

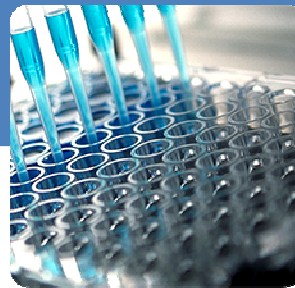


September 19, 2013

Tanya Antonille

ITN TrialShare

Advancing clinical trial transparency through data sharing



INNOVATION • COLLABORATION

ITN Mission Statement

Our Mission

is to advance the clinical application of immune tolerance by performing high quality clinical trials of emerging therapeutics integrated with mechanism-based research.

In particular, we aim to:

- establish new tolerance therapeutics
- develop a better understanding of the mechanisms of immune function and disease pathogenesis
- Identify new biomarkers of tolerance and disease

Our Purpose

is to achieve immune tolerance to prevent and cure human disease.



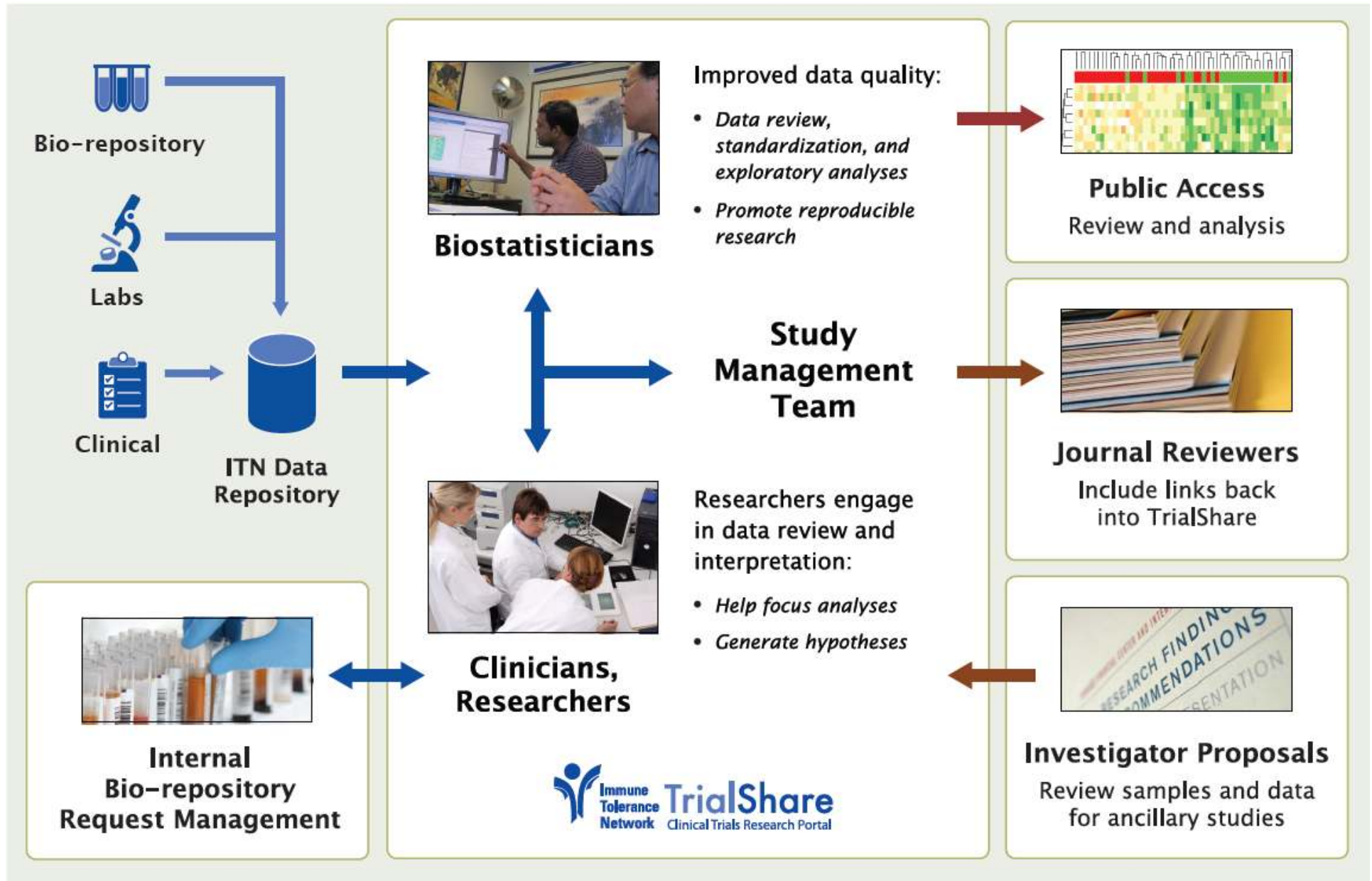
ITN TrialShare History & Mission

- **2011 LabKey Selection, Requirements, Prototype**
- **2012 Beta Testing**
- **2013 Public Launch**


The primary goal of ITN TrialShare is to speed translational research through better data integration and presentation allowing ITN researchers and domain experts to more easily access research results and collaborate to generate scientific insights.

Internal Facing

External Facing



Public Facing Site

**TrialShare**
Clinical Trials Research Portal

INNOVATION • COLLABORATION
A clinical research consortium funded by NIAID

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Highlights

Welcome

Getting Started

Highlights

Study Catalog

Welcome trialsharedemo

Using ITN TrialShare, you can review ITN data, analyses and sample repository information for ITN studies as well as request samples from closed studies for independent investigation.

The study navigation tree on the right shows ITN studies with data available based on your access credentials. There are currently 10 studies with data accessible to the general public.

Recent Highlights

The data and figures for the manuscript *Efficacy of Remission-Induction Regimens for ANCA-Associated Vasculitis (NEJM, 2013)* are now available.

The NEW ENGLAND JOURNAL of MEDICINE

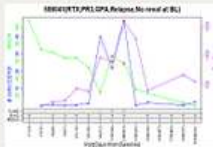
ORIGINAL ARTICLE

Efficacy of Remission-Induction Regimens for ANCA-Associated Vasculitis

Ulrich Specks, M.D., Peter A. Merkel, M.D., M.P.H., Philip Seo, M.D., Robert Spiera, M.D., Carol A. Langford, M.D., M.H.S., Gary S. Hoffman, M.D., Cees G.M. Kallenberg, M.D., Ph.D., E. William St. Clair, M.D., Barri J. Fessler, M.D., Linna Ding, M.D., Ph.D., Lisa Viviano, R.N., Nadia K. Tchao, M.D., Deborah J. Phippard, Ph.D., Adam L. Asare, Ph.D., Noha Lim, Ph.D., David Ikle, Ph.D., Brett Jepson, M.S., Paul Brunetta, M.D., Nancy B. Allen, M.D., Fernando C. Fervenza, M.D., Ph.D., Duvuru Geetha, M.D., Karina Keogh, M.B., B.Ch., Eugene Y. Kissin, M.D., Paul A. Monach, M.D., Ph.D., Tobias Peikert, M.D., Coen Stegeman, M.D., Ph.D., Steven R. Ytterberg, M.D., Mark Mueller, B.S., C.C.R.P., Lourdes P. Sejismundo, R.N., Kathleen Mieras, C.C.R.P., and John H. Stone, M.D., M.P.H., for the RAVE-ITN Research Group*

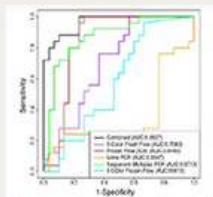
RAVE Participant Data

Participant level data views show relationships among flare events, ANCA, B-Cell, T-cell, BVAS, and prednisone levels.



FACTOR Interactive Analysis Reports and Tools

Multi assay predictive modeling of biomarkers: an enhanced interactive R report.



ROC			
	Number	Area	Standard Error
Control (n=10)	21	0.8076	
Test (n=10)	4	0.8076	

View Studies

- Transplant
 - WISP-R ITN029ST Public
 - FACTOR ITN507ST Public
- Autoimmune
 - RAVE ITN021AI Public
 - STAYCIS ITN020AI Public
 - Diamond-Wofsy ITN002AI Public
 - Khoury ITN006AI Public
- Type I Diabetes
 - IL2-RAPA ITN018AI Public
 - AbATE ITN027AI Public
 - Shapiro ITN005CT Public
 - Orban ITN012AI Public
- Allergy
 - Casale ITN019AD Public
- Specimen Only Studies
 - PART ITN011AI Public
 - Herold ITN007AI Public
 - Herold II ITN017AI Public
 - GAMBIT ITN503ST Public
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Internal Facing – Operational Studies

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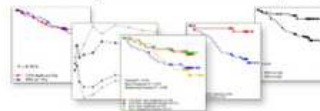
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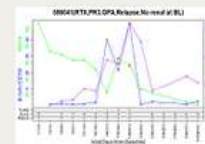
Ulrich Specks, M.D., Peter A. Merkel, M.D., M.P.H., Philip Seo, M.D., Robert Spiera, M.D., Carol A. Langford, M.D., M.H.S., Gary S. Hoffman, M.D., Cees G.M. Kallenberg, M.D., Ph.D., E. William St. Clair, M.D., Barri J. Fessler, M.D., Linna Ding, M.D., Ph.D., Lisa Viviano, R.N., Nadia K. Tchao, M.D., Deborah J. Phippard, Ph.D., Adam L. Asare, Ph.D., Noha Lim, Ph.D., David Ikle, Ph.D., Brett Jepson, M.S., Paul Brunetta, M.D., Nancy B. Allen, M.D., Fernando C. Fervenza, M.D., Ph.D., Duvuru Geetha, M.D., Karina Keogh, M.B., B.Ch., Eugene Y. Kissin, M.D., Paul A. Monach, M.D., Ph.D., Tobias Peikert, M.D., Coen Stegeman, M.D., Ph.D., Steven R. Ytterberg, M.D., Mark Mueller, B.S., C.C.R.P., Lourdes P. Sejismundo, R.N., Kathleen Mieras, C.C.R.P., and John H. Stone, M.D., M.P.H., for the RAVE-ITN Research Group[☆]

Click here to go to the manuscript figures



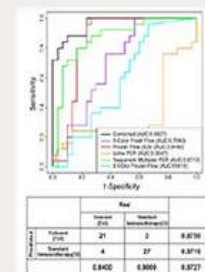
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View Studies

Transplant

- WISP-R ITN029ST Operational
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- AWISH ITN030ST Operational
- GAMBIT ITN503ST Riset Operational
- FACTOR ITN507ST Operational
- FACTOR ITN507ST Public
- TILT ITN024ST Operational

Autoimmune

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- RAVE ITN021AI Public
- STAYCIS ITN020AI Operational
- STAYCIS ITN020AI Public
- Diamond-W ITN002AI Operational
- Diamond-Wofsy ITN002AI Public
- HALT-MS ITN033AI Operational
- HALT-MS ITN033AI Reviewer
- ACCESS ITN034AI Operational
- Khouri ITN006AI Operational
- Khouri ITN006AI Public

Type I Diabetes

- IL2-RAPA ITN018AI Operational
- IL2-RAPA ITN018AI Public
- AbATE ITN027AI Operational
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- Shapiro ITN005CT Operational
- Shapiro ITN005CT Public
- Orban ITN012AI Operational
- Orban ITN012AI Public
- START ITN028AI Operational
- START ITN028AI Public
- T1 DAL ITN045AI Operational

Allergy


- Casale ITN019AD Operational
- Casale ITN019AD Public
- LEAP ITN032AD Operational

Specimen Only Studies

Other Places

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Study View

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INNOVATION + COLLABORATION
A clinical research ecosystem funded by NIAID

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Casale ITN019AD: Allergen Immunotherapy Co-Administered with Omalizumab

OverviewData & ReportsParticipantsSpecimensSubmit ProposalsFiles

Study Overview

Efficacy and Safety Evaluation of Allergen Immunotherapy Co-Administered With Omalizumab, an Anti-IgE Monoclonal Antibody

Protocol Chair: Thomas B. Casale, M.D.

This Phase II double-blinded, parallel group, multi-center, placebo-controlled study examined whether pre-treatment of participants with Omalizumab followed by rush immunotherapy (RIT), followed by dual therapy with Omalizumab plus immunotherapy (IT) is safer and more effective in preventing symptoms in ragweed-induced seasonal allergic rhinitis (SAR) versus omalizumab alone, IT alone or placebo. Omalizumab (or placebo) was given every 2 or 4 weeks prior to RIT or placebo RIT. RIT was completed at least 3 weeks prior to the start of ragweed season. After RIT, participants received weekly maintenance ragweed IT or placebo IT, and omalizumab or placebo, every 2 or 4 weeks for 12 weeks. These 12 weeks began prior to the ragweed season, continued through the ragweed season, and for some participants, may extend beyond the ragweed season. A follow-up period examined whether persistent immunologic and clinical tolerance has been achieved.


Study Result


Omalizumab pretreatment enhances the safety of RIT (Ragweed immunotherapy) for ragweed allergic rhinitis. Furthermore, combined therapy with omalizumab and allergen immunotherapy may be an effective strategy to permit more rapid and higher doses of allergen immunotherapy to be given more safely and with greater efficacy to patients with allergic diseases.

Ragweed immunotherapy induced serum regulatory antibodies that partially blocked binding of allergen-IgE complexes to B cells. Additional treatment with anti-IgE, by directly blocking IgE binding to CD23, completely inhibited allergen-IgE binding.



Cohort	Description
Omalizumab/Ragweed	Omalizumab pre-treatment, ragweed RIT, omalizumab + ragweed IT
Omalizumab/Placebo	Omalizumab pre-treatment, placebo RIT, omalizumab + placebo IT
Placebo/Ragweed	Placebo omalizumab pre-treatment, ragweed RIT, placebo omalizumab + ragweed IT
Placebo/Placebo	Placebo omalizumab pre-treatment, placebo RIT, placebo omalizumab + placebo IT

ClinicalTrials.gov #: NCT00078105

 Study Protocol Synopsis


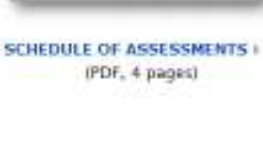


STUDY NAVIGATOR




SCHEDULE OF ASSESSMENTS

(PDF, 4 pages)




TRIAL SCHEME




View Studies

- Transplant
- Autoimmune
- Type 1 Diabetes
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Shortcuts

Reports



Data & Reports

Data Reports

Name	Type	Details	Status	Modified	Author
Interactive Analysis Reports and Tools					
Biomarker Multi Assay Predictive Modeling	Link Re...			2012-10-19	Noha Lim
Manuscript Figures – JCI 2010, B-Cell Signature					
fig1: Hierarchical clustering heatmap of 31 differentially expressed genes (from Microarray data)	R View			2012-11-03	Zhong Gao
fig2: Real-time PCR gene expression analyses of urine sedimentary cells	R View			2012-10-29	Zhong Gao
fig3: Hierarchical clustering heatmap of 31 differentially expressed genes (from Sequenom data)					
fig4: Transcripts that best distinguish TOL from SI					
fig5: Box plots of log2 normalized mRNA copy numbers for the 3 genes					
fig6: 5-color flow cytometry of whole blood samples shows different numbers of B cell subsets					
fig7: 9-color flow cytometry of frozen PBMCs					
fig8: Intracellular cytokine staining of sorted B cells					
Peripheral Blood Gene Expression – PCR					
Multiplex PCR Periph Blood IGKV4-13					
Multiplex PCR Peripheral Blood IGKV4-1					
Multiplex PCR Peripheral Blood IGL1					

fig2: Real-time PCR gene expression analyses of urine sedimentary cells

Source: Manuscript Figures – JCI 2010, B-Cell Signature

Created By: Michael Stahly

Author: Zhong Gao

Type: R View

Status: Final

https://www.itntrialshare.org/study-reports/Studies/ITN507STPUBLIC/Study Data/runRReport.view?Dataset.reportId=db:400

Pathology image data

Screenshot of the TrialShare website showing pathology image data for a participant.

The browser address bar shows the URL: https://www.itntrialshare.org/study/Studies/ITN0295TPUBLIC/Study%20Data/participant/view?participantId=WISPR_149406

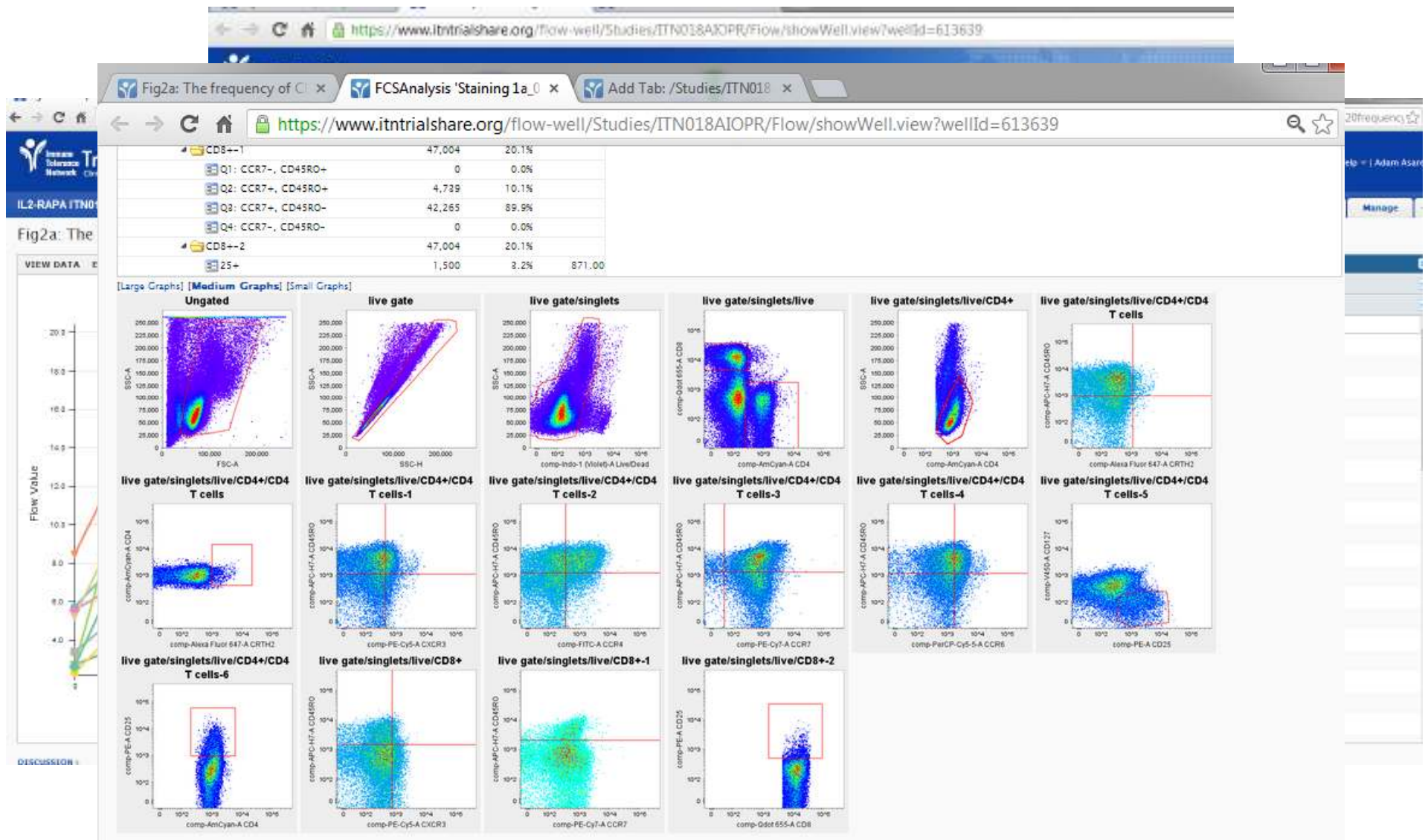
The TrialShare logo and navigation bar are visible at the top. The study title is "WISPR-ITN0295T: Immunosuppression Withdrawal for Pediatric Liver Recipients".

The participant ID is "Participant - WISPR_149406".

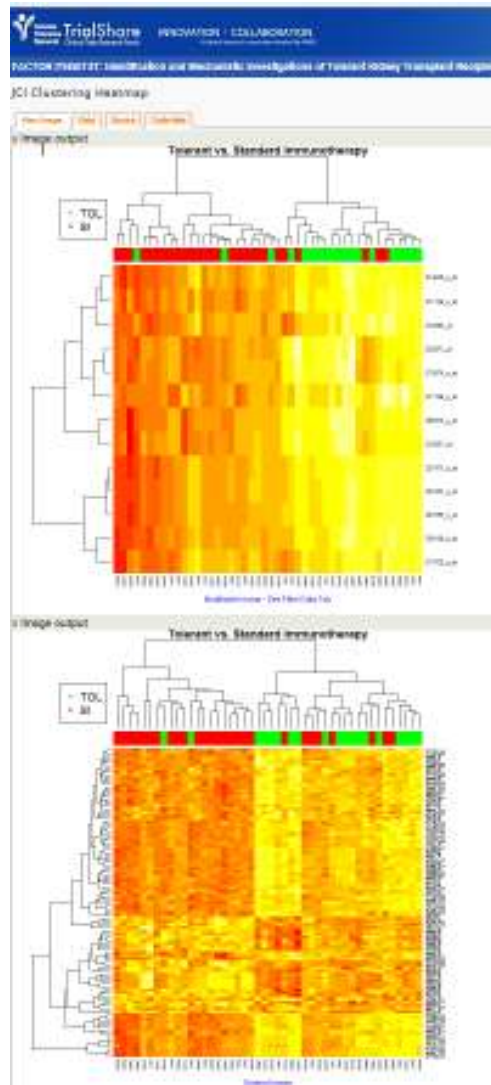
The "Pathology Reports" section is highlighted, showing a large histological image of liver tissue. The image displays a dense field of hepatocytes with prominent nuclei and surrounding connective tissue. A small inset image in the top left corner of the main image shows a green line, likely a scale bar or a reference marker.

The left sidebar contains navigation tabs: "DEMOGRAPHICS DATA", "TIMELINE", and "PATHOLOGY".

Flow Gating data



Manuscript figures with data and analysis code

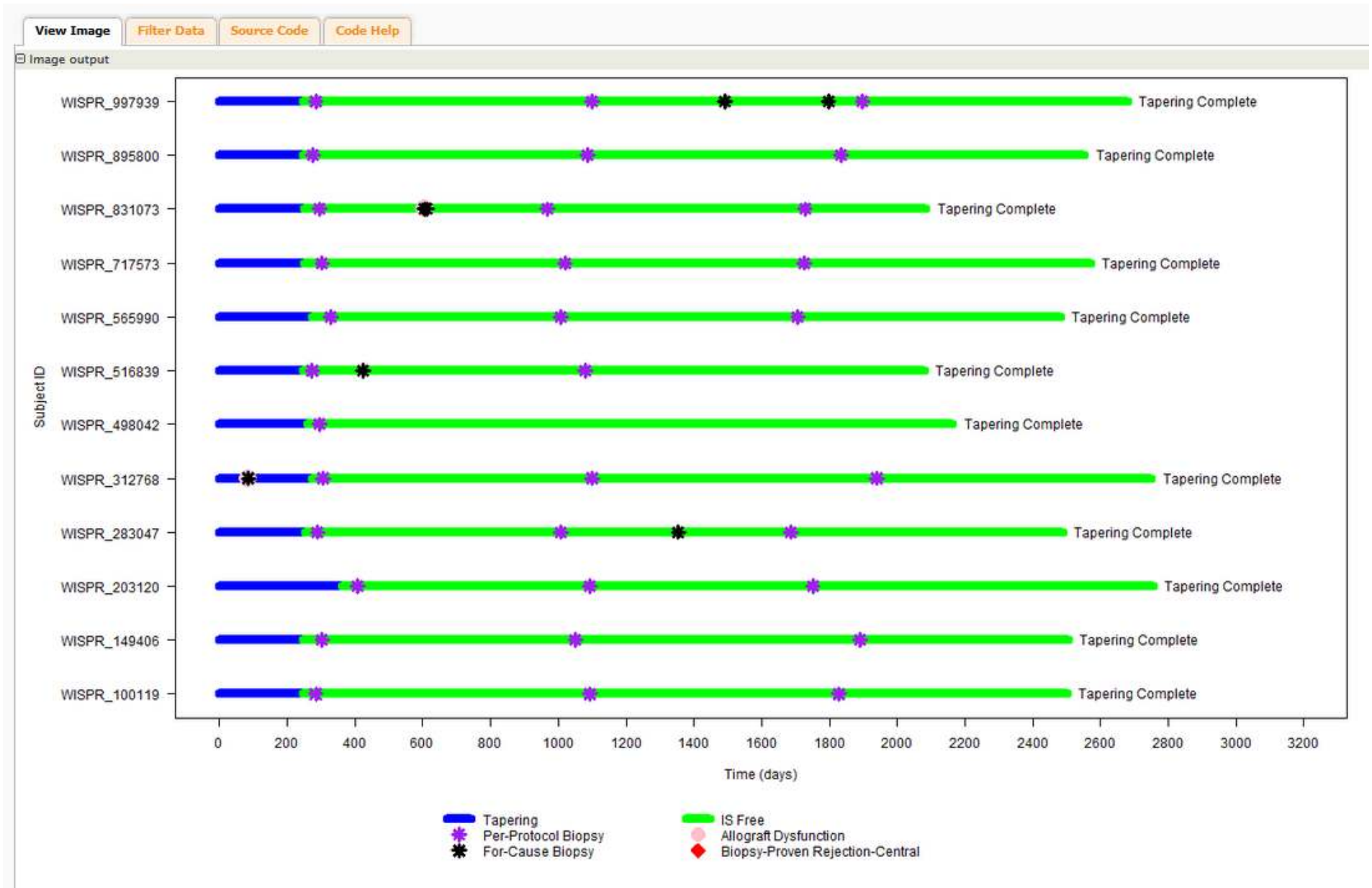


*Original
Analysis*

User-defined Filters

[illegible]

Custom R Plots



Custom R Plots



Towards a new paradigm in research publishing

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Efficacy of Remission-Induction Regimens for ANCA-Associated Vasculitis

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ABSTRACT

BACKGROUND

The 18-month efficacy of a single course of rituximab as compared with conventional immunosuppression with cyclophosphamide followed by azathioprine in patients with severe (organ-threatening) antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis is unknown.

FOR ANCA-ASSOCIATED VASCULITIS

by means of a Poisson regression model. Time-to-event comparisons were performed with the use of a log-rank test. Descriptive statistics were generated for analyses of time to event and were tested with the use of the Wilcoxon rank-sum test. Data sets for these analyses are accessible through TrialShare, a public Web site that was developed and is managed by the Immune Tolerance Network (<https://trialshare.org/trave.html>). Further details about TrialShare and the methods of the censoring and imputation of data and adjustments of the analysis for specific variables are provided in the Supplementary Appendix.

RESULTS

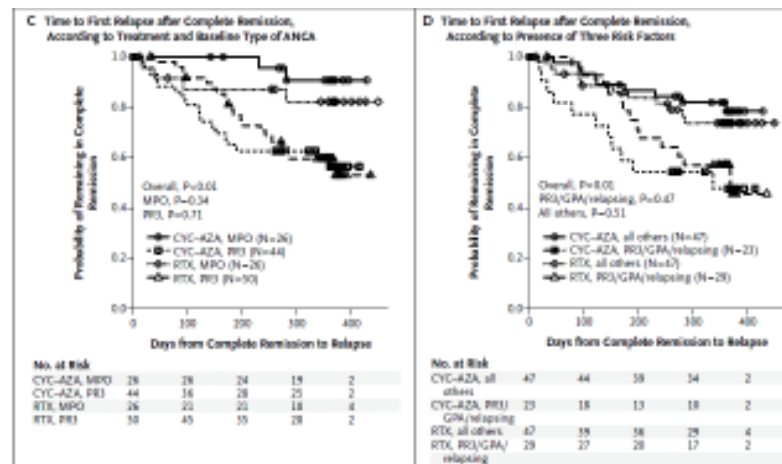


Figure 2. Kaplan-Meier Plots of the Risk of Disease Relapse after Complete Remission.

Panel A shows the time to the first disease relapse after complete remission according to treatment group (rituximab [RITX] or cyclophosphamide-azathioprine [CYC-AZA]). Panel B shows the time to the first disease relapse after complete remission according to baseline type of antineutrophil cytoplasmic antibody (ANCA) (perinuclear 3-ANCA [PR3] or myeloperoxidase-ANCA [MPO]). Panel C shows the time to the first disease relapse after complete remission according to baseline type of ANCA in each treatment group. Panel D shows the time to the first disease relapse after complete remission among patients with a diagnosis of granulomatosis with polyangiitis (GPA) who were also positive for perinuclear 3-ANCA and had a severe relapse at baseline, as compared with all other patients in each treatment group. In Panels C and D, the overall P values are for the comparison of the four patient groups, whereas the other P values are for the comparisons between the two treatment groups within each defined patient subgroup. For additional details, see www.trialshare.org/RAVEITNmonfig7.html.



Simplified navigation and filters

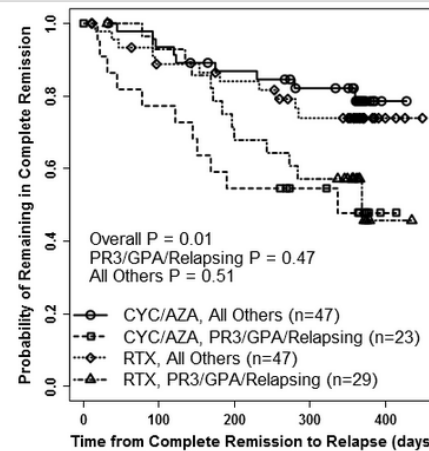
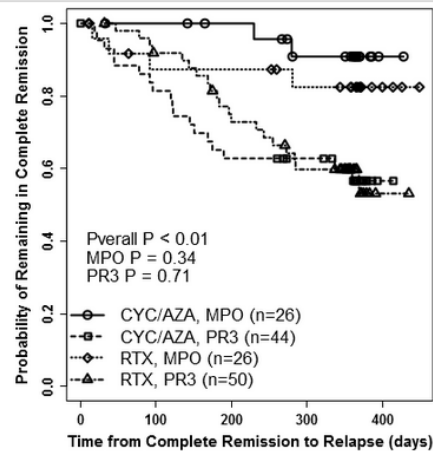
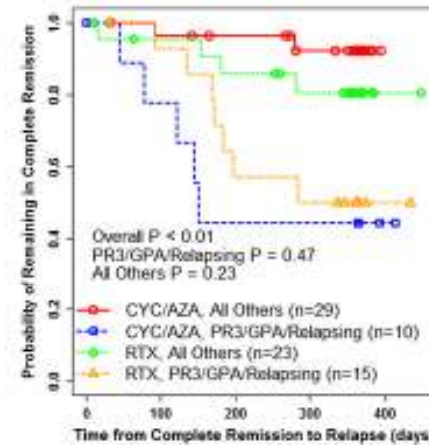
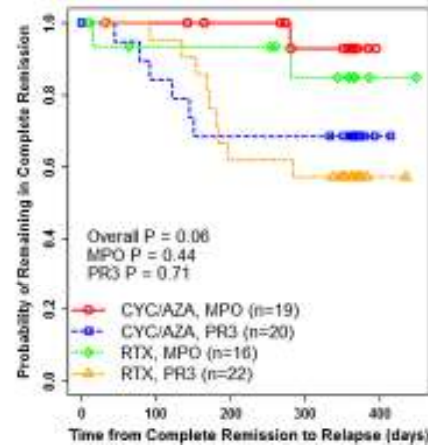
Figure 2

Options

New Diagnosis at Enrollment: ☒ All ☐ Yes ☐ No

Major Renal Involvement at Baseline: ☐ All ☒ Yes ☐ No

APPLY



CYC/AZA, MPO
CYC/AZA, PR3
RTX, MPO
RTX, PR3

Time from Complete Remission to Relapse (days)	26	26	24	19	2
26	26	24	19	2	
44	36	28	25	2	
26	21	21	18	4	
50	45	35	28	2	

Number at risk

CYC/AZA, All Others
CYC/AZA, PR3/GPA/Relapsing
RTX, All Others
RTX, PR3/GPA/Relapsing

Time from Complete Remission to Relapse (days)	47	44	39	34	2
47	47	44	39	34	2
23	18	13	10	2	
47	47	39	36	29	4
29	27	20	17	2	

Number at risk

Benefits Realized

- **Higher quality operational and mechanistic data**
 - Data exercise
 - Data visibility/accessibility
- **Manuscript development**
 - Rapid review of data and analysis approaches by study team internally for manuscript development
- **Public resource for reference datasets and analysis approaches**
 - Published and negative data
 - Data pulled directly to NIAID repository of record

Lessons Learned

- **Systems ≠ data management**

- Better systems raise expectations for timeliness, transparency, data quality
- New systems require additional data cleaning and reconciliation

- **Open source ≠ free**

- Requires investment in resources (IT*, staff)
- Substantial effort in maintaining, configuring and customizing

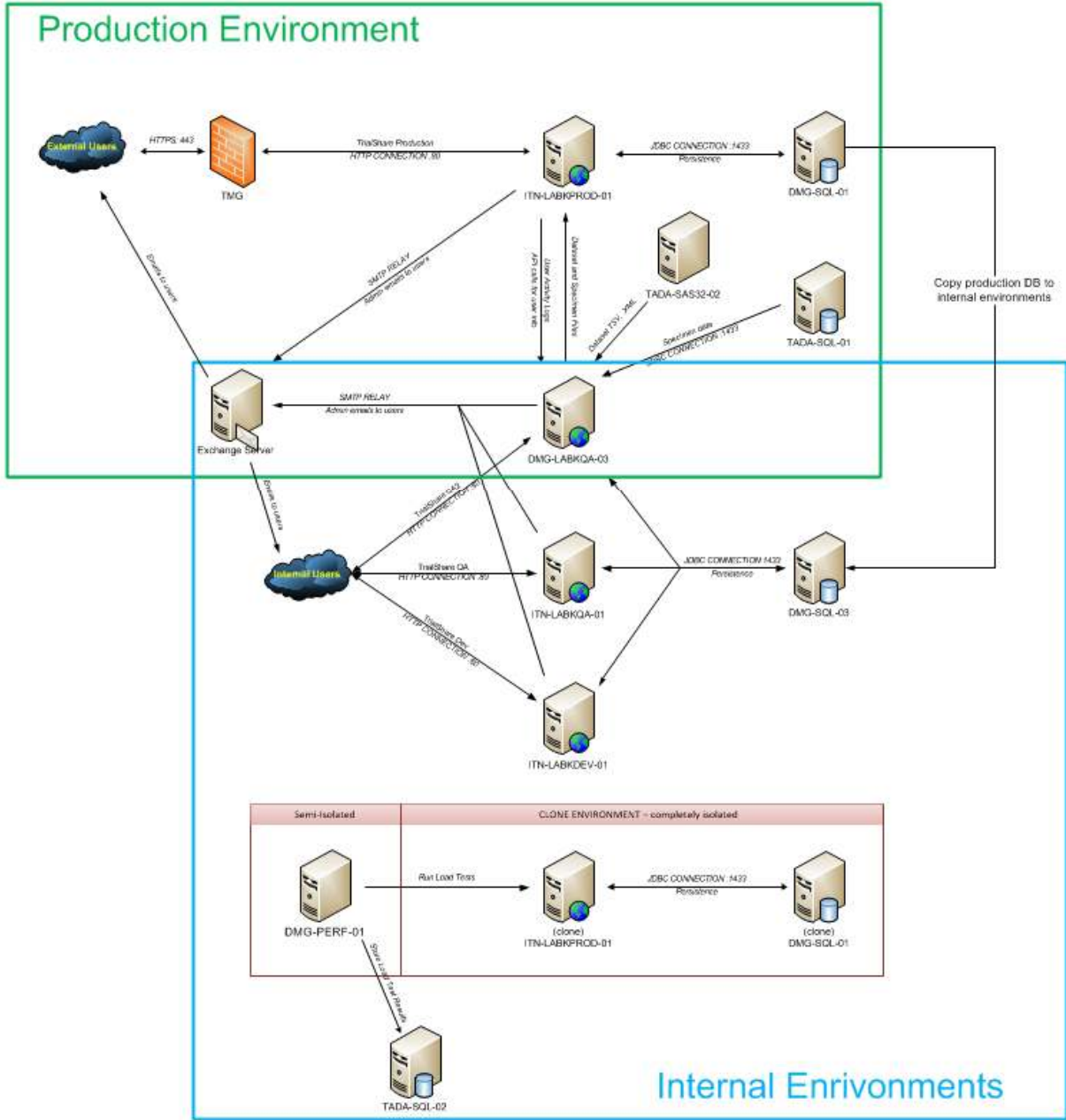
- **Open access ≠ no user management**

- Significant effort required for user account management
- Tracking user behavior allows more targeted improvements**

- **URL confusion**

- Always communicate important edits with a new document version
- Plan for redirects to be necessary

*TrialShare IT infrastructure



TrialShare Exclusive:

CPU Cores: 67

Memory: 268 GB

Storage: 4.93 TB

Shared:

CPU Cores: 7

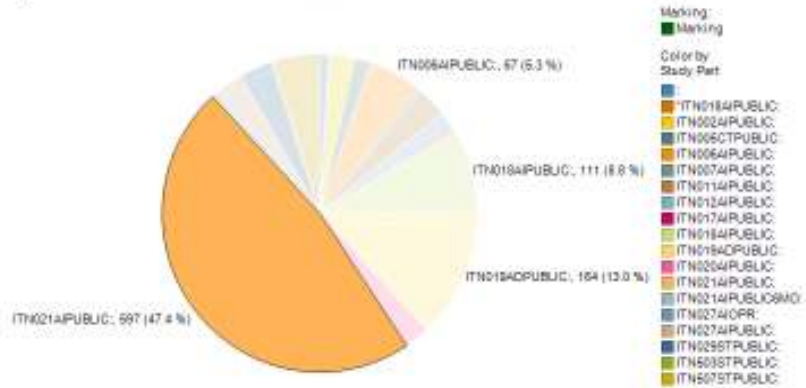
Memory: 21 GB

Storage: 2.03 TB

**Track usage -> Target improvement

RAVE Access

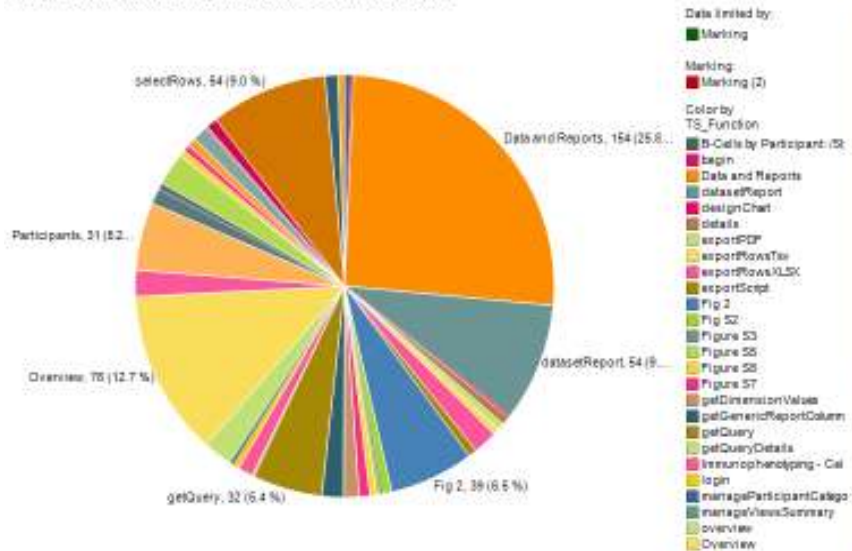
Study or Parent Section Accessed - Pie Chart



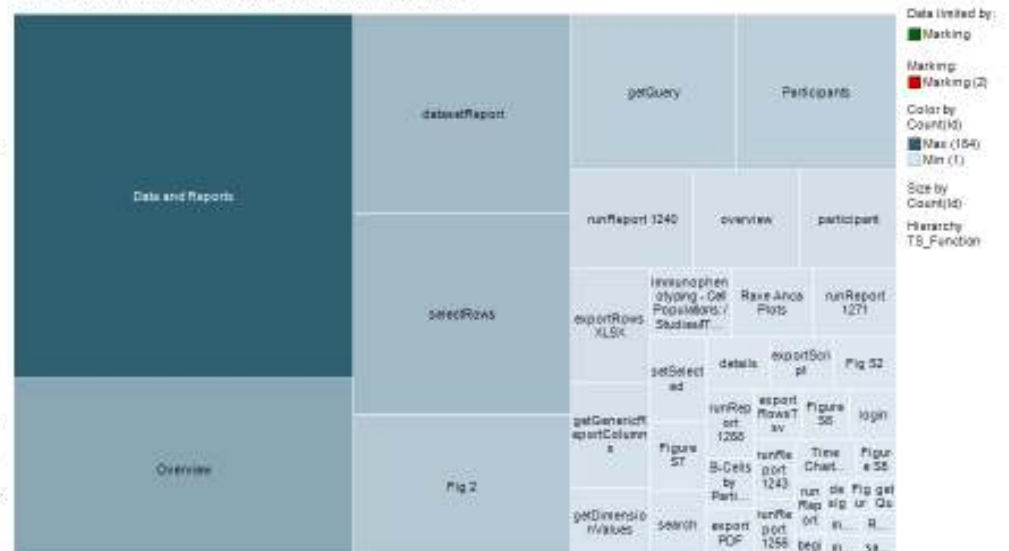
Study or Parent Section Accessed Pie Chart - Tree Map



Detail Function with Study or Parent Section - Pie Chart

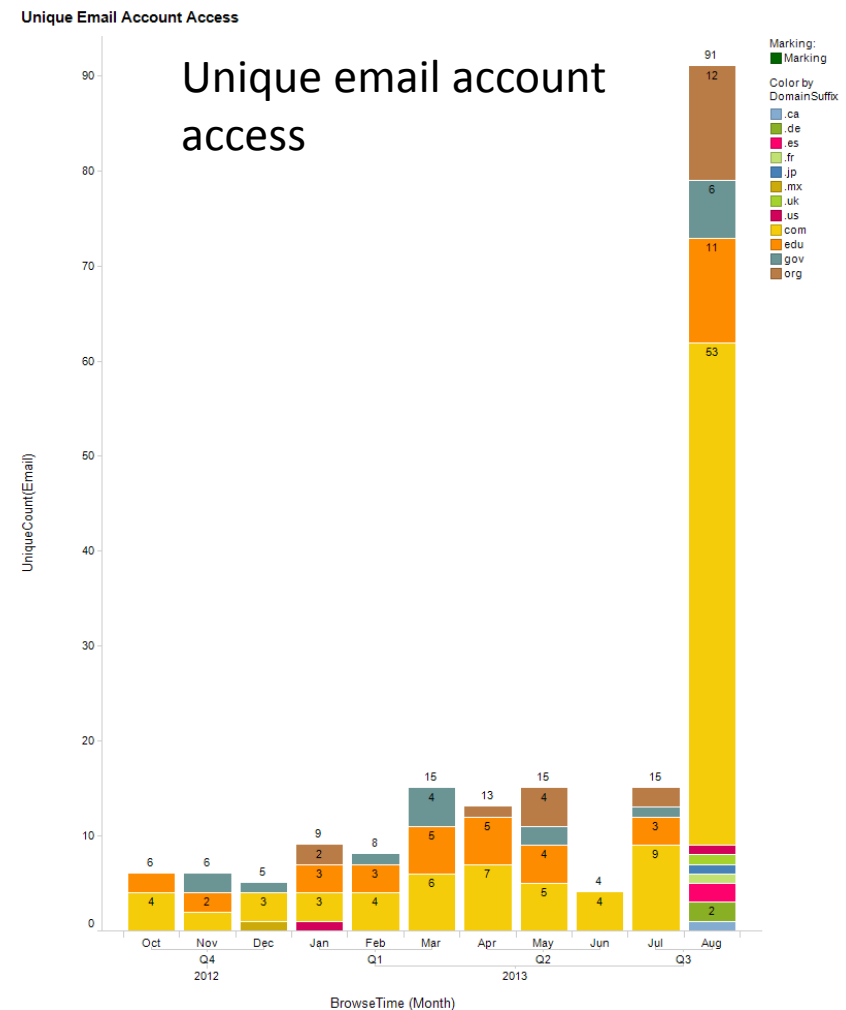
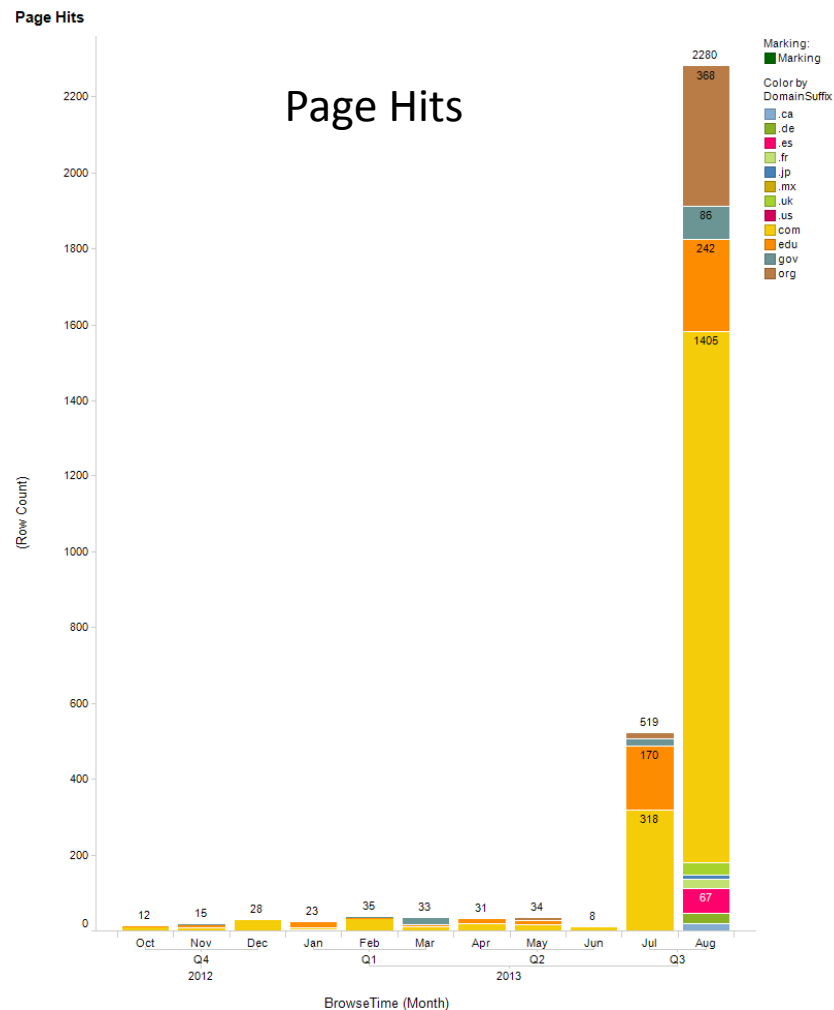


Detail Function within Study or Parent Section - Tree Map



**Track usage -> Target improvement

Monthly counts (non-ITN users)



Filter Settings

- BrowseTime: (10/7/2012 4:23:37 AM <= BrowseTime <= 8/19/2013 2:00:57 PM) without empty values
- Filtered out at 5:20:02 PM: (Untagged)

HIPAA Compliance

Policies Developed

- Data Sharing Policy
- Data Access and Use Policy
- System Terms of Use

Compliance Activities

- HIPAA Staff Training
- UCSF Privacy Office review
- Independent HIPAA/HITECH Audit

De-identification

- No Personally Identifiable Information (PII) in system
- No Protected Health Information (PHI) in public studies
- Privacy Protection Plan by study with individual field level review
 - Free-form text fields such as AE verbatim removed
 - Dates shifted or removed
 - Participant IDs masked or removed
 - Site names removed

Future directions

- **Improved search**
 - Meta-data mapping and tagging
- **Integrated operational workflows**
 - Nearer real time specimen refresh
 - Specimen requests
 - Operational reporting
- **Extend analysis tool integration**

Acknowledgments

Senior Director

Adam Asare, PhD

Biostats, Bioinformatics

Noha Lim, PhD

Sai Kanaparthi, MS

Zhong Gao, PhD

Project Management

Tanya Antonille, MPH

Science

Operations

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Smita Asare

Tracia Debnam

Eduard Chani, PhD

Software Development

Dennis Wightman

Peter Riggs

Data Management

Amy Feng

Aditya Badhwar

Sachin Hebbar

Jie Zhou

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Debs Phippard, PhD

Michael Howell, PhD

Kristina Harris, PhD

Jorge Pardo, MS

Requirements, Technical support

Mike Stahly

Robert Yates



LabKey Software™

Adam Rauch



