
Cancer Clinical Trials 2008

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3% of patients with cancer participate in clinical trials....WHY?

- Lack of trials available
 - Lack of participation by oncologists
 - Regulatory burden is great
 - Time intensive and costly
 - Eligibility criteria too strict
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Why clinical research has not always yielded the desired advances?

- Quality of trials ranges from poor to excellent
- Underpowered studies
- Major selection bias in un-randomized trials
- Unselected patient population studies yield small group benefits even if individuals are benefitting
- Pharma-driven research has some limitations
 - Lack of cooperation with other companies

What about the NCI?

The U.S. Cooperative Group System is
in serious need of reform!

And the NCI AGREES

- NCI provided 7.1 million dollars in 2006 to begin changes recommended by a Clinical Trials Working Group on more efficient operation of the clinical trial system
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NCI anticipates 60% decline in number of new trials by Cooperative Groups

- 10% budget cut for NCI-supported groups would force the elimination of 95 new clinical trials
- Reduce patient enrollment by 3000
- 60% of 150 new trials started each year would be eliminated

Where to start....

- Studies are significantly under-funded
 - Including many unfunded mandates
- Dependence on pharmaceutical industry buy-in
- Best phase I and II ideas are “lost” in cooperative group setting or never introduced
 - Why?

The real problem is INITIATING
studies

Inefficiency: the Low Hanging Fruit:

What happens when trials are not initiated in a timely manner?

- Trial design frequently becomes obsolete
 - Rapidly changing nature of cancer care
 - Investigators become discouraged
 - Sites become disinterested
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Process to activate phase III trials

■ Methods:

- Interview CALGB headquarters and statistical center staff and committee chairs to discover steps to transit from concept development to final study activation
- Review procedure manuals
- Inspect all study records, documents, and emails to identify additional steps
- Collected calendar time for each step

Review of Clinical Trial Process

- 13 phase III trials activated by CALGB from 5/02 to 5/05 were reviewed
- 370 distinct processes were required for study activation
 - 317 work steps
 - 42 decision points
 - 63% outside of CALGB
 - 29 processing loops
- Median days to activate: 580 (range 295 to 1,248) from concept to approval and 784 days (range 537-1130) from initial conception of study—1.5 years to 3.1 years!
- Then you have to conduct the study!!!

Table 1. Number of Steps, Individuals, and Signatures Required to Activate a Phase III Study

	Community Practice Site*	Comprehensive Cancer Center*	CALGB
No. of process steps	< 60	> 110	> 370
No. of groups or individuals involved	13-27	< 27	> 30
No. of signatures required	4-12	13-27	> 70
Decision points	NA	NA	42
Processing loops	NA	NA	29

Abbreviations: CALGB, Cancer and Leukemia Group B; NA, not available.

*See Dilts et al.²

Table 2. Calendar Days From Initiation to Final Approval for Each Major Process Step Required to Activate a Phase III Study

	No.	Median (days)	Range (days)
Initial development			
Concept development	8	193	77-309
CTEP concept review*	13	126	28-562
Study development			
Protocol development	13	477	266-1,200
CTEP protocol review*	13	277	83-467
Forms/database development	13	434	259-1,183
CDE compliance*	7	240	83-361
Grant development	5	222	169-302
Regulatory affairs development	6	350	113-496
FDA review*	4	100	43-157
Central institutional review board review*	13	111	46-320
Total days from initial concept receipt to study activation†	8	784	537-1,130
Total days from CALGB executive review to study activation	13	580	295-1,248

What this analysis does not tell us...

- How many trials were never activated during this time despite approval of a concept
- What studies accrue poorly because by the time they are activated the question is obsolete?
- What trials were never brought up because investigators were frustrated by the system
- How to solve the problem of bureaucratically entrenched stakeholders (NCI, US FDA, CTEP, IRB's, drug companies, academic centers)
- No real sense of urgency and desperation
 - Contrast with patients in the physician's office