

Cooperative Groups and Cost Analysis

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Outline of Presentation

- 'Payment 101' for Cooperative Groups
 - Basics of how NCI pays Groups
- The current Cooperative Group fiscal climate
- Cost analysis and related issues
- The fiscal future for Cooperative Groups

'Payment 101' for Cooperative Groups

A brief summary of how NCI pays
Cooperative Groups and their sites
for performing clinical trials

Sources of NCI Payments

- Main source – the Cancer Therapy Evaluation Program (CTEP) in the Division of Cancer Treatment and Diagnosis
- All US Cooperative Groups except ACOSOG also are “research bases,” separately funded by the Division of Cancer Prevention (DCP) for performing cancer control and prevention trials

Types of U10 Payments

CTEP and DCP award to Cooperative Groups, under U10 cooperative agreements, 2 categories of payments, for

- Each Group's centralized functions
 - Protocol development, data management, statistical analysis, centralized specimen processing, and Group administration
- Per-accrual payments to member sites for Group-led and endorsed studies

Group Central Office Support

- Because of NCI funding limitations in recent years, U10 support is roughly 30% to 50% less than each Group's detailed application
- A recent NCI policy statement encourages supplemental support of Group activities by biopharmaceutical manufacturers
 - It is too soon to evaluate the impact, if any, of this policy pronouncement

Per-accrual Site Payments

- NCI's standard \$2,000-per-accrual rate has not changed in 7 years
 - In some Groups, sites (e.g., 'main members') receive direct U10's or Group subgrants based on anticipated accruals
- CTEP is in final stages of developing a 'trial complexity' payment mechanism
 - However, the additional support for complex trials will, overall, be relatively limited

Per-accrual Site Payments (2)

- NCI is separately the source of per-accrual funds for treatment trial accruals
 - when a site's Group is not the lead or an endorsing group
 - for accruals by independent, non-Group sites
 - these funds flow to Groups, and then to trial sites, via the Cancer Trials Support Unit (CTSU)

Other NCI Payments to Sites

- CTEP U10 funds are also disbursed by Groups to their member sites
 - For follow-up efforts (e.g., \$50 per pt. annually)
 - For specimen submissions (a multi-tier system of standardized payment rates is currently being implemented by CTEP)
- DCP pays \$250 per patient for some trials with a QOL component

Supplemental Industry Support

- For Groups' centralized activities
 - Specific correlative studies
 - Additional CRF requirements (e.g., for registration trials)
 - Accelerated data management/QA efforts
- For sites
 - Reimbursement for non-standard of care tests
 - Additional required data submissions
 - Special submissions (e.g., for independent post-study review of disease-status MRI or CT scans)

'Mechanics' of Industry Support

- Drug manufacturer negotiates a contract with, and pays, the Lead Group
- The Lead Group
 - Disburses funds directly to its sites
 - For members of other Groups, disburses funds to sites, via either the applicable Group or the CTSU

Cooperative Groups' Current Fiscal Climate

Accomplishments of Cooperative Groups

- Over their 50+ years of activity, each Cooperative Group has maintained a broad portfolio of cutting-edge trials
- Many major cancer breakthroughs resulted directly from Group trials
 - A forthcoming special issue of *Seminars in Oncology* will contain papers detailing each Group's accomplishments

Accomplishments of Cooperative Groups (2)

- Despite limited resources, Cooperative Groups have achieved much
 - FDA often accepts Group study results as registration trials for new indications (sNDAs and sBLAs)
 - Groups have collaborated with NCI in increasing their site and central office efficiency (e.g., RDE Project, OPEN system, other CTSU enhancements)
- Industry recognizes that Group trials offer a significant 'bargain'

The Biopharmaceutical Industry and Cooperative Groups

- Cooperative Groups continue to accrue >22,000 patients every year, about half of the nation's total accrual to treatment trials
- Group trials have become attractive to industry
 - Group thought leaders are involved with pharmas
 - Groups are a bargain source of data for supplemental registration trials
- However, FDA's recent insistence on additional data requirements will add substantially to costs of Groups' registration trials

Key Barriers to the Advancement of Effective Clinical Trials are Related to:

- Insufficient financial support for publicly funded clinical trials and their infrastructure;
- Constrained and deteriorating finances of physician practices and institutions that limit discretionary spending to internally support trials;
- Shortages of vital manpower, in particular sub-specialties and trained physician researchers;
- Limited participation in cancer clinical trials by both clinicians and patients, including minority populations;

The Challenge of New Molecules

- The pharmaceutical industry reports 96 new molecules under development*
 - 79 in industry-sponsored Phase I trials
 - Another 17 are in Phase II trials
- The trial pipeline also includes many biotechnology products
- Few new molecules are finding their way into Cooperative Group trials - see next slide

* Source: PhRMA/Wolters Kluwer Health Adis R&D Insight on-line database (accessed 6/10/08 at <http://newmeds.phrma.org/results>)

But Group Submissions of New LOIs and Concepts Are Greatly Reduced

- Between 2005 and preliminary data for 2008,
 - New Phase III trial concepts submitted to NCI by Groups are down ~75%
 - Concepts approved for development of protocols are down > 90%
 - New Phase II LOIs are down ~90%

Source: Presentation by John E. Neiderhuber, MD, Director, NCI, to Cooperative Group Chairs, Chicago, IL 5/30/08

Fewer NCI New Trials May Produce a Perverse Result

- Until the trend is substantially reversed, fewer trials and accruals will cause sites to receive lower total capitation payments than previously
- Groups & U10-funded sites will be able to reallocate capitation funds to other needs

Other Fiscal Pressures Continue

- The basic NCI \$2,000 stipend has been constant for 7 years
 - the average actual site cost is much greater
 - anticipated supplemental NCI payments for “trial complexity” will offer only limited relief
- Overall reductions in hospital & physician fee payment levels have caused sites to increase attention to clinical trial costs
 - Such activities are often seen as not essential to the institution’s mission

... Leading to a Dispirited Clinical Research Enterprise

- As trials become more complex & costly, those local fiscal pressures constrain the incentive to do clinical research
 - Both academic centers and community practices are affected
 - Other sessions have reviewed the adverse impact on oncologists' willingness to perform clinical trials

The Climate for Cost Analysis and Other Cost Issues

Current Efforts Are Often
At Cross-Purposes

Efficiency: Best Achieved by Focusing on Accrual Potential

- Yet efforts continue to broaden trial menu choices
 - DCP trials are soon to be added to the CTSU menu
- Availability of more trials encourages sites to activate despite low accrual potential
 - Many sites accrue no patients to a high proportion of their IRB-approved trials
 - In 2004, 57% of all patients were accrued to Group trials by only 10% of the sites; 36% of sites were responsible for 88% of all patients*

* Comis, RL, Miller, JD, An Analysis of Quarterly Reports from a National Sample of Cancer Clinical Trial Sites, Coalition of Cancer Cooperative Groups & Northwestern Univ., 2006

One Study: A \$3,000-6,000 Median Site Cost per Pt. for Group Trials

Reported Study Cost per Subject					
		Per Subject Reimbursement	Median	25 th Percentile	75 th Percentile
Randomized Phase II	Government-Sponsored	\$2,000	\$6,266	\$3,618	\$9,001
	Industry-Sponsored	Variable	\$8,450	\$4,713	\$9,473
Phase III	Government-Sponsored	\$2,000	\$3,427	\$1,966	\$6,950
	Industry-Sponsored	Variable	\$4,696	\$2,532	\$9,850

Total Revenue by Source and Revenue per Subject by Trial Sponsor

Revenue Centers	AMC		Non-AMC		All Sites	
Average non-trial source of revenue as percent of total research revenue	28%	(6)	33%	(5)	29%	(11)
Median revenue per subject, Government-sponsored trials	\$2,716	(6)	\$1,000	(4)	\$2,276	(10)
Median revenue per subject, industry-sponsored trials	\$2,676	(6)	\$2,510	(2)	\$2,676	(8)

Cost Analysis May Be Counter-Productive

- Refining and substantiating site-related trial cost details can be problematic for sites
 - Little prospect of an overall NCI funding ↑ for Groups, despite NCI's 'bypass budget' FY2009 request for 15.2% additional support
 - Substantiating previously hidden costs encourages 'compliance' efforts to restrict clinical research with built-in deficits

Exemplary Attributes of a Clinical Trial Site

- A recent ASCO report (*JCO 26:2562, May 20, 2008*) proposes criteria for an 'exemplary clinical trial site'
 - These sites 'could contribute to improved accrual and assist in maximizing the opportunities ... to participate in the clinical trial process'
- While itself exemplary, the proposal will exacerbate the typical site's clinical research deficit

The Issue of Paying for Research Related Procedures

- Specifics to come, later in this session
- In the past, protocol-required tests/etc. were often, routinely, “billed to insurance”
- No aggregate data are available about the costs involved
- Compliance-related scrutiny and major fraud settlements have especially impacted academic medical centers
- No clear rules on what is “standard care”

Health Insurance and Clinical Trials

- Medicare has worked with NCI and FDA to pioneer broadened support for clinical trials, as we will hear shortly
- Similarly, United HealthCare has been a leader among private insurers
- However, payment reluctance still persists because of the impact on insurance costs
 - The high cost of newly developed drugs and biologics is an important consideration for both insurers and patients

**Baseline Study of Patient Accrual onto Publicly
Sponsored US Cancer Clinical Trials:**
An Analysis Conducted for the Global Access Project of
the National Patient Advocate Foundation

Philadelphia, PA, 2006

Aggregate Accrual Patterns Results

- 70,853 clinical treatment trial registrations over the 2.5-year baseline period
- 1,129 different Phase I-III treatment trials
 - 531 (47%) were sponsored by Cooperative Groups

Characteristics of the Entire CDUS Study Cohort

Variable	No. of pts (N=70,853)	%
<u>Race</u>		
American Indian/Alaska Native	329	0.5
Asian/Pacific Islander	1887	2.8
Black or African American	5392	8.0
White	59544	88.6
Multiple	82	0.1
<u>Method of Payment</u>		
Private insurance	34952	54.4
Medicare	5858	9.1
Medicare & Private insurance	8011	12.5
Medicaid	3592	5.6
Medicaid & Medicare	653	1.0
Military/VA	1220	1.9
No insurance (no means of self pay)	2294	3.6
Other	7659	11.9

Characteristics of the Entire CDUS Study Cohort

Variable	No. of pts (N=70,853)	%
<u>Institution Type</u>		
Academic	24150	34.1
Community	30467	43.0
Children's	3224	4.6
Military/VA	690	1.0
Foreign/Unknown	12322	17.4

Report to Global Access Project, 2006

Baseline Study of Patient Accrual Onto Publicly Sponsored US Cancer Clinical Trials

The Growing Need for Correlative and Translational Studies, But . . .

- Dedicated NCI resources are currently limited
- Many labs are no longer subsidized from other academic resources
- Constrained resources affect both concurrent studies and retroactive studies of banked materials
- It is often hard to convince pharma of the importance of these studies

The Fiscal Future for Cooperative Groups

Summing Up...

- Cooperative Groups and their member sites see no relief ahead, from the continuing scarcity of resources
- At the same time, Groups face new pharmacogenomic-related demands
- Efficiencies such as the RDE system will eventually help
- For 2008-2009, additional resources need to be obtained, to improve the outlook for the Groups

If current trend continues:

- Further disincentive to enter academic medicine
- Increased schism between laboratory and clinical medicine
- Increased reliance on pharmaceutical industry
- Decreased incentives to develop
 - tumor banks
 - contribute to public sector clinical trial design/accrual

Assault on Clinical Research

- Undervalued
 - in terms of time, effort, costs, importance
 - by academics, government, media, carriers
- Regulatory complexity increases time, effort, costs
 - Medicare modifiers
 - trial registration

Assault on Clinical Research Cont'd

- Who pays = battle between pharma vs. carriers
- Driven by volunteers with substantial institutional subsidies (philanthropy)
- Public sector trials at grave risk
- Effects of Health Care enterprise component changes on research