

# New HIV Cases Still Increasing in MSM Population

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SAN FRANCISCO — New HIV and AIDS cases still occur most commonly in the gay male population, and one of the reasons may be because a substantial proportion of infected persons do not know that they are infected.

“We increasingly have been focused on [new infection cases in] women, but the only group in which we have evidence that

HIV or AIDS cases are increasing is in the group of men who have sex with men,” Dr. Susan Buchbinder said at a meeting on HIV management sponsored by the University of California, San Francisco.

A high proportion of infected persons are not aware of their serostatus; they engage in risky behavior and come in for testing and treatment way too late, said Dr. Buchbinder, the director of the HIV research section of the San Francisco Department of Public Health.

About 40% of all new HIV/AIDS diagnoses in 2001 were in men who have sex with men (MSM), and by 2004, that figure had risen to 45%, according to Dr. Buchbinder.

Figures from the Centers for Disease Control and Prevention indicate that there were 16,625 new cases in the transmission category of male-to-male sexual contact in 2001. By 2004, there were 18,203.

The annual number of cases in other transmission categories—including intravenous drug use and heterosexual contact—remain flat or are declining.

Another salient feature of the epidemic's evolution is that although roughly 80% of cases still occur in major metropolitan areas, increasing numbers of HIV/AIDS cases are occurring among women in suburban and rural areas, Dr. Buchbinder noted. A disturbing feature of these cases is that almost half of the women are getting infected through heterosexual contact with a man whose risk factor they do not know.

“This is that hidden epidemic ... that is increasingly moving into less populated areas and heavily impacting women in this country,” she said.

Dr. Buchbinder also discussed the new CDC guidelines for HIV testing adopted in September 2006, which call for “opt-out” testing, meaning that all patients are informed that they will undergo testing unless they choose to forgo it.

The rationale for the new guidelines is based on the estimation that at least 25% of infected persons in the United States are not aware of their serostatus, and that too many people seek treatment when it is too late.

Dr. Buchbinder said that in some populations, the number of people who are not aware that they are HIV positive might be even higher than the estimated one-quarter. In 2004-2005, the CDC randomly interviewed and tested gay men in four cities and found that 48% of those tested were unaware of their infection (MMWR 2005;54:597-601).

Moreover, of those testing positive for the virus the first time, 38% do so within 1 year of developing AIDS. That is too late, said Dr. Buchbinder. People who know that they are HIV positive report that they change their behavior, and the earlier treatment starts, the better, she added.

In a large retrospective review of data from Kaiser Permanente patients going back to the mid-1990s, the investigators found that 43% of patients had a CD4 cell count of fewer than 200 cells/mL when they first were tested as positive, and an-

other 19% had CD4 cell counts of 200-350 cells/mL, the point at which it is advised that antiviral treatment should start (J. Acquir. Immune Defic. Syndr. 2003;32:143-52).

Those patients could perhaps have been detected earlier because the group had been in the Kaiser system for a mean of 5 years before testing positive. However, only 26% of the patients had their intravenous drug abuse history or their homosexual activity—possible pointers to infection risk factors—documented in their charts before they tested positive, Dr. Buchbinder noted.

Dr. Buchbinder also discussed the practice of “serosorting.” In serosorting, men who know they are HIV positive modify their behavior depending on their partner's HIV status, such that they have sex only with other men who are positive, or always use a condom when having sex with a negative partner, or ensure that the positive partner is always the receptive partner when having anal sex with a negative partner because of the perceived lower risk of transmission.

She added that data from San Francisco and California suggest that since the late 1990s, the number of MSMs who have unprotected anal sex and the number of cases of rectal gonorrhea and syphilis have increased. However, in San Francisco—where many infected men report that they have sex with uninfected partners less frequently since becoming aware of their serostatus—the HIV infection rates do not seem to be increasing to the same extent. ■

## LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION

(3% and <1%); Anorgasmia (2% and <1%). \*Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo B Lexapro: headache, upper respiratory tract infection, back pain, pharyngitis, inflicted injury, anxiety. †Primarily ejaculatory delay. ‡Denominator used was for males only (N=225 Lexapro; N=188 placebo). †Denominator used was for females only (N=490 Lexapro; N=404 placebo). **Generalized Anxiety Disorder Table 3** enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia (see TABLE 3). **TABLE 3. Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Generalized Anxiety Disorder\* (Lexapro (N=429) and Placebo (N=427)).** **Autonomic Nervous System Disorders:** Dry Mouth (9% and 3%); Sweating Increased (4% and 1%); **Central & Peripheral Nervous System Disorders:** Headache (24% and 17%); Paresthesia (2% and 1%); **Gastrointestinal Disorders:** Nausea (18% and 8%); Diarrhea (8% and 6%); Constipation (5% and 4%); Indigestion (3% and 2%); Vomiting (3% and 1%); Abdominal Pain (2% and 1%); Flatulence (2% and 1%); Toothache (2% and 0%); **General:** Fatigue (8% and 2%); Influenza-like symptoms (5% and 4%); **Musculoskeletal:** Neck/Shoulder Pain (3% and 1%); **Psychiatric Disorders:** Somnolence (13% and 7%); Insomnia (12% and 6%); Libido Decreased (7% and 2%); Dreaming Abnormal (3% and 2%); Appetite Decreased (3% and 1%); Lethargy (3% and 1%); Yawning (2% and 1%); **Urogenital:** Ejaculation Disorder<sup>†</sup> (14% and 2%); Anorgasmia<sup>‡</sup> (6% and <1%); Menstrual Disorder (2% and 1%). \*Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo B Lexapro: inflicted injury, dizziness, back pain, upper respiratory tract infection, rhinitis, pharyngitis. †Primarily ejaculatory delay. ‡Denominator used was for males only (N=182 Lexapro; N=195 placebo). †Denominator used was for females only (N=247 Lexapro; N=232 placebo). **Dose Dependency of Adverse Events** The potential dose dependency of common adverse events (defined as an incidence rate of 15% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). **Table 4** shows common adverse events that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group. **TABLE 4: Incidence of Common Adverse Events\* in Patients with Major Depressive Disorder Receiving Placebo (N=311), 10 mg/day Lexapro (N=310), 20 mg/day Lexapro (N=125); Insomnia (4%, 7%, 14%); Diarrhea (5%, 6%, 14%); Dry Mouth (3%, 4%, 9%); Somnolence (1%, 4%, 9%); Dizziness (2%, 4%, 7%); Sweating Increased (<1%, 3%, 8%); Constipation (1%, 3%, 6%); Fatigue (2%, 2%, 6%); Indigestion (1%, 2%, 6%).** \*Adverse events with an incidence rate of at least 5% in either of the Lexapro groups and with an incidence rate in the 20 mg/day Lexapro group that was approximately twice that of the 10 mg/day Lexapro group and the placebo group. **Male and Female Sexual Dysfunction with SSRIs** Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experiences and performance cited in product labeling are likely to underestimate their actual incidence. **Table 5** shows the incidence rates of sexual side effects in patients with major depressive disorder and GAD in placebo-controlled trials. **TABLE 5: Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials (In Males Only: Lexapro (N=407) and Placebo (N=383)); Ejaculation Disorder (primarily ejaculatory delay) (12% and 1%); Libido Decreased (6% and 2%); Impotence (2% and <1%). (In Females Only: Lexapro (N=137) and Placebo (N=636)); Libido Decreased (3% and 1%); Anorgasmia (3% and <1%).** There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Pripriam has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. **Vital Sign Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. **Weight Changes** Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. **Laboratory Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. **ECG Changes** Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.7 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. **Other Events Observed During the Premarketing Evaluation of Lexapro** Following is a list of WHO terms that reflect treatment-emergent adverse events, as defined in the introduction to the **ADVERSE REACTIONS** section, reported by the 1428 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. All reported events are included except those already listed in **Tables 2 & 3**, those occurring in only one patient, event terms that are so general as to be uninformative, and those that are unlikely to be drug related. It is important to emphasize that, although the events reported occurred during treatment with Lexapro, they were not necessarily caused by it. Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in less than 1/100 patients but at least 1/1000 patients; cardiovascular - *Frequent:* palpitation, hypertension, *Infrequent:* bradycardia, tachycardia, ECG abnormal, flushing, varicose vein. *Central and Peripheral Nervous System Disorders - Frequent:* light-headed feeling, migraine, *Infrequent:* tremor, vertigo, restless legs, shaking, twitching, dysequilibrium, tic, carpal tunnel syndrome, muscle contractions involuntary, sluggishness, coordination abnormal, faintness, hyperreflexia, muscular tone increased. *Gastrointestinal Disorders - Frequent:* heartburn, abdominal cramp, gastroenteritis, *Infrequent:* gastroesophageal reflux, bloating, abdominal discomfort, dyspepsia, increased stool frequency, belching, gastritis, hemorrhoids, gagging, polyposis gastric, swallowing difficult. *General - Frequent:* allergy, pain in limb, fever, hot flushes, chest pain, *Infrequent:* edema of extremities, chills, tightness of chest, leg pain, asthenia, syncope, malaise, anaphylaxis, fall. *Hemic and Lymphatic Disorders - Infrequent:* bruise, anemia, nosebleed, hematoma, lymphadenopathy cervical. *Metabolic and Nutritional Disorders - Frequent:* increased weight, *Infrequent:* decreased weight, hyperglycemia, thirst, bilirubin increased, hepatic enzymes increased, gout, hypercholesterolemia. *Musculoskeletal System Disorders - Frequent:* arthralgia, myalgia, *Infrequent:* jaw stiffness, muscle cramp, muscle stiffness, arthritis, muscle weakness, back discomfort, arthropathy, jaw pain, joint stiffness. *Psychiatric Disorders - Frequent:* appetite increased, lethargy, irritability, concentration impaired, *Infrequent:* jitteriness, panic reaction, agitation, apathy, forgetfulness, depression aggravated, nervousness, restlessness aggravated, suicide attempt, amnesia, anxiety attack, bruxism, carbohydrate craving, confusion, depersonalization, disorientation, emotional lability, feeling unreal, tremulousness nervous, crying abnormal, depression, excitability, auditory hallucination, suicidal tendency. *Reproductive Disorders/Female - Frequent:* menstrual cramps, menstrual disorder, *Infrequent:* menorrhagia, breast neoplasm, pelvic inflammation, premenstrual syndrome, spotting between menses. % based on female subjects only. N= 905 *Respiratory System Disorders - Frequent:* bronchitis, sinus congestion, coughing, nasal congestion, sinus headache, *Infrequent:* asthma, breath shortness, laryngitis, pneumonia, tracheitis. *Skin and Appendages Disorders - Frequent:* rash, *Infrequent:* pruritus, acne, alopecia, eczema, dermatitis, dry skin, folliculitis, ligoma, funiculosis, dry lips, skin nodule. *Special Senses - Frequent:* vision blurred, linnitus, *Infrequent:* taste alteration, earache, conjunctivitis, vision abnormal, dry eyes, eye irritation, visual disturbance, eye infection, pupils dilated, metallic taste. *Urinary System Disorders - Frequent:* urinary frequency, urinary tract infection, *Infrequent:* urinary urgency, kidney stone, dysuria, blood in urine. **Events Reported Subsequent to the Marketing of Escitalopram** - Although no causal relationship to escitalopram treatment has been found, the following adverse events have been reported to have occurred in patients and to be temporally associated with escitalopram treatment during post marketing experience and were not observed during the premarketing evaluation of escitalopram: abnormal gait, acute renal failure, aggression, akathisia, allergic reaction, anger, angioedema, atrial fibrillation, chorea, chorea, delirium, delusion, diplopia, dysarthria, dyskinesia, dystonia, ecchymosis, erythema multiforme, extrapyramidal disorders, fulminant hepatitis, hepatic failure, hypoaesthesia, hypoglycemia, hypokalemia, INR increased, gastrointestinal hemorrhage, glaucoma, grand mal seizures (or convulsions), hemolytic anemia, hepatic necrosis, hepatitis, hypotension, leucopenia, myocardial infarction, myoclonus, neuroleptic malignant syndrome, nightmare, nystagmus, orthostatic hypotension, pancreatitis, paranoia, photosensitivity reaction, priapism, prolactinemia, prothrombin decreased, pulmonary embolism, QT prolongation, rhabdomyolysis, seizures, serotonin syndrome, SIADH, spontaneous abortion, Stevens Johnson Syndrome, tardive dyskinesia, thrombocytopenia, thrombosis, torsade de pointes, toxic epidermal necrolysis, ventricular arrhythmia, ventricular tachycardia and visual hallucinations.

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## HAART Halt Did Not Lead to Neuro Decline

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LOS ANGELES — Relatively healthy individuals who opted to discontinue highly active antiretroviral therapy did not appear to suffer any neurocognitive repercussions and in fact performed better on a standard battery of neuropsychological tests during their drug vacations.

“This was not what we expected,” said Kevin Robertson, Ph.D., who presented the findings at the 14th Conference on Retroviruses and Opportunistic Infections.

An initial group of 167 HIV-infected patients was enrolled in the observational, multicenter study when they made a decision to discontinue highly active antiretroviral therapy (HAART).

At study entry, their mean age was 42 years and they had spent 4.5 years on HAART. They represented a “uniquely healthy population,” Dr. Robertson stressed, with a mean baseline peripheral blood CD4 count of 833 cells/mL and a low viral load (71% had fewer than 50 copies/mL plasma HIV RNA).

A brief neuropsychological battery of tests, including Trailmaking A/B and Digit Symbol, was administered at 24 weeks, 48 weeks, 72 weeks, and 96 weeks to assess psychomotor speed, attention, concentration, cognitive sequencing, and shifting cognitive sets—skills known to be affected by HIV.

“We felt that when subjects stopped HAART, it would lead to a decline in neuropsychological performance,” said Dr. Robertson, director of neuropsychology and a member of the NeuroAIDS Working Group at the University of North Carolina at Chapel Hill.

In fact, the opposite occurred, with mean neuropsychological summary (NPZ3) scores improving by 0.22, 0.39, 0.52, and 0.74 over the course of the 96-week study.

Among a group of 46 subjects who eventually decided to reinstate HAART,

there was no significant change in composite neurocognitive scores over 72 weeks of follow-up, although Dr. Robertson noted that the final study group represented a “very small sample size” of 37 patients by week 24 of the follow-up study.

Numerous possible confounding factors were explored by the investigative team from the University of North Carolina; Harvard University, Boston; the University of California, San Francisco; and Baystate Medical Center, Springfield, Mass. However, they statistically ruled out a practice effect, selection bias, or a possible link between neurocognitive function and efavirenz-containing HIV regimens.

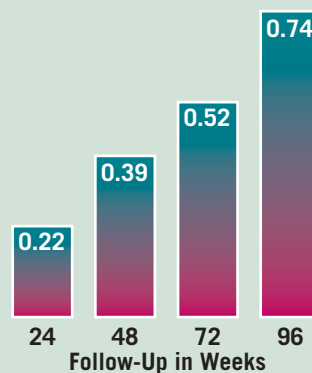
“Many people in this room, myself included, have shown improvement [in neurocognitive function] with ART, especially in later disease,” said Dr. Robertson from the podium during his presentation.

“This study does not suggest you shouldn't take your antiretroviral treatment at all.

“What we know is that HIV gets into the CNS within days. ... The virus is presumably chipping away,” he said.

He suggested that further research should focus on “potential sources of HAART toxicity on CNS function,” because neurocognitive decline did not follow discontinuation of the powerful therapies in healthy subjects who were able to remain off HAART for extended periods of time. ■

### Neuropsychological Summary Score Improvement After HAART Discontinuation



Note: Based on a study of 167 HIV-infected patients.  
Source: Dr. Robertson