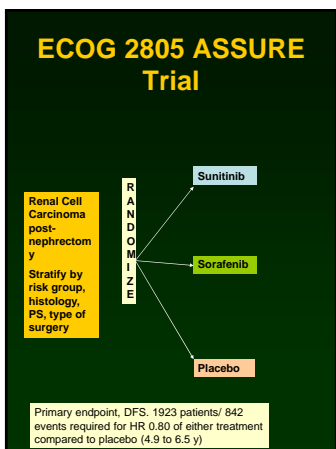
Compare Treatments from Different Sponsors

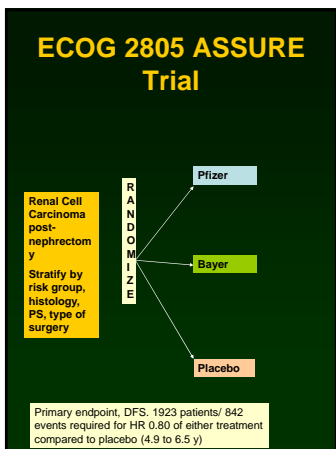






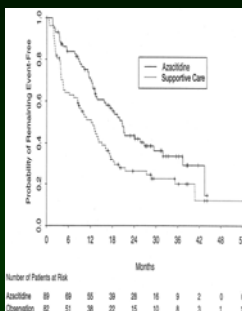






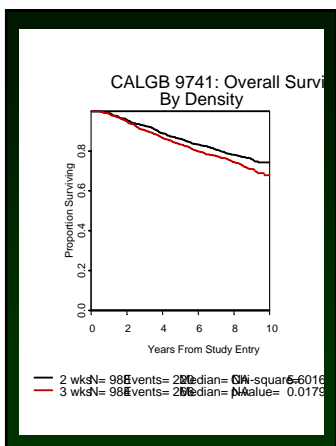
Rare Disease Treatments

5-Azacitidine in MDS

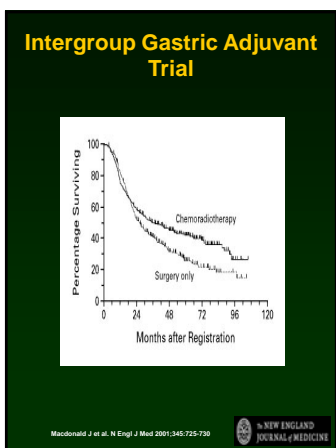


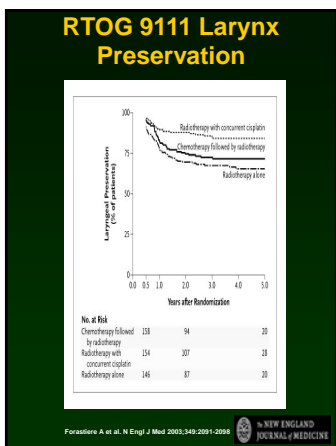
Silverman, L. R. et al. J Clin Oncol. 20:2429-2440 2002

Optimize Dosing

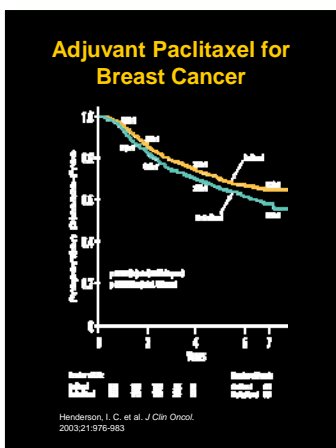


Combine Treatment Modalities



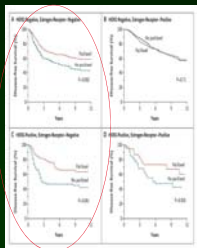


Identify Patient Subsets



Who Benefits from Adjuvant Paclitaxel?

Adjuvant paclitaxel primarily benefits women with ER negative and/or Her2 positive breast cancer

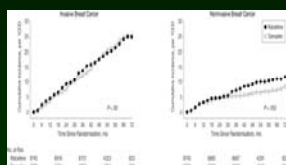


Hayes D et al. N Engl J Med 2007;357:1496-1506

Study Prevention Strategies

STAR Trial Breast Cancer

Comparative Evaluation of Systemic Treatment in Breast Cancer

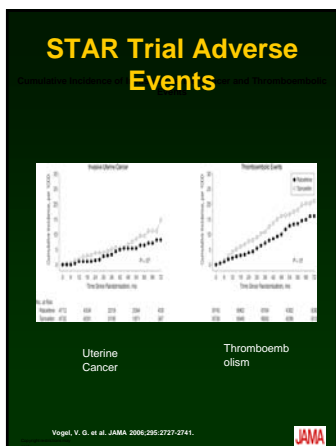


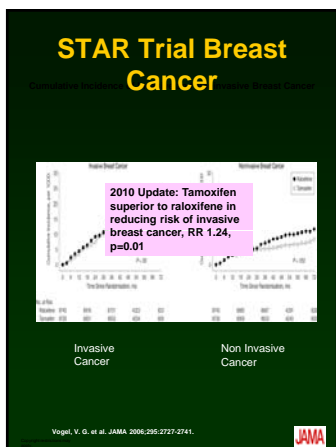
Invasive Cancer

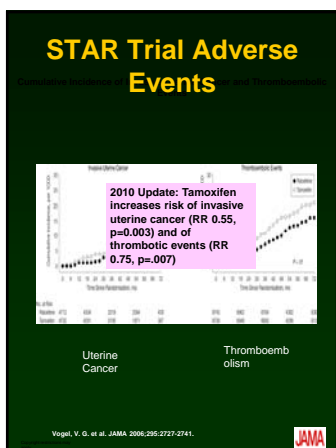
Non Invasive Cancer

Veget, V. G. et al. JAMA 2006;295:2727-2741.



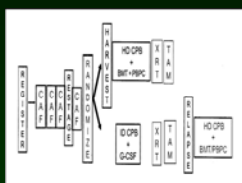






Publish Negative Results

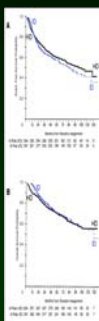
CALGB 9082 High Dose Chemotherapy for High Risk Breast Cancer



Peters, W. P. et al. J Clin Oncol; 23:2191-2200 2005

[View Full Text](#)

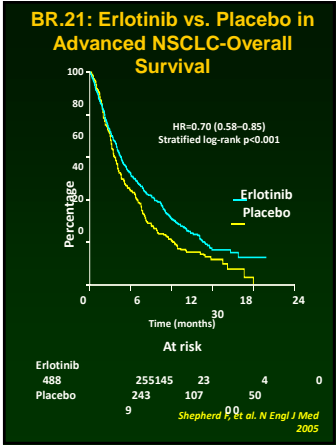
CALGB 9082 Outcomes



Peters, W. P. et al. J Clin Oncol; 23:2191-2200 2005

[View Full Text](#)

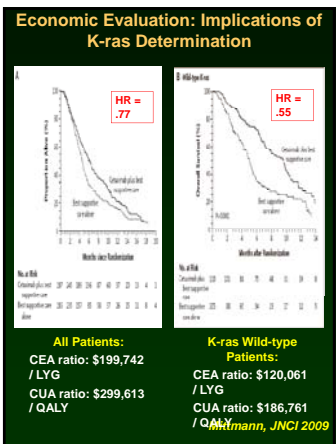
Assess Cost Effectiveness



BR.21 Cost Effectiveness

- Median overall survival benefit: 2 months
- Incremental cost effectiveness ratio: \$94,638/year of life saved
- ICER for EGFR amplified subset: \$33,353
- ICER for Never-smoker subset: \$39,487

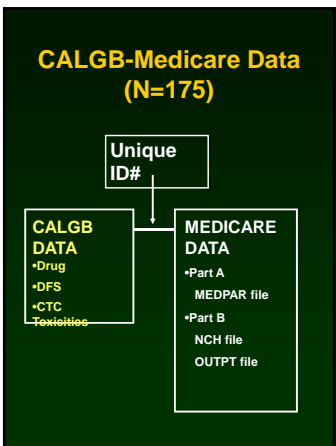
Bradbury, et. al. JNCI 102:1-9, 2010

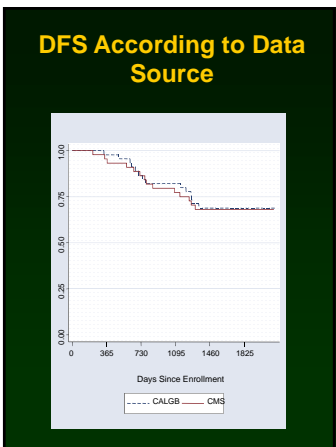


Provide Gold Standard Databases

Practical Problem

- Most people who are diagnosed with cancer are elderly
- Most people who are on clinical trials of anti-cancer therapy are not elderly
- The risks and benefits of anti-cancer therapies in the elderly is uncertain



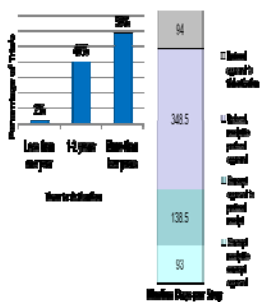


- ### Advantages of Groups
- Access to large, diverse (unique) patient populations
 - Research resources: administrative and data management centers; specimen repositories; reference laboratories; image archives
 - Quality assurance procedures in place
 - Staff and investigator training and mentoring
 - Study results definitive

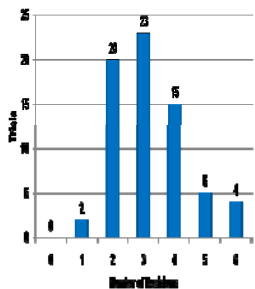
Disadvantages of Groups

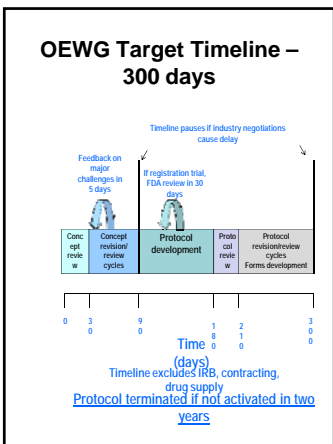
- Cumbersome bureaucracy with review at many levels
- Years to launch and complete may limit relevance
- Results may not be reproducible in "real world" patients
- Uniform tissue handling and acquisition of complex data sets difficult
- Competing priorities with industry

Time to Activation of Cooperative Group Phase III Trials (2006 – 2008)



Review/Revision of Phase III Protocols (2006 – 2008)





IOM Report on CER

“Comparative effectiveness research is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat and monitor a clinical condition or to improve the delivery of care.

The purpose of CER is to assist consumers, clinicians, purchasers and policy makers to make informed decisions that will improve healthcare at both the individual and population levels.”

Characteristics of CER

- CER has the objective of directly informing a specific clinical decision from a patient perspective or a health policy decision from the population perspective.
- CER compares at least two alternative interventions, each with the potential to be “best practice”.
- CER describes results at the population and subgroup levels.
- CER is conducted in settings that are similar to those in which the intervention will be used in practice.

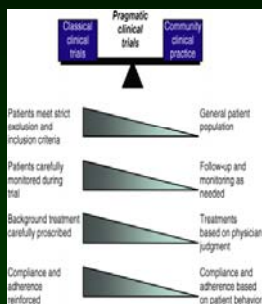
Cooperative Groups and CER

- Specialists from all oncology modalities and scientific disciplines
- Studies broadly accessible to patients through national networks
- Investigator-initiated trials that directly compare therapies
- Collect cancer outcomes and QoL data
- High quality biospecimens to identify/assess subsets

CER Strategies

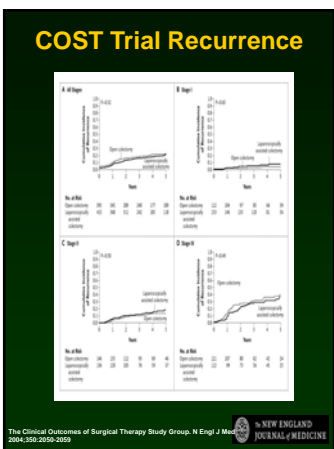
- "Pragmatic" clinical trials
- Prospective observational studies
- Prospective or retrospective registries
- Meta analyses
- Literature review
- Technology assessments

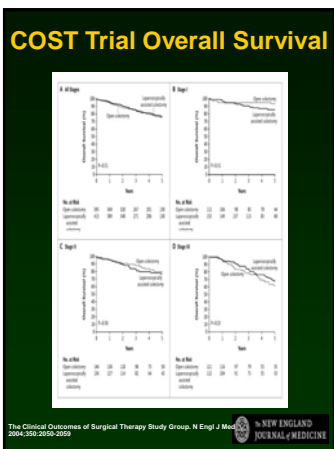
Pragmatic Clinical Trials

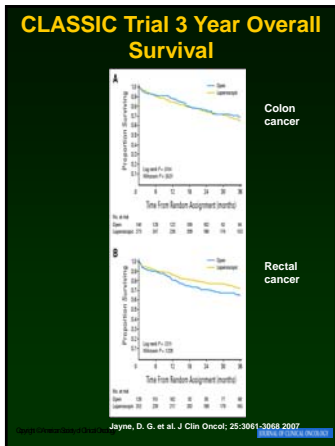


Brass, EP, Clin Pharm Ther 87:351, 2010

The Case of Laparoscopic Colectomy







Laparoscopic Colectomy Can Work!

Laparoscopic Colectomy Can Work!

But Does It?
