

NCI Special Symposium:
Using Team Science Approaches for the NCI Drug Program
Friday, January 11th (2013)

Attendees

Non-Federal:

Ken Anderson
Chandra Belani (phone)
Jan Beumer
Lewis Cantley
Michael Carducci
John Carpten
Diana Chingos
Adam Dicker
Robert DiPaola
Afshin Dowlati (phone)
Charles Erlichman
David Gandara
Levi Garraway
Elizabeth Garrett-Mayer
Steven Grant
Mike Grever
Donald Kufe
Steven Larson (phone)
Glenn Liu
Pat LoRusso
Edward Newman
Amit Oza
John Perentesis
Mark Ratain
Gary Rosner
Michelle Rudek
Lesley Seymour (phone)
Charles Shapiro
Lillian Siu
David Spriggs
Walter Stadler

Dan Sullivan
Ken Turteltaub
Miguel Villalona
Brenda Weigel
Patrick Wen
Jedd Wolchok (phone)
James Yao

Federal:

Sherry Ansher
L. Michelle Bennett
Joanna Brell
Alice Chen
Helen Chen
Barbara Conley
Myrtle Davis
James Doroshow
Austin Doyle
Greg Evans
Amy Gravell (contractor)
Paulette Gray
Ed Harlow
Pam Harris
Toby Hecht
Jeff Hildesheim
Andrew Hruszkewycz
Percy Ivy
Debbie Jaffe
LeeAnn Jensen
Kim Jessup
Gary Kelloff
Frank Lin

Jean Lynn
Cheryl Marks
Richard Mazurchuk
Lisa McShane
Anne Menkens
Lori Minasian
Bill Merritt
Jeff Moscow
Barbara Mroczewski
Anthony Murgo
Ray Petryshyn
Richard Piekarz
Sheila Prindiville
Steven Reeves
Larry Rubinstein (phone)
Elad Sharon
Dinah Singer
Gary Smith
Howard Streicher
Sudhir Srivastava
Naoko Takebe
William Timmer
Joe Tomaszewski
Peter Ujhazy
Bhadrasain Vikram
Linda Weiss
Mary Wolpert
John Wright
Roy Wu
Stephen Yoo
James Zwiebel

Moderator: Ed Harlow

NCI Special Symposium: Using Team Science Approaches for the NCI Drug Program

1. **Welcome/Introduction:** James Doroshow welcomed IDSC members and NCI staff to the Special Symposium.
2. **Overview of the Early Therapeutics – Clinical Trials Network** (*Percy Ivy*):

The NCI CTEP Early Experimental Therapeutics program has had a longstanding mission that is focused on the research and development of new treatments for cancer. To that end our program plays a number of roles. First, recognizing the importance of combination therapies, CTEP has succeeded in working with our collaborators to combine investigational new drugs. Our program also incorporates biomarker development and qualification for use in clinical trials. In addition, we seek a better understanding of cancer biology and how it relates to drug development. Drug development now requires new approaches, including the full molecular characterization of patients' tumors. To address these new challenges and opportunities, the NCI has initiated a full redesign of its early experimental therapeutics program, encompassing phase 0 through phase 2.

The new Experimental Therapeutics Clinical Trials Network (ETCTN) will employ a team science approach for drug development, while integrating research resources and programs across the NCI. Teams will work together to define the best path forward for the development of a new drugs. This team science approach should allow NCI-sponsored investigators to perform high impact clinical trials enriched with molecular characterization of patients and sophisticated scientific research. The goal is to move toward the more precise selection of patients for participation on clinical studies. Along the way we hope to enhance interaction and collaboration as well as improving the training of the next generation of drug developers.

The National Cancer Institute will build on its existing infrastructure including its grants and contracts for phase 1 and 2 clinical trials and plans to strengthen its collaborations with other NCI-sponsored agreements and programs. Many complex pieces will be cohesively brought together in a way that allows us to better understand patients' tumors and the best treatment for them.

3. **Team-Based Science Recommendations and Obstacles:**

Ed Harlow introduced the esteemed group of speakers to participants and outlined the session for the symposium. Follow the links for Presenter slide decks.

Ken Anderson (SPORE)

Lewis Cantley (Stand Up to Cancer Dream Team)

Levi Garraway (Broad Institute)

Ken Turteltaub (Lawrence Livermore National Library)

L. Michelle Bennett (NHLBI) discussed team science strategies and obstacles.

Recommendations from the session are listed below.

4. Recommendations for “Successful” Team Science:

1. Must have a clear goal that is achievable in the funding period.
2. Fosters partnerships of academia, pharmaceuticals, NCI, regulatory agencies, and advocacy to fast forward progress.
3. Must have clear, achievable **milestones with a timeline**. Frequent teleconferences and/or face-to-face meetings are required to verify that the milestones are being met.
4. May want to develop a “prenuptial” contract for scientist, which outlines what is expected of leadership, team members, and timelines.
5. Facilitates iterative bench to bedside and back research which has markedly improved patient outcome.
6. Leverages multiple resources. There must be sufficient funds to achieve the goal(s).
7. Deep and sustained collaborations are essential.
8. An escalating budget rather than fixed yearly budget is usually better. Some members of the team only become relevant at late stages of the project.
9. **The Leader is critical:** the Leader must be fully engaged in achieving the goal and must be willing to cede senior authorship on key papers to members of the team who achieve their assigned tasks (motivation). Ideally, the Leader should have a working knowledge of all aspects of technologies/disciplines utilized by the team (or be willing to learn these at a level that allows evaluation of quality).
10. **The Leader (or leadership team) must have the ability to re-distribute resources** in a timely manner to solve unanticipated problems that arise or replace team members who, for whatever reason, are not meeting their milestones.
11. Model of team development includes: forming, storming, norming, and performing. This model is cyclical and arises each time the team is changed/alterd.
12. Trust must be established with all team members.
13. Mentors should be available for new Team members.
14. Able to resolve conflict swiftly and effectively (developing ways to circumvent conflict).
15. All members of the team believe that the goal is a worthy one **AND** that it is achievable with the technology, expertise and funds available to the team.

16. Each member of the team must understand her/his role in achieving the goal, and must feel that she/he will get credit for making this contribution.
17. Metric of success is improved patient outcome.
18. Funds infrastructure for translational research and tissue banks.

5. Reasons that Team Science can fail or underachieve:

1. The goals are ambiguous, too broad, or premature with existing knowledge or tools.
2. Poor leadership. Members don't like or trust each other and thus, don't exchange ideas or even attend meetings.
3. Some members of the team are only there for the money (or fame).
4. A key technology needed for success is premature or oversold.
5. Success depends on making a highly unlikely "Discovery". Most members of the team twiddle their thumbs waiting for someone to make the "Discovery" or perfect the technology needed for their role to become relevant.
6. The funds are divided up at the beginning with no ability of the leader to shift funds from non-performers to performers.
7. There are insufficient funds to achieve the goal.
8. Bureaucratic and logistical delays.
9. Publication/authorship considerations – members don't feel valued.

6. Open Discussion (areas that should be worked on or are concerns of the group) – Ed Harlow.

1. Currently the process for the new ET-CTN is being structured by agent. There was some concern regarding using this approach by IDSC and other attendees. Target/pathway may be a better way to organize.
2. Could drugs outside of the CTEP portfolio be studied with yearly ET-CTN funds that are set-aside? Reallocation of resources has to be discussed internally through CTEP.
3. Several IDSC members were concerned that CTEP have the flexibility to bring in the "best" agents not just what comes through NCI NExT (NCI Experimental Therapeutics Program). A look at the NExT process is needed.
4. Flexibility to change teams and leadership was discussed. More than one Team leader and one leader should select other.
5. Finding the right team leader will be essential to the ET-CTN process (should be organized, unique, dual team leaders, timelines, milestones, etc),
6. Communication process should encompass small groups, not 20-30 people on a teleconference line.
7. Storming was a concern brought up by several IDSC members (conflict resolution).
8. Need concise SOPs developed.

7. Conclusion:

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Quality Team-based Science is critical to the success of clinical trials supported by the Division of Cancer Treatment and Diagnosis (DCTD) in the National Cancer Institute (NCI). The need for a stronger emphasis on global collaboration, technology expertise, molecular characterization, combination therapy development, validated assays, and an enhanced understanding of signaling pathways prompted NCI leadership to call for a redesign of the NCI Early Phase Experimental Therapeutics Program (Phase 1 Program).

Demonstrating the ability to be team builders and to work with others is important. The team should decide, along with company interest, what kind of studies will be done. That teams, along with IDSC buy-in and NCI staff participation should develop the LOI and protocols. NCI needs to ensure that there is a mechanism for non-Network investigators to collaborate with Network investigators and that the “best” agents are funneled through the NCI Experimental Therapeutics (NExT) Program.

Through the presentations today, we can see the components which make up “good or successful” team science endeavors and behaviors that can lead to “bad” collaborative efforts.

Good team science: Strong leadership, trust is built; milestones and timelines are adhered to, clear goals that are achievable, ability to circumvent conflict (storming), and leverage multiple resources.

Bad team science: Poor leadership, key technology is premature or oversold, trust is lacking between team members, storming is not handled properly, and goals/timelines are ambiguous or lacking.

Areas that should be focused on from IDSC discussion by NCI CTEP:

- Currently the process for the new ET-CTN is being structured by agent. There was some concern regarding using this approach by IDSC and other attendees. Target/pathway may be a better way to organize.
- Could drugs outside of the CTEP portfolio be studied with yearly ET-CTN funds that are set-aside? Reallocation of resources has to be discussed internally through CTEP.
- Several IDSC members were concerned that CTEP have the flexibility to bring in the “best” agents not just what comes through NCI NExT (NCI Experimental Therapeutics Program). A look at the NExT process is needed.
- Concise SOPs should be developed for the ET-CTN.