



ETCTN

Experimental Therapeutics Clinical Trials Network

Team Driven. Cancer Therapy Focused.

Phase 2 Clinical Trial Component of the ETCTN

Jeff Moscow

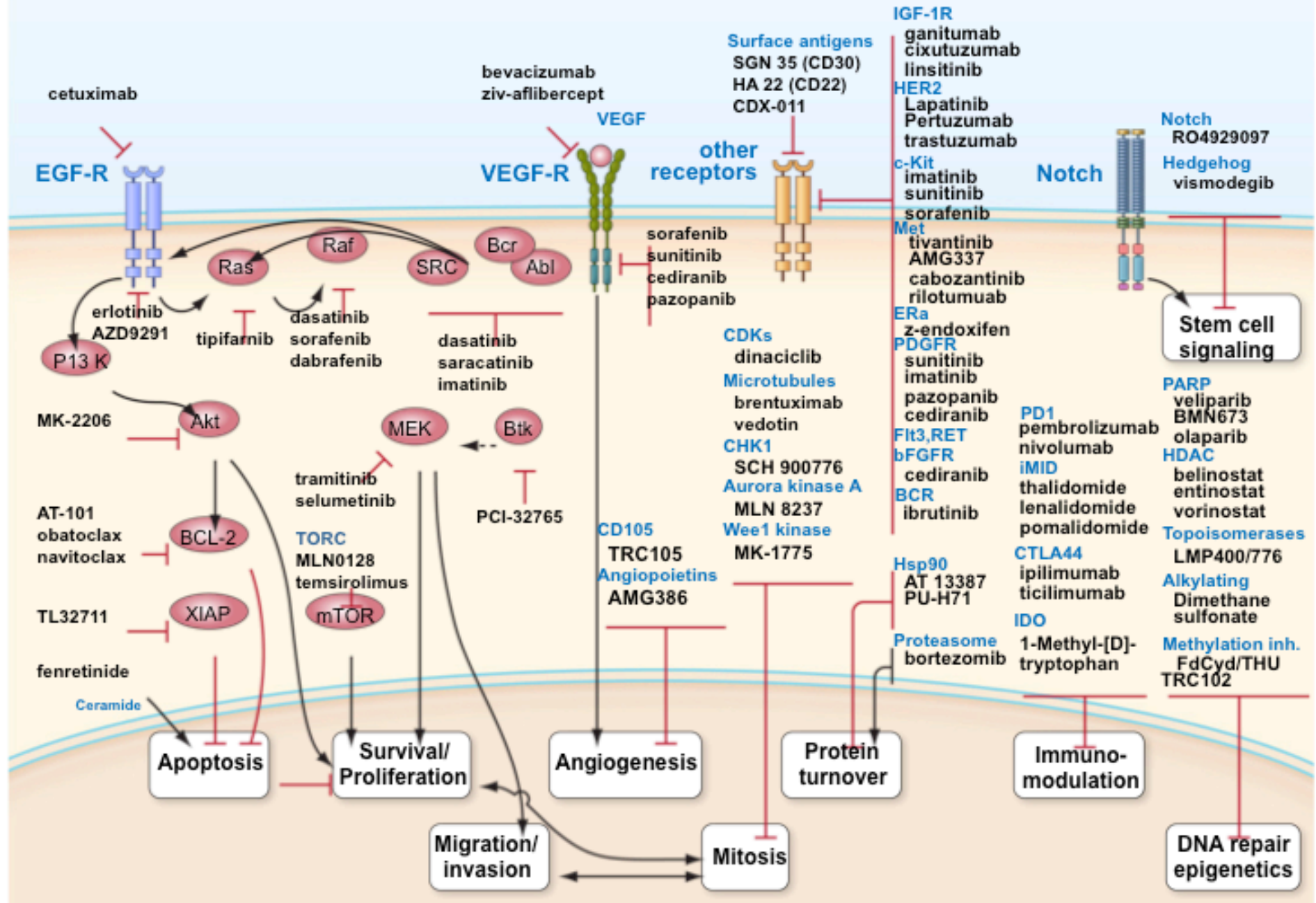
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Role of NCI/DCTD in Early Clinical Development of New Cancer Therapies

- NCI/DCTD forms collaborations with Pharma and academic medical centers to develop new anticancer agents and new combinations of agents
- Underlying concept is that important public health needs are not met by Pharma activities alone – role of NCI/DCTD is to expand clinical indications for novel agents as well as the understanding of their biology
- Many interrelated NCI programs are devoted to this effort, in a continuum from evaluation of proposed collaborations through the initial clinical evaluation of these agents.

High Priority Targets and DCTD/CTEP Agents



Recently developed NCI IND agents

Agents that have achieved FDA approval based *in part* on early development in CTEP collaborative early phase programs

| Agent | Indication |
|-----------------------------|--------------------------------------|
| Azacytidine | Myelodysplastic syndrome (secondary) |
| Bortezomib | Mantle Cell Lymphoma (secondary) |
| Ipilimumab | Melanoma (primary) |
| Lenalidomide and bortezomib | Multiple Myeloma (secondary) |
| Oxaliplatin | Colorectal Cancer (primary) |
| Romidepsin | CTCL (primary) PTCL (secondary) |
| Sorafenib | Thyroid Cancer (secondary) |
| Ziv-aflibercept | Colorectal Cancer (secondary) |

Pending FDA approval

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|-----------------------|-------------------------|
| Dinutuximab (ch14.18) | Neuroblastoma (primary) |
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In pivotal trials based on development in CTEP program

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|------------------------|----------------------------|
| Cediranib and Oliparib | Ovarian Cancer |
| Selumetinib | Uveal Melanoma (secondary) |

Role of ETCTN in NCI Drug Development

- The Experimental Therapeutics Clinical Trials Network (ETCTN) is the network of clinical trial sites and infrastructure that is solely devoted to the conduct of the earliest clinical studies of these Investigational New Drugs (INDs) sponsored by NCI.
- Assures the development of NCI IND agents up to the point of hand-off to NCTN and/or back to Pharma: defining dose, schedule, target engagement, biomarkers of response, and demonstration of clinical activity
- Involves and maintains an experienced network of extramural investigators focused on mechanism-based early phase studies that require intensive monitoring for safety and intensive intervention for correlative studies

Consolidating the NCI ETCTN initiative

- The ETCTN is currently composed of two distinct clinical components: Phase 1 UM1 grant program and Phase 2 N01 contract program
- Both the phase 1 and phase 2 programs consist of lead organizations, either the grant or contract holders, and multiple affiliated centers that contribute to accrual and scientific goals
- The Phase 1 program was recently re-competed as part of the formation of ETCTN
- The expiration of contracts for the phase 2 program is an opportunity to develop ETCTN into a unified grant program to adapt to the era of targeted therapies
- As clinical science has evolved, current programmatic separation of phase 1 and 2 activities is not desirable.

Evolution of the science of early phase trials

Requirements for early phase trials have evolved:

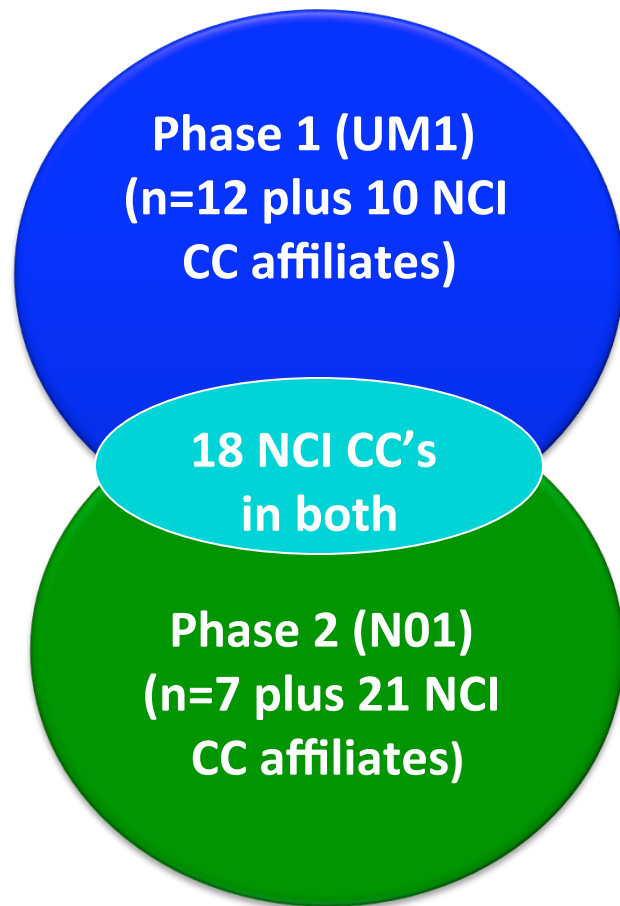
- Disease-focused context traditionally associated with phase 2 trials now frequently required in phase 1 studies, because targeted therapies are tested only against tumors that express the target
- Biomarker incorporation into trials, both for eligibility and proof of target engagement, is now usually required in early stage drug development
- Pharma has already adopted flexible early phase study design, quickly building phase 2 endpoints into phase 1 studies when signal of activity is detected
- As line becomes blurred between phase 1 and phase 2, placing pharmacology-focused investigators (phase 1) with disease-focused investigators (phase 2) within the same program provides flexibility required to nimbly develop trials of NCI IND agents

Phase 2 Program goals: How do we make the program fit the science?

Program goals reflecting new realities:

- Shorter duration from phase 1 initiation through proof-of-activity – flexibility to quickly explore signals of activity
- Enhance biomarker incorporation into phase 2 study design
- Maintain experienced phase 2 (disease-specific) investigators in ETCTN and on ETCTN project teams that develop early phase studies
- Expand pool of eligible patients for rare tumor subtypes
- Further leverage ETCTN centralized clinical trial support resources

Separate vs unified ETCTN structure



Current



Proposed

ETCTN Core Grant Program

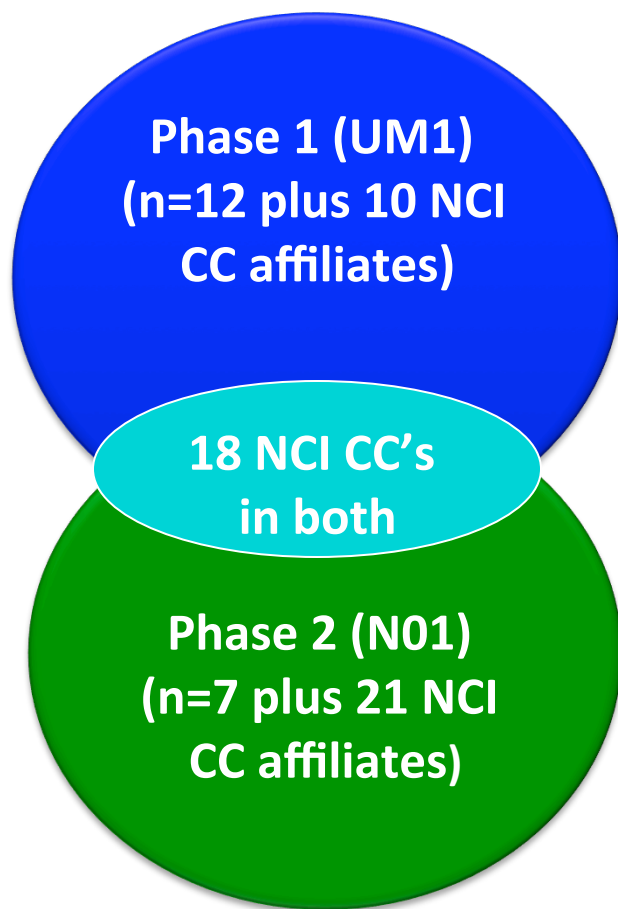
- Current phase 1 grantees would compete for supplements to expand phase 2 expertise
 - Could include current NCI phase 2 programs or new, qualified experimental therapeutics programs at other NCI CC's – these CC's would be part of a consortium arrangement with the grantee institution
 - Opportunity to redistribute the 31 NCI CCs currently affiliated with the phase 2 contract program into more streamlined alignments
 - 7 NCI CC's affiliated with different UM1 and N01 LAO's
 - Flexibility in number of supplements requested to optimize network
- An FOA would be required for competitive supplement; focus will be on scientific leadership/expertise for ETCTN phase 2 studies

Budget recommendation for UM1 supplements

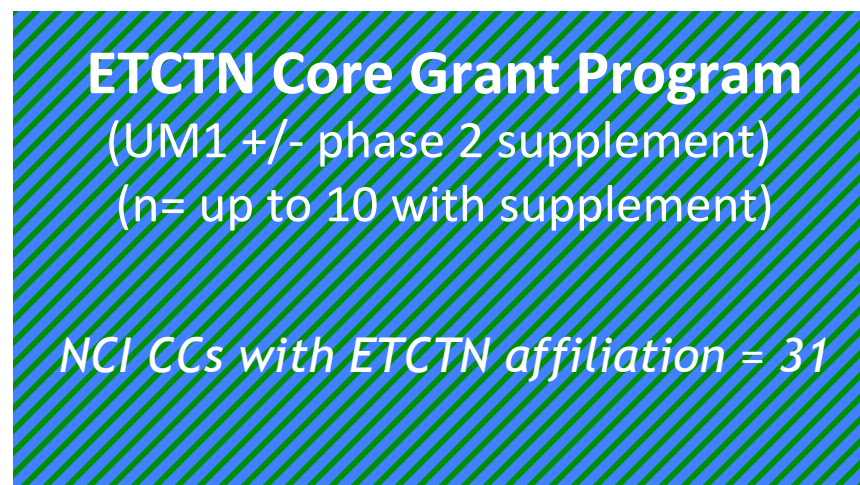
Proposed Annual Allocation of Funds for UM1 supplements: \$9,000,000 per year

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| Total Funding Per Site (example of n=7 supplements) | \$1,250,000 | |
| <u>Unrestricted Funding</u> | <u>\$1,000,000</u> | <u>80%</u> |
| Salary support and travel | \$100,000 | 8% |
| Per-case patient accrual (n=130) and biopsy acquisition | \$900,000 | 72% |
| <u>Restricted funding</u> | <u>\$250,000</u> | <u>20%</u> |
| Biomarker studies | \$250,000 | 20 |

ETCTN Pilot Collaboration with NCI CC Program



Current



Proposed

NCI Early Therapeutics Opportunity Program – Pilot collaboration with NCI cancer centers program

- Proposal designed to greatly expand participation in early drug development studies for both physician-scientists and patients
 - Study leadership proposal
 - Phase 2 study participation proposal

NCI Cancer Centers and ETCTN Phase 2 study leadership

- In the NCI Early Therapeutics Opportunity Program, an investigator from any clinical NCI-designated cancer center could submit an Letter of Intent (LOI) to CTEP and, if approved by the Protocol Review Committee (PRC), the PI could receive:
 - Full ETCTN clinical trial support for the study – including CIRB, registration and data management support, and accrual from ETCTN sites
 - Funds for salary reimbursement (% effort)
 - Funds for accrual to the study at the PI's home institution
- LOIs must be approved and submitted by cancer center
- Administered as a P30 administrative supplement after LOI approved by PRC

NCI Cancer Centers and ETCTN Phase 2 study accrual

- NCI Cancer Centers would be able to open selected ETCTN phase 2 studies that require screening for rare tumor subsets.
- Reimbursement via P30 supplement with some restricted funding.
- Overall additional accrual to ETCTN trials with both proposals is up to 91 patients per year
 - Study leadership n=16
 - Rare population accrual n=75
- Proposal coordinated with assistance & guidance from the cancer centers program (Linda Weiss)

Budget request for Pilot NCI CC collaboration

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| NCI Cancer Centers Pilot Collaboration with ETCTN | \$1,000,000 |
| Study leadership supplements (n=4 @ \$62,500/supplement) | \$250,000 |
| Supplements for study accrual (n=15 @ \$50,000/supplement) | \$750,000 |

Metrics for 3-year pilot period (FY16-18)

- Number of accepted LOI's
- Accrual to studies opened through leadership supplement
- Number of NCI CC's participating in both programs
- Accrual to studies for rare tumors

Renewal would depend on performance of pilot program

Total budget recommendation

Total Proposed Annual Allocation of Funds \$10,000,000 per year

Proposed Annual Allocation of Funds for UM1 supplements: \$9,000,000 per year

| | | |
|--|--------------------|------------|
| UM1 Phase 2 Supplements | \$9,000,000 | |
| <u>Unrestricted Funding</u> | <u>\$7,200,000</u> | <u>80%</u> |
| Salary support and travel | \$1,000,000 | 8% |
| Per-case patient accrual and biopsy acquisition | \$6,200,000 | 72% |
| | | |
| <u>Restricted funding – For Biomarker Studies</u> | <u>\$1,800,000</u> | <u>20%</u> |
| | | |
| NCI Cancer Centers Pilot Collaboration with ETCTN | \$1,000,000 | |
| Study leadership supplements (n=4 @ \$62,500/supplement) | \$250,000 | |
| Supplements for study accrual (n=15 @ \$50,000/supplement) | \$750,000 | |

The background features a light gray gradient with a faint, circular arrangement of stylized human figures. Each figure is composed of a circular head and a triangular body with arms and legs, all rendered in a light gray tone. They are positioned as if standing in a circle, facing inward.

Open for discussion