Studies of Ocular Complications of AIDS (SOCA)

Curriculum Vitae

16 November 2015

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Background and purpose

The Studies of Ocular Complications of AIDS (SOCA) is a collaborative multicenter research effort whose objective is to evaluate strategies for the treatment and prevention of ocular complications associated with AIDS. Ophthalmologic disorders are commonly associated with the acquired immunodeficiency syndrome (AIDS), and blindness is among its many complications. Two of these ophthalmic clinical manifestations occur in patients with AIDS with sufficient frequency that further study is warranted through clinical trials and other epidemiological studies. Cytomegalovirus (CMV) retinitis is an opportunistic infection of the retina characterized by white infiltrates and hemorrhages. This ocular complication of AIDS leads to necrosis and atrophy of the retina and is the major cause of visual loss and blindness in patients with AIDS. Although it appears to occur in the more severely immunocompromised patients with AIDS, little is know about other risk factors that influence the development or prognosis of this ocular disease.

This has led to an RFA (88-EY-01), The Ocular Complications of AIDS, to which two applications have been submitted from the Johns Hopkins University: one for a Chairman's Center and one for a Coordinating Center and represent a joint effort. Additionally, collaboration with the Fundus Photograph Reading Center, located in Madison, Wisconsin was included in the RFA under the cooperative agreement.

SOCA began in 1989 through funding from the National Eye Institute, started enrollment of patients in March of 1990, and completed five clinical trials. The SOCA clinical trials were conducted over a nine year period (1989 through 1998), and were designed to examine the effects of current and emerging treatments for cytomegalovirus retinitis in patients with AIDS. The treatment strategies utilized in each of the five trials are summarized in study-specific design tables located in this document. The SOCA trials focused on cytomegalovirus (CMV) retinitis. The prevalence of CMV retinitis in patients with AIDS rose from 25% to 45% following institution of primary prophylaxis against pneumocystis carinii infection. Improved survival in patients with AIDS may also have contributed to the increased prevalence of CMV retinitis. It is estimated that more than 20,000 new cases of CMV retinitis occur annually in the United States. Evidence of active CMV infection (i.e., CMV isolated from urine, blood, or saliva) can be found in the majority of AIDS patients. CMV retinitis progressively destroys retinal tissue resulting in vision loss. Current treatment slows progression and in some cases stops it. Complex treatment regimens as well as viral resistance have complicated treatment and continues to adversely affect quality of life. Laboratory assessments will continue to be included in future studies to examine the pathogenesis of CMV infections. The SOCA research group is committed to developing standards and new methodologies for long term epidemiological investigations of the progression and outcome of ocular complications of AIDS.

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Background and purpose

The Studies of Ocular Complications of AIDS (SOCA) is a collaborative multicenter research effort whose objective is to evaluate strategies for the treatment and prevention of ocular complications of AIDS. Three SOCA studies were proposed:

1988-1993

- a randomized clinical trial of existing (ganciclovir) and new antiviral agents (as they become available) for the treatment of CMV retinitis;
- a prospective cohort study of epidemiological investigations of the CMV retinitis in newly diagnosed AIDS patients; and
- a prospective cohort study of the ocular manifestations of HIV infection in inidividuals who have not yet developed AIDS.

1993-1998

Administrative renewal. Continuation of the aims listed above.

The Longitudinal Studies of Ocular Complications of AIDS (LSOCA), a long term prospective epidemiological study, began in August 1998. Enrollment in LSOCA was discontinued on 31 July 2011 with a total of 2,392 patients. LSOCA is in its third 5-year funding cycle. The following summarizes the stated aims within each of the previous 5-year funding periods: 1998 through 2013.

1998-2003

- To monitor secular trends in the incidence of ocular complications of AIDS;
- To determine the effect of highly active anti-retroviral therapy (HAART - induced) changes in immune status on the incidence and course of ocular complications of AIDS; and
- To determine the characteristics of patients that place them at high risk for ocular complications; and
- To evaluate the effects of treatments for CMV retinitis and other ocular complications on visual function, quality of life and survival.

2003-2008

- To determine the characteristics (clinical, virologic, and immunologic) of and risk factors for CMV retinitis and other ocular complications of AIDS in the era of HAART;
- To monitor trends in the incidence and prevalence of CMV retinitis and other ocular complications of AIDS; and
- To evaluate the outcomes of CMV retinitis and other ocular complications of AIDS and determine risk factors for adverse outcomes.

2008-2013

- To evaluate the long-term outcomes of ocular opportunistic infections;
- To evaluate visual impairment among patients without ocular opportunistic infections; and

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Background and purpose

- To evaluate the host genetic risk factors for and immunologic mechanisms of ocular complications and their outcomes

With the introduction of highly active antiretroviral therapy (HAART), AIDS has converted to being a chronic disease with the attendant issues of chronic disease management. Hence, a consequence of improved lifespan for patients with AIDS is accelerated aging resulting in increased incidence of dyslipidemia, diabetes, and cardiovascular disease. Preliminary data from LSOCA suggests accelerated aging in the eye, including a higher prevalence of cataracts in younger people and a greater rate of cataract surgery. Also, the prevalence of large drusen at a younger age is evident and is associated with early age-related macular degeneration. The diameter of central retinal arteries and venules in patients with AIDS are comparable to those in an older population. These emerging trends are of significant interest for continued research. Toward this end, plans are underway to submit a competitive renewal application to the NEI in September 2012 for an additional five years of funding for LSOCA.

2013-2018 (Not funded)

- To evaluate prevalence and incidence of and risk factors for evidence of accelerated aging (eg, large drusen, cataracts, etc.)
- To evaluate genomics of intermediate and AMD in patients with AIDS
- To evaluate effect of inflammation on accelerated aging of the eye in patients with AIDS

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Funding history

LSOCA Total Awarded Dollars

	1999 - 2003	2003 - 2008	2008 - 2013	2013 - 2018†
CC & BioFisher	9,882,711	11, 416,094	8,637,771	7,404,200
Clinic	10,503,125	17,082,055	16,916,565	4,208,565
Patient cost	6,592,400	6,326,303	5,433,109	3,958,080
SUN	0	0	962,827	0
Peter Hunt	0	0	0	1,193,500
CO	2,179,853	2,469,137	2,178,704	1,717,000
RC	1,359,709	1,167,682	1,032,443	732,600
Total Cost	**30,517,798**	**38,461,271**	**35,161,419**	**19,214,345**

†Years 26 - 30 preliminary budget proposal

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Chronology

25	Mar	88	RFA released from NEI
15	Aug	88	Funding initiated
17	Mar	89	Release of RFP by Coordinating Center to clinics
15	Jun	89	Clinics selected
17	Nov	89	1st meeting of SOCA Research Group
08	Jan	90	1st PDMB meeting
13	Mar	90	1st patient enrolled into Foscarnet-Ganciclovir CMV Retinitis Trial (FGCRT)
07	Oct	91	FGCRT protocol suspended due to a mortality difference
17	Oct	91	Clinical Alert regarding mortality difference in FGCRT
23	Jan	92	FGCRT: Mortality results paper published *(N Engl J Med)*
01	Feb	92	FGCRT: Rationale, design and methods paper published *(Controlled Clin Trials)*
17	Dec	92	1st patient enrolled into CMV Retinitis Retreatment Trial (CRRT)
	Jun	92	Mortality data sets placed on reposit at NTIS
02	Nov	93	FGCRT forms archived at Medical Archives Office, off-site Records Center
21	Apr	94	1st patient enrolled into HPMPC Peripheral CMV Retinitis Trial (HPCRT)
	Jul	94	FGCRT visual outcomes by treatment group *(Ophthalmology)*
03	Aug	94	FDA imposed moratorium on enrollment into HPCRT due to new carcinogenicity information
21	Oct	94	Enrollment reinstituted into HPCRT
		94	FGCRT Visual Outcomes data sets placed on reposit at NTIS
09	Jan	95	FGCRT: Morbidity and toxicity effects paper published *(Arch Intern Med)*
06	Mar	95	CRRT recruitment closed based on recommendation of PDMB
10	Apr	95	CRRT protocol suspended due to positive treatment effect of combination therapy
31	Jul	95	CRRT close of data collection
14	Sep	95	1st patient enrolled into Monoclonal Antibody CMV Retinitis Trial (MACRT)
		95	FGCRT Morbidity data sets placed on reposit at NTIS
		95	Anti-retroviral treatment of Fos/Gan on p24 data sets placed on reposit at NTIS
01	Jan	96	CRRT: Combination foscarnet and ganciclovir therapy vs. monotherapy *(Arch Ophthalmol)*
08	Apr	96	CRRT forms archived

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Chronology

01	Mar	96	HPCRT protocol suspended due to positive treatment effect of HPMPC
15	Mar	96	HPCRT results presented to FDA
14	Aug	96	MACRT protocol suspended due to no treatment effect
		96	CRRT Combination Fos and Gan vs Monotherapy for treatment of CMVR data sets placed on reposit at NTIS
15	Feb	97	HPCRT: Parenteral cidofovir for CMV retinitis in patients with AIDS paper published *(Ann Intern Med)*
30	Jun	97	1st patient enrolled into Ganciclovir-Cidofovir CMV Retinitis Trial (GCCRT)
	Aug	97	FGCRT: Retinal detachment paper published *(Am J Ophthalmol)*
	Aug	97	FGCRT: Clinical features paper published *(Am J Ophthalmol)*
	Dec	97	MACRT: MSL-109 adjuvant therapy paper published *(Arch Ophthamol)*
		97	HPCRT Parenteral cidofovir for CMVR results data sets placed on reposit at NTIS
		97	MACRT MSL-109 adjuvant therapy for CMVR results placed on reposit at NTIS
02	Sep	98	1st patient enrolled into the LSOCA
10	Sep	99	GCCRT protocol revised; patients to be randomized to systemic therapy rather than cidofovir
26	Apr	00	PDMB recommendation to close GCCRT
28	Apr	00	GCCRT enrollment suspended; clinics notified of closeout procedures
30	Jun	00	GCCRT close of data collection
	Jul	00	HPCRT: Long-term followup *(AIDS)*
	Sep	00	FGCRT: Risk factors for adjuvant of CMV retinitis *(Arch Ophthalmol)*
31	Oct	00	GCCRT database closed
	Feb	01	Patient notification and followup after suspension of treatment protocols *(Controlled Clin Trials)*
	Apr	01	GCCRT: Ganciclovir implant plus oral ganciclovir versus parenteral cidofovir for treatment of CMV retinitis *(Am J Ophthalmol)*
30	May	01	Certificate of Confidentiality distributed to clinic
19	Jul	01	OHRP suspends enrollment in human research at JHU
22	Aug	01	JHU received expedited IRB review and approval to enroll patients
		01	GCCRT: GCV implant plus oral ganc vs parenteral cidofovir results placed on reposit at NTIS
	Jan	02	LSOCA: Characteristics of patients with CMVR in the era of HAART published *(Am J Ophthalmol)*

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Chronology

26	Feb	02	LSOCA Specimen Banking and Use Statements added to Consent/Assents
29	Mar	02	GCSF bacterial infections paper published *(AIDS)*
02	Apr	02	MACRT: Influence of filgrastim (granulocyte - stimulating factor) on HIV-1 RNA published *(J Inf Dis)*
12	Apr	02	GCSF HIV and CMV viral load outcomes paper published *(AIDS)*
03	Jul	02	Role of anti-CMV antibody avidity in progression of CMV disease (ancillary study approved by SO)
07	Aug	02	Comparison of clinician vs reading center determination of CMV retinitis (ancillary study approved by SO)
01	Sep	02	SOCA Competitive Grant application submitted to NEI
07	Jan	03	SOCA: Visual loss in patients with CMV retinitis and AIDS before widespread availability of HAART *(Arch Ophth)*
25	Aug	03	Notice of Grant Award from NEI for continued funding, 2003-2008
19	Sep	03	Tropical storm (Hurricane Isabel) flooding at Ann Street
01	Nov	03	Restart of enrollment
24	Nov	03	Data entry begins on new dedicated server
	Feb	04	GCCRT: Complications of Ganciclovir Implant Surgery paper published *(Retina)*
	Mar	04	Avidity of Antibodies to Cytomegalovirus paper published (*Viral Immunol)*
	Apr	04	LSOCA: Results of a CMV specific CD8+/Interferon cytokine flow cytometry assay (*J Infect Dis)*
01	Jun	04	Submission of annual non-competitive renewal for LSOCA (Yr 17)
03	Jun	04	Quota lifted to allow open enrollment through 31Jul04 (PPM 62)
03	Jun	04	Enrollment quota lifted to allow open enrollment through 31Jul04
06	Jul	04	Approved Study: Virologic/immunologic predictors of CMV-retinitis in LSOCA (H.Farzadagan)
	Dec	04	Leukocyte specimens (1,751) shipped from Cryonix to S. O'Brien for ancillary study regarding genetic markers
	Dec	04	LSOCA: Course of CMV in era of HAART: 1. Retinitis progression (*Ophthalmology)*
	Dec	04	LSOCA: Course of CMV in era of HAART: Second eye involvement and retinal detachment (*Ophthalmology)*
03	Jan	05	Collection of additional blood for cell viability testing
21	Apr	05	Revised Fundus Photograph schedule: 5-year photos for all patients
	May	05	LSOCA: Risk factors for mortality in patients with AIDS in era of HAART *(Ophthalmology)*
30	Sep	05	Revisions to the annual enrollment quota (5 patients/clinic/year) and patient payment
12	Jan	06	Cell Viability Testing, Year 2

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Chronology

14	Mar	06	Distribution of LSOCA Newsletter
	May	06	LSOCA: Risk of immune recovery uveitis in patients with AIDS and CMV retinitis (*Ophthalmology)*
	May	06	LSOCA: Factors affecting attrition in a longitudinal study of patients with AIDS *(AIDS CARE)*
17	Jan	07	Indiana University notified of termination (effective 1 Aug 08)
17	Jan	07	Cell viability testing, Year 3 (PPM 102)
19	Jan	07	University of Southern California notified of termination (effective 1 Aug 08)
02	Feb	07	Conversion from full threshold to SITA Standard protocol for Humphrey visual field testing
07	Mar	07	Study Chairman (D. Jabs) moves to MSMC; continues in role of LSOCA Study Chairman
	Apr	07	The effects of CMV retinitis on the risk of visual acuity loss among patient with AIDS *(Ophthalmology)*
	Apr	07	LSOCA: Ocular diagnosis at enrollment *(Ophthalmology)*
	Apr	07	LSOCA: Ocular examination results at enrollment *(Ophthalmology)*
01	May	07	LSOCA 5 -year competitive renewal due date
10	Aug	07	Jennifer Thorne designated as Deputy Director
14	Aug	07	Receipt of competitive renewal summary statement from NEI
01	Jan	08	Merger of Fisher Clinical Services with Cryonix
22	Jan	08	Start of transition to Digital photography (PPM119)
22	Jan	08	Cell Viability Testing, Year 4
24	Jan	08	LSOCA: Poor predictive value of CMV-specific T-Cell assays for the development of CMV retinitis in patients with AIDS *(Clin Infect Dis)*
15	Feb	08	LSOCA: Vision function in HIV- infected individuals without retinitis *(Am J Ophthalmol)*
19	Jun	08	IRB approval at MSSM for Hep C study
02	Jul	08	IRB approval of ancillary studies titled: “Hepatitis C Virus Infections and Ocular Outcomes in LSOCA”
07	Jul	08	LSOCA Certificate of Confidentiality extended to July 2013
28	Jul	08	Notice of Grant Award from NEI for continued funding 2008-2013
31	Jul	08	IU, USC discontinuation of LSOCA funding (closeout complete cessation of contract)
01	Aug	08	Enrollment quota reinstated (5 patients/clinic/year)
14	Aug	08	Relocation of LSOCA Chair’s Office to MSSM
15	Aug	08	LSOCA: AIDS and ophthalmology *(Arch Ophthalmol)*
28	Aug	08	Implementation of lens grading (AREDS)
01	Sep	08	Protocol 6.0 distributed
11	Dec	08	Site visit to Thermofisher specimen repository

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14	Dec	08	Site visit to Chairman's Office at MSSM
31	Jan	09	RUSH, NJMS, UCI discontinuation of LSOCA funding (closeout complete cessation of contract)
06	Mar	09	Brainstorming meeting re: paper writing
27	Mar	09	Site visit to Archive Storage Facility
23	Apr	09	Resignation of A. Hillis (PDMB)
02	Jul	09	D. Musch to replace A. Hillis on PDMB
28	Jul	09	Handbook Version 8.0 distributed
29	Jul	09	Site visit to Thermofisher specimen repository
02	Jul	09	UTMB discontinuation of LSOCA funding (closeout complete cessation of contract)
10	Aug	09	LSOCA accepted into NA-ACCORD
02	Sep	09	Harmon Smith resigns from PDMB
17	Dec	09	Igor Kozak replaces William Freeman as PI at UCSD
20	Jan	10	Transition from film to digital images for Fundus Photography
20	Jan	10	Enrollment quota lifted for all clinics
27	Jan	10	Leslie Wolf replaces Harmon Smith as LSOCA Ethicist (PDMB)
8-12	Feb	10	Coordinating Center closed due to blizzard
20	Feb	10	Site visit to ThermoFisher re: labeling concerns
04	Mar	10	Fundus Photographers training review (San Antonio)
19	Aug	10	NEI approved replacement PI (Steven Yeh) to replace S. Srivastava at Emory
23	Sep	10	Fundus Photographers training review
15	Jul	10	LSOCA Chair's Office MSSM IRB approval of project entitled: "Standardization of Uveitis Nomenclature (SUN)"
14	Oct	10	IRB approval of ancillary study titled: "Nervefiber thickening in people with AIDS and abnormalities of contrast sensitivity and color vision"
19	Oct	10	IRB approval of revised LSOCA Research Plan regarding termination of NJMS, RUSH, UCI and UTMB
19	Nov	10	IRB approval of ancillary study entitled: "Inflammation, senescense, and mortality in relation to HIV infection"
23	Nov	10	SOCA archive materials for FGCRT, CRRT, MACRT, HPCRT and LSOCA removed for destruction by Vangel Paper Company
17	Dec	10	I Kozak replaces W. Freeman as PI at UCSD
28	Jan	11	Meeting to discuss competitive renewal
21	Feb	11	Enrollment quota removed to enable clinics
31	Jul	11	End of LSOCA patient enrollment
12	Oct	11	LSOCA website move to new server
27	Oct	11	Implementation of National Death Index
31	Oct	11	Steve Oversby works with N. Kurinij in role as LSOCA Project Officer (PO)
16	Dec	11	1st Competitive renewal meeting to 'brainstorm' ideas (Baltimore)

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31	Dec	11	Data for NYU 'duplicate' patient will not be in data sets for future analysis
15	Mar	12	National Death Index approved LSOCA Phase 2 request
23	Mar	12	Clinics given instructions to send patient search materials to National Death Index
26	Mar	12	Competitive renewal conference call with FPRC
04	May	12	PI meeting in Ft. Lauderdale regarding 5-year renewal
01	June	12	NEI Annual Renewal application submitted for Year 25
19	Jun	12	Signed letters of Intent received from all 13 clinical sites to continue in LSOCA for 5-year renewal.
11	Jul	12	Study Officers voted on revised patient closeout plan
19	July	12	C Meinert notified editors of Health and Quality of Life Outcomes and Editor of American Journal of of Ophthalmology regarding 'duplicate' patient and determination of 'no effect' on data outcomes of 4 LSOCA publications
25	Sep	12	Deadline due date for submission of competitive renewal to NEI
27	Sep	12	Submission of competitive renewal application to NEI
31	Oct	12	NYU clinic at Bellevue Hospital closed due to hurricane
06	Dec	12	Cheryl Arcinue replaces Igor Kozak as PI at UCSD
10	Dec	12	Patient Closeout and Appreciation letter
31	Dec	12	N. Kurinij retires and is replaced by S. Oversby as NEI Project Officer
28	Jan	13	Clinics notified LSOCA not funded
31	Jan	13	Review of LSOCA Competitive Renewal
07	Feb	13	Bellevue Hospital reopens after hurricane
29	Apr	13	Request for extension of Certificate of Confidentially
23	May	13	Re-Submission of Competitive Renewal Application to NEI
31	Jul	13	End of NIH funding
15	Aug	13	Clinics provided instructions for archiving study data and related documents
26	Oct	13	Transfer of specimens (>100,000) from ThermoFisher repository to Johns Hopkins Biological Repository
31	Oct	13	Steve Oversby, NEI Project Officer, retires
01	Nov	13	Louise Wideroff replaces S. Oversby as LSOCA/NEI Project Officer
06	Nov	13	NEI IRG review of LSOCA re-submission application
20	Dec	13	M. L. Van Natta replaces C. Meinert as LSOCA Coordinating Center Director
31	Dec	13	Last date the Coordinating Center to accept patient data
15	Jan	14	Site visit to JHU Biological Repository
23	Jan	14	NEI Council meets
20	Feb	14	Destruction of study documents
30	Jan	15	L. Wideroff replaced by D. Everett as Project Officer
31	Jul	15	End of LSOCA funding

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Specimen Repository History

Biomedical Research Institute (BRI): Rockville MD, James Leef (Director)

- 28 June 1990; Preliminary negotiations with ERC
- October 1990: Initial deposit of specimens (FGCRT)
- July 1991: Site visit
- June 1992: FGCRT specimen repository closed

Ogden BioServices: Gaithersburg MD, Harrison Hoppes (President)

- July 1992: FGCRT specimen repository transferred to Ogden BioServices
- CMV Retinitis Retreatment Trial (CRRT): December 1992 *(1st patient enrolled) - July 1995 (data collection closed)*
- August 1993: Site visit
- October 1994: Site visit
- HPMPC CMV Retinitis Trial (HPCRT): *April 1994 (1st patient enrolled) - March 1996 (data collection closed)*

University of Texas Medical Branch (UTMB) - James Richardson (Director)

- 1995: Monoclonal Antibody CMV Retinitis Trial (MACRT): *September 1995 (1st patient enrolled) - November 1996 (data collection closed)*

McKesson BioServices Corporation: Rockville MD, Donald Nolde

- December 1995: McKesson BioServices acquires Ogden BioServices
- February 1998: Meeting with McKesson BioServices Director - Donald Nolde
- Ganciclovir Cidofovir CMV Retinitis Treatment (GCCRT): *June 1997 (1st patient enrolled) - June 2000 (data collection closed)*

Cryonix Incorporated: Rockville MD, Jim Stavinoha (Director)

- June 1997: repository for LSOCA specimens
- 1999: Cryonix and McKesson jointly act as repositories
- LSOCA/Cryonix third party airbill for specimen shipments
- May 2001: Cryonix to replace McKesson BioServices

ThermoFisher, Rockville MD, Bruce Simpson (Director)

- December 2005: Merger of ThermoFisher Scientific with Cryonix

Fisher BioServices, Bruce Simpson (Director)

- January 2008: Merger of ThermoFisher and Fisher BioServices
- October 2013: Transfer of Specimens from ThemoFisher to JHBR

Johns Hopkins Biological Repository (JHBR), Homeyoon Farzedagam (Director)

- October 2013; Transfer of specimens from ThermoFisher repository to JHBR.

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Foscarnet-Ganciclovir CMV Retinitis Trial (FGCRT): ACTG 129

Status

- Completed (data collection closed as of 1 October 1992)
- 240 patients[†] enrolled at 12 clinics (March 1990-October 1991)
- Followup for vital status continued to death of last patient (December 1996)

Objectives

- Determine the relative safety and efficacy of foscarnet compared with ganciclovir for treating CMV retinitis in people with AIDS
- Compare the relative benefits of immediate treatment with foscarnet or ganciclovir with deferral of treatment in zones 2 & 3 retinitis

Trial characteristics

- Phase 3/4; Multicenter treatment trial

Treatment groups

- Ganciclovir (127 patients); Foscarnet (85 patients); Deferred (24 patients; restricted to patients with small peripheral lesions only)

Treatment administration

- Foscarnet: 60mg/kg of body weight every 8 hrs. **(induction)**; 90 mg/kg of body weight every 24 hours **(maintenance)**
- Gauciclovir: 5 mg/kg every 14 hrs **(induction)**; 5 mg/kg every 24 hrs **(maintenance)**

Inclusion criteria

- Males and females with AIDS, age 13 or older
- Newly diagnosed CMV retinitis

Masking

- Treatment administration unmasked
- Fundus photography reading masked

Other features of trial

- IND held by SOCA Coordinating Center
- Patient preference design for patients eligible for deferral

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[†]Including 20 startup patients

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Foscarnet-Ganciclovir CMV Retinitis Trial (FGCRT): ACTG 129

Results

- Equal efficacy of foscarnet and ganciclovir in treating CMV retinitis
- No difference between foscarnet and ganciclovir for preventing progression of retinitis
- Excess mortality associated with ganciclovir compared to foscarnet
- p24 antigen levels associated with mortality, but not with treatment assignment
- Characterization of patients with newly diagnosed CMV retinitis
- Comparison of centralized fundus photography readings with clinician interpretations
- Development of quality of life instrument
- Positive CMV cultures at baseline associated with increased risk of retinitis progression and mortality
- Foscarnet associated with adverse drug reactions; however, these reactions rarely had long-term effects
- Retinal detachments associated with increasing lesion size over time

Support

- Funding: NIH
- Drug support for patients provided by Astra, Syntex, and Burroughs-Wellcome

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CMV Retinitis Retreatment Trial (CRRT): ACTG 228

Status

- Completed (data collection closed as of 31 July 1995)
- 279 patients enrolled at 12 clinics (December 1992-February 1995)
- Followup for vital status continues to death of last patient

Objectives

- Compare the safety and efficacy of three aggressive therapeutic regimens in patients with AIDS-related CMV retinitis previously treated with foscarnet or ganciclovir whose retinitis progresses or recurs
- Compare the safety and efficacy of continuing to treat patients with the same anti-CMV drug versus switching to the alternative drug

Trial characteristics

- Phase 3/4; Multicenter treatment trial

Treatment groups

- Ganciclovir (94 patients); Foscarnet (89 patients); Combination ganciclovir and foscarnet (96 patients)

Treatment administration

- **Foscarnet group:** Induction with foscarnet sodium at 90mg/kg intravenously every 12 hours for 2 weeks followed by maintenance at dosage of 120 mg/kg per day.
- **Ganciclovir group:** 5 mg/kg intravenously every 12 hours for 2 weeks followed by maintenance at 10 mg/kg everyday
- **Combination therapy group:** Continuation of previous maintenance therapy plus induction with other drug (either ganciclovir or foscarnet) for 2 weeks followed by maintenance therapy with both drugs: ganciclovir sodium at 5 mg/kg per day and foscarnet sodium at 90 mg/kg per day

Inclusion criteria

- Males and females with AIDS, age 13 or older
- Relapsed CMV retinitis

Masking

- Treatment administration unmasked
- Fundus photography reading masked

Other features of trial

- Protocol suspended before planned sample size of 300 reached
- IND held by SOCA Coordinating Center

CMV Retinitis Retreatment Trial (CRRT): ACTG 228

Results

- Combination therapy most effective treatment in controlling CMV retinitis
- For monotherapy patients, switching to alternative drug was no more effective than continuing the same drug
- Survival advantage associated with prior foscarnet use
- GCSF use not associated with decreased bacterial infections
- GCSF use associated with increased survival

Ongoing analysis

- Quality of life comparisons among the 3 treatment groups

Support

- Funding: NIH
- Drug support for patients provided by Amgen, Astra, Bristol-Myers Squibb, Syntex, and Burroughs-Wellcome

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HPMPC Peripheral CMV Retinitis Trial (HPCRT): ACTG 281

Status

- Completed (data collection closed as of 1 September 1996)
- 64 patients enrolled in 13 clinics (April 1994 to March 1996)
- Followup for vital status continues to death of last patient

Objectives

- Evaluate safety and tolerance of intravenous HPMPC (cidofovir) in patients with CMV retinitis
- Obtain data on the safety and efficacy of two different dose regimens of HPMPC

Trial characteristics

- Phase 2/3; Multicenter treatment trial

Treatment groups

- Deferral of treatment (26 patients)
- H-3: Induction with HPMPC at 5mg/kg/wk and maintenance at 3mg/kg/2wks (26 patients)
- H-5: Induction with HPMPC at 5mg/kg/wk and maintenance at 5mg/kg/2wks (12 patients)

Treatment administration

- **Deferral:** treatment deferred until CMV retinitis progresses
- **Low-dose cidofovir:** 5 mg/kg once a week for 2 weeks followed by maintenance therapy with cidofovir of 3 mg/kg once every 2 weeks
- **High-dose cidofovir:** 5 mg/kg once weekly for 2 weeks followed by maintenance therapy with cidofovir of 5 mg/kg once every 2 weeks.

Inclusion criteria

- Males and females with AIDS, age 13 and older
- Newly diagnosed patients with peripheral CMV retinitis involving less than 25% of the retina

Masking

- Treatment assignment unmasked
- Fundus photography reading masked

Other features of trial

- Protocol suspended before planned sample size of 90 reached
- IND held by Gilead Sciences, Inc.

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HPMPC Peripheral CMV Retinitis Trial (HPCRT): ACTG 281

Results

- Cidofovir is effective in treatment of CMV retinitis at both 3mg/kg and 5mg/kg maintenance doses
- Cidofovir toxicity typically resolves with discontinuation of treatment. Discontinuation at the earliest sign of toxicity may prevent permanent complications.

Status

- Completed data collection

Support

- Funding: NIH and Gilead Sciences
- Drug support for all patients provided by Gilead Sciences

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Monoclonal Antibody CMV Retinitis Trial (MACRT): ACTG 294

Status

- Completed (data collection closed as of 15 November 1996)
- 209 patients enrolled at 15 clinics (September 1995 to November 1996)
- Followup for vital status continues to death of last patient

Objectives

- Evaluate safety and efficacy of human anti-CMV monoclonal antibody (MSL 109) as an adjunct treatment for CMV retinitis in patients with AIDS
- Evaluate the CMV viral load in patients with CMV retinitis

Trial characteristics

- Phase 2/3; Multicenter treatment trial

Treatment groups

- MSL 109, concurrent with active primary treatment for CMV retinitis (104 patients)
- Matched placebo for MSL 109, concurrent with active primary treatment for CMV retinitis (105 patients)

Treatment administration

- MSL-109 at 60 mg intravenously every 2 weeks
- Placebo

[Randomization stratified on basis of whether patients had untreated or relapsed CMV retinitis. Primary drug therapy for CMV retinitis was determined by treating physicians]

Inclusion criteria

- Males and females with AIDS, age 13 years or older
- Diagnosis of active CMV retinitis (new or relapsed)

Masking

- Treatment assignment masked
- Fundus photography reading masked

Other features of trial

- Protocol suspended before planned sample size of 325 reached
- IND held by Protein Design Labs

Results

- MSL 109 ineffective as adjunct treatment for CMV retinitis
- Excess mortality in patients receiving MSL 109 as compared to placebo group in patients with relapsed CMV at baseline

SOCA CV

Monoclonal Antibody CMV Retinitis Trial (MACRT): ACTG 294

Ongoing analysis

- CMV and HIV viral load

Support

- Funding: NIH and Protein Design Labs
- Drug supported patients provided by Protein Design Labs

SOCA CV

Ganciclovir Cidofovir CMV Retinitis Trial (GCCRT): ACTG 350

Status

- Completed data collection 30 June 2000
- 61 patients enrolled at 17 clinical centers (June 1997 to April 2000)
- Followup for vital status continues

Objectives

- To compare the efficacy of two treatment regimens in preventing vision loss as measured by visual acuity and visual field for patients with AIDS and CMV retinitis
- To compare a treatment regimen that incorporates highly active local therapy with a treatment regimen that does not

Trial characteristics

- Phase 4; Multicenter treatment trial

Treatment groups

- Ganciclovir intraocular device plus oral ganciclovir; Intravenous cidofovir

Treatment administration

- Ganclovir implant plus oral ganciclovir: 1 gm three times daily
- Intravenous cidofovir at 5 mg/kg once weekly for 2 doses followed by 5 mg/kg every other week.

Inclusion criteria

- Males and females with AIDS, age 13 years or older
- Diagnosis of active CMV retinitis (new or relapsed)

Masking

- Treatment administration unmasked
- Fundus photography reading masked

Other features of trial

- Surgical Quality Assurance Committee (SQAC)
- Visual Function Quality Assurance Committee (VFQAC)

Results

- In the era of highly active antiretroviral therapy, the regimens were similarly effective for controlling cytomegalovirus retinitis and preventing vision loss
- Side effects are different between the two groups

Support

- Funding: NIH
- Drug support for hardship patients provided by Chiron and Gilead

SOCA CV

Longitudinal Study of Ocular Complications of AIDS (LSOCA)

Status

- Enrolling (first patient enrolled 02 Sept 1998)
- Enrollment ended 31 July 2011

Current Objectives (2008-2013)

- Evaluate the long-term outcomes of ocular opportunistic infections (OOIs) among patients with AIDS;
- Evaluate visual impairment among patients with AIDS and without ocular opportunistic infections (No OOIs; and
- Evaluate (a) host genetic risk factors and (b) immunologic mechanisms of these ocular complications and their outcomes.

Original Objectives

- To monitor secular trends in the incidence of CMV retinitis and other complications of AIDS
- To determine the effect of HAART-induced changes in immune status on the risk of CMV retinitis and other complications of AIDS
- To determine the characteristics (clinical, virologic, hematologic and biochemical) of populations at high risk for CMV retinitis and other complications of AIDS
- To evaluate the effects of treatment for CMV retinitis and other ocular complications on visual function, quality of life and survival

Study characteristics

- Prospective, observational study
- Multicenter
- Sample size: 2,300 patients over a 10-year enrollment period; increased enrollment to 2,800 patients for years 2008-2013

Original Inclusion criteria

- Diagnosis of AIDS according to the 1993 CDC diagnostic criteria (with or without clinical symptoms of CMV retinitis or other ocular complications of AIDS)
- Males and females with AIDS, age 13 years or older
- Signed consent statement

Amended inclusion criteria

- Patients diagnosed with AIDS on or after 1 January 2001; or patients with newly diagnosed (within 45 days of enrollment) ocular opportunistic infections (OOIs)

Support

- Funding: NIH
- Currently in 4th year of 5 year funding cycle (2008-2013)

Ongoing analysis

- Secular trends of ocular complications
- Changes in HIV, CMV and CD4+ T cells
- Clinical course of ocular complications
- Mortality by CMV retinitis status

Longitudinal Study of Ocular Complications of AIDS (LSOCA)

End of enrollment

- 31 July 2011
- 2,392 patients enrolled from Sep 1998 to 31 July 2011

Status of study closeout

- IRG review of re-submission of application (6 Nov 2013)
- LSOCA notified of IRG critiques and likely not to be funded (14 Nov 2013)
- End of LSOCA funding (31 July 2015)

SOCA CV

Enrollment by clinic and study

Clinics	FGCRT	CRRT	HPCRT	MACRT	GCCRT	LSOCA
BCM	44	35	3	15	1	209
EU	--	--	0	1	3	136
IU	--	--	--	--	3	74
JHU	43	38	9	24	10	196
LSU	8	22	1	16	8	170
MSK	17	23	0	9	5	114
MSMC	10	19	3	7	--	--
NJMS	--	--	3	5	5	125
NU	30	22	3	19	0	120
NYU	26	21	6	19	0	108
PENN	--	--	--	--	1	171
RUSH	--	--	--	--	--	64
UCI	--	--	--	--	3	69
UCLA	14	23	6	19	2	174
UCSD	20	25	6	13	2	89
UCSF	10	23	11	19	0	123
UM	18	26	7	18	3	13
UNC	--	2	5	6	1	107
USC	--	--	--	--	2	67
USF	--	--	1	19	6	130
UTMB	--	--	--	--	5	133
WU	--	--	--	--	1	--
Total	**240**	**279**	**64**	**209**	**61**	**2,392**

*See page 58 for dates of clinic participation

SOCA CV

Baseline characteristics and followup status

	Trial					
	FGCRT	**CRRT**	**HPCRT**	**MACRT**	**GCCRT**	**LSOCA**
Number of patients	240	279	64	209	61	2,392
Demographic characteristics						
Mean age (yrs)	38	39	39	40	39	43
% white	72	61	58	64	29	45
% male	92	92	92	90	81	80
HIV exposure category*						
% men having sex with men	82	80	84	80	47	55
% injection drug users	10	9	8	3	24	13
% heterosexual contact	15	16	9	13	43	26
% blood product exposure	3	4	3	4	4	2
% other/unknown	3	1	2	5	0	4
CMV history						
% with extraocular CMV	0†	20	0†	20	12	6
% with newly dx CMVR	100†	0†	100†	40	80	5
Medication history (% ever taken)						
HAART	0	0	0	0	0	90
Mean Karnofsky score	82	78	81	79	81	83
Data collection statistics						
Date of start of study (mo/yr)	3/90	12/92	4/94	9/95	6/97	9/98
Length of study (years)	2.6	2.6	2.4	1.2	2.9	14.7
Cumulative person-years	217	215	63	125	76	17,335
% missed visits	¶	8.2	13.9	10.7	25.2	27
% patients dropout‡	¶	2.9	9.4	5.7	14.8	22

*Some patients may fall into multiple categories
†Forced because of inclusion/exclusion criteria
‡Defined as missing the last three or more visits prior to death or the close of data collection at suspension of the protocol
¶Not available

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70. Jabs DA, Ahuja A, Van Natta ML, Dunn JP, Yeh S for the Studies of Ocular Complications of AIDS Research Group. Comparison of treatment regimens for cytomegalovirus retinitis in patients with AIDS in the era of highly active antiretroviral therapy. *Ophthalmology* 2013; 120(6):1262-70. PMC:3660467.

71. Krauskopf K, Van Natta ML, Danis RP, Gangaputra S, Ackatz L, Addessi A, Federman AD, Branch AD, Meinert CL, Jabs DA for the Studies of Ocular Complications of AIDS Research Group. Correlates of hypertension in patients with AIDS in the era of highly active antiretroviral theraphy. *JIAPAC* 2013; 12:325. PMC:4100586.

72. Branch AD, Drye LT, Van Natta ML, Sezgin E, Fishman SL, Dieterich DT, Meinert CL, Jabs DA, Evaluation of Hepatitis C Virus as a Risk Factor for HIV- Associated Neuroretinal Disorder. *Clin Infect Dis* 2013; 57(11):1618-25. PMC:3814824.

Publications

73. Serrano-Villar S, Sainz T, Lee SA, Hunt PW, Sinclair E, Shacklett BL, Ferre AL, Hayes TL, Somsouk M, Hsue PY, Van Natta ML, Meinert CL, LedermanMM, Hatano H, Jain V, Huang Y, Hecht FM, Martin JN, McCune JM, Moreno S, Deeks SG, HIV-infected Individuals with Low CD4/CD8 Ratio despite Effective Antiretroviral Therapy Exhibit Altered T Cell Subsets, Heightened CD8+ T Cell Activiation, and Increased Risk of Non-Aids Morbidity and Mortality. *PLOS Pathog* 2014; 10(5):E1004078. PMC:4022662.

74. Hunt PW, Sinclair E, Rodriguez B, Shive C, Clagett B, Funderburg N, Robinson J, Huang Y, Epling L, Martin JN, Deeks SG, Meinert CL, Van Natta M, Jabs DA, Lederman MM. Gut Epithelial Barrier Dysfunction and Innate Immune Activation Predict Mortality in Treated HIV Infection. *J Infect Dis* 2014 Oct 15; 210(8): 1228-38. PMC:4192038.

75. Lee SA, Sinclair E, Jain V, Huang Y, Epling L, Van Natta M, Meinert CL, Martin JN, McCune JM, Deeks SG, Lederman MM, Hecht FM, Hunt PW. Low Proportions of CD28-CD8+ T cells Expressing CD57 Can Be Reversed by Early ART Initiation and Predict Mortality in Treated HIV Infection. *J Infect Dis* 2014 Aug 1;210(3):374-82. PMC:4110459.

76. Kozak I, Vaidya V, Van Natta ML, Pak JW, May KP, Thorne J for the Studies of Ocular Complications of AIDS Research Group. The prevalence and incidence of epiretinal membrances in eyes with inactive extramacular CMV retintis. *IOVS* 2014 Jun 12;55(7):4304-12. PMC:4098061.

77. Kempen JH, Sugar EA, Varma R, Dunn JP, Heinemann MH, Jabs DA, Lyon AT, Lewis RA, Studies of Ocular Complications of AIDS Research Group. Risk of Cataract among subjects with Acquired Immune Deficiency Syndrome Free of Ocular Opportunistic Infections. *Ophthalmology*. 2014 Dec; 121(12):2317-24. PMC:4252252.

78. Jabs DA, Drye L, Van Natta ML, Thorne JE, Holland GN, Studies of Ocular Complications of AIDS Research Group. Incidence and Long-term Outcomes of the Human Immunodeficiency Virus Neuroretinal Disorder in Patients with AIDS. *Ophthalmology*. 2015 Apr;122(4):760-8. PMC:4372475.

79. Jabs DA, Van Natta ML, Sezgin E, Pak JW, Danis R, Studies of the Ocular Conplications of AIDS Research Group. Prevalence of Intermediate-Stage Age-Related Macular Degeneration in Patients with the Acquired Immunodeficiency Syndrome. *Am J Ophthalmol*. 2015 Mar 10. PMID: 25769246.

80. Jabs DA, Ahuja A, Van Natta ML, Lyon AT, Yeh S, Danis R, Studies of the Ocular Complications of AIDS Research Group. Long-term Outcomes of Cytomegalovirus Retinitis in the Era of Modern Antiretrovial Therapy: Results from a United States Cohort. *Ophthalmology*. 2015 Apr 16. PMID: 25892019.

81. Ashraf DC, May KP, Holland GN, Van Natta ML, Wu AW, Thorne JE, Jabs DA, for the Studies of the Ocular Complications of AIDS Research Group. Relationship between Human Immunodeficiency Virus neuroretinal disorder and vision-specific quality of life among people with AIDS, (submitted to Ophthalmology June 2015).

Publications

82. Sezgin E, Van Natta ML, Thorne JE, Puhan MA, Jabs DA on behalf of the Studies of the Ocular Complications of AIDS (SOCA) Research Group. Secular trends in AIDS defining opportunistic infections, cancers, and mortality in patients with AIDS in the cART era (to be submitted).

83. Jabs DA, Van Natta ML, Danis R for the Studies of the Ocular Complications of AIDS Research Group. Cytomegalovirus retinitis among patients with the acquired immune deficiency syndrome initiating antiretroviral therapy. (to be submitted).

Publications over time by study

	FGCRT	CRRT	HPCRT	MACRT	GCCRT	LSOCA	Total
1992-1993	2						2
1994-1995	3						3
1996-1997	7	1	2	1			11
1998-1999							
2000-2001	1	1	1		1	2	6
2002-2003				3		4	7
2004-2005					1	7	8
2006-2007						9	9
2008-2009						3	3
2010-2011						10	10
2012-2013						13	13
2014-2015						8	8
Total	13	2	3	4	2	56	80

SOCA CV

Selected presentations and abstracts

1991

Davis MD: NEI sponsored clinical studies for CMV retinitis (SOCA). American Academy of Ophthalmology. Anaheim, CA; October 1991.

Studies of Ocular Complications of AIDS Research Group in Collaboration with the National Eye Institute: FGCRT - Mortality results. Press conference, October 1991.

Meinert CL: SOCA CMV retinitis trial mortality results. FDA Antiviral Advisory Board, Washington DC. November 1991.

Jabs DA: Foscarnet vs. Ganciclovir as initial treatment of CMV retinitis. Presented to the NIH AIDS Program Advisory Committee. Bethesda, MD, November 1991.

Jabs DA: Results from SOCA study: Foscarnet-Ganciclovir CMV Retinitis Trial. Presented to the AIDS Clinical Trials Group, Washington DC, December 1991.

1992

Jabs DA, for the Studies of Ocular Complications of AIDS (SOCA) Research Group in collaboration with the AIDS Clinical Trials Group (ACTG). Studies of Ocular Complication of AIDS Forscarnet-Ganciclovir Cytomegalovirus Retinitis Trial: Mortality results. *ARVO Abstracts Invest Ophthalmol Vis Sci* (suppl 33: 751). Tampa FL, May 1992.

Mowery R: SOCA study, an update. Presented to the National Advisory Eye Council, Washington DC, February 1992.

Meinert CL: Mortality in patients with AIDS treated with either foscarnet or ganciclovir for CMV retinitis: Results from a randomized trial. Presented to the European AIDS conference, Paris France, March 1992.

1993

Wu AW, Coleson LC, Holbrook JT, Jabs DA: A questionnaire to measure visual function and quality of life in CMV retinitis. Abstracts of the IX International Confererence on AIDS/IV STD World Congress. Berlin, Germany, June 1993.

Kempen JH, Martin BK, Wu AW, Barron B, Thorne JE, Jabs DA: The Studies of Ocular Complications of AIDS Research Group. The impact of cytomegalovirus retinitis on the quality of life of patients with the acquired immune deficiency syndrome. *ARVO Abstracts. Invest Ophtahlmol Vis Sci 44:E-Abstract 3127,* 1993

1993 (cont'd)

Holbrook JT, Jabs DA, Jacobson MA, Mendez P, Min Y, Murphy R: Foscarnet-related abnormalities in serum creatine, calcium, and magnesium in patients with CMV retinitis. *Presented to IX International AIDS Conference,* Berlin Germany, June 1993.

1996

Jacobson MA, Drew WL, Dunn JP, Feinberg J, Holbrook J, Martin B, Min N, Murphy R: Foscarnet-ganciclovir CMV retinitis trial: CMV culture results and clinical outcomes in AIDS patients with CMV retinitis treated either with foscarnet or ganciclovir. *Presented to XI International AIDS Conference,* Vancouver BC, July 1996.

Lawrence DW, Jacobson MA, Dunn JP, Feinberg J, Holbrook J, Martin B, Min N, Murphy R: Incidence of drug resistant CMV culture isolates and association with clinical outcomes in AIDS patients with CMV retinitis treated with either foscarnet (PFA) or ganciclovir (GCV). *Presented to XI International AIDS Conference,* Vancouver BC, July 1996.

Holbrook J, Davis M, Gilpin AK, Hubbard L, Martin B: Association of cytomegalovirus (CMV) retinitis characteristics with disease progression and vision loss. *Presented to XI International AIDS Conference,* Vancouver BC, July 1996.

Dieterich D for the SOCA Research Group - Monoclonal Antibody CMV Retinitis Trial: preliminary results. *Presented to the 36th Interscience Conference on Antimicrobial Agents and Chemotherapy,* New Orleans LA, September 1996.

1997

Wu AW for the SOCA Research Group: Clinical trials: future study design and methodology-Issues of concern to patients - quality of life. *Presented to the California Intercampus Ophthalmology Symposium,* San Francisco CA, February 1997.

Jabs DA for the SOCA Research Group: Cidofovir (HPMPC) for the treatment of CMV retinitis: the HPMPC Peripheral CMV Retinitis Trial. *Presented to the Macula Society Meeting,* Florence Italy, June 1997.

1998

Wu AW for the SOCA Research Group: Reliability, validity and responsiveness of patient reported health and vision measures in AIDS-related CMV retinitis. *Presented to the Drug Information Association,* January 1998.

Martin B for the SOCA Research Group: Effect of CMV retinitis treatment on patient-reported and objective measures of vision. *Presented to the International Society for Quality of Life Research*, November 1998.

SOCA CV

Selected presentations and abstracts

1999

Wu AW for the SOCA Research Group: The importance of patient-reported vision in CMV retinitis. *Presented at Yosemite CA,* February 1999.

Martin B for the SOCA Research Group: Evaluating disease-specific quality of life measures in a clinical trial for cytomegalovirus retinitis. *Presented to the Epidemiology Department, Johns Hopkins University,* Baltimore MD, March 1999.

2000

Van Natta M L and Min Y-I: Bias in "as treated" analysis using time-varying treatment (poster). Controlled Clin Trials 21: 133S. *Presented at the 21st Annual Meeting of the Society for Clinical Trials,* Toronto Canada, 2000.

Davidson M, Min YI, Holbrook JT, Quinn TC, Murphy R, Jabs DA, Welch W, Meinert CL, for the SOCA Research Group: Influence of granulocyte colony-stimulating factor on HIV 1 RNA in patients with CMV retinitis. AIDS 4:575. *Presented at the XIII International AIDS Conference, Durban South Africa*, July 2000.

Shah KH, Holland GN, Van Natta ML, for the SOCA Research Group: Contrast sensitivity in individuals with AIDS: Severely immunosuppressed individuals versus individuals with immune reconstitution. *Presented at the 2001 Association for Research in Vision and Ophthalmology Annual Meeting*, 2000.

Davidson M, Min Y-I, Holbrook JT, Van Natta ML, Jabs DA, Murphy R, Welch W, Meinert CL for the Studies of Ocular Complications of AIDS (SOCA): Influence of granulocyte colony stimulation factor (G-CSF). Use on bacterial infections and mortality in advanced AIDS. *Presented at the XIII International AIDS Conference, Duban South Africa,* July 2000.

2001

Jabs DA: The ganciclovir implant plus oral ganciclovir versus parenteral cidofovir for the treatment of cytomegalovirus retinitis in patients with AIDS: The Ganciclovir Cidofovir Cytomegalovirus Retinitis Trial. *Presented at the Macula Society Meeting,* 2001.

Kempen JH: Ganciclovir implant and oral ganciclovir vs cidofovir for cytomegalovirus retinitis in patients with AIDS: The Ganciclovir Cidofovir Cytomegalovirus Retinitis Trial. *Presented at the Association for Research in Vision and Ophthalmology Annual Meeting*, 2001.

Holbrook JT: Workshop in Closeout Procedures for Clinical Trials. Patient notification and followup after suspension of treatment protocols. Controlled Clin Trials 22: (2S): 22S. *Presented at the 22nd Annual Meeting for the Society of Clinical Trials,* 2001.

Martin BK, Gilpin AMK, Jabs DA, Wu AW: Evaluation of a general and disease-specific quality of life instrument for cytomegalovirus retinitis. *Presented at the 8th Annual Meeting of the International Society of Quality of Life Research,* Amsterdam, 2001.

SOCA CV

Selected presentations and abstracts

2002

Thorne JE, Kempen JH, Wu A, Martin BK, Barron B, Jabs DA for the Studies of Ocular Complications of AIDS Research Group: The impact of CMV retinitis on Quality of Life of patients with AIDS (LSOCA). *Presented at the Wilmer Residents Association Meeting*, Baltimore 2002.

2003

Kempen JH: The impact of CMV retinitis on Quality of Life of patients with AIDS. *Presented at the Association for Research in Vision and Ophthalmology Annual Meeting,* 2003.

Jacobson MA for the Studies of Ocular Complications of AIDS Research Group: HIV: Toxicity, Transmission, and Treatment. *Presented at the Infectious Diseases Society of America (ISDA),* 2003.

Holland GN for the Studies of Ocular Complications of AIDS Research Group: Factors related to the opacity of cytomegalovirus retinitis lesions in patients with AIDS (LSOCA). *Presented at the Association for Research in Vision and Ophthalmology Annual Meeting,* 2003.

2004

Jabs DA: Risk factors for mortality in patients with AIDS in the era of HAART. *Presented at the 11th Conference on Retroviruses and Opportunistic Infections,* 2004.

Jabs DA, Van Natta ML, Thorne JE, Weinberg DV, Meredith TA, Kuppermann BD, Sepkowitz K, Li HK and the Studies of Ocular Complications of AIDS Research Group: Course of CMV retinitis in the era of highly active anti-retroviral therapy. Abstracts for the Association for Research in Vision and Ophthalmology Annual Meeting, April 2004.

Weinberg DV, Holbrook J, Jabs DA, Holland GN, Vanderhoof Young M, Hurlburt D, Hubbard LD, David MD and the Studies of Ocular Complications of AIDS Research Group: Clinician vs. Reading center assessment of cytomegalovirus retinitis lesion area. *Abstracts at the Association for Research in Vision and Ophthalmology Annual Meeting,* Ft Lauderdale FL, April 2004.

Holbrook J: CMV retinitis is a risk factors for mortality in patients with AIDS in the era of HAART. *Presented at the Association for Research in Vision and Ophthalmology Annual Meeting,* 2004.

2005

Thorne JE: Visual acuity loss among patients with AIDS and CMV retinitis in the era of HAART. *Presented at the American Uveitis Society Meeting,* 2005.

Kempen JH, Min YI, Freeman WR, Holland GN, Friedberg DN, Dieterich DT, Jabs DA: Studies of Ocular Complications of AIDS Research Group. Risk of immune recovery uveitis in patients with cytomegalovirus retinitis and the acquired immune deficiency syndrome. *Abstracts at the Association for Research in Vision and Ophthalmology Annual Meeting*, Ft Lauderdale FL, 2005.

SOCA CV

Selected presentations and abstracts

2006

Thorne JE: Visual acuity loss among patients with AIDS and CMV retinitis in the era of HAART. *Presented at the Association for Research in Vision and Ophthalmology Annua l Meeting, Ft. Lauderdale FL, April 2006.*

Kempen JH, Thorne JE, Holbrook JT, Jabs DA, Nichols CW, Meinert CL for the Studies of Ocular Complications of AIDS Research Group: Risk of loss of visual acuity for patients with AIDS. *Abstract at Association for Research in Vision and Ophthalmology Annual Meeting, Ft. Lauderdale FL, May 2006.*

Gaynes B: Maculopathy with prior CMV retinitis in patients receiving HAART as depicted by OCT (LSOCA). *Presented at Association for Research in Vision and Ophthalmology Annual Meeting,, Ft. Lauderdale FL, 2006.*

2007

Kempen JH: Cataract risk among patients with AIDS.*Presented at the Symposium on Ocular Epidemiology, January 2007.*

Thorne JE, Jabs DA, Kempen JH, Holbrook JT, Nichols C, Meinert CL, for the Studies of Ocular Complications of AIDS Research Group: Visual acuity loss among patients with AIDS and cytomegalovirus retinitis in the era of highly active antiretroviral therapy. *Abstracts at the German Uveitis Patient Interest Group (Deutsche Arbeitsgemeinschaft (DUAG), Paris France, October 2007.*

2009

Holland GN, Kim CJ, Van Natta ML, Jacobson MA, Dunn JP, Meredith TA, Jabs DA for the SOCA Research Group. Immunologic and virologic laboratory parameters associated with active AIDS-related cytomegalovirus retinitis in the era of highly active antiretroviral therapy. *Abstract at the Association for Research in Vision and Ophthalmology Annual Meeting,* Ft Lauderdale, FL 2009.

2011

Limou S, Van Natta M, Jabs DA, Multi-cohort genome-wide association study reveals a new signal of protection against HIV-1 acquisition. Abstract at the International Congress of Human Genetics 2011.

2012

Hunt P, Rodrigquez B, Shive C, Clagett B, Funderburg N, Van Natta ML, Medvik K, Huang Y, Meinert C, and Lederman M: Gut Epithelial Barrier Dysfunction, Inflammation, and Coagulation Predict Higher Mortality during treated HIV/AIDS. Abstract at the 19th Conference on Retroviruses and Opportunistic Infections, 2012

Meetings

	Date		Place
Research group/Coordinators	**1990**	08 Feb	Baltimore
		16 Oct	Baltimore
	1991	16 May	Houston
		11 Oct	Baltimore
		07 Nov	Baltimore, AD Hoc
	1992	10 Apr	Baltimore
		29 May	Baltimore, PDMB
		18 Oct	San Diego
	1993	25 Apr	Baltimore
		01 Sep	Conference call
		14 Oct	Baltimore
		Nov	Conference call
	1994	02 Mar	Conference call
		18 Apr	Baltimore
		03 Aug	Conference call
		21 Nov	Baltimore
	1995	01 Feb	Conference call
		10 Apr	Washington DC
		09 Nov	New Orleans
	1996	07 Feb	Conference call
		29 Apr	Baltimore, MD
		07 Aug	Conference call
		14 Aug	Conference call
		30 Sep	Baltimore, MD
	1997	05 Feb	Conference call
		03 Apr	Miami
		06 Aug	Conference call
		20 Oct	Annapolis

SOCA CV

Meetings

	Date		Place
Research group (cont'd)	**1998**	04 Feb	Conference call
		19 Feb	Training Session
		20 Apr	Columbia, MD
		05 Aug	Conference call
		01 Oct	Chicago
	1999	03 Feb	Conference call
		22 Sep	Baltimore, MD
		03 Nov	Conference call
	2000	07 Feb	Santa Monica
		05 Apr	Conference call
		03 Aug	Baltimore - presented GCCRT results
		01 Nov	Conference all
	2001	05 Mar	Tampa
		04 Apr	Conference call
		30 Nov	Baltimore, MD
	2002	01 Mar	New Orleans - RG & Coords'
		01 May	Conference call
		19 Sep	Houston, TX
	2003	05 Feb	Conference call
		21 Feb	Atlanta, RG - Coords' Mtg
		04 Jun	Conference call
		17-18 Oct	Baltimore, MD
	2004	04 Jan	Conference call
		20 Feb	San Antonio, Coords' Mtg
		03 Mar	Conference call
		01 Jun	Conference call
		29 Sep	Baltimore, MD
	2005	13 Feb	Tucson, Coords' Mtg,
		3 Mar	San Francisco, Coords' Mtg
		06 Apr	Conference Call
		15 Sep	San Diego

SOCA CV

Meetings

	Date		Place
Research group (cont'd)	**2006**	06 Apr	Conference call
		18 Sep	Baltimore, MD
	2007	22-23 Feb	New Orleans - Coords' Mtg
		10 Sep	Baltimore, MD
	2008	21-22 Feb	Orlando, FL - Coordinators'
		10 Jun	Conference call
		2-3 Oct	Tampa, FL
	2009	26-27 Feb	Charleston - Coordinators'
		01 Apr	Conference call
		10-11 Sep	Washington, DC
	2010	27 Apr	Conference call
		23 Sep	Santa Monica
	2011	15-16 Sep	Baltimore, MD
	2012	29 May	Conference Call
		27-28 Sep	Chicago, IL
	2013	23 Apr	Conference Call
Steering Committee	**1989**	6-7 Feb	Baltimore, MD
		24 Jul	Baltimore, MD
		25 Jul	Baltimore, MD
	1990	25 Jul	Dallas
		15 Oct	Baltimore, MD
	1991	16 May	Houston
		07 Nov	Baltimore, MD
	1992	31 Jan	Dallas
	1997	06 Aug	Conference call
	2001	17 Jan	Conference call
	2002	31 May	Conference call

Meetings

	Date		Place
Steering Committee (cont'd)	**2003**	07 Feb	Conference call
		06 Aug	Conference call
	2004	05 May	Conference call
	2005	18 May	Conference call
		16 Sep	San Diego
		09 Dec	Conference call
	2006	09 Dec	Conference call
	2007	26 Jan	Dallas, TX
		13 Feb	Conference call
	2008	10 Jun	Conference call
	2009	08 Apr	Conference call
	2010	14 Apr	Conference call
		23 Sep	Santa Monica - RG/SC
	2011	19 Jan	Conference call
		06 Apr	Conference call
		15 Sep	Baltimore - RG/SC
	2012	27-28 Sep	Chicago, IL
Policy and Data Monitoring Board (PDMB)	**1990**	08 Jan	Dallas,Tx
		17 Sep	Chicago
		27 Nov	Interim data monitoring report (31Oct90) distribute)
	1991	07 Feb	Interim data monitoring report (31Oct90) distribute)
		05 Apr	Dallas, Tx
		31 May	Interim data monitoring report (28Feb91) distribute)
		05 Aug	
		28 Aug	Chicago

SOCA CV

Meetings

	Date		Place
PDMB (cont'd)	**1991**	07 Oct	Baltimore, MD
	1993	09 Mar	Baltimore, MD
		22 Sep	Baltimore, MD
		20 Dec	Conference call
	1994	25 Feb	Conference call
		06 Apr	Baltimore, MD
		27 Jul	Conference call
		19 Sep	Baltimore, MD
		19 Oct	Baltimore, MD
	1995	11 Jan	Baltimore, MD
		31 May	Conference call
		11 Sep	Baltimore, MD
	1996	01 Mar	Baltimore, MD
		16 Apr	Conference call
		30 May	Conference call
		03 Jun	Conference call
		07 Aug	Conference call
	1997	04 Feb	Conference call
	1998	09 Jan	Baltimore, MD
		18 Nov	Conference call
	1999	28 Jan	Conference call
		12 Mar	Baltimore, MD
		12 May	Baltimore, MD
		30 Jun	Conference call
		29 Oct	Baltimore, MD
	2000	26 Apr	Conference call
		14 Jul	Baltimore, MD
		21 Nov	Conference
	2001	17 Jan	Conference call
		10 Oct	Baltimore, MD
	2002	26 Jan	Baltimore, MD
		26 Jun	Baltimore, MD

SOCA CV

Meetings

	Date		Place
PDMB (cont'd)	**2003**	11 Apr	Baltimore, MD
		17 Sep	Conference call
	2004	14 Apr	Baltimore, MD
	2005	09 May	Baltimore, MD
		09 Nov	Conference call
	2006	24 Apr	Baltimore, MD
		09 Nov	Conference call
	2007	10 Jan	Conference call
		02 Mar	Baltimore, MD
		26 Oct	Baltimore, MD
		10 Dec	Conference call
	2008	10 Oct	Baltimore, MD
	2009	22 Apr	Conference call
	2010	29 Apr	Conference call
		19 Nov	Baltimore, MD
	2011	11 Apr	Conference call
		04 Nov	Baltimore, MD
	2012	29 May	Conference call
	2013	18 Jul	Conference call
Coordinator's Meeting	**2000**	05 Mar	Tampa
	2002	01 Mar	New Orleans
		19 Sep	Houston
	2003	21 Feb	Atlanta
		17 Oct	Baltimore
	2004	20 Feb	San Antonio
		29 Sep	Baltimore, RG/CC
	2005	03 Mar	San Francisco
		15 Sep	San Diego, RG/CC
	2006	13-14 Feb	Tucson, AR

SOCA CV

Meetings

	Date		Place
Coordinator's meeting (cont'd)	**2007**	22-23 Feb	New Orleans
		10 Sep	Baltimore, RG/CC
	2008	08 Feb	Orlando, FL
		2-3 Oct	Tampa, RG/CC
	2009	25-27 Feb	Charleston, SC
		10 Sep	Washington DC, RG/CC
	2010	04 Mar	San Antonio, TX
		24 Sep	Santa Monica, RG/CC
	2011	3-4 Mar	Las Vegas, NV
		15-16 Sep	Baltimore, MD RG/SC/CC
	2012	28-30 Mar	San Diego, CA
		27-28 Sep	Chicago, IL
	2013	Jul	Conference call

SOCA Ancillary studies

Title:	**Hepatitis C Virus Infection and Ocular Outcomes in LSOCA (Douglas Dieterich , MSSM)**
Primary Objective:	Test hypothesis that there is an increased incidence of presumed HIV-associated neuroretinal disorder (HIV-NRD) and an increased incidence of cataracts in subjects with chronic HCV infection compared to subjects without HCV infection.
Resources/timepts:	2,195 Banked specimens: plasma (1 mL) Baseline, or if only one remaining aliquot of baseline sample is banked, then the sample tested will be from earliest time point where at least two samples are banked
Estimated duration:	2 years
Shipment/# specimens:	1st shipment: 383 samples - HCV Ab and HCV RNA tests 2+ shipment: 1812 samples - HCV Ab and HCV RNA if HCV Ab+
Funding mechanism:	Release of restricted LSOCA funds
Date of Initiation: *(as of IRB approval)*	**2 July 2008**

Title:	**Inflammation, Senescence, and Mortality in relation to HIV Infection** (Peter Hunt, UCSF)
Primary Objective:	To determine the relative contributions of inflammation and T-cell senescence in predicting mortality among 100 HIV-infected individuals maintaining treatment-mediated viral suppression who died matched with 200 controls.
Resources/timepts:	Soluble markers of inflammation and microbial translocation, T-cell activation, memory T-cell senescence at last visit before death
Estimated duration:	2 years
# specimens:	300 leukocyte specimens and 300 plasma specimens
Funding mechanisms:	**R21**
Date of Initiation: *(as of IRB approval)*	**19 November 2010**

Title:	**Administrative Supplement: Change in Hepatitis C Virus status - incidence, clearance, and reactivation** (D. Dieterich, MSSM)
Primary Objective:	1) To determine clearance rate in patients with chronic HCV at baseline; 2) to determine sustainability of clearance among patients with cleared HCV at baseline; 3) To determine incidence of chronic HCV among patients with uninfected HCV at baseline; 4) To adjust for CMV Ab status
Resource/timepts:	1) 348 last visit samples + 720 serial samples for HCV RNA; 2) 910 serial samples for HCV RNA; 3) 1,734 last visit samples for HCV Ab + 2,250 serial samples for HCV RNA
Estimated duration:	2 years
# specimens:	6,592 plasma specimens
Funding mechanism:	**Administrative (ARRA) Supplement**
Date of Initiation: *(date of award)*	**1 September 2009**

Title:	**Nerve fiber thickening in people with AIDS and abnormalities of contrast sensitivity and color vision** (G Holland, UCLA)
Primary Objective:	To evaluate structural abnormalities of the retina, by OCT, in LSOCA participants with abnormalities in contrast sensitivity and color vision, longitudinally.
Resource/timepts:	15-20 LSOCA participants without OOI. This is a single center study.
Estimated duration:	First report in 3 months and to continue to obtain longitudinal data for OCT and color vision.
#specimens:	Not applicable
Funding mechanism:	**Not contingent upon funding**
Date of Initiation: *(as of IRB approval)*	**14 October 2010**

SOCA CV

Host genetic risk factors for ocular complications of AIDS and their outcomes*

Type of study

- Nested case control
- Longitudinal

Objective: Evaluate effect of host genes on occurrences & course of CMV and HIV-NRD

Methods

- Examine AIDS restriction genes, known to influence AIDS progression and look for additional candidate genes
- Examine candidate genes polymorphisms for association with CMV susceptibility and pathology
- Perform a series of genetic tests on selective allele populations

Inclusion criteria

- Participants both with CMV and without CMV infection

Number of participants: One specimen each from patients

Duration: Four years

Specimens needed: Cryo-preserved PDBM pellet transformed in EBV to lymphoblastoid cell lines

Other resources

- CMV status
- HIV viral load
- CD4 cell count
- CMV date
- AIDS diagnosis
- Age/Gender/Ethnicity

Statistical analysis

- Linkage equilibrium
- Other genetic association analyses

Status of IRB approval: NCI Approved

Funding: Cost of specimen shipping

Other assistance needed: Analytical collaboration with LSOCA biostatisticians

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*Initially an ancillary study in 1998, host genetic risk factors became a primary aim of LSOCA in 2003-2008 funding cycle.

Support funding

The Studies of Ocular Complications of AIDS (SOCA) is supported by cooperative agreements from the National Eye Institute to The Johns Hopkins University Bloomberg School of Public Health (U10EY 08057), the Fundus Photograph Reading Center, (EY 80867) and the Chairman's Office (EY 08052).

Data sharing

LSOCA & NA-ACCORD agreement began in August 2009

The North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) is part of the International Epidemiologic Databases to Evaluate AIDS (IeDEA). NA-ACCORD is designed to be widely representative of HIV care in the United States and Canada, and includes investigators who have a high level of scientific expertise and clinical experience and constitutes an efficient structure for harmonization of data and the conduct of analyses.

Genetics Core Facility of the Frederick National Laboratory for Cancer Research (FNLCR) agreement began in August 2004

Since 2004, SOCA had a productive collaboration with the Frederick National Laboratory for Cancer Research (FNLCR); formerly known as Laboratory of Genomic Diversity, investigating host genetic factors influencing infectious and non-infectious ocular complications of AIDS. FNLRC began operations under the authority of the National Cancer Institute (NCI) in June 1972 upon transfer of 70 acres and 67 buildings formerly owned by the U.S. Department of Health and Human Services, National Institutes of Health (NIH). FNLCR partners with university, government, and corporate scientists to speed the translation of laboratory research into new diagnostic tests and treatments for cancer and AIDS, and has become an internationally recognized center of scientific excellence. With a unique array of advanced technologies, FNLCR aims to bridge the gap between discovery and healthcare delivery. In 2012, SOCA started to collaborate with Dr. Cheryl Winkler, head of molecular genetic epidemiology studies, of FNLCR to continue genetic studies with the SOCA cohort. SOCA will collaborate with Dr. Winkler's group to determine the impact of genetic risk factors for age-related eye complications such as Age-related macular degeneration (AMD), cataract, and retinal vasculature.

SOCA CV

NA-ACCORD/LSOCA Publications (as of 28 May 2015)

1. Althoff KN, Gebo KA, Gange SJ, Klein MB, Brooks JT, Hogg RS, Bosch RJ, Horberg MA, Saag MS, Kitahata MM, Eron JJ, Napravnik S, Rourke SB, Gill J, Rodriguez B, Sterling TR, Deeks SG, Martin JN, Jacobson LP, Kirk GD, Collier AC, Benson CA, Silverberg MJ, Goedert JJ, McKaig RG, Thorne J, Rachlis A, Moore RD, Justice AC for the North American AIDS Cohort Collaboration on Research and Design. CD4 count at presentation for HIV care in the United States and Canada: Are those over 50 years more likely to have a delayed presentation? AIDS Res Ther 2010; 7 (1): 45- 50. PMC:3022663.

2. Sterling TR, Lau B, Zhang J, Freeman A, Bosch RJ, Brooks JT, Deeks SG, French A, Gange S, Gebo KA, Gill MJ, Horberg MA, Jacobson LP, Kirk GD, Kitahata MM, Klein MB, Martin JN, Rodriguez B, Silverberg MJ, Willig JH, Eron JJ, Goedert JJ, Hogg RS, Justice AC, McKaig RG, Naprivnik S, Thorne JE, Moore RD for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of the International Epidemiologic Databases to Evaluate AIDS (IeDEA). Risk factors for tuberculosis after highly active antiretroviral therapy initiation in the United States and Canada: Implications for Tuberculosis Screening Strategies. J Infect Dis 2011; 204 (6): PMC:21849286.

3. Abraham Ag, Lau B, Deeks S, Moore RD, Zhang J, Eron JJ, Harrington R, Gill MJ, Kitahata MM, Klein MB, Napravnik S, Rachlis AR, Rodriquez B, Rourke SB, Benson CA, Bosch RJ, Collier AC, Gebo KA, Goebert JJ, Hogg RS, Horberg MA, Jacobson LP, Justic AC, Kirk GD, Martin JN, McKaig RG, Silverberg MJ, Sterling TR, Thorne J, Willig J and Gauge SJ for the North American AIDS Cohort Collaboration on Research and Design. Missing data or the estimation of the prevalence of accumulated HIV drug resistance in antiretroviral-treated patients in North America. Am J Epidemiol 2011; 174(6):727-735. PMC:3202147.

4. Silverberg MJ, Lau B, Justice AC, Engels E, Gill MJ, Goedert JJ, Kirk GD, D'Souza G, Bosch RJ, Brooks JT, Napravnik S, Hessol NA, Jacobson LP, Kitahata MM, Klein MB, Moore RD, Rodriguez B, Rourke SB, Saag MS, Sterling TR, Gebo KA, Press N, Martin JN, Dubrow R; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of IeDEA. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. Clin Infect Dis. 2012;54(7):1026-34. PMC:3297645.

5. Althoff KN, Buchacz K, Hall HI, Zhang J, Hanna DB, Rebeiro P, Gange SJ, Moore RD, Kitahata MM, Gebo KA, Martin J, Justice AC, Horberg MA, Hogg RS, Sterling TR, Cescon A, Klein MB, Thorne JE, Crane HM, Mugavero MJ, Napravnik S, Kirk GD, Jacobson LP, Brooks JT; North American AIDS Cohort Collaboration on Research and Design. U.S. trends in antiretroviral therapy use, HIV RNA plasma viral loads, and CD4 T-lymphocyte cell counts among HIV-infected persons, 2000 to 2008. Ann Intern Med. 2012;157(5):325-35. PMC:3534765.

6. Hanna DB, Buchacz K, Gebo KA, Hessol NA, Horberg MA, Jacobson LP, Kitahata MM, Korthuis PT, Moore RD, Napravnik S, Patel P, Silverberg MJ, Sterling TR, Willig JH, Collier A, Samji H, Thorne JE, Althoff KN, Martin JN, Rodriguez B, Stuart EA, Gange SJ; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of the International Epidemiologic Databases to Evaluate AIDS (IeDEA). Association between U.S. State AIDS Drug Assistance Program (ADAP) Features and HIV Antiretroviral Therapy Initiation, 2001-2009. PloS One, 2013; 8(11). PCM:3657490.

7. Lucas GM, Jing Y, Sulkowski M, Abraham AG, Estrella MM, Atta MG, Fine DM, Klein MB, Silverberg MJ, Gill MJ, Moore RD, Gebo KA, Butt AA; NA-ACCORD of the IeDEA. Hepatitis C viremia and the risk of chronic kidney disease in HIV-infected individuals. J Infect Dis 2013; 208(8): 1240-9. PMC:3778973.

8. Hanna DB, Buchacz K, Gebo KA, Hessol NA, Horberg MA, Jacobson LP, Kirk GD, Kitahata MM, Korthuis PT, Moore RD, Napravnik S, Patel P, Silverberg MJ, Sterling TR, Willig JH, Lau B, Althoff KN, Crane HM, Collier AC, Samji H, Thorne JE, Gill MJ, Klein MB, Martin JN, Rodriguez B, Rourke SB, Gange SJ; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of the International Epidemiologic Databases to Evaluate AIDS. Trends and disparities in antiretroviral therapy initiation and virologic suppression among newly treatment eligible HIV-infected individuals in North America, 2001-2009. Clin Infect Dis. 2013; 56(8): 1174-82. PMC:3657490.

9. Rebeiro P, Althoff KN, Buchacz K, Gill J, Horberg M, Krentz H, Moore R, Sterling TR, Brooks JT, Gebo KA, Hogg R, Klein M, Martin J, Mugavero M, Rourke S, Silverberg MJ, Thorne J, Gange SJ; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Retention among North American HIV-infected persons in clinical care, 2000 to 2008. J Acquir Immune Defic Syndr. 2013; 62(3): 356-62. PMC:3661708.

10. Justice AC, Modur SP, Tate JP, Althoff KN, Jacobson LP, Gebo KA, Kitahata MM, Horberg MA, Brooks JT, Buckhacz K, Rourke SB, Rachlis A, Napravnik S, Eron J, Willig JH, Moore R, Kirk GD, Bosch R, Rodriguez B, Hogg RS, Thorne J, Goedert JJ, Klein M, Gill J, Deeks S, Sterling TR, Anastos K, Gange SJ; North American AIDS Cohort Collaboration on Research Design (NA-ACCORD) and VACS Project Teams. Predictive accuracy of the Veterans Aging Cohort Study index for mortality with HIVE infection: a North American cross cohort analysis. J Acquir Immune Defic Syndr. 2013;62 (2): 149-63. PMC:3619393.

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11. Althoff KN, Rebeiro B, Brooks JT, Buckharcz K, Gebo K, Martin J, Hogg R, Thorne JE, Klein M, Gill JM, Sterling TR, Yehia B, Silverberg MH, Crane H, Justice AC, Gange SJ, Moore R, Kitahata MM, Horberg MA for the North American AIDS Cohort Collabration on Research and Design (NA-ACCORD). Disparities in the Quality of HIV Care When Using US Department of Health and Human Service Indicators. Clin Infect Dis 2014; 58(8): 1185-1189. PMC:3967825

12. Abraham AG, Althoff KN, Jing Y, Estrella MM, Kitrahata MM, Wester CW, Bosch RJ, Crane H, Eron J, Horberg MA, Justic AC, Klein M, Mayor AM, Moore RD, Palella FJ, Parikh CR, Silverberg MJ, Golub ET, Jacobson LP, Napravnik S, Lucas GM; for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of the International Epidemiologic Database to Evaluate AIDS (IeDEA). End-Stage Renal Disease among HIV-infected Adults in North America. Clin Infecd Dis 2015; 60(6): 941-9. PMC:4357817.

13. Yehia BR, Rebeiro P, Althoff KN, Agwa AL, Horbert MA, Samji H, Napravnik S, Mayer K, Tedaldi E, Silverberg MJ, Thorne JE, Burchell AN, Rourke SB, Rachlis A, Mayor A, Gill MJ, Zinksi A, Ohl M, Anastos K, Abraham AG, Kitahata MM, Moore RD, Gebo KA; for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). The Impact of Age on Retention in Care and Viral Suppression. J Acquir Immune Defic Syndr 2015; 68(4): 413-9. PMC:4334738.

Genetics Core Facility FNLCR Publications

Limou S, Delaneau O, van Manen D, An P, Sezgin E, Le Clerc S, Coulonges C, Troyer JL, Veldink JH, van den Berg LH, Spadoni J-L, Taing L, Labib T, Montes M, Delfraissy J-F, Schacter F, O'Brien SJ, Buchbinder S, Van Natta ML, Jabs DA, Froguel P, Schuitemaker H, Winkler CA, Zagury J-F. Multicohort genomewide association study reveals a new signal of protection against HIV-1 acquisition. J Infect Dis 2012;205:1155-1162. PMCID:3295605.

Malov S, Cherkasov N, Dobrynin P, Guan L, Geerts P, Troyer JL, Hendrickson SL, Dilks HH, Oleksyk T, Donfield S, Gomperts E, Jabs DA, Van Natta ML, Harrigan R, Brumme Z, O'Brien SJ, for the SOCA Research Group. Gene Discovery and Data Sharing in Disease Association Analyses across the Genome. Nature Biotech (Submitted).

Archived datasets and documents

Trial	Document/dataset	NTIS* Accession #
FGCRT	Protocol	PB93-231298
	Handbook	PB93-231280
	Data collection forms	PB93-231306
CRRT	Protocol	PB96-109715
	Handbook	PB96-109749
	Data collection forms	PB96-109723
HPCRT	Protocol	PB97-170310
	Handbook	PB97-170328
	Data Collections forms	PB97-170195
GCCRT	Protocol	PB2002-107314
	Handbook	PB2002-107310
	Data collection forms	PB2002-107315
MACRT	Protocol	PB97-170336
	Handbook	PB97-170344
	Data Collection forms	PB97-170351
SOCA	SOCA General Handbook	PB2002-107311
LSOCA	Protocol	PB2002-107309
	Handbook	PB2002-107316
	Data Collection forms	PB2002-107312
All Trials	SOCA CMV Grading Protocol	PB97-192082

*National Technical Information Service

SOCA CV

Quality assurance and procedures

Data monitoring and analysis

- Double data entry
- Ongoing data editing and analysis
- Data Quality Queries to resolve edits
- Vital Status Audits
- Interim data monitoring reports reviewed by the Policy and Monitoring Board
- Performance Guidelines
- Outlier detection

Safety monitoring

- Adverse events (trials only) and deaths are faxed to the CC within 24 hours of clinical notification
- Adverse event reports (trials only) and death reports are reviewed for completeness and correctness upon receipt
- The CC safety monitor contacts clinics to gather additional information on adverse events as necessary (trials only)
- Adverse events are reviewed by the CC safety monitor as well as drug company safety monitors as applicable (trials only)
- Maintain compliance with FDA regulations regarding IND safety reporting requirements (trials only)

Clinic and staff certification

- Certification of personnel is required for the following key positions:
  - Ophthalmologist
  - Infectious disease specialist
  - Clinic coordinator
  - Pharmacist (trials only)
  - Visual acuity examiner
  - Visual field examiner
  - Photographer
  - Research nurse (trials only)
- All new personnel must be certified
- Any personnel who take on a new function within the clinic must be certified for the new function
- Visual function training sessions (Photography, examination procedures for visual fields (Humphrey and Goldmann), visual acuity and Pelli-Robson contrast sensitivity)

Site visits

- Site visits to clinics and Resource centers, every 12-18 months
- Interim site visits, as needed
- Conference telephone call site visits, as needed

SOCA CV

Participating Centers (as of Nov 2013)

Clinics

Baylor College of Medicine: Richard Alan Lewis, MD, MS
Emory University Clinic: Steven Yeh, MD
Johns Hopkins University: James P. Dunn, MD
LSU Medical Center: Donald Bergsma, MD
Memorial Sloan-Kettering Cancer Center: Murk-Hein Heinemann, MD

NYU Medical Center: Dorothy Friedberg, MD, PhD
Northwestern University: Alice Lyon, MD
University of California at Los Angeles: Gary N. Holland, MD
University of California at San Diego: Cheryl Arcinue, MD
University of California at San Francisco: Jacque Duncan, MD

University of North Carolina: Travis Meredith, MD
University of Pennsylvania: Charles Nichols, MD
University of South Florida: Peter Reed Pavan, MD

Chairman's Office: Douglas Jabs, MD, MBA (Chairman); Jill Slutsky (Administration Manager): Mount Sinai School of Medicine
Coordinating Center: Curtis Meinert, PhD (Director); Jennifer Thorne, MD, PhD (Deputy Director)
Fundus Photography Reading Center: Ronald Danis, MD (Director)
National Eye Institute: Steve Oversby, PsyD (NEI Project Office)
Central Laboratories/Repository: Bruce Simpson; Thermofisher Scientific

Committees

Study Officers: Douglas A. Jabs, MD, MBA (Chairman); Curtis L. Meinert, PhD (LSOCA Director); Ronald Danis, MD (Director, FPRC); Matthew Davis, MD (FPRC); Steve Oversby, PsyD (NEI Representative); Jennifer Thorne, MD, PhD (LSOCA Deputy Director)

Steering Committee (as of Nov 2013): Douglas A. Jabs, MD, MBA (Chairman); Curtis L. Meinert, PhD (Vice-Chairman); Ronald Danis (FPRC); J. P. Dunn, MD (JHU); Dorothy Friedberg, MD (NYU); Gary N. Holland, MD (UCLA); Milana Isaacson (CC); Mark Jacobson, MD (UCSF); Alice Lyon, MD (NU); Steve Oversby, PsyD (NEI); Ann Johiro (UCLA); Frank Palella (NU); Christine Romero (LSU); Jennifer Thorne (CC)

Policy and Data Monitoring Board (as of Nov 2013): John Phair, MD (Chairman); Brian P. Conway, MD; Barry Davis, MD, PhD; David Musch, PhD, MPH; Robert Nussenblatt, MD; Richard J. Whitley, MD; Leslie Wolf, JD, MPH; Ronald Danis, MD; Matthew D. Davis, MD; Douglas A. Jabs, MD, MBA; Steve Oversby, PsyD; Curtis Meinert, PhD

SOCA CV

SOCA Clinical Centers: Start and departure dates

(as of 24 October 2011)

Baylor College of Medicine (BCM):	1 Aug 1989 - 30 Nov 2013
University of Alabama (UAB):	11 Mar 1994 - 15 Feb 1995
Emory University (EU):	31 Jan 1997 - 30 Nov 2013
Indiana University (IU):	9 Oct 1997 - 31 Jul 2008
The Johns Hopkins University (JHU):	1 Aug 1989 - 30 Nov 2013
Louisiana State University (LSU):	1990 - 1 Sep 2013
Memorial Sloan Kettering (MSK):	1 Aug 1989 - 28 Jun 2013
Mount Sinai Medical Center (MSMC):	1 Aug 1089 - 1 Oct 1998
New Jersey Medical Center (NJMS):	25 Apr 1995 - 31 Jan 2009
Northwestern University (NU):	1 Aug 1989 - 6 Nov 2013
New York University (NYU):	1 Aug 1989 - 1 Nov 2013
University of Pennsylvania (PENN):	11 Sep 1998 - 30 Nov 2013
RUSH Presbyterian (RUSH): (as an independent clinic)	14 Jun 2001 - 31 Jan 2009
University of California, Irvine (UCI):	6 Apr 1998 - 31 Jan 2009
University of California, Los Angeles (UCLA):	1 Aug 1989 - 30 Nov 2013
University of California, San Diego (UCSD):	1 Aug 1989 - 15 Nov 2013
University of California, San Francisco (UCSF):	1 Aug 1989 -
University of Miami (UM):	1 Aug 1989 - 2 Aug 2000
University of North Carolina (UNC):	18 Oct 1994 - 31 Oct 2013
University of South Florida (USF):	27 Jul 1995 - 30 Sep 2013

SOCA CV

Glossary of abbreviations

AIDS	Acquired Immune Deficiency Syndrome
AREDS	Age-related Eye Disease Study
CC	Coordinating Center
CMV	Cytomegalovirus
CO	Chairmans Office
CRRT	CMV Retinitis Re-treatment Trial
FDA	Food and Drug Administration
FGCRT	Foscarnet Ganciclovir CMV Retinitis Trial
FPRC	Fundus Photography Reading Center
GCCRT	Ganciclovir Cidofovir CMV Retinitis Trial
G-CSF	Granulocyte-colony stimulating factor
HAART	Highly Active Anti-Retroviral Treatment
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
HIV-NRD	HIV-associated neuroretinal disorder
HPCRT	HPMPC Peripheral CMV Retinitis Trial
IND	Investigational new drug
IRB	Institutional Review Board
LSOCA	Longitudinal Study of the Ocular Complications of AIDS
MACRT	Monoclonal Antibody CMV Retinitis Trial
NA-ACCORD	North American AIDS Cohort Collaboration on Research and Design
NCI	National Cancer Institute
NEI	National Eye Institute
NIH	National Institutes of Health
No OOI	No Ocular Opportunistic Infections
NTIS	National Technical Information Service
OCT	Optical Coherence Tomography
OHRP	Office of Human Research Protection
OOI	Ocular Opportunistic Infections
PI	Principal Investigator
PDMB	Policy and Data Monitoring Board
PPM	Policy and Procedure Memoranda
PO	Project Officer
RFA	Request for Application
RFP	Request for Proposal
SO	Study Officers

SOCA CV

Glossary of abbreviations

SOCA	Studies of Ocular Complications of AIDS
SUN	Standardization of Uveitis Nomenclature

SOCA public website

SOCA website: https://jhucct.com
The following information can be accessed through the public portion of the SOCA website.

SOCA

- SOCA General Handbook
- LSOCA Competitive Renewal 2008-2013 Research Plan
- SOCA CV
- Access to Social Security Death Index
- HIV/AIDS-related acronym list
- Other documents

LSOCA

- Patient newsletter
- LSOCA General Knowledge Assessment
- Protocol version 6.0
- LSOCA Consent Statement
- LSOCA Handbook version 8.0
- LSOCA Data System Manual
- Procedures for standard field color fundus images using film and digital imaging
- Forms
- LSOCA Form FAQs
- Drug Codebook
- Amendments to Certificate of Confidentiality

JHSPH Students involved in SOCA

Janet Holbrook
Michael Davidson
Camara Jones
Jennifer Thorne
Claudine Woo

Nancy Min
Aynur Arida-Unalp
Laura Murrow
Emily West
Shoshana Reshef

Pam Scott
Winifred Werther
Alexandra Jabs