ETCTN

Experimental Therapeutics Clinical Trials Network

Team Driven. Cancer Therapy Focused.

ETCTN Brief Overview

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Program Director, ETCTN
Associate Chief, Investigational Drug Branch
Cancer Therapy Evaluation Program

Experimental Therapeutics Clinical Trials Network (ETCTN)

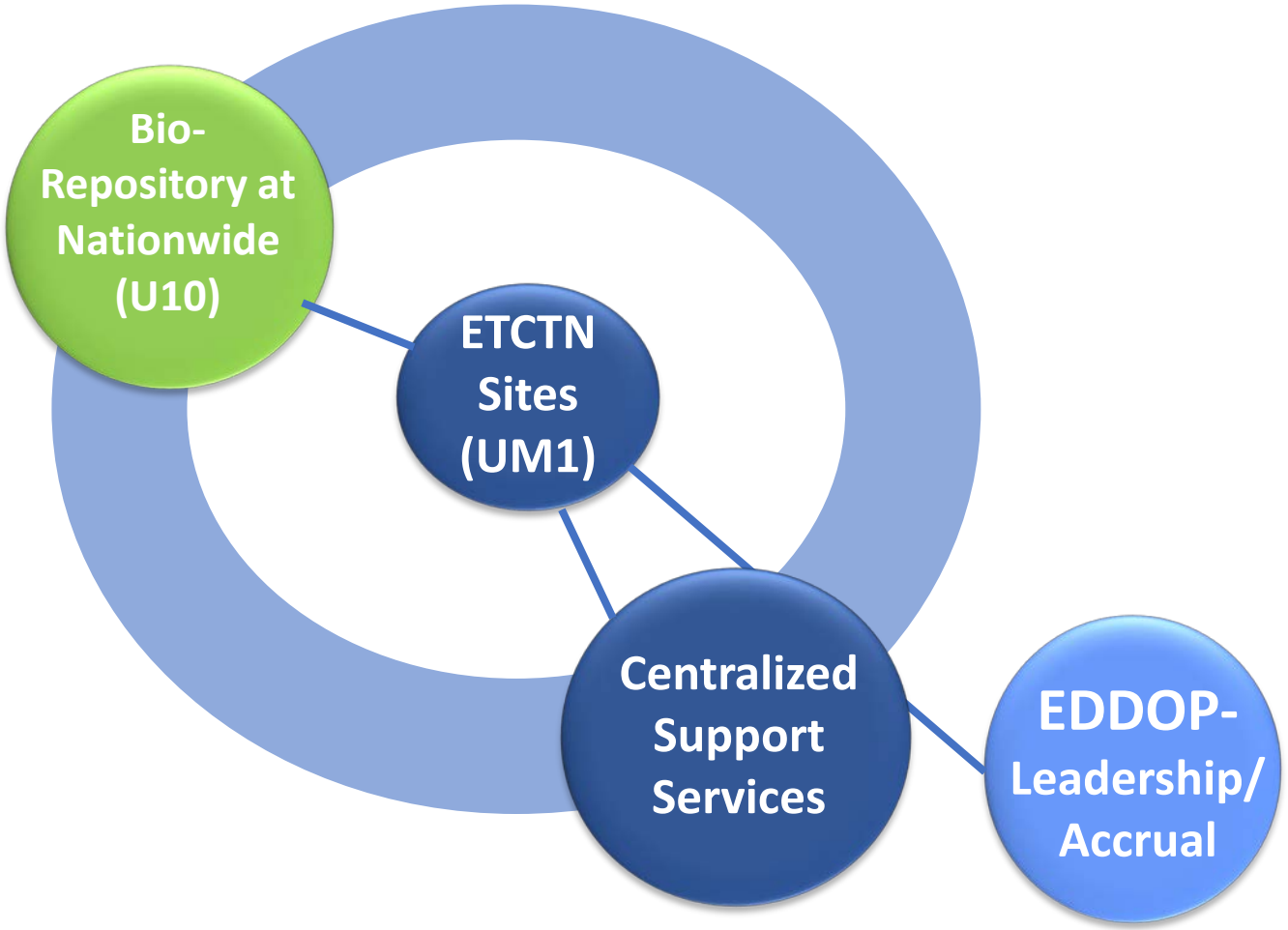
≈ 41 enrolling North American sites

UM1 network first renewal RFA/FOA

- **12** Lead Academic Organization (LAO) sites (includes NCI-Clinical Center)
- **29** Affiliated Organizations (AO) sites
- **2120** patients enrolled through Q4 2017

Clinical trials

- Activated studies: **82**
- Ongoing studies: **132**
- Closed studies: **37**
- Completed/Admin Completed studies:**11**



Goals and Objectives of Experimental Therapeutics Clinical Trials Network

Research, development and improvement of cancer treatments

- Advance the clinical development of NCI-IND agents with early phase studies
  - *Complementary collaboration with pharma partners*
- Determine dose, schedule and sequence for NCI-IND agents and combination regimens
- Perform disease-specific activity studies of NCI-IND-agents and combinations
  - *Prioritize cancers and cancer subsets where industry is not investing*

Biomarker and cancer biology-driven studies using patient derived specimens

- Acquire high quality patient tumor specimens for correlative studies
- Incorporate fit-for-purpose PD/biomarker assays into ETCTN trials

Career enhancement for early career investigators

- Experience leading clinical trials in the ETCTN
- Play a significant role on the drug development Project Teams

ETCTN – Transformation to a Network Structure

- **Collaborative approach to clinical trial development and implementation**
  - Moved from mass solicitations to **extramural project teams** early in clinical development planning
  - Involve **disease-specific clinical** expertise from all sites
  - Enhance **study participation** across the network

- **Assuring Reproducible Translational Science**
  - Transformed the approach to **biomarkers** from laboratory developed tests (**LDTs**) to analytically **validated, fit for purpose bioassays**

- **Site Re-Organization and Infrastructure Support**
  - Moved from siloed sites to a **unified trials network** with centralized infrastructure support
  - Further enhanced **GCP principles** in all aspects of ETCTN trials

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Evaluation of the Experimental Therapeutics Clinical Trials Network (ETCTN)

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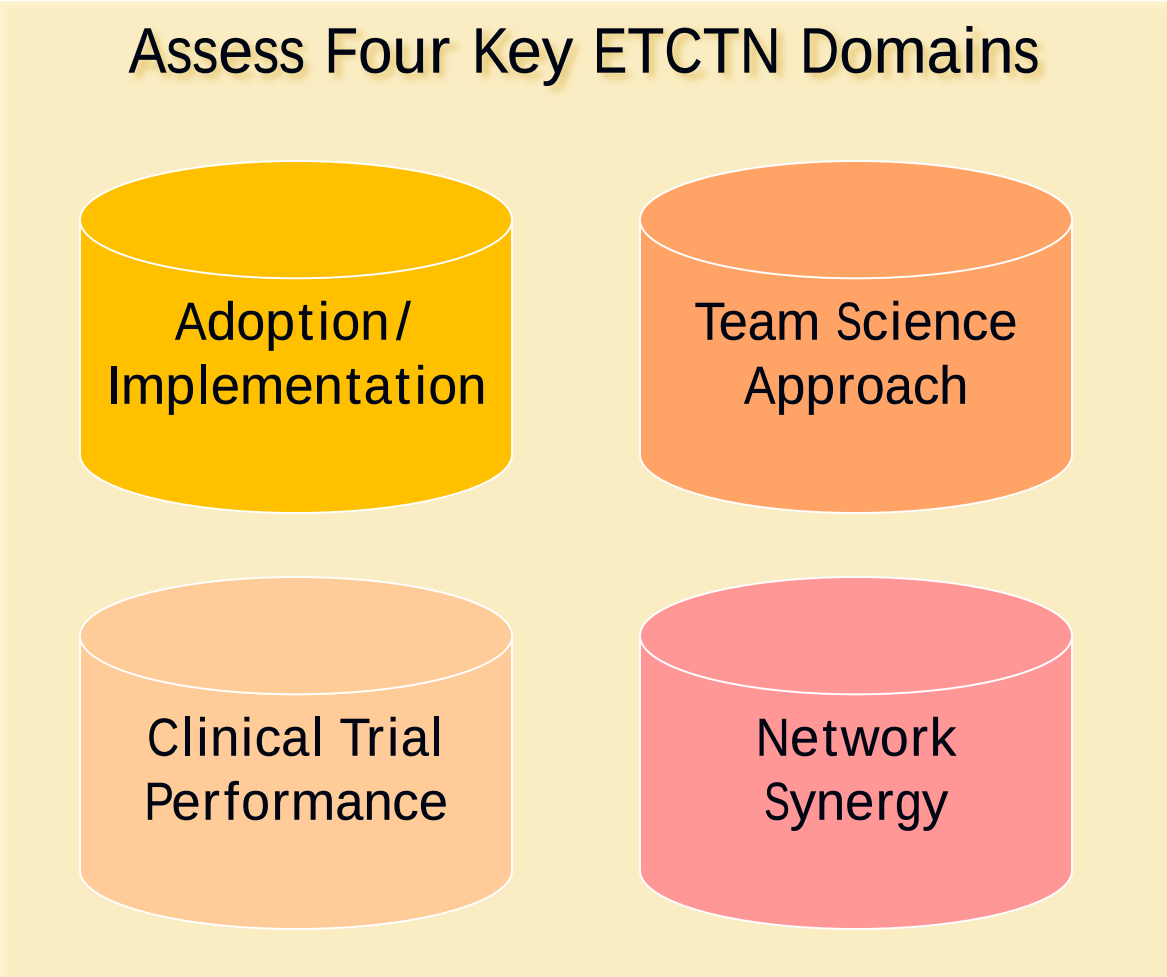
Grace Mishkin, MPH
Martha Krum, MS, RAC
Cancer Therapy Evaluation Program/NCI

36th meeting of the Clinical Trials and Translational Research Advisory Committee (CTAC), July 11, 2018

3-Year process evaluation of ETCTN

Goals:

1. Document ETCTN's implementation
2. Identify course corrections if needed
3. Provide data to guide decision making for program's subsequent funding cycle



Survey

Online survey to assess:

- Satisfaction with ETCTN processes, resources and portfolio
- Team approach and interaction among network

- Investigator Sample:
  - LAO Grant PIs & Investigators who directly participated in ETCTN to date
  - Surveys administered the month after grant year ended (Years 1-3)

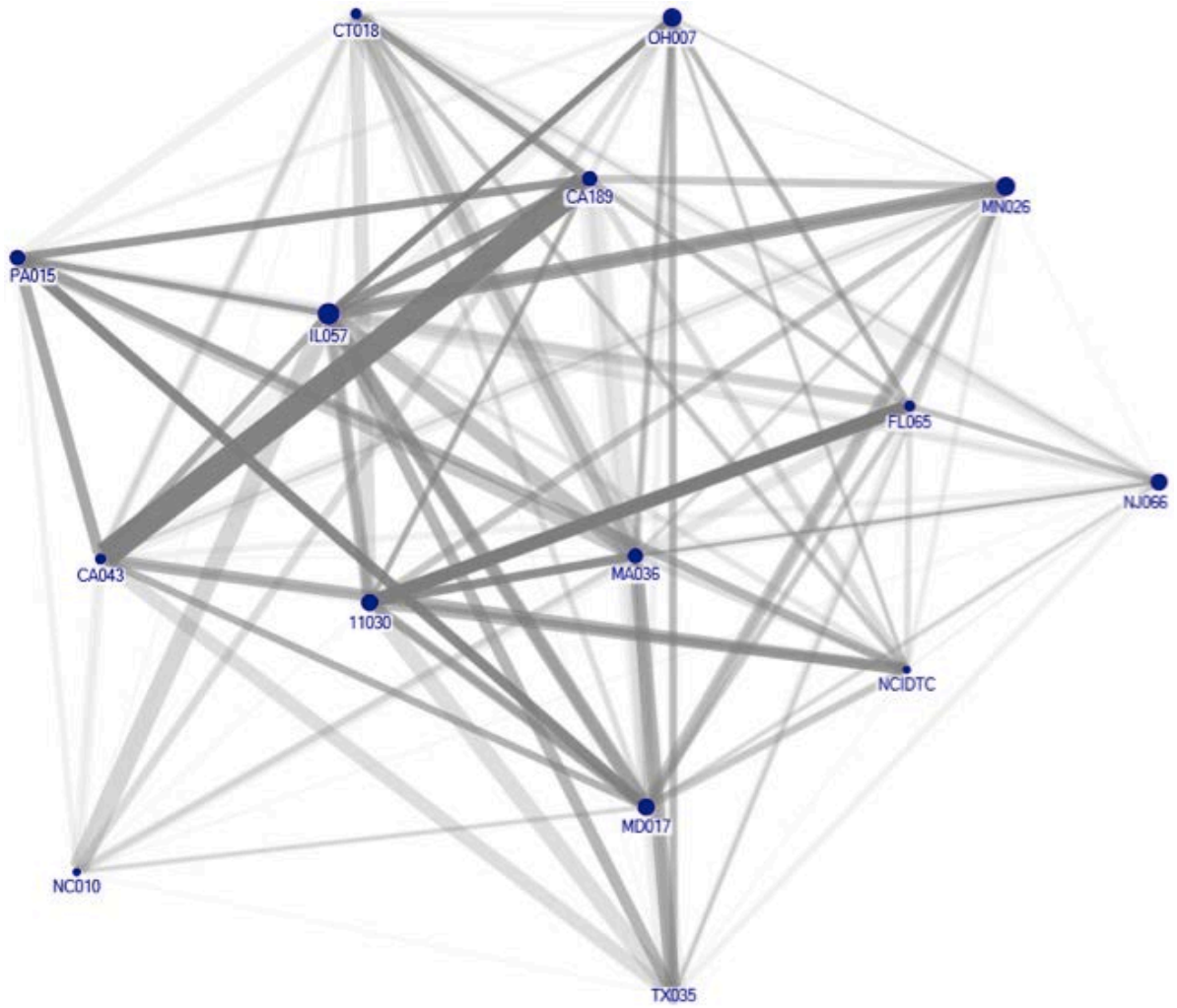
Investigators	Invited (N)	Completed (N)	Response rate (%)
Year 1	129	105	81.4
Year 2	154	152	98.7
Year 3	185	171[a]	92.4

ETCTN as a Network

A well-connected network from the beginning

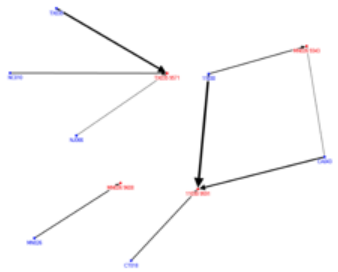
Year 1

Network metric	Value
Number of organizations	15
Number of total ties	313
Average degree centrality	12.7
Network density	90.5%
Transitivity	75.7%

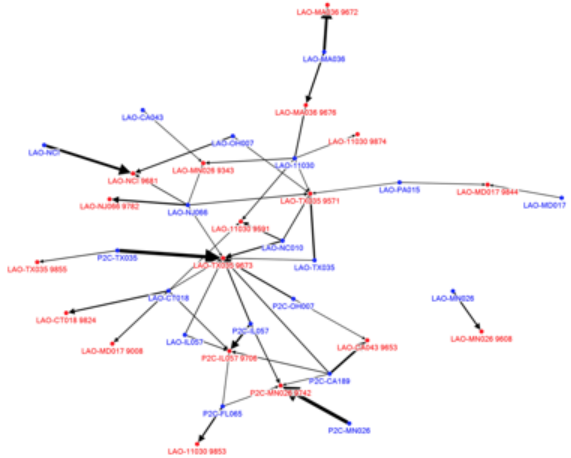


Accrual Network: Year 1 to Year 4

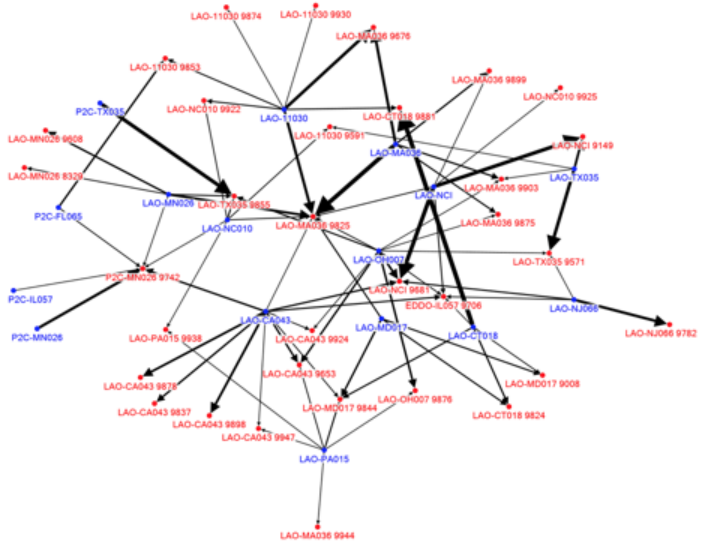
Year 1



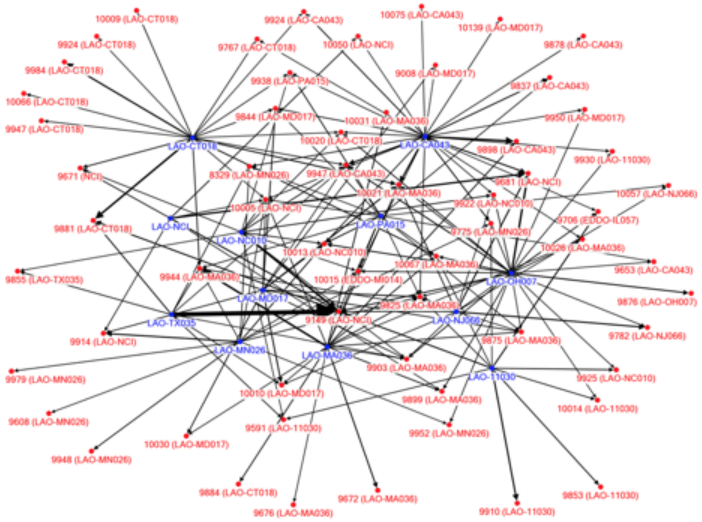
Year 2



Year 3

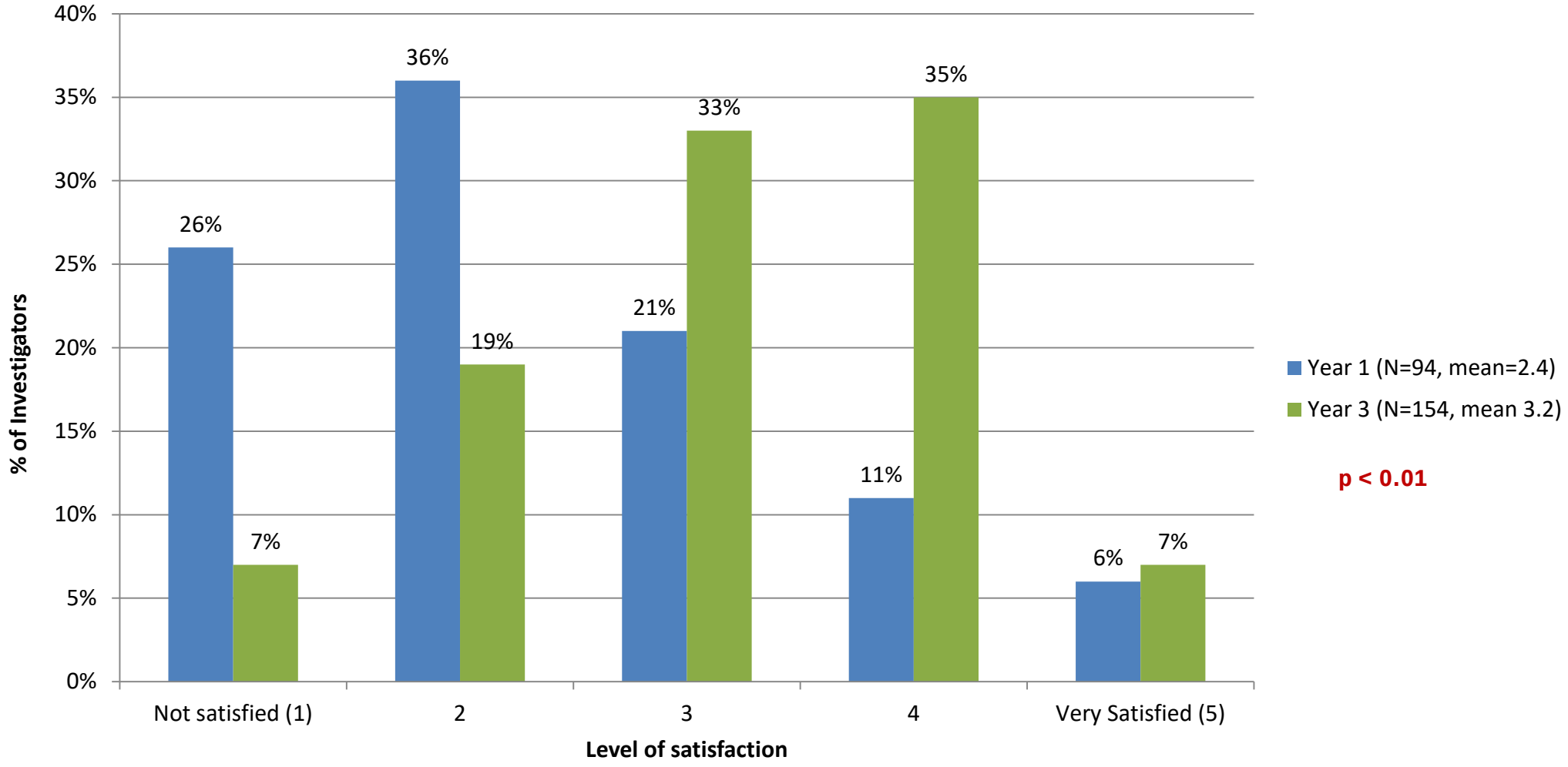


Year 4

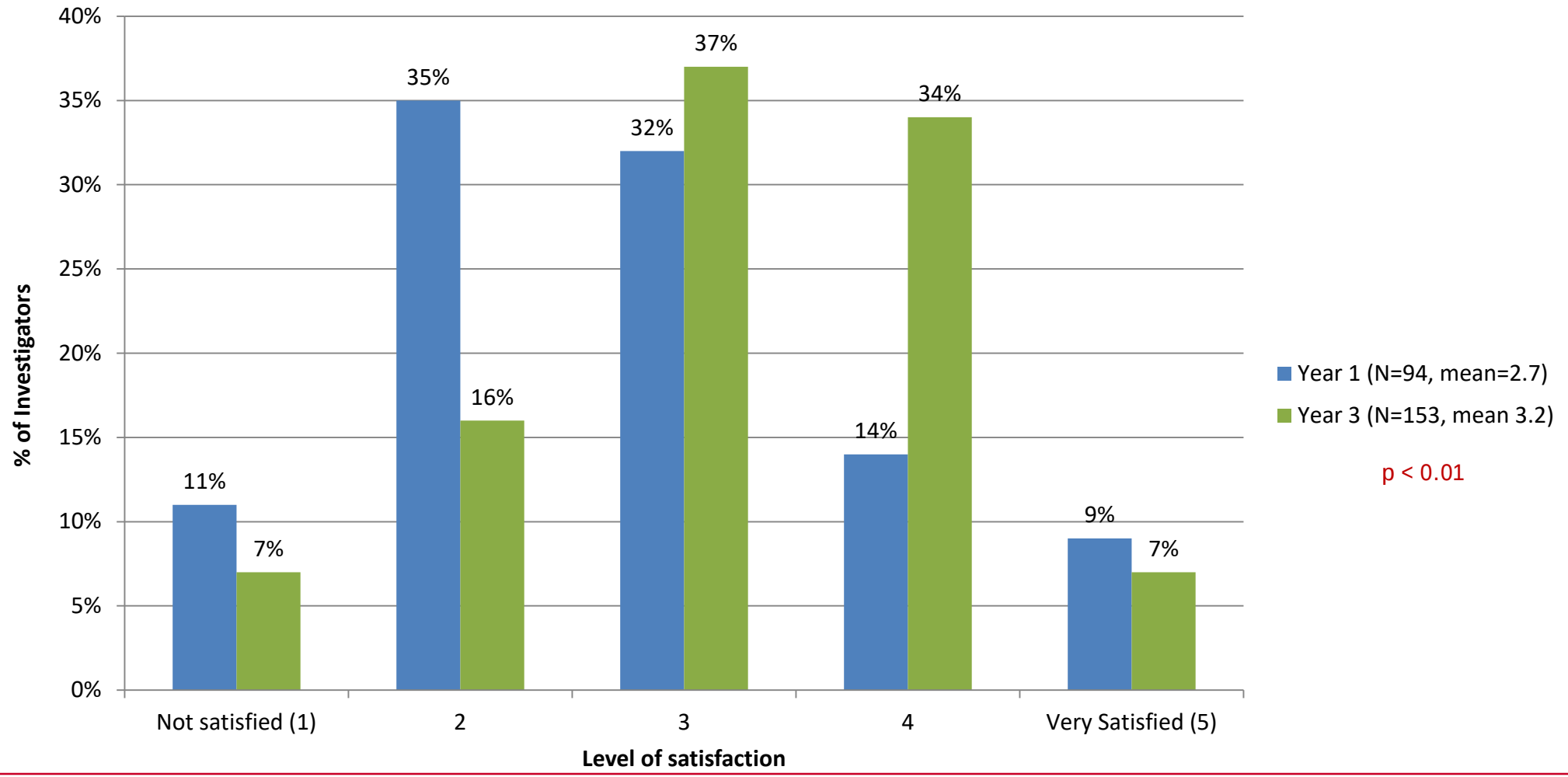


Investigator Satisfaction with Science

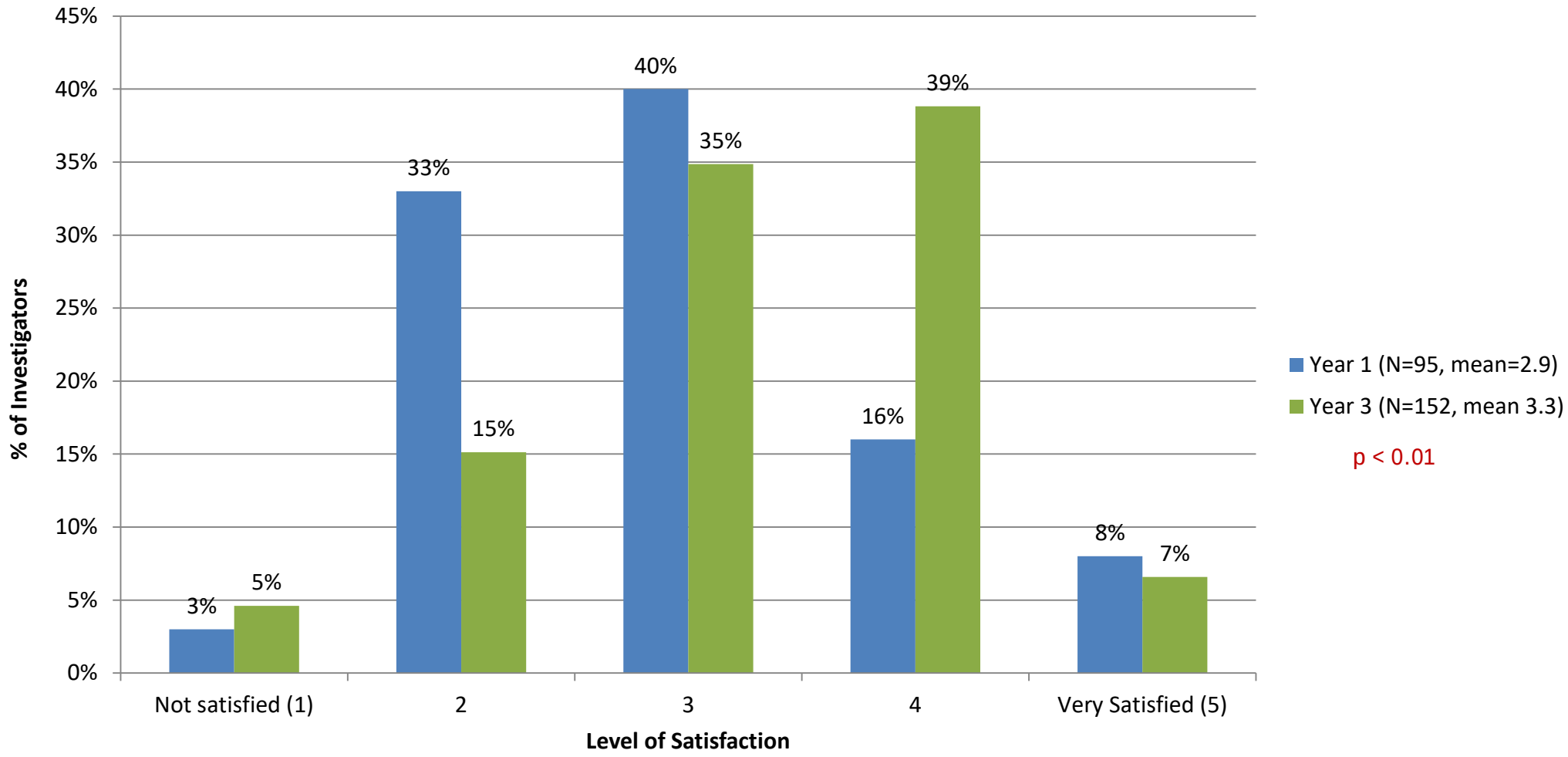
Satisfaction with # of trials in ETCTN portfolio—Year 1 vs. 3



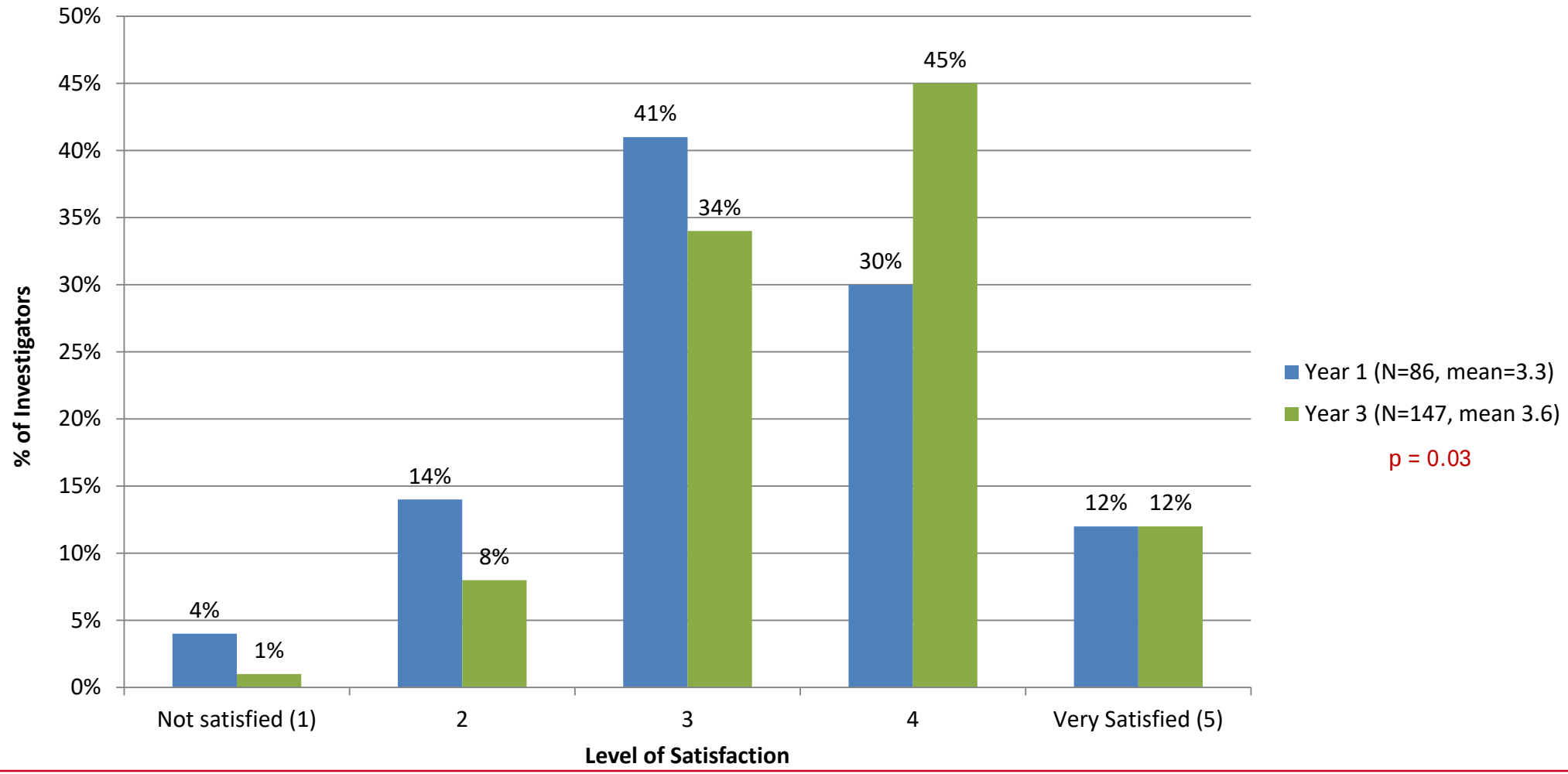
Satisfaction with therapeutic classes in portfolio—Year 1 vs. 3



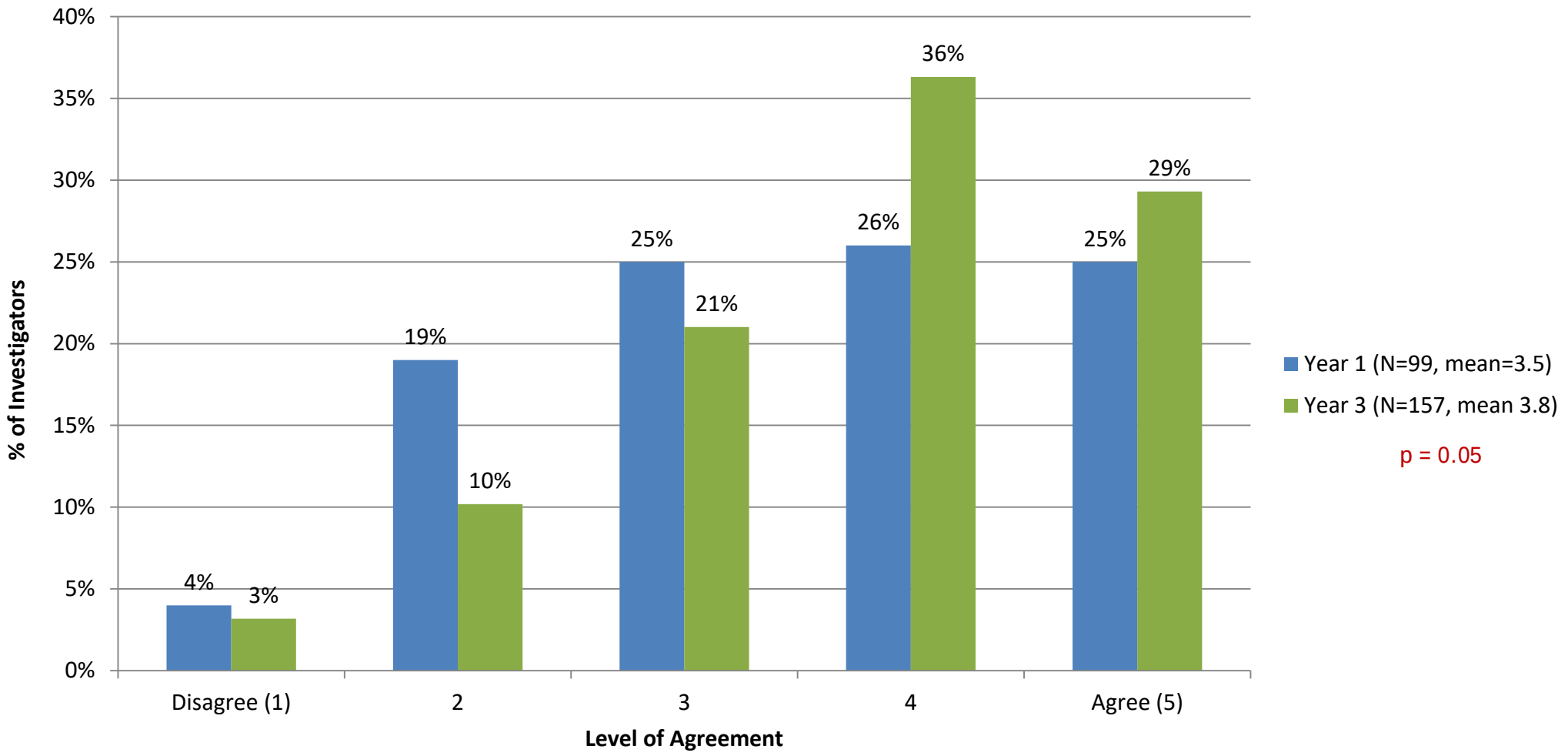
Satisfaction with scientific balance of portfolio—Year 1 vs. 3



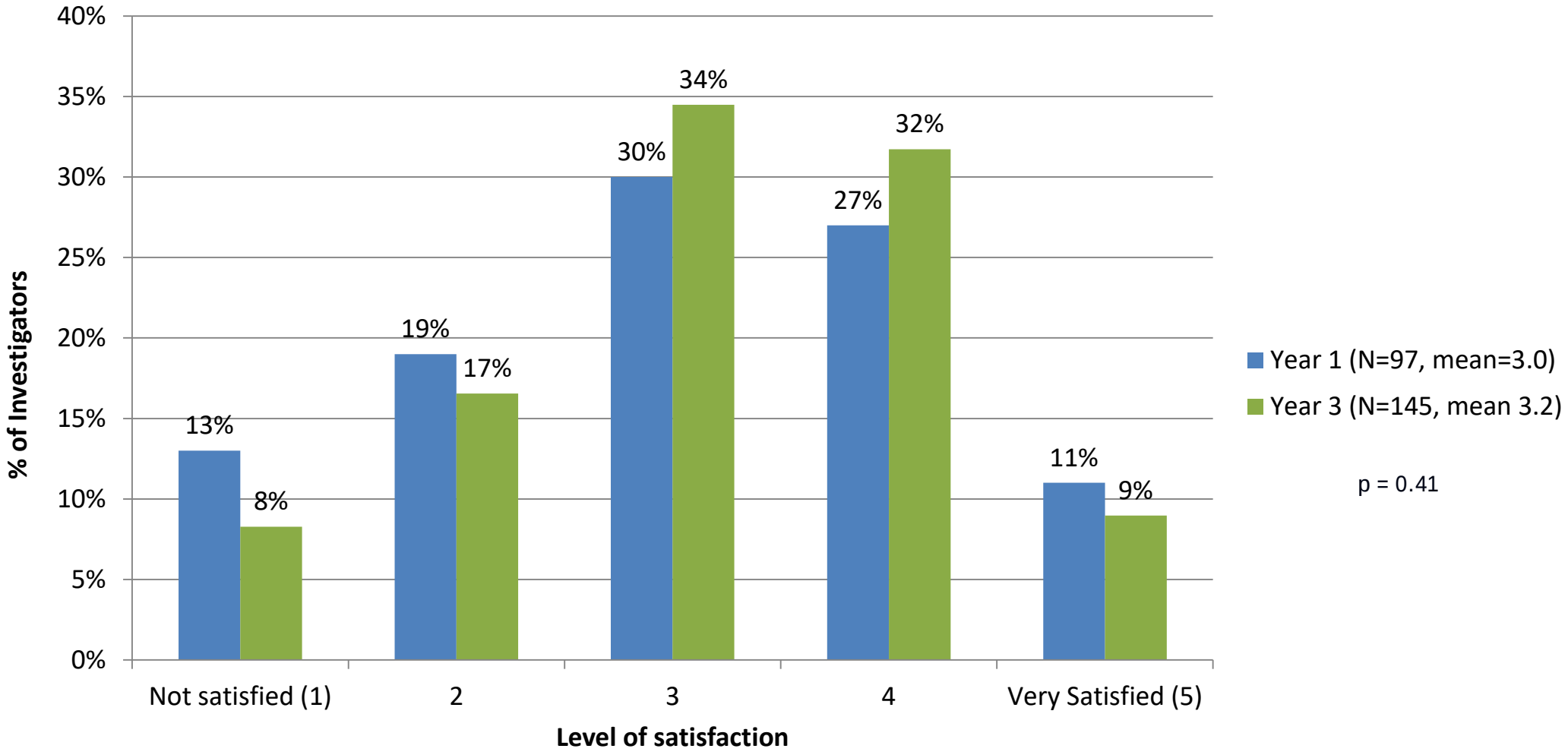
Satisfaction with integration of preclinical findings—Year 1 vs. 3



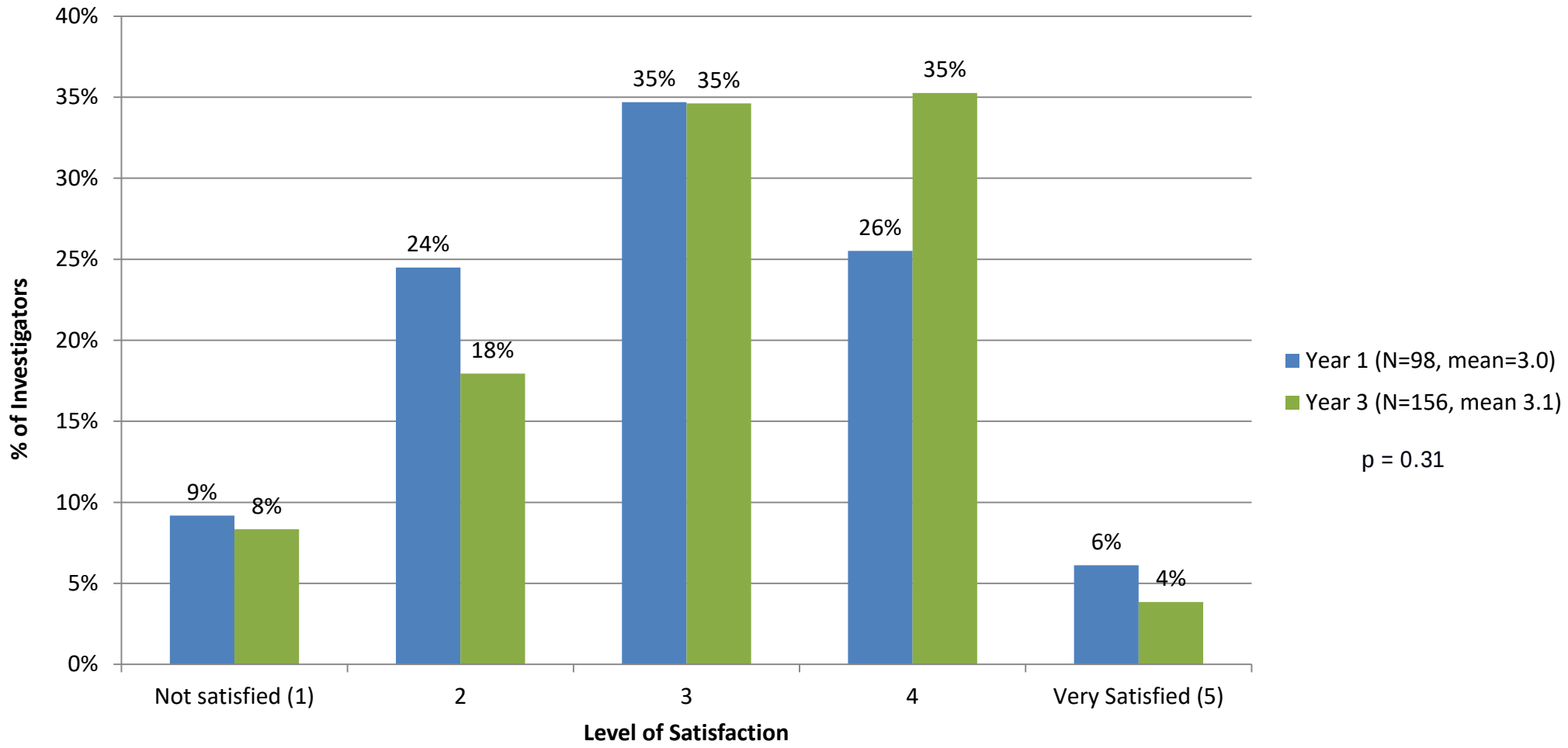
ETCTN opens opportunities for junior PIs—Year 1 vs. 3



Satisfaction with # of drugs available for LOIs—Year 1 vs. 3



Overall satisfaction with ETCTN portfolio—Year 1 vs. 3



Grant PI interviews (January, 2017)

- 60 minute phone interviews with ETCTN Grant PIs from each LAO
  - Emphasis on recommendations to improve ETCTN system
    - What are the greatest challenges to trial activation and accrual within your LAO?
    - What can be done to improve the process?

Grant PI key concerns and changes made

1. No incentive to lead trials (as have to give slots away to other LAOs) & it requires a lot of resources to activate niche trials.

   Change: CTEP now provide incentives for sites (via accrual credits) to lead new ETCTN studies as well as activate others' studies.

2. Sites need more information sooner to determine disease-specific interest in trial and make decisions around portfolio planning.

   Changes:

   - Created user-friendly email newsletters sent monthly to all ETCTN PIs based on their disease specialty: active trials & changes, protocols soon to active, and protocols in development)
   - Developed online, interactive flowcharts of ETCTN trials by disease
   - Now provide one-page Physician-Fact sheets for each trial upon activation (summarizes key trial information and is posted on CTSU)

Grant PI key concerns and changes made

3. Once a protocol is activated it still takes enormous time to “build” it into a Center’s Electronic Health Record (EHR) system.

   Change: CTEP is piloting the use of Excel spreadsheets to provide necessary information that can be used as the basis for EHR builds for newly activated protocols.

4. Catch 22 with ETCTN trials: Many are niche trials yet these are hard to sell to their leadership (pressure to not open and/or close as “not performing” with only 1-2 accruals).

   Changes:

   - Now seek out site champions for challenging trials early on (with potential for authorship)
   - CTEP leadership is working with NCI-CC Program to engage Cancer Centers’ directors more directly in UM1 grant activity

Grant PI key concerns and changes made

5. OEWG timeline takes too long to activate ETCTN trials. Specifically:
   - Both the LOI and Protocol development processes are seen as inefficient and frustrating
   - CIRB review results in numerous changes that take a lot of time to address
   - There is no consistency in when a protocol will be activated and therefore it's difficult to build into their Centers' planning process and/or prioritize

   Changes:

   - CTEP now provides centralized contract support to author all ETCTN approved LOIs
     - Increases quality of writing & reduces time (60 day limit)
   - Now limit number of protocol reviews to two revisions prior to CIRB
   - Removed "Recommendations" from Consensus Reviews and only send PI required changes
   - In process: Developing CTEP checklists and reviewing biomarker processes to improve efficiencies

In summary…

- ETCTN is a highly connected network, professionally and with trial accrual
  - Provides opportunities for junior PIs to advance careers
- ETCTN investigators are supportive of the network's scientific portfolio:
  - # trials, balance of portfolio and therapeutic classes, & integration of pre-clinical findings
  - However, satisfaction with # of available drugs and overall portfolio remains stagnant
- CTEP has identified and is addressing key process challenges:
  - Provide accrual incentives to lead new ETCTN studies and activate others'
  - Created numerous venues to increase awareness and educate PIs about ETCTN pipeline
  - Seek out site champions for challenging trials
  - Targeting key OEWG barriers to reduce activation timelines w/o compromising science

Many thanks to many people!

- Grant PIs for your continued support of our efforts
- Research teams for all your hard work and great input
- NCI Leadership for your openness and receptivity to the data, both hearing and acting on the findings
- NCI colleagues who work very hard to keep the systems running smoothly
  - Martha Krum, MS, RAC, Deputy Program Manager, Protocol and Information Office (PIO)
- NCI contractors for your dedicated work
  - Westat
  - Emmes
  - Theradex

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