Research Priorities and Current Studies

End Organ Disease and Inflammation Transformative Science Group



Turner Overton, MD, ITSG Chair Netanya Utay, MD, ITSG Vice Chair







End-organ Disease and Inflammation TSG Scientific Research Objectives

- 1. To identify strategies to reduce HIV-associated immune activation and inflammation.
- 2. To elucidate the specific drivers of HIV pathogenesis that can be targeted to prevent specific comorbidities common among treated HIV-infected persons.
- 3. To assess the impact of treatment strategies on surrogate markers of immune dysfunction and end-organ disease.
- 4. To test whether promising treatment strategies emerging from pilot studies decrease morbidity in treated HIV infection in larger clinical endpoint trials.

Many Challenges in Treating HIV Patients

- Comorbidities
 - Cardiovascular and Cerebrovascular disease
 - Insulin resistance/Diabetes
 - Hypertension
 - CKD
 - NAFLD/NASH
 - Malignancies
- Neuropsychiatric Complications
 - Cognitive Impairment
 - Depression/Anxiety
- Polypharmacy due to Multimorbidity
 - Drug-Drug Interactions (DDIs)
- Frailty and Functional Impairment
- Social Isolation
- Substance use and abuse

NW329: Activation, Inflammation and Non-HIV Related Events in Antiretroviral Treated and Suppressed HIV

- Case control study of 458 participants from ALLRT (longitudinal cohort study)
- Aim: to define the association of non-AIDS events with inflammation and immune activation in the setting of controlled HIV.



Areas of Focus for ITSG (Targets for Intervention)

<u>Leaves</u> End-organ diseases

 <u>Branches</u>
 Systemic inflammation (IL-1β, IL-6, TNF)
 Hypercoagulability (D-dimer)
 Lymphoid Tissue Fibrosis

Roots

HIV reservoirs CMV and other co-infections Gut mucosal dysregulation Unhealthy fat accumulation Mitochondrial dysfunction Aging

Where Have We Been? Cardiovascular Disease

- ART decreases vascular inflammation
 - A5224s (ATV/r or EFV + ABC/3TC or FTC/TDF)
 - ART reduces proteinuria and albuminuria
 - ART reduces inflammation and endothelial activation markers
 - A5248 (RAL + FTC/TDF)
 - Raltegravir based therapy markedly decreases inflammatory biomarkers
 - LPS, IL-6, D-dimer, TNFR1, sCD14
 - Still higher than negative controls
 - A5260s (DRV/r vs. ATV/r vs. RAL + FTC/TDF)
 - Inflammatory biomarkers associated with oxidized lipoproteins
 - Incomplete reversal: inflammatory biomarkers declined with ART (differences based on 3rd agent): hsCRP, IL-6, D-dimer, sCD163, T cell activation

ART improves endothelial function

- A5152s (3 class sparing regimens: NNRTI/PI, NNRTI/NRTIs, PI/NRTIs)

• ART improves flow-mediated dilation (FMD)

Wyatt CM. JAIDS. 2014;67: 36-44. McComsey et al. AIDS; 2012; 26: 1371. Funderburg N. PLoS One. 2013 Dec 18;8(12):e83514. Stein JH. AIDS. 2013;27:929-37. Kelesidis T. AIDS. 2016;30:2625-33. Torriani FJ. JACC. 2008;52:569-76.

Where Have We Been? Cardiovascular Disease/Lipids

• ART has complicated effects on lipids

– A5260s (DRV/r vs. ATV/r vs. RAL + FTC/TDF)

• oxLDL increases with ART; oxHDL decreased with ART

– Potentially due to excess oxidative stress?

- changes in lipids do not correlate with CIMT changes
- A5248 (RAL + FTC/TDF)
 - RAL increases LDL-c, oxLDL, and TG levels
 - RAL improved HDL composition and function
 - HDL cholesterol efflux function improvement
 - » Correlated with 10% reduction in future CVD events

Where Have We Been? Recent Cardiovascular Disease Focused Studies

- A5275: Atorvastatin on Lipids, Immune Activation, and Inflammatory Biomarkers
- 98 ppts on ART, Median CD4 ct 552 c/mm3, LDL < 130mg/dL
- Results:
 - Robust reduction of LDL-C (\downarrow 38%), oxLDL (\downarrow 33%)
 - No effect on biomarkers of interest
 - IL-6, sCD14, sCD163, MCP-1, IP-10, hsCRP, CD40L
 - T cell and monocyte activation
 - Long viral suppression at entry with very low inflammatory biomarkers at entry
- A5331: Aspirin on Flow-Mediated Dilation and Immune Activation
- 121 ppts on ART, Median Age 49 yrs, Median CD4 ct 599 c/mm3
- Results:
 - Significant reduction of serum thromboxane levels
 - No effect on FMD
 - No effect on biomarkers of interest
 - IL-6, sCD14, sCD163, D-dimer
 - T cell and monocyte activation
 - Very low inflammatory biomarkers at entry

Where Have We Been? Bone Disease

- BMD declines 2-6% with ART initiation
 - A5224s (ATV/r or EFV + ABC/3TC or FTC/TDF)
 - Greater BMD loss with TDF
 - A5260s (DRV/r vs. ATV/r vs. RAL + FTC/TDF)
 - Higher baseline inflammation biomarkers and markers of cellular activation and senescence predicted BMD loss
 - A5303 (DRV/r +FTC + MVC vs. TDF)
 - Greater BMD loss with TDF (\downarrow 2.4%) vs. MVC (\downarrow 1.5%) at hip
- Bisphosphonates improve BMD in treated HIV
 - Weekly alendronate improved BMD (A5163)
- VitD/calcium mitigate BMD loss with ART initiation
 A5280 (EFV/FTC/TDF + VitD/Ca)

McComsey GA. JID. 2011; 203:1791-801. Brown TT. JID. 2015; 212:1241-9. Taiwo BO. CID. 2015;61:1179-88. McComsey GA. AIDS. 2007;21: 2473-82. Overton ET. Ann Int Med. 2015; 162:815-24.



Where Have We Been? Bone Disease

 Persistent BMD loss despite suppressive ART vs. HIV neg – A5224s/A5318



- Fracture incidence higher in first 96 weeks after ART initiation
 - ALLRT (A5001) Longitudinal cohort
- HCV treatment and BMD
 - A5178 (pIFN/RBV treatment of HCV/HIV coinfection)
 - IFN-based therapy reduces BMD
 - Bone turnover markers decline after HCV cure

Grant P. JID. 2016. Yin M. AIDS 2012. Kendall. ARHR 2015. Bedimo R. ARHR 2016.

Where Have We Been? Neuropsychiatric Disease

- A5271: International Neurocognitive (NC) Normative Study
 - NC Performance Even in Treated HIV Patients Worldwide is Often Not Normal



- ALLRT (A5001) Aging and Neurocog Function
- 3313 ppts; median age 38 yrs; 12% >50 yrs
 - NC performance improved with ART duration
 - Despite ART, age remains a risk factor for NCI
 - Potential explanations
 - Greater comorbidities:
 - HTN, DM, Lipid disorder
 - Greater ART toxicities

Probability of NC Impairment



Robertson K. J Neurovirol. 2016; 22: 472-8. Coban H. AIDS 2017; 31: 1565-71.

Tenorio A. JID. 2015;211: 780-90. Sandler NG. JID. 2014;210: 1549-54.

Where Have We Been? Gut Mucosal Health

- A5286: Rifaximin to Reduce Immune Activation
 - Hypothesis: Bind bacteria in gut/Prevent translocation
 - Enrolled 65 ppts (43 Rifaximin; 22 controls)
 - Median age: 50 yrs; Median CD4 236 c/mm3 on suppressive ART
 - Results
 - Marginal Change in HLA-DR+/CD38+ CD8 cells, sCD14, LPS
 - No effect on other inflammatory biomarkers
 - D-dimer, IL-6, hsCRP
- A5296: Sevelamer to Reduce Microbial Translocation
 - Hypothesis: Bind LPS and decrease systemic inflammation
 - Enrolled 40 ppts to sevelamer; no control arm
 - Median age: 50 yrs; Median CD4 236 c/mm3 not on ART
 - Results
 - No effect on markers of microbial translocation: LPS, sCD14
 - Modest effect on lipids
 - Decreased T chol, LDL, oxLDL
 - No effect on HDL, TG, and fasting glucose





Short interventions

Where Are We Now/Where Are We Going: End-organ Disease and Inflammation TSG Scientific Research Objectives

- 1. To identify strategies to reduce HIV-associated immune activation and inflammation.
- To elucidate the specific drivers of HIV pathogenesis that can be targeted to prevent specific comorbidities common among treated HIV-infected persons.
- 3. To assess the impact of treatment strategies on surrogate markers of immune dysfunction and end-organ disease.
- 4. To test whether promising treatment strategies emerging from pilot studies decrease morbidity in treated HIV infection in larger clinical endpoint trials.

A5314: Effect of Reducing Inflammation with Low Dose Methotrexate on Inflammatory Markers and Endothelial Function in Treated and Suppressed HIV Infection

Protocol Co-Chairs: Priscilla Hsue and Judith Currier

Enrollment:

200 HIV participants on ART, CD4 >400 c/mm³, documented CVD or CVD risk



Rationale

- LDMTX decreases vascular events in observational studies of HIV-uninfected persons

Key Study Objectives

- To evaluate safety of low dose methotrexate (LDMTX) therapy (<u>Primary</u>)
- To demonstrate LDMTX improves endothelial function (brachial artery FMD) (Secondary)

176 participants enrolled; study completed; analysis ongoing

A5314: Methotrexate Results

Safety:

- 12.8% of individuals in LDMTX met primary safety endpoint vs. 5.6% in the placebo group (P=0.037)
 - The difference was lower than anticipated.

<u>FMD:</u>

• No change in endothelial function as assessed by FMD (%)



Contributors to End-Organ Disease in HIV-Infected Patients Well Controlled on Antiretroviral Therapy Protocol Co-Chairs: Jordan Lake and Netanya Utay **Enrollment:** 54 HIV participants on ART for at least 48 weeks, HIV-1 RNA <200 copies/ml for at least 24 weeks and < 50 copies/ml at screening Blinded **ART + telmisartan** weeks **ART** alone

A5317: Effects of Telmisartan on Fibrotic and Inflammatory

<u>Rationale</u>

 Telmisartan is an angiotensin receptor blocker and partial PPAR gamma agonist with putative anti-fibrotic and anti-inflammatory properties

Key Study Objectives

 To evaluate whether adding telmisartan for 48 weeks to a suppressive ART regimen decreases lymphoid and/or adipose tissue fibrosis

44 participants randomized; study completed; analysis ongoing

A5317: Telmisartan Results

- Median CD4 ct 588 c/mm³
- 35 participants in the per protocol analysis
 - 22 telmisartan
 - 13 control



Telmisartan did not decrease LN or adipose tissue fibrosis more than ART alone

A5325/30s: A Prospective Randomized Controlled Study to Evaluate the Effect of Isotretinoin on Immune Activation Among HIV-1 Infected Subjects with Incomplete CD4+ T Cell Recovery on Suppressive ART

Protocol Co-Chairs: Nina Lin and Douglas Kwon

Enrollment:

81 HIV participants on suppressive ART for at least 12 months, CD4+ count < 350 c/mm³



- Rationale:
 - Profound gut CD4+ T cell depletion occurs early in infection
 - Retinoic acid plays a prominent role in regulation of immunologic pathways, and contributes to gut mucosal integrity
- Objectives
 - Evaluate changes in CD8+ T cell activation with isotretinoin in suppressed HIV
 - Evaluate CD4+ T cell reconstitution in the gut mucosa (A5330s substudy)

76 participants enrolled in A5325; 24 in A5330s; study completed; analysis ongoing

A5325/30s: Isotretinoin Results

- Median CD4 ct 552 c/mm3
 34% <350 c/mm3
- Study completion
 - 40 in isotretinoin completed therapy
 - 26 in control arm
- Primary results:

	%DR+/CD38+	Isotretinoin (n=39) Median [95% Cl]	No treatment (n=26) Median [95% CI]	P-value
BL - wk 16	CD8+ T-cells	+3.24 [1.44, 6.29]	+0.52 [-0.36, 2.41]	0.03
	CD4+ T-cells	+1.01 [0.37, 2.26]	+0.17 [-0.79, 0.91]	0.05

- Conclusions
 - Isotretinoin increases circulating activated CD8+ and CD4+ T cells during treatment
 - Not durable increases
 - Similarly, several inflammatory markers increased but effect not sustained.
 - IL-6, hsCRP, sCD163, sCD14

A5350/52s: Effect of Probiotics on Gut Microbiome and Immune Activation Markers

Protocol Co-Chairs: Turner Overton and Adriana Andrade

The trial will randomize 90 HIV-infected adults 18 years of age and older - On ART, with CD4 count >200 c/mm³, and HIV VL < 50cp/mL



led	45 participants on ART + Visbiome ES X 24 we	eks	Fo add
slinc	45 participants on ART + placebo X 24 weeks		off afte pro

Followed for an additional 12 weeks off study therapy after completion of probiotic/placebo

Rationale

- Potential to increase Th17 T cell population in gut
- Potential to shift monocyte population to less pro-inflammatory phenotype and potentially less likely to induce cardiovascular events
- Mediated through improved gut permeability

Primary Study Objective

- Assess changes in inflammatory biomarkers (main study)
- Assess changes in CD4+ cells in gut mucosa (substudy)



A5336: Effect of Ruxolitinib on Inflammation and Immune Activation

Protocol Co-Chairs: Vincent Marconi and Jeffrey Lennox

The trial will randomize 60 HIV-infected adults 18 years of age and older - On ART, with CD4 count >350 c/mm³, and HIV VL < 50cp/mL



ded	40 ppts on ART +Ruxolitinib X 5 wks	Followed for an additional 7 weeks off study therapy after completion of ruxolitinib
linc	20 ppts on ART + no drug X 12 wks	
B		

Rationale

- Janus Kinase 1&2 inhibitors decrease inflammatory cytokines in myelofibrosis, RA, psoriasis
- Potential to reduce inflammation in HIV-infected adults
- Mediated through improved gut permeability

Primary Study Objectives

- Evaluate Safety and Tolerability of Ruxolitinib
- Assess changes in inflammatory biomarkers

A5351s: CMV Reactivation with Immunomodulatory Therapies

Prospective, observational study of participants on suppressive ART and enrolled in the ruxolitinib or sirolimus (Cure TSG) study or future studies of immunomodulatory agents as they are approved for development



Genital secretions, oral swabs, stored urine will be collected longitudinally

A5336: Ruxolitinib

A5337: Sirolimus

Rationale

- Persistent sub-clinical CMV replication in genital and oral secretions and urine is frequently found in HIV-infected individuals and is associated with increased systemic immune activation, T cell proliferation and exhaustion, and larger HIV DNA reservoir
- Therefore, it is important to capture the extent of sub-clinical CMV replication in clinical trials evaluating inflammation-related outcomes.

Primary Study Objectives

- To determine the effect of immune-modulatory interventions on seminal CMV shedding during suppressive ART
- CMV shedding in female genital tract, oral mucosa, and urine will also be evaluated

A5324: Integrase & Maraviroc Intensification in Neurocognitive Dysfunction (InMIND)

Protocol Co-Chairs: Kevin Robertson and Serena Spudich

The trial will randomize 186 HIV-infected adults 18 years of age and older - On ART, with HIV VL < 50cp/mL and NCI



Rationale

- NCI remains prevalent despite ART; CNS is a protected compartment
- Novel mechanisms may reduce CNS virus activity
 - R5 inhibition & integrase inhibition
- Mediated through improved gut permeability

Primary Study Objectives

Assess changes in neurocognitive function with ART intensification

Randomized Trial to Prevent Vascular Events in HIV REPRIEVE (A5332/33s)



Funded by NHLBI and NIAID. Supported by KOWA Pharmaceuticals.

REPRIEVE Substudies

- A5333s: Mechanistic Substudy: CCTA at 0 and 24 months (PI: Hoffman/Ribaudo; funded by NHLBI)
 - 704/800 enrolled
 - Assess effects of pitavastatin on critical plaque and inflammatory biomarkers
- Kidney substudy (PI: Overton; funded by NIDDK)
 - 2558 enrolled
 - Assess changes in kidney function
 - Serum and urine markers
- Sex Differences substudy (PI: Zanni/Looby; funded by NIAID)
 - 4636 enrolled
 - Assess sex-based differences in Immune activation and statin-induced immunomodulation
 - Characterize the role of menopause status and ovarian reserve
- A5361s: Physical Function and Frailty (PI: Erlandson; funded by NIA)
 - 436/600 enrolled
 - Assess statin effects on physical function and muscle quality

A5322 (HAILO): The HIV Infection, Aging and Immune Function Long-Term Observational Study

- 1035 Participants (81% male, 48% white)
 - Median age 51 years
 - Median CD4 ct at ART initiation: 228 c/mm3
 - Median CD4 ct at study entry: 621 c/mm3
 - HIV VL <50 cp/mL at study entry: 61%
 - Median years of ART: 7.2 years
- Many data elements/samples available
 - Labs (CD4, VL, CBC, CMP, lipids, urine)
 - Neurocognitive examination
 - Questionnaires/assessments
 - Smoking, frailty, substance use, medical insurance, behavioral data, physical activity, ADLs

A5322 Non-AIDS Events Through 2016

Clinical Event Category	Observed event rate per 100 person- years since A5001	Expected event rate per 100	
	(#events/total person years)	person-years*	
Cardiovascular Diseases	0.83 (19 / 2294.91)	0.48	
Thrombosis/Embolism	0.39 (9 / 2302.35	0.12	
Diabetes	2.61 (53 / 2027.86)	1.10	
Hepatobiliary Disorders	0.30 (7 / 2307.3)	0	
Neoplastic Disease	0.52 (12 / 2301.64)	0.41	
Renal Disorders	0.58 (12 / 2076.27)		
Bone fractures due to falls	0.79 (18 / 2291.57)	0.15	
Bone fractures due to trauma	0.44 (10 / 2297.81)		
Death	0.43 (10 / 2312.91)	0.88	

Creation of 5 Working Groups to Seek Independent Funding:

- Cardiovascular Disease
- Kidney Disease
- Frailty/Physical Function
- Neuropsychiatric issues
- Cancer



Rationale

 Persistent sub-clinical CMV replication in genital and oral secretions and urine is frequently found in HIV-infected individuals on ART and is associated with increased systemic immune activation, T cell proliferation and exhaustion, and larger HIV DNA reservoir

Primary Study Objective

- To evaluate safety and tolerability of Triplex in HIV-infected persons (Primary)
- To determine effects of Triplex on CMV DNA levels

A5363: Effects of Cenicriviroc on Arterial Inflammation in People Living with HIV

Protocol Chair: Janet Lo Vice Chairs: Judith Currier & Ned Tawakol

The trial will randomize 93 HIV-infected adults ≥45years of age on suppressive ART for ≥48 weeks with at least one cardiovascular disease risk factor



Rationale

Blindec

- Monocyte/macrophage activation is increased in HIV infection and plays a key role in cardiovascular events
- CCR2 and CCR5 mediate monocyte migration and are thought to contribute to atheroslerosis
- Cenicriviroc (CVC) is a CCR2/CCR5 antagonist

Primary Study Objective

 To assess whether CVC decreases arterial inflammation as measured by 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT) imaging of the carotid arteries and aorta

A5371: Treatment of NAFLD: A Metabolic Syndrome

Protocol Chairs: Kristine Erlandson and Jordan Lake



Lead-in (12 weeks)

<u>Rationale</u>

- Non-alcoholic fatty liver disease (NAFLD) is associated with cardiovascular events in the general population and affects 30-40% (or more) of HIV-infected adults.
- NAFLD may have unique origins in HIV infection

Primary Study Objective

 To assess whether sitagliptin or liraglutide for 36 weeks decreases MRI-quantified intrahepatic triglyceride deposition by proton MR spectroscopy (MRS)

In development

What our current portolio can teach us?

In the next few years, we should know more about

- Whether probiotics can facilitate gut healing, and if so, if this attenuates inflammation (A5350/52s)
- Relative contribution of CMV to systemic inflammation in chronic treated HIV infection (A5351s, A5355)
- Role of Jak/Stat signaling in driving chronic inflammation in treated HIV infection (A5336)
- Effects of systemic inflammation on HIV persistence and transcriptional activation (A5337, A5336, A5346)
- Role of macrophage recruitment via CCR2/CCR5 in vascular inflammation, neurocognitive function, liver steatosis (A5363)
- Drivers of hepatic steatosis in HIV infection (A5371)
- Specific mechanisms behind accelerated CVD in HIV (A5332/33s)

Ultimately, these studies will lead to a greater understanding of HIV pathogenesis in the next several years

Unanswered Questions to Address

• What are the drivers of persistent inflammation?

- GI mucosal dysregulation/microbial translocation
- Unhealthy fat accumulation, particularly NAFLD→NASH
- HIV persistence
- Other pathogens (Hepatitis and Herpes viruses)
- Mitochondrial dysfunction
- Severity of immune deficit
- Does sustained ART and virologic suppression reduce inflammation adequately?
- Can we do anything about it beyond ART to prevent diseases of interest?
 - Treating early has incomplete benefit
 - Various treatment strategies being evaluated
- What is the role in chronic inflammation in HIV persistence?
- If we effect a cure, what are the consequences on end organ disease/comorbidities?
 - Remains unknown with only 1 cure to date
 - Even if a cure is identified, roll-out to almost 37 million people will take time and money and
 - People have comorbidities now



Critical Neurological Topics Requiring Ongoing Investigation

- Optimal cART for the brain compartment (A5303, A5324)
- CNS compartment (A5321, A5341s, biorepository studies, biomarker development, viral escape characteristics)
- Impact of anti-inflammatory approaches on brain/csf inflammatory response (**needs better plans – 5332, 5336)
- Vascular disease (Stroke, brain perfusion as source and/or measure of HAND)
- Aging/Degenerative Dx (A5322 HAILO neurological component, frailty)
- Co-morbidity (CMV, HCV)

Current Red Line

- Psychiatric disease
- Sleep (glymphatics and degeneration)
- CNS opportunistic infections (crypto, TB, toxo, JC)
- Peripheral neuropathy

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Inflammation International

- Greater ART access with initiation at higher CD4 cell counts
 BUT
- Morbidity and Mortality remains higher in low and middle income countries
 - Bacterial infections
 - Malnutrition
 Non-AIDS diseases (CVD, obesity, DM, HTN)
- **A5175** secondary analyses (ART initiation)

— TB

- Baseline and persistently elevated inflammatory biomarkers associated with TB, AIDS, and Mortality
- Weight gain associated with increases in inflammatory biomarkers despite ART
- Key questions for international studies:
 - How will anti-inflammatory therapies work?
 - Are drivers of persistent inflammation different?
 - What is the role of late ART initation, i.e. low CD4 count?
 - CVD is a common comorbidity in these settings (A5332)?

Pathways Forward

- Utilize existing data and samples for secondary analyses
 - NWCS 329
 - A5224s/A5260s data
 - ALLRT/HAILO
 - Longitudinal follow up in 5320; A5321/41
 - REPRIEVE (a treasure trove)
- Systems Biology Approach to completed studies
 - Find the unexpected
- Select the appropriate study population
 - CD4 count
 - Evidence or risk factors for end organ disease
- Partner with experts within the ACTG
 - Hepatitis Committee: NAFLD/NASH working group
 - WHISC: the role of sex and sex hormones
 - Cure TSG: 5354, ATIs
 - TB: biomarker development
 - ARTS: long acting agents; studying hard to reach populations (A5359); metabolic consequences of bNAbs
 - International sites and partners: different drivers in developing world

- Partnerships with NIH Institutes for Studies
 - A5224s: NIAID
 - A5260s: NHLBI
 - A5314: NHLBI
 - REPRIEVE: NHLBI, NIAID, NIDDK, NIA
 - NAFLD/NASH: NIDDK 10/20/17 meeting

Partnerships with Industry

- A5363: Allergan
- A5346: Merck
- A5371: Nordisk; Merck
- Engage experts from specific areas
 - NAFLD/NASH: Kara Chew
 - Frailty/Physical function: Marcus Bamman
 - Mucosal immunology: Jason Brenchley





Pathways Forward

- What are the strengths of the ITSG?
 - Investigators and Breadth of Knowledge
 - Diversity of areas of research
 - Collaborations between Clinicians and Laboratorians
 - Strong Statistical Support
 - Availability of large repository of samples and data
- What are we not doing well?
 - Soliciting studies from non-ACTG investigators
 - Difficult process getting protocols from genesis to enrollment
 - Utilizing existing samples/data
 - Engaging International investigators
 - Collaborating with TB investigators
- Are there new opportunities in this field that the ITSG should pursue?
 - Utilizing newer imaging techniques
 - Collaboration with industry and other groups
 - Example: NASH Clinical Research Network
 - Collaborating with NIH Institutes beyond NIAID
 - Identifying novel therapeutic agents
 - Example: IDO inhibitors, cancer therapeutics
 - Targeting endpoints beyond biomarkers



Our People Provide Our Expertise

- Turner Overton
- Netanya Utay
- Adriana Andrade
- Donald Anthony
- Roberto Arduino
- Francesca Aweeka
- Jason Baker
- David Clifford
- Robert Coombs
- Kristina Crothers
- Michael Dube
- Kristine Erlandson
- Nicholas Funderburg
- Sonya Heath
- Peter Hunt
- Nichole Klatt
- John Koethe
- Nagalingeswaran Kumarasamy
- Jordan Lake
- Alan Landay
- Bernard Macatangay

- Carlos Malvestutto
- Christina Marra
- Vidya Mave
- Grace McComsey
- Mosepele Mosepele
- Fred Sattler
- Thomas Uldrick
- Sara Weibel
- Michael Yin
- Doug Kitch (Statistical and Data Analysis Center)
- Carlee Moser (SDAC)
- Heather Ribaudo (SDAC)
- Baljinder Singh (SDAC)
- Karin Klingman (DAIDS representative)
- Dave Rusin (Data Management Center representative)
- Stanford Chimutimunzeve (Community Scientific Subcommittee)
- David Palm (CSS)
- Andrea White (Coordinator)
- Reena Masih (Coordinator)

