1980s
Kaposi’s Sarcoma and Pneumocystis Pneumonia
Among Homosexual Men — New York City and California

During the past 30 months, Kaposi’s sarcoma (KS), an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men (20 in New York City [NYC]; 6 in California). The 26 patients range in age from 26-51 years (mean 39 years). Eight of these patients died (7 in NYC, 1 in California)—all 8 within 24 months after KS was diagnosed. The diagnoses in all 26 cases were based on histopathological examination of skin lesions, lymph nodes, or tumor in other organs. Twenty-five of the 26 patients were white, 1 was black. Presenting complaints from 20 of these patients are shown in Table 1.

Skin or mucous membrane lesions, often dark blue to violaceous plaques or nodules, were present in most of the patients on their initial physician visit. However, these lesions were not always present and often were considered benign by the patient and his physician.

A review of the New York University Coordinated Cancer Registry for KS in men under age 50 revealed no cases from 1970-1979 at Bellevue Hospital and 3 cases in this age group at the New York University Hospital from 1961-1979.

Seven KS patients had serious infections diagnosed after their initial physician visit. Six patients had pneumonia (4 biopsy confirmed as due to Pneumocystis carinii [PC], and one had necrotizing toxoplasmosis of the central nervous system. One of the patients with Pneumocystis pneumonia also experienced severe, recurrent, herpetic simplex infection; extensive candidiasis; and cryptococcal meningitis. The results of tests for cytomegalovirus (CMV) infection were available for 12 patients. All 12 had serological evidence of past or present CMV infection. In 3 patients for whom culture results were available, CMV was isolated from blood, urine and/or lung of all 3. Past infections with amebiasis and hepatitis were commonly reported.

**TABLE 1. Presenting complaints in 20 patients with Kaposi’s sarcoma**

<table>
<thead>
<tr>
<th>Presenting complaint</th>
<th>Number (percentage) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin lesion(s) only</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Skin lesions plus lymphadenopathy</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Oral mucosal lesion only</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Inguinal adenopathy plus perirectal abscess</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Weight loss and fever</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Weight loss, fever, and pneumonia (one due to <em>Pneumocystis carinii</em>)</td>
<td>2 (10%)</td>
</tr>
</tbody>
</table>
Trends in Age-Adjusted* Rate of Death due to HIV Infection, USA, 1987-2000

*Using the year 2000 US standard population.
†Preliminary mortality data for 2000

Year

Note: For comparison with data for 1999-2000, data for 1987-1998 were modified to account for ICD-10 rules instead of ICD-9 rules.
A TRIAL COMPARING NUCLEOSIDE MONOTHERAPY WITH COMBINATION THERAPY IN HIV-INFECTED ADULTS WITH CD4 CELL COUNTS FROM 200 TO 500 PER CUBIC MILLIMETER

SCOTT M. HAMMER, M.D., DAVID A. KATZENSTEIN, M.D., MICHAEL D. HUGHES, PH.D., HOLLY GUNDACKER, M.S., ROBERT T. SCHOOLEY, M.D., RICHARD H. HAUBRICH, M.D., W. KEITH HENRY, M.D., MICHAEL M. LEDERMAN, M.D., JOHN P. PHAIR, M.D., MANETTE NIU, M.D., MARTIN S. HIRSCH, M.D., AND THOMAS C. MERIGAN, M.D., FOR THE AIDS CLINICAL TRIALS GROUP STUDY 175 STUDY TEAM*
TREATMENT OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION WITH SAQUINAVIR, ZIDOVUDINE, AND ZALCITABINE

ANN C. COLLIER, M.D., ROBERT W. COOMBS, M.D., PH.D., DAVID A. SCHOFIELD, PH.D., ROLAND L. BASSETT, M.S., JOSEPH TIPMONE, M.D., ALICE BARUCH, M.D., PH.D., MICHELLE JONES, M.SC., KAREN FACEY, PH.D., CAROLINE WHITACRE, PH.D., VINCENT J. MCAULIFFE, M.D., HARVEY M. FRIEDMAN, M.D., THOMAS C. MERIGAN, M.D., RICHARD C. REICHMAN, M.D., CAROL HOOPER, M.D., AND LAWRENCE COREY, M.D., FOR THE AIDS CLINICAL TRIALS GROUP

Abstract  Background. In patients with human immunodeficiency virus (HIV) infection, combined treatment with several agents may increase the effectiveness of antiviral therapy. We studied the safety and efficacy of saquinavir, an HIV-protease inhibitor, given with one or two nucleoside antiretroviral agents, as compared with the safety and efficacy of a combination of two nucleosides alone.

Methods. In this double-blind trial, patients with HIV infection were randomly assigned to receive either saquinavir (1800 mg per day) plus both zidovudine (600 mg per day) and zalcitabine (2.25 mg per day) or zidovudine plus either saquinavir or zalcitabine. The 302 patients enrolled had CD4+ counts of 50 to 300 cells per cubic millimeter and had previously received zidovudine for a median of 27 months. The study lasted 24 weeks, with an optional double-blind extension period of an additional 12 to 32 weeks.

Results. Ninety-six percent of the patients completed the 24-week study. In all three treatment groups, CD4+ cell counts rose at first and then fell gradually. The normalized area under the curve for the CD4+ cell count was greater with the three-drug combination than with either saquinavir and zidovudine (P = 0.017) or zalcitabine and zidovudine (P < 0.001). There were significantly greater reductions in plasma HIV with the three-drug combination than with the other regimens when peripheral-blood mononuclear cells were cultured for HIV and HIV RNA was assessed, and there were greater decreases in serum neopterin and beta2-microglobulin levels. There were no major differences in toxic effects among the three treatments.

Conclusions. Treatment with saquinavir, zalcitabine, and zidovudine was well tolerated. This drug combination reduced HIV-1 replication, increased CD4+ cell counts, and decreased levels of activation markers in serum more than did treatment with zidovudine and either saquinavir or zalcitabine. Studies are warranted to evaluate whether the three-drug combination will reduce morbidity and mortality. (N Engl J Med 1996;334:1011-7.)

©1996, Massachusetts Medical Society.
Trends in Age-Adjusted* Rate of Death due to HIV Infection, USA, 1987-2000

*Using the year 2000 US standard population.
†Preliminary mortality data for 2000

Note: For comparison with data for 1999-2000, data for 1987-1998 were modified to account for ICD-10 rules instead of ICD-9 rules.
Trends in Age-Adjusted* Rate of Death due to HIV Infection, USA, 1987-2000

Deaths per 100,000 Population

*Using the year 2000 US standard population.
†Preliminary mortality data for 2000

Note: For comparison with data for 1999-2000, data for 1987-1998 were modified to account for ICD-10 rules instead of ICD-9 rules.
<table>
<thead>
<tr>
<th>Primary or secondary cause</th>
<th>1996</th>
<th>1997</th>
<th>2003</th>
<th>2004</th>
<th>( P ) (test for trend)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>2783</td>
<td>3156</td>
<td>3602</td>
<td>3414</td>
<td></td>
</tr>
<tr>
<td>Person-years of observation</td>
<td>2189</td>
<td>2503</td>
<td>3183</td>
<td>3075</td>
<td></td>
</tr>
<tr>
<td>Primary or secondary cause</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AIDS</td>
<td>83 [3.79]</td>
<td>47 [1.88]</td>
<td>27 [0.85]</td>
<td>10 [0.32]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>All non-AIDS</td>
<td>20 [0.91]</td>
<td>25 [1.0]</td>
<td>20 [0.63]</td>
<td>17 [0.55]</td>
<td>0.524</td>
</tr>
<tr>
<td>Unknown</td>
<td>50 [2.28]</td>
<td>19 [0.76]</td>
<td>8 [0.25]</td>
<td>13 [0.42]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total</td>
<td>153 [7.0]</td>
<td>91 [3.64]</td>
<td>55 [1.73]</td>
<td>40 [1.30]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bacteremia/sepsis</td>
<td>3 [0.14]</td>
<td>3 [0.12]</td>
<td>1 [0.03]</td>
<td>1 [0.03]</td>
<td>0.476</td>
</tr>
<tr>
<td>Neurologic disorders</td>
<td>3 [0.14]</td>
<td>4 [0.16]</td>
<td>1 [0.03]</td>
<td>3 [0.10]</td>
<td>0.256</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>7 [0.32]</td>
<td>11 [0.44]</td>
<td>7 [0.22]</td>
<td>4 [0.13]</td>
<td>0.170</td>
</tr>
<tr>
<td>Gastrointestinal disease</td>
<td>2 [0.09]</td>
<td>4 [0.16]</td>
<td>5 [0.16]</td>
<td>3 [0.10]</td>
<td>0.588</td>
</tr>
<tr>
<td>Hepatic disease</td>
<td>1 [0.09]</td>
<td>8 [0.36]</td>
<td>5 [0.31]</td>
<td>4 [0.16]</td>
<td>0.100</td>
</tr>
<tr>
<td>Non-AIDS malignancy</td>
<td>3 [0.14]</td>
<td>1 [0.04]</td>
<td>1 [0.03]</td>
<td>4 [0.13]</td>
<td>0.696</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>8 [0.37]</td>
<td>11 [0.44]</td>
<td>3 [0.09]</td>
<td>4 [0.13]</td>
<td>0.038</td>
</tr>
<tr>
<td>Renal disease</td>
<td>5 [0.23]</td>
<td>2 [0.08]</td>
<td>3 [0.09]</td>
<td>3 [0.10]</td>
<td>0.836</td>
</tr>
</tbody>
</table>
Increased COPD Among HIV-Positive Compared to HIV-Negative Veterans*

Kristina Crothers, MD; Adeel A. Butt, MD, MS; Cynthia L. Gibert, MD; Maria C. Rodriguez-Barradas, MD; Stephen Crystal, PhD; and Amy C. Justice, MD, PhD; for the Veterans Aging Cohort 5 Project Team

HIV Infection and Risk for Incident Pulmonary Diseases in the Combination Antiretroviral Therapy Era

Kristina Crothers¹,², Laurence Huang³, Joseph L. Goulet², Matthew Bidwell Goetz⁴, Sheldon T. Brown⁵, Maria C. Rodriguez-Barradas⁶, Krisann K. Oursler⁷, David Rimland⁸, Cynthia L. Gibert⁹, Adeel A. Butt¹⁰, and Amy C. Justice²,¹¹
Why Might HIV Increase COPD Risk?

Smoking?
Why Might HIV Increase COPD Risk?

Smoking?

Bacterial pneumonia?
Respiratory Infections May Increase Rate of Lung Function Decline in COPD
Lung Function Decline

**FEV\textsubscript{1} decline in smokers and non-smokers**

- **FEV\textsubscript{1}** (% of value at age 25)
- **Disability**
- **Death**

**Age (years)**

- **Never smoked or not susceptible to smoke**
- **Susceptible smoker**
Lung Function Decline

FEV₁ decline in smokers and non-smokers

- Never smoked or not susceptible to smoke
- Susceptible smoker

Age (years)

Disability
Death
Respiratory Infections May Increase Rate of Lung Function Decline in **COPD**

Table 5. Estimates of the Effect of Lower Respiratory Illness Physician Visits (LRI) on the 5-yr Averaged Annual Rate of Decline of the FEV₁

<table>
<thead>
<tr>
<th>Number of MD LRI Visits/yr</th>
<th>Sustained Quit</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated Mean Change in FEV₁*</td>
<td>Estimated Mean % from LRI†</td>
<td>Estimated Mean Change in FEV₁*</td>
<td>Estimated Mean % from LRI†</td>
</tr>
<tr>
<td>0–0.24</td>
<td>−13.1 (764)‡</td>
<td>+0.0</td>
<td>−32.6 (1,191)</td>
<td>−0.7</td>
</tr>
<tr>
<td>0.25–0.49</td>
<td>−27.6 (74)</td>
<td>−0.0</td>
<td>−25.2 (143)</td>
<td>−6.4</td>
</tr>
<tr>
<td>0.50–0.99</td>
<td>−24.0 (39)</td>
<td>−0.0</td>
<td>−35.3 (137)</td>
<td>−8.7</td>
</tr>
<tr>
<td>1.00–1.49</td>
<td>−20.3 (32)</td>
<td>−0.0</td>
<td>−40.7 (63)</td>
<td>−15.3</td>
</tr>
<tr>
<td>≥ 1.50</td>
<td>−12.0 (17)</td>
<td>+0.1</td>
<td>−52.0 (35)</td>
<td>−36.0</td>
</tr>
</tbody>
</table>

* The rate of change in FEV₁ is in ml/yr.
† The effect of LRIs is expressed as a mean predicted percentage of the rate of change in FEV₁. A negative sign indicates that the effect was to accelerate the rate of decline.
‡ The numbers in parentheses are the number of participants in each subcategory.

Respiratory Infections May Increase Rate of Lung Function Decline in HIV

Figure 1. Changes in pulmonary function after infection with PCP or BP. *p < 0.05, †p < 0.01, and ‡p ≤ 0.001.

Why Might HIV Increase COPD Risk?

- Smoking?
- Bacterial pneumonia?
- Pneumocystis jiroveci colonization?
**Pneumocystis Colonization in COPD**

*Figure 1.* Percentage of subjects colonized with *Pneumocystis* according to GOLD stage. GOLD = Global Health Initiative on Obstructive Lung Disease. Number of subjects per group: 0 = 10, I = 10, II = 10, III = 8, IV = 30.

Morris A. Am J Respir Crit Care Med 2004.
Pneumocystis Colonization in HIV

A. 

Percent

FEV₁ predicted  FEV₁/FVC

p=0.02

Pc-colonized  Pc-negative

p=0.009

B. 

% with airway obstruction

Pc-colonized  Pc-negative

p=0.03

L7 - THE LUNG HIV MICROBIOME PROJECT: VALIDATION, HEALTHY VOLUNTEERS, AND DISEASED STATES

CME Credits: N/A

Sunday, May 20 2012 - 12:00PM - 1:00PM

Room 2016-2018 (West Building, Level 2)
Moscone Center, West Building

Target Audience: Clinicians, researchers, healthcare workers, and trainees with an interest in the lung microbiome.

OBJECTIVES

At the conclusion of this session, the participant will be able to:

- understand the NHLBI-funded HIV Lung Microbiome Study and its goals and objectives;
- describe the complexities in cross-validating metagenomic data;
- understand how studies of the microbiome may lead to better patient care.

The Lung HIV Microbiome Project (LHMP) will characterize the microbiome of the lung alone or in combination with the nasal and/or oropharyngeal cavities in HIV-infected individuals and matched HIV-uninfected controls using molecular techniques to identify bacteria and other organisms. In this session, we will describe the structure of the project, present results from a validation study across six sequencing centers, discuss a study to compare non-HIV infected smokers to non-smokers, and address applications of the microbiome to clinical studies.

Session Organizer

- Hannah H. Peavy

Chairing

- J. M. Beck, MD, Denver, CO
- S. Colombini-Hatch, MD, Bethesda, MD

Featured Speaker(s)

12:00PM Introduction To The Lung HIV Microbiome Study
- K. Jablonski, PhD, Rockville, MD
- G. Weinstock, PhD, St. Louis, MO

12:15PM Analysis Of The Complexity Of Cross Validating Metagenomic Data
- A. M. Morris, MD, MS, Pittsburgh, PA

12:30PM Differences In The Bacterial Population Of HIV-Uninfected Smokers And Non-Smokers
- S. V. Lynch, PhD, San Francisco, CA

12:45PM Lung Microbiome In Cohort Of HIV-Infected Persons
Why Might HIV Increase COPD Risk?

Smoking?

Bacterial pneumonia?

Pneumocystis jiroveci colonization?

CD8+ T-cells?
CD8+ Cell Proliferation in Lung and Airways in **COPD**


CD8+ Alveolitis in HIV

Drummond MB. Presented at Conference of Retroviruses and Opportunistic Infections, March 2012.
Effect of CD4 count on lung function decline

Adjusted for sex, age, race, pack-years and current smoking, BMI, pneumonia

HIV-: p=0.03 vs. CD4 100-199 & p<0.01 vs. CD4<100
CD4≥200: p=0.05 vs. 100-199 & p<0.01 vs. <100

Drummond MB. Presented at Conference of Retroviruses and Opportunistic Infections, March 2012.
Effect of HIV viral load on lung function decline

Drummond MB. Presented at Conference of Retroviruses and Opportunistic Infections, March 2012.
Ongoing RCT

HIV-infected patients with CD4+ counts >500 cells/mm³
n = 4,000 (237 sites)

Strategic Timing of AntiRetroviral Therapy (START) Trial

HIV-infected patients with CD4+ counts >500 cells/mm³
n = 1,000 (85 sites)

Early ART group
Initiate ART immediately following randomization
n = 500

*Baseline + Annual*
- Spirometry
- SGRQ-C
- Respiratory medication assessment
- Respiratory illness assessment
- Smoking assessment

Deferred ART group
Defer ART until CD4+ count declines to < 350 cells/mm³ or AIDS develops
n = 500

Main trial study procedures,

Main Trial

Ancillary Study
Why Might HIV Increase COPD Risk?

- Smoking?
- Bacterial pneumonia?
- *Pneumocystis jiroveci* colonization?
- CD8+ T-cells?
- Oxidative stress / Inflammation?
Non-Infectious Pulmonary Disease in the cART Era

• COPD
  – HIV is an independent risk factor for COPD
  – Most common incident pulmonary disease in HIV
  – Several mechanistic hypotheses
  – COPD is the 3rd leading cause of death in the U.S.

• Lung cancer

• Pulmonary HTN
# Lung Cancer in HIV

**TABLE 2.** Cause of Death Rates and Distribution of Causes of Death Among HOPS Patients, 1996–2004

A. Cause of Death Rates Among HOPS Patients, 1996–2004

<table>
<thead>
<tr>
<th>Year of Death</th>
<th>1996</th>
<th>1997</th>
<th>2003</th>
<th>2004</th>
<th>( P ) (test for trend)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>1 [0.03]</td>
<td>0.476</td>
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<tr>
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<td>3 [0.14]</td>
<td>4 [0.16]</td>
<td>1 [0.03]</td>
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Palella F. JAIDS 2006
HIV Infection and Risk for Incident Pulmonary Diseases in the Combination Antiretroviral Therapy Era

Kristina Crothers¹,², Laurence Huang³, Joseph L. Goulet², Matthew Bidwell Goetz⁴, Sheldon T. Brown⁵, Maria C. Rodriguez-Barradas⁶, Krisann K. Oursler⁷, David Rimland⁸, Cynthia L. Gibert⁹, Adeel A. Butt¹⁰, and Amy C. Justice²,¹¹
Types of NADMs and incidence

Over 176,775 person-years, 880 patients developed a new NADM
Incidence: 4.98/1000 PY, 95% CI [4.65, 5.31]

*Pancreatic cancer, esophageal cancer, gall bladder cancer

Wurm S. Presented at Conference of Retroviruses and Opportunistic Infections, March 2012.
5-year Survival After Cancer Diagnosis by HIV Status

**Prostate**
- 5-yr survival: HIV- 90.6%, HIV+ 84.3%
- HR=2.2 (1.2-4.3)

**Anal**
- 5-yr survival: HIV- 66.5%, HIV+ 57.2%
- HR=1.7 (0.6-5.4)

**Colorectal**
- 5-yr survival: HIV- 61.6%, HIV+ 59.5%
- HR=1.6 (0.8-3.1)

**Hodgkin**
- 5-yr survival: HIV- 87.3%, HIV+ 64.9%
- HR=3.0 (0.8-10.8)

<table>
<thead>
<tr>
<th></th>
<th>Younger at dx?</th>
<th>Worse stage at dx?</th>
<th>Reduced survival?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td></td>
<td></td>
<td>Y</td>
</tr>
<tr>
<td>Anal</td>
<td>Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
</tr>
<tr>
<td>Colorectal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hodgkin</td>
<td></td>
<td>?</td>
<td>Y</td>
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</tbody>
</table>

Thus, continued focus on cancer prevention in HIV(+) patients is essential.

Silverberg et al., CROI 2012
5-year Survival After Cancer Diagnosis by HIV Status

<table>
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<tbody>
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<td>Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Y</td>
<td></td>
<td></td>
</tr>
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<td>Hodgkin</td>
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Thus, continued focus on cancer prevention in HIV(+) patients is essential.
Non-Infectious Pulmonary Disease in the cART Era

• COPD
  – Most common incident pulmonary disease
  – HIV associated with increased risk
  – Several mechanistic hypotheses
  – COPD is the 3rd leading cause of death in the U.S.

• Lung cancer
  – Most common incident NADM in HIV infection
  – HIV associated with increased risk
  – Very poor survival

• Pulmonary HTN
Table 1. Revised WHO Classification of PH

1. Pulmonary arterial hypertension (PAH)
   1.1. Idiopathic (IPAH)
   1.2. Familial (FPAH)
   1.3. Associated with (APAH):
      1.3.1. Connective tissue disorder
      1.3.2. Congenital systemic-to-pulmonary shunts
      1.3.3. Portal hypertension
      1.3.4. HIV infection
   1.3.5. Drugs and toxins
   1.3.6. Other (thyroid disorders, glycogen storage disease, Gaucher's disease, hereditary hemorrhagic telangiectasia, hemoglobinopathies, chronic myeloproliferative disorders, splenectomy)
   1.4. Associated with significant venous or capillary involvement
      1.4.1. Pulmonary veno-occlusive disease (PVOD)
      1.4.2. Pulmonary capillary hemangiomatosis (PCH)
   1.5. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension with left heart disease
   2.1. Left-sided atrial or ventricular heart disease
   2.2. Left-sided valvular heart disease

3. Pulmonary hypertension associated with lung diseases and/or hypoxemia
   3.1. Chronic obstructive pulmonary disease
   3.2. Interstitial lung disease
   3.3. Sleep disordered breathing
   3.4. Alveolar hypoventilation disorders
   3.5. Chronic exposure to high altitude
   3.6. Developmental abnormalities

4. Pulmonary hypertension due to chronic thrombotic and/or embolic disease (CTEPH)
   4.1. Thromboembolic obstruction of proximal pulmonary arteries
   4.2. Thromboembolic obstruction of distal pulmonary arteries
   4.3. Nonthrombotic pulmonary embolism (tumor, parasites, foreign material)

5. Miscellaneous
   Sarcoidosis, histiocytosis X, lymphangiomatosis, compression of pulmonary vessels (adenopathy, tumor, fibrosing mediastinitis)
Pulmonary HTN in HIV

Prevalence of HIV-related Pulmonary Arterial Hypertension in the Current Antiretroviral Therapy Era

Olivier Sitbon¹, Caroline Lascoux-Combe², Jean-François Delfraissy³, Patrick G. Yeni⁴, François Raffi⁵, Dominique De Zuttere⁶, Virginie Gressin⁷, Pierre Clerson⁸, Daniel Sereni², and Gérald Simonneau¹


35 / 7,648 = 0.46% [95% CI: 0.32% – 0.64%]
Prevalence Not Associated with HIV Factors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall Population</th>
<th>Per-Protocol Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, mean (SD)</td>
<td>41.91 (9.56)</td>
<td>42.29 (8.90)</td>
</tr>
<tr>
<td>Males, %</td>
<td>67</td>
<td>55</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>75</td>
<td>73</td>
</tr>
<tr>
<td>Black</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>Asian</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mode of HIV infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men having sex with men</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>IV drugs</td>
<td>16</td>
<td>26</td>
</tr>
<tr>
<td>Heterosexual contact</td>
<td>43</td>
<td>44</td>
</tr>
<tr>
<td>Transfusion</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Undetermined</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Duration of HIV infection, yr, mean (SD)</td>
<td>10 (6)</td>
<td>10 (6)</td>
</tr>
<tr>
<td>Viral load, copies/ml, &lt; 400, %</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>CD4$^+$ count/mm$^3$ &lt; 200, %</td>
<td>13</td>
<td>20</td>
</tr>
</tbody>
</table>

Non-Infectious Pulmonary Disease in the cART Era

• **COPD**
  – Most common incident pulmonary disease
  – HIV associated with increased risk
  – Several mechanistic hypotheses
  – COPD is the 3rd leading cause of death in the U.S.

• **Lung cancer**
  – Most common incident NADM in HIV infection
  – HIV associated with increased risk
  – Very poor survival

• **Pulmonary HTN**
  – Relatively uncommon, but serious
  – Risk factors unknown
The Burden of Smoking in HIV
HOST FACTORS

SYSTEMIC AND LUNG EFFECTS

AGING

Chronic inflammation

HIV persistence and immune dysfunction

Respiratory infections/colonization

Oxidative stress

Potential pathogenetic mechanisms
- Inflammation
- Immune dysfunction
- Apoptosis
- Protease/anti-protease imbalance

Lung function decline

COPD, other chronic lung disease

Additional cofactors
- Occupational and environmental exposures
- Malnutrition
- Genetic susceptibility
- Impact of antiretroviral treatment unknown

Crothers K. Am J Respir Crit Care Med 2012.
Summary

• After 15+ years of HAART, pulmonary complications of HIV have shifted from opportunistic infections to non-infectious complications such as COPD, Lung cancer, and Pulmonary HTN
• HIV increases risks of COPD, Lung CA, Pulmonary HTN
  – Mechanisms unclear
  – Rich areas of research relevant to HIV and non-HIV lung disease
• Smoking cessation efforts critical to future HIV care
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Thank you!

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