

25 years of information, inspiration and advocacy for people living with HIV/AIDS

TOP STORIES

“Treatment as prevention” proposed as element of the National HIV/AIDS Strategy

A significant question that has perplexed and even divided HIV experts in recent years is whether and how “Test & Treat” programs to assure that a greater percentage of HIV-positive people learn their serostatus and take antiretroviral medications might serve to reduce new cases of HIV infection. Several studies have concluded that viral suppression resulting from effective HIV therapy makes it less likely that an HIV-positive person can transmit HIV to an HIV-negative partner, even in the absence of condom use during sex. Statistical models have come to different conclusions about the extent to which programs to increase the diagnosis and treatment of HIV-positive people might reduce HIV transmission on a population-wide basis, but various models have concluded that they would have impact.

In December 2009, Project Inform and Community HIV/AIDS Mobilization Project (CHAMP) convened a multi-disciplinary group of HIV experts to consider whether implementing a strategy to significantly increase participation in HIV testing, care and treatment could help the US accomplish three important goals: 1) to increase the percent of HIV-positive Americans who know their status, 2) to improve the health outcomes of individuals who are HIV-positive, and 3) to reduce HIV incidence.

Based upon a review of currently available data and existing programs from multiple jurisdictions, the Think Tank resulted in a recommendation that a new effort called Testing & Linkage to Care Plus, or TLC+ (the Plus referring to Treatment), has significant potential to help the US meet the three goals described above. (A review of this scientific literature is available at [www.projectinform.org/tlc+/.](http://www.projectinform.org/tlc+/)) The participants also concluded that TLC+ should become a key element of the National HIV/AIDS Strategy, currently under development by the Obama Administration, because of its additional potential to support the three stated objectives of the Summary. (An article discussing the National HIV/AIDS Strategy appears on page 12).

TLC+ proposes a standard of care in which all public and private testing providers work intensively with HIV-positive people as soon after diagnosis as possible to link them voluntarily to primary medical care, prevention with positives counseling, as well as social services that can support them to engage in and maintain participation in HIV treatment. Its components are designed to benefit people newly diagnosed with HIV, those who have not previously been ready or able to engage in care and treatment owing largely to a lack of needed social services to support their readiness, and those who have been lost to systems of care and treatment.

CONTENTS

- 1–9 Top stories
- 10–12 Hepatitis C information
- 12–16 Project Inform’s policy work
- 16–20 HIV treatment information
- 20–24 Current drugs in clinical study

A thorough description of TLC+ can be read at www.projectinform.org/tlc+/. Briefly, it includes:

- Assuring that HIV-positive individuals know their status as soon after infection as possible;
- Effective and timely linkage of newly diagnosed HIV-positive people to primary medical care and social services that will prepare them to consider initiation of treatment, as well as efforts to re-engage individuals who have been lost to systems of care;
- Prompt evaluation of eligibility and readiness for HIV therapy, and support for its initiation;
- Effective efforts to support retention in care and adherence to HIV therapy to maintain viral suppression;
- HIV prevention counseling and support; and
- STI screening and treatment.

TLC+ would promote much-needed integration of existing testing, care and treatment, support services and prevention programs at all levels of government and create specific and measurable outcomes for those efforts. While some medical providers and local jurisdictions are already taking steps to implement it, the Think Tank concluded that TLC+ should become a national program, delivered through intensive collaborations of state and local health departments, medical providers, social services agencies, and AIDS service organizations — including prevention-focused agencies. Its further design and implementation necessitate an unprecedented level of coordination among the National Institutes of Health (NIH), Centers for Disease Control & Prevention, Department of Health & Human Services and other federal agencies responding to HIV/AIDS, as well as intensive efforts to assure that these agencies' funding streams are combined to enable such a strategy at the local level.

The NIH is currently conducting a study of the feasibility of implementing Test & Treat as a potential tool in prevention. We nevertheless believe that TLC+ can and should become a part of the National HIV/AIDS Strategy and be implemented nationally in the near future. It would not be ethical to delay improved efforts to increase the percentage of HIV-positive Americans who know their serostatus and are engaged in care and treatment that may protect their health, in addition to the possible benefits for prevention accruing from this strategy.

The Think Tank also highlighted a set of issues that serve as significant barriers to strengthening the health outcomes of HIV-positive people, and that will reduce the potential effects of TLC+ if they are not addressed. It was therefore recommended that the National HIV/AIDS Strategy establish policies and programs to address these conditions:

- Stigma and discrimination continue to act as powerful barriers to an individual's willingness to be tested for HIV and engage in care and treatment if they are HIV-positive. Major national efforts, including visible Presidential leadership, are needed to address these barriers.
- It is clear that many primary medical providers are failing to encourage patients to be tested for HIV and to follow up in sensitive and helpful ways because they are uneasy about sex, sexual identity, race, drug use and other social and behavioral factors associated with HIV and AIDS. A significant national effort that includes national medical associations and medical schools must be launched to establish standards of care regarding the offering of HIV testing, care and treatment, and to encourage providers to follow them. Presidential leadership is also necessary on this point.



**For more
treatment and
health care
information, call
Project Inform's
toll-free
National HIV
Treatment
Hotline at
1-800-822-7422.
HOURS:
10a–4p, M–F**

- Similarly, there is evidence that many people at risk for HIV are failing to be tested or to enter care and treatment based on a serious misunderstanding of their benefits, the effectiveness of HIV treatment, and the availability of low or no cost care and treatment. A significant national campaign is needed to help people at risk for HIV infection better understand the benefits of knowing their serostatus and addressing HIV disease, and even to promote testing, care and treatment.
- California has passed a law requiring that all insurers and payer sources reimburse for HIV testing whenever ordered by a medical provider. Additional state and/or Federal legislation to this effect may be needed to ensure universal access to testing. President Obama has commissioned a study of this issue, and related issues, by a panel of the Institute of Medicine.
- Adequate resources do not currently exist to assure that all HIV-positive Americans are able to receive affordable or no-cost care and treatment. Without such a guarantee, the US will never be able to fully control this epidemic. National healthcare reform, establishing HIV care and treatment as an entitlement program, or significant increases in Ryan White funding will be essential to the success of this strategy.

Project Inform believes that TLC+ has enormous potential to support many thousands of Americans to preserve their health and well-being, and to help the US gain much greater control of the AIDS epidemic. Along with members of a national TLC+ Work Group that was formed to continue the work started at the Think Tank, we will continue to work with the newly appointed President's Advisory Council on HIV/AIDS, the Office of National AIDS Policy, and all relevant federal agencies to further develop the policies and programs that will be necessary to implementing TLC+ on a national basis. Regular updates on the status of this effort will appear at www.projectinform.org.

Federal guidelines updated December 1, 2009

On World AIDS Day in 2009, the US DHHS released an updated version of the *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*, in a move that harkens back to the "Hit Hard, Hit Early" era. The two major updates include changes to when to start and what to use as first line therapy. These changes reflect the challenging discussions that have taken place over the past couple of years in reaction to newer data on when to start.

When to start therapy moved to earlier starting point

The previous edition of the Federal HIV Treatment Guidelines recommended as an "option" to start therapy between 350 and 500 CD4s. The current edition has changed and now recommends that everyone with CD4s below 500 be on therapy. Some Guidelines Panel members even recommend starting at CD4s above 500. While more convincing study data point to the benefits of starting before CD4s drop below 500, the data for starting above 500 CD4s are not as strong. Some experts on the Guidelines Panel disagree with this last point, however.

This edition marks a significant development in updating the Guidelines. With any recommended change, the Panel seeks agreement by at least 2/3 of its members. This did not happen this time around. Despite agreeing on starting between 350 and 500, the Panel was divided on the strength of the data that supports this change. For the first time, the Guidelines state that the

“Panel was divided on the strength of this recommendation: 55% of Panel members for strong recommendation and 45% for moderate recommendation”. Then, a second statement was made regarding starting therapy above 500 CD4s: half the Panel favored starting therapy while the other half viewed it as optional.

The benefit of starting therapy at higher CD4s comes from several retrospective studies (such as the large NA-ACCORD) that have generated useful information but are not the gold standard method used in randomized, prospective studies. A large international when-to-start study (START) is now underway, but its results may not be available until 2012 or later. Given the mix of data from these retrospective studies and the absence of data from randomized studies, the Panel members came to their new conclusions in the Guidelines.

The possible benefits of starting treatment earlier include lower rates of many non-AIDS conditions due to reducing inflammation and immune activation, better overall health, longer-term survival, use of current therapy that's more effective and easier to take and tolerate, and lower rates of passing HIV onto others. The possible risks of starting earlier include higher risk of short- or long-term drug complications, drug resistance, and running out of options earlier.

As with the previous edition, these Guidelines continue to recommend that anyone with an AIDS-defining condition or with CD4s below 350 should be on therapy, as should anyone who is pregnant, has HIV-related kidney disease or has hepatitis B where treatment is warranted, regardless of their CD4 count.

What drugs to start also changed

Two noteworthy changes took place in the section on what to start. The first added the new integrase inhibitor, Isentress (raltegravir), as a *preferred* drug. The second down-graded Kaletra (lopinavir/ritonavir) from *preferred* to an *alternative* option, except in pregnant women where it's still a preferred option.

The new list of *preferred* HIV drugs for first line therapy now includes Isentress, Prezista (darunavir) boosted with ritonavir, boosted Reyataz (atazanavir), and Sustiva (efavirenz). For a full potent regimen, each of these should be combined with Truvada (Emtriva + Viread). Atripla (Emtriva + Viread + Sustiva) is the only one-pill, once-a-day regimen out of the 4.

In addition to consulting these new Guidelines, Project Inform recommends that anyone who considers starting treatment weigh the potential benefits and risks of lifelong HIV therapy. Deciding to start therapy creates a significant change in a person's life and it should be individualized and based on up-to-date information. The decision should also take into account a person's ability to adhere to the regimen and other lifestyle factors that could impact therapy.

Other notable updates: Resistance testing

The resistance testing section was updated to reflect using genotypic tests as the preferred method to test for resistant HIV in recently diagnosed individuals (most effective at viral loads above 1,000) as well as for people on their first and second regimens. This is mostly due to a faster turnaround for results, lower cost and higher accuracy on detecting resistant virus. Phenotypic tests are recommended as an added method for cases where there's a known or suspected complex drug resistance mutation pattern, particularly to protease inhibitors.

Go online and get connected to treatment information around the clock and in the privacy of your home!

Conditions favoring the start of therapy

Despite the Guidelines recommending an earlier start to HIV therapy, some individuals may choose not to start. However, many conditions point to more urgent situations where starting is more warranted. These include pregnancy, CD4s below 200, rapidly declining CD4s (>100 cells/year), an AIDS-defining condition, acute opportunistic infections, higher viral loads above 100,000, hepatitis B treatment, and HIV-related kidney disease.

HIV-2 infection and treatment

This new section was added with respect to treating people with HIV-2. HIV-2 is mostly found in West Africa, so the testing and treatment of HIV-2 should be considered in people of West African origin and those who have had sexual contact or shared needles with persons of West African origin. HIV-2 disease progression is somewhat different from HIV-1 and co-infection with both viruses is possible, so additional considerations are necessary when treating HIV-2 disease.

Hepatitis C co-infection

A new large section on hepatitis C evaluation and treatment has been added. About 1 in 4 people with HIV also live with chronic hepatitis C, so additional guidance around evaluating liver health and the need for treatment has been included.

Side effects and drug interactions

New side effects information based on the most recent published data in the newest approved agents is now included in the guidelines.

Secondary prevention

A new section on preventing secondary infection with HIV has been added. It covers the somewhat neglected opportunity of providing prevention messages during doctor visits; encouraging strategies to change risky behaviors such as safer needle use and safer sex; and the role of HIV therapy in preventing HIV transmission.

Keeping America healthy through meaningful health care reform

Meaningful health care reform that will provide comprehensive, quality coverage to people with HIV has been and will continue to be a top priority for Project Inform. In early 2009, the Obama Administration led the way, prioritizing health care reform as critical to ensuring both the health of Americans and supporting economic recovery. Extensive and contentious debate took place in Congress, resulting in several bills in both the House and Senate by mid-year.

Project Inform's policy team was actively engaged in efforts to monitor the bills and advocate with Congressional leaders to ensure that the needs of those living with and at risk for HIV were addressed in legislative proposals. Working in coalition with the HIV Health Care Access Working Group, we focused on ensuring that reform proposals addressed access to high-quality, affordable care, treatment, and prevention and screening. The working group developed a 2009 Health Care Reform Policy Platform, outlining key priorities for the HIV community. We also advocated on provisions in the bill as they were brought forward, sent letters regarding priorities for the HIV community to committee members as they developed bills, and met with key members of Congress.

Mobilizing people living with HIV and their allies in the fight for quality health care reform was an important part of our efforts. To ensure the voices of people living with and at risk for HIV and advocates were included in the health care reform debate, Project Inform convened regular HIV Community Health Care Reform Conference Calls. These included updates on Congressional health care reform activities and provided an opportunity for broader community input into priority issues and legislative strategy. We worked with our partners to disseminate frequent Action Alerts providing updates on legislation and opportunities to participate in the debate by signing on to important letters and contacting elected officials and the Administration.

In late August 2009, prospects for health care reform were dealt a blow with the death of Senator Ted Kennedy, one of Congress' most powerful proponents of health care reform. Senator Kennedy's death came at the end of a Congressional recess filled with vitriolic disruptions of district town hall meetings, staged by opponents to health care reform aimed at preventing thoughtful discussion of reform, scaring Americans, and politicizing the debate. Project Inform and our partners responded with a sign-on letter to President Obama strongly supporting the need for health care reform and outlining the components most important for people living with and at risk for HIV. Over 1,000 people and organizations signed on to the letter — one of the strongest responses from the community in years.

By December 2009, the Senate and House had each passed health care reform legislation and negotiations began to create a final bill. Although both bills included provisions important for people living with and at risk for HIV/AIDS, the House bill was much stronger in most areas. As negotiations continued, it appeared that some provisions from both bills would appear in the final bill. However, the process stalled once again when the special election for the late Senator Kennedy's seat was won by a Republican, causing the Democrats to lose the 60 votes necessary to stop a filibuster (preventing a vote) in the Senate.

There is, however, still strong hope for meaningful reform. There are mechanisms by which the bill can pass both houses. The President and Congressional leaders who have spent months working on the effort remain committed to delivering health care reform now. Senator Al Franken said at a recent conference, "We can't walk away from the health care reform empty-handed and we won't." And Speaker Nancy Pelosi stated, "We'll go through the gate. If the gate is closed, we'll go over the fence. If the fence is too high, we'll pole vault in. If that doesn't work, we'll parachute in. But we're going to get health care reform passed for the American people."

It is essential, however, that we continue our efforts to demand that our Congressional leaders pass a health care reform bill. If this effort stalls or fails, the likelihood of meaningful reform during the first term of the Obama presidency decreases dramatically.

Advocates in the broader health care reform community as well as Project Inform and our partners have rallied to urge Congress to pass this reform. Once the bill passes, there will be a tremendous amount of work, much of which may fall to the state level, to monitor implementation in order to ensure that people living with and at risk for HIV get the health care they need to live healthy lives.

Updates on health care reform and recommended community actions can be found on Project Inform's website at www.projectinform.org/advo/hc/index.shtml.

Aging and HIV

As a result of tremendous community outcry for more attention to the topic of aging and HIV, Project Inform sponsored a forum on “The Consequences and Management of Aging and HIV” in September 2009. As anticipated, the San Francisco LGBT Center was packed as presentations on the clinical and psychosocial aspects of aging with HIV were presented. Steven Deeks MD UCSF, Peter Carnini MFT, New Leaf and Matt Sharp from Project Inform led the forum.

Our society is aging. Baby boomers are reaching their senior years and the impact on our health care infrastructure is being felt. In California, half of the state’s population will reach 65 years old or older in the next ten years.

Due to the success of antiretroviral therapy, people with HIV are also living longer and into their senior years. Today in the UK, nearly one-third of people with HIV are more than 45 years old. In the US, it’s predicted that by 2015 half of people with HIV will be over 50. In San Francisco, 27% of people with HIV were over 50 in 2003, but by 2008 40% were older than 50. This growing number will impact social service delivery and affect our already fragile health care system. Providers are generally not sensitive to the concerns and needs of an aging HIV population.

Fifteen percent of newly diagnosed people with HIV are over 50 years old. Since this population is mostly heterosexual, it raises many concerns over the lack of targeted prevention for older people in a society that stigmatizes them as a population of people who don’t or shouldn’t have sex.

The remaining aging population has been on HIV treatment for a long time and is generally healthier, having returned to work or at least maintained a reasonable quality of life. We know that the cumulative survival rate is going up due to this success, but it is also an odd paradox that many who have been successfully treated and reached undetectability are also now at increased risk for certain diseases commonly seen in the elderly.

The fact remains that life expectancy is lower for those who started HIV treatment late or their CD4 cells never increased as a result of therapy. The Antiviral Therapy Collaborative Cohort Study showed life expectancy has increased due to therapy but has not reached the same level seen in the HIV-negative population. Our work is cut out for us.

The physical effects of aging are well known. However, the consequences of aging and HIV are interrelated. But it is still not completely understood if HIV causes premature aging or if aging makes HIV disease worse. Researchers are looking for answers in ongoing and planned laboratory and clinical research.

Non-AIDS events

Today, a third or more of deaths most common in older people with HIV are not caused by AIDS. Most of these clinical issues are known as non-AIDS events, which are illnesses not related to HIV. These events are also being seen more often than in the earlier days of the epidemic. Before HAART, the biggest cause of mortality was due to opportunistic infections in people with severe CD4 loss. Non-AIDS events such as cardiovascular disease and malignancies are most often caused by direct viral infection, a sub-optimal CD4 response to therapy and by inflammation.

Despite effective HAART, there remains a low level of latent virus that leads to inflammation which causes some of the non-AIDS events such as heart disease. Also, many of the non-AIDS conditions are also common in older people in general, so as HIV+ people grow older the risks become greater.

**Become
a fan of
Project Inform
on Facebook!**

Simply go to
[www.facebook.com/
ProjectInform](http://www.facebook.com/ProjectInform)
to become a fan.

*Project Inform
posts important HIV
news several days each
week to help you stay
informed!*

Heart disease has long been a concern in HIV, and especially in recent years as the HIV population ages and cumulative data on different markers for heart disease, including heart attacks, are growing. Heart disease is the most important cause of death in the general population and is higher in people with HIV. Heart attack risk is increased with Ziagen or Epzicom although the reason has not been established. Protease inhibitors increase lipids that are associated with heart disease, however newer drugs may be less of a problem. Other lipid-friendly regimens exist, so providers should individualize therapy based on risk factors for heart disease. More long-term research is needed in people with HIV to understand the cumulative effect of HIV therapy as they grow older.

The liver is the body's critical filtering mechanism. It makes sense that, over time, the liver wears down, especially in co-infection with HIV and hepatitis B or C. Inflammation and low CD4s are related to liver disease. In aging populations of people with HIV alcohol, obesity and poly-pharmacy, or the use of many drugs together, are also factors related to liver disease.

AIDS-related cancers such as non-Hodgkins lymphoma and Kaposi's sarcoma have declined in the HAART era. However, most malignancies occur as people age, and as time passes older people with HIV will be at a higher risk for cancer. In HIV, Hodgkins lymphoma, anal, throat, liver and head and neck cancers are the most common malignancies. These cancers are most often caused by an infectious agent such as hepatitis B or C, or human papillomavirus. Low CD4 cells and inflammation are also related.

Today, AIDS dementia is also less common due to HAART because neurocognitive decline is greatly slowed with effective HAART. But some are concerned that many effective HIV drugs do not penetrate the central nervous system, which may lead to mild neurocognitive symptoms that are quite common in older people with HIV. Alzheimers disease and senility have been a big concern in the general aging population, but persistent HIV and inflammation are contributing to these already debilitating and frustrating conditions in older people with HIV.

Bone fractures and osteoporosis (loss of bone density) are also common in older people. Yet, osteoporosis is three times higher in people with HIV. Osteopenia (thinning of the bone mass) is even higher. Long-term HIV disease, inflammation and non-HIV related factors such as alcohol use are all risks to good bone health in older people with HIV. There has been some concern regarding Viread (tenofovir) causing bone disease, however this has not been borne out in studies thus far. Doctors suggest using vitamin D supplements and calcium where appropriate.

Frailty is characterized as unintentional weight loss, exhaustion, low physical activity, weakness and slowness. It includes poor general health, risk of falling, poor appetite, loss of muscle mass and bone demineralization. It is a common geriatric condition but is now being seen in older people with HIV. Again, persistent inflammation and low CD4 counts are related to this condition.

The consequences of low-level, persistent HIV

Despite effective treatment, HIV persists in small amounts (millions of copies) in various "reservoirs" in the body where it can lay silent in cells that are "asleep." These cells must be activated to release new virus, which in turn starts a normal immune response. Since this is an ongoing low-level response, inflammation can remain as long as virus is present. This low level is not detected by standard tests, but researchers detect it in highly sensitive assays that reach below 1 copy.

Viral proteins released by this persistent virus in the latent reservoir can be toxic to the body and also cause immune activation. HIV persistence is being researched and may lead to what is being called "functional cure."

Inflammation is a normal immune process involving specific cells and cytokines that in HIV are switched on due to chronic immune responses (either due to sub-optimal treatment or low level persistent HIV). Inflammation does decrease w/ HAART but never returns to normal.

A process called microbial translocation is seen within a few weeks of HIV infection and can weaken a person's immune capacity, possibly never being fully restored. After infection, HIV targets CD4 cells in the gut, demolishing a large part of the body's important immune reserves. Then, bacterial microbes travel outside of the gut and enter the bloodstream where the immune system responds to them, activating T cells that are infected with HIV. More HIV is produced leading to further immune damage. This is one of the most important physiological reasons for stopping virus as soon as possible after infection.

Aging and HIV and the immune system

As we grow older certain aging processes are similar to what chronic HIV does to our bodies. *Apoptosis* is our natural mechanism to rid our bodies of unnecessary, weak or damaged cells. Apoptosis can lead to suppression of the immune system which can also lead to cancers. It is a process that most likely occurs more often in older people with HIV.

HIV damages lymph node structure and thymic dysfunction, and there is a cumulative effect as people with HIV grow older. Over long-term HIV infection, the thymus loses its function and fewer crucial T cells are produced, causing low CD4 and CD8 ratios and low memory to naïve cell ratios. This leads to further immune system damage.

Another process that becomes dysregulated in aging and HIV is called immunosenescence. This is another word for "immunologic aging" or "exhaustion" of T cells. This can cause a destructive high T cell turnover and may be part of premature "aging" of the immune system.

In HIV disease and in older people the immune system's functional capacity decreases. This is what causes a poor response to vaccines and the TB skin test. Oxidative stress occurs in both the elderly and people with HIV. Over time this can create further suppress the immune system.

Research is needed

Although we have made huge progress with HIV therapy, the effects of living longer with HIV despite viral control are still not completely understood. It is clear that this issue requires more research, although it's hard to know if there will be clear answers anytime soon. There are still many unknowns in HIV pathogenesis, technical laboratory issues, new assays needing development and clinical studies will be challenging to design and recruit.

Much that scientists are learning about aging and HIV is daunting and most of the news is sobering. Yet people with HIV are gaining years on their lives, and surviving despite critical odds. People with HIV can maintain health through a few practical management tips such as monitoring for and treating underlying cardiovascular disease, screening and reducing risk for cancers, individualizing HIV treatment, appropriate exercise, healthy diets and stress reduction. Importantly, research is promising on immune related therapies and better, less toxic HIV drugs that have the potential to take us into a different paradigm of living with HIV.

HEPATITIS C INFORMATION

Project Inform expands hepatitis C advocacy efforts

2009 marked a significant year for Project Inform, as we greatly expanded our hepatitis C (HCV) policy agenda at the federal, state and local levels. We began HCV advocacy in 2007 in response to the number of people living with HIV who are co-infected with HCV. It became immediately apparent that in addition to the need to address co-infection, there was a great need for increased policy and grassroots advocacy on behalf of the millions who are infected only with HCV and often have less access to the treatment and health care they need to survive than those who are co-infected.

Between 3 and 4 million Americans are living with chronic hepatitis C and the overwhelming majority are not aware of their status. Chronic HCV can lead to cirrhosis, liver failure, and is the leading cause of liver cancer in the US. Nearly 15,000 people die per year from this preventable disease. In addition, an estimated 25–30% of people with HIV are co-infected with HCV. End-stage liver disease is now a leading cause of death among people with HIV.

Despite these staggering statistics, the response by all levels of government has been abysmal. The federal government provides less than \$20 million per year for viral hepatitis prevention services and there is no effort to establish programs to provide access to care and treatment for uninsured people living with HCV. Meanwhile, most states and localities lack resources and a plan to offer adequate screening, testing, care, and prevention services.

Project Inform is working in coalition with national, state and local partners to advocate for a comprehensive strategy to address the HCV epidemic. At the national level, we advocate for increased federal funding through our participation in the Hepatitis C Appropriations Partnership, led by the National Alliance of State and Territorial AIDS Directors (NASTAD). Our advocacy led to a \$1 million increase in 2009. While highly inadequate, this represented the largest increase in several years.

We also participate in the steering committee of the National Viral Hepatitis Roundtable (NVHR), a national coalition of hepatitis B and C advocates. NVHR is leading efforts to pass the Viral Hepatitis and Liver Cancer Control and Prevention Act, which would establish a national hepatitis surveillance, prevention, screening, and testing program. We are also taking the lead in organizing the first hepatitis B and C rally at the Capitol on World Hepatitis Day, May 19, 2010.

At the California state level, we participate on the steering committee of the California Hepatitis Alliance (CalHEP), a statewide coalition of hepatitis B and C advocates. CalHEP played a major role in the development of the recently released California Adult Hepatitis Prevention Strategic Plan, a proposed roadmap to addressing the hepatitis epidemic in the state, and will focus on its implementation in 2010. To that end, we will be organizing a hearing in the California State Legislature on World Hepatitis Day.

In San Francisco, we played a leadership role in establishing the San Francisco Mayor's Hepatitis C Task Force and chair its Public Policy Subcommittee. The task force was formed in September 2009, and is composed of 32 advocates, medical and social service providers, and people living with HCV. Its goal is to develop a list of recommendations to the Mayor to improve San Francisco's response to the hepatitis C epidemic. For more information about the task force structure and goals, visit www.projectinform.org/advo/hepc/011210.shtml.

World Hepatitis Day

May 19, 2010

Check www.projectinform.org for more information on Project Inform's activities for World Hepatitis Day, or go to www.ami.number12.org.

Promising new drugs for hepatitis C on the horizon

In many ways, 2009 brought significant changes to viral hepatitis with promising new drug development and increased national advocacy. In terms of drug development, the treatment pipeline for hepatitis C (HCV) is very robust. Two protease inhibitors, telaprevir and bocepravir, are in final Phase 3 studies and if approved this year, will add an adjunct therapy to the standard of care (pegylated interferon + ribavirin) for HCV mono-infected individuals. Over 50 new therapies from several classes — including HCV inhibitors, anti-inflammatory drugs, immunomodulators, new interferon drugs and vaccines — are all in early and mid-stage studies. Advocates, including Project Inform, have also pushed for the development of studies in people living with both HCV and HIV, which will follow results from mono-infection studies, but pose new challenges for a more difficult to treat population.

The year also heralded the announcement of a strategy called *Specifically Targeted Antiviral Therapy* for hepatitis C (STAT-C), which is attempting to effectively treat HCV without using pegylated interferon and ribavirin. If this strategy proves effective it may usher in a new era of HCV treatment since pegylated interferon and ribavirin are highly toxic and not effective in everyone.

In any case, HCV drug development is complex and the offering of so many clinical studies of different drugs from so many different classes presents unique challenges to the field. However, these challenges will eventually pay off for people who need new HCV treatments. It is extremely encouraging to see the motivation and interest in the research. For more information on the status of hepatitis C clinical studies, go to www.HCVadvocate.org or www.clinicaltrials.gov.

Advocacy efforts are building through the Viral Hepatitis and Liver Cancer Control and Prevention Act of 2009 bill that was introduced at the same time as the AASLD meeting in Boston last fall. Advocates have worked for years for legislation to increase funding for testing, care and treatment of HCV. Project Inform has also joined with Treatment Action Group and other hepatitis C advocates nationally to create a Hepatitis C Treatment Issues Committee which will work to monitor the abundant drug development. We have learned significant lessons through the years of HIV drug development that are likely to support HCV drug development.

Immune gene may help predict effectiveness of hepatitis C therapy

As discussed earlier, newer hepatitis C treatments are currently being studied that hopefully will not only cure more people but will also reduce its many side effects and length of therapy. In the meantime, a gene called IL28B has been found that may help predict how effective hepatitis C therapy will be in certain people. Not only is it associated with long-term responses to current standard therapy, it also helps forecast how fast the treatment response is.

In November 2009, results from the IDEAL study of 1,600 people showed that the “CC” version of IL28B (getting the gene from both parents) is associated with the best response to treatment. The “TC” type (only one IL28B gene from one parent) and “TT” type (no gene from either parent) were associated with poorer outcomes. Other factors that influenced treatment outcomes were hepatitis C viral load, ethnicity, liver fibrosis and fasting blood sugar. This gene will also have to be studied in all of the newer drugs now in study.

Confirming these results with more research is the next step. Nevertheless, developing a test that detects this gene could change medical practice for treating hepatitis C. Test results would give doctors and patients alike more information to make better decisions before starting therapy. Hopefully a new test will be developed quickly, perhaps before the end of 2010.

PROJECT INFORM'S POLICY WORK

Significant policy victories in 2009

2009 brought some major policy victories that will greatly improve the lives of people living with and at risk for HIV/AIDS:

- **Reversal of syringe exchange funding ban:**

In December 2009, Congress finally lifted the federal funding ban on syringe exchange programs. Even though these programs have been proven to reduce HIV transmission without increasing drug use, Congress would not allow any federal funding for them for over 20 years. Thanks to tireless efforts of our advocacy partners, this ban is now history, an important step forward in assuring that science determines how HIV prevention dollars should be spent.

- **Renewal of Ryan White Program:**

On October 30, 2009, President Obama signed the Ryan White Treatment Extension Act. This bill renews the lifesaving Ryan White Program for another three years. The program provides vital care, treatment, and support services to over 100,000 low-income and uninsured people living with HIV/AIDS. The extension will allow for continued services while Congress continues developing health care reform legislation.

- **Lifting of HIV immigration ban:**

In November 2009, President Obama ended one of the country's most shameful policies by lifting the ban on HIV-positive immigrants and travelers. The ban was first implemented in 1987 and prohibited HIV-positive foreign nationals from entering the country without obtaining a waiver for short-term travel. As a result, the International AIDS Conference has lifted its boycott of the US and the 2012 conference will be held in Washington, DC.

Development of the National HIV/AIDS Strategy now underway

In 2008, more than 500 AIDS service organizations from across the nation called on candidates for the Presidency to commit to developing a National HIV/AIDS Strategy. Project Inform has served as a member of the Steering Committee of the coalition that made this call. During his campaign, then Senator Barack Obama enthusiastically embraced the need for a Strategy to bring greater urgency, innovation and coordination to bear to address slow progress in further controlling the domestic epidemic. As President, Mr. Obama has convened an interagency panel of high-level representatives of all Federal agencies involved in the response to HIV to actually develop the Strategy with three critical outcomes in mind:

- To increase the percentage of HIV-positive Americans who are engaged in care and treatment for their infection, because nearly 50% of HIV-positive people either do not know their HIV status or are not engaged in care;

- To reduce the number of Americans who become newly infected with HIV each year, because for the past decade, the number of new HIV cases has remained constant at 56,300 a year;
- To reduce the substantial disparities that women and people of color experience in HIV health, both with respect to the disproportionate number of new infections affecting these groups and the poorer HIV health outcomes they suffer.

To manage the development of the National HIV/AIDS Strategy, President Obama also agreed to the community's request that he re-invigorate the Office of National AIDS Policy (ONAP) within the Domestic Policy Council of the White House. In early February 2010, Mr. Obama also appointed a new President's Advisory Commission on AIDS (PACHA) and selected the highly respected HIV expert Dr. Helene Gayle to serve as its chairperson. PACHA, which includes representatives of community-based HIV agencies where the interagency panel does not, will review a draft of the Strategy and will apparently play a significant role in monitoring its implementation. The Administration hopes to complete work on the Strategy in June 2010.

To receive community input into the development of the Strategy, ONAP conducted a series of 14 Town Hall meetings across the country at which people living with and at risk for HIV, service providers and concerned citizens provided recommendations about what should be contained in the plan. The Steering Committee of the Campaign for a National/HIV AIDS Strategy also convened a series of four community consultations to develop recommendations to the interagency panel about key issues and needs it must address in order for the Strategy to be effective.

Great hope is being placed in President Obama to assure that the Strategy resolves many questions about how the US will make further progress against the epidemic through a series of bold, evidence-based and innovative new approaches. Hope also exists that the Strategy will increase coordination and cooperation among key government agencies, as well as among governmental and non-governmental organizations, to assure deeper impact on the epidemic.

Project Inform will continue to do its utmost as a member of the Steering Committee of the Campaign for a National HIV/AIDS Strategy to assure the success of this much needed effort. Updates will regularly appear at www.projectinform.org and at www.nationalaidsstrategy.org.

Protecting people with HIV in the California budget

California has been facing a massive budget deficit for the past several years, a problem that is expected to continue for the next several budget years. A weak economy, structural barriers to increasing revenues, "solutions" from previous budgets that imposed future costs, earmarked revenues and limited options to balance the budget are some of the contributors to the difficulty the state faces. Governor Schwarzenegger and the Legislature have chosen to cut spending in essential social programs rather than show the leadership necessary to adequately address the state's fiscal crisis by examining appropriate revenue sources in addition to cutting state spending.

In February 2009, the Legislature and the Governor passed a budget for the 2009–10 fiscal year. The budget contained a shortfall that needed correction almost as soon as it was signed into law. The Governor proposed severe cuts to health and human services in a budget amendment process that started in early spring. That proposal included an \$85 million cut from HIV services,

eliminating state funding for Education and Prevention, Home and Community-based Care, the Therapeutic Monitoring Program, Early Intervention programs, Housing, and Epidemiology and Surveillance. It also reduced funding to the State Office of AIDS and to the AIDS Drug Assistance Program (ADAP).

Project Inform and our partners mounted a strong advocacy campaign, including a rally in Sacramento, lobbying, and compelling testimony from people living with HIV, providers, and doctors. The Legislature restored the worst of the cuts only to have the Governor remove even more state general fund from the programs with his veto of the Legislature's proposal. By August, the state was reeling from deep cuts to HIV services, Medi-Cal and other important programs that people with HIV depend on to stay healthy.

In spite of protests, many of which were organized by Project Inform and our partners, and law suits questioning the cuts, the money was not restored and the fight against HIV in California has suffered a serious blow. As local health jurisdictions struggle to find innovative ways to continue essential services, it is unclear what the overall impact of the cuts will be.

In fall 2009, the Governor and his administration began development of the FY 2010–11 budget and it became clear that ADAP was moving quickly towards a large shortfall in funding. Advocates estimated that \$100 million more would be needed to ensure that ADAP could continue to serve all who qualify and need the services. The Legislative Analyst's Office later confirmed the amount.

Again, advocacy campaigns were mounted, with press conferences and rallies. People with HIV and their allies turned out in force, attending events and contacting the Governor. More than 80 organizations signed on to a letter demanding that the Governor fully fund ADAP in his budget proposal. In spite of a budget deficit of close to \$20 billion and proposed cuts to many important health and human services programs, the Governor put \$97 million in state general fund into ADAP, allowing it to serve all who need it, with one important exception. ADAP will no longer serve 36 municipal jails, resulting in a \$9.5 million reduction in the overall program, and raising concerns that those in municipal jails may not continue to get the HIV treatment they need during their stay in jail and as they transition back to the community.

Currently, the Legislature is developing its response to the Governor's proposal. We have an uphill battle to ensure that ADAP retains the necessary increase it received in the Governor's budget and that people in municipal jails get the treatment they need. Medi-Cal serves about 50% of those with HIV in California and we will also have to fight against the devastating cuts that have been proposed for that program. In addition, California is preparing to renew its Medi-Cal waiver, the plan that outlines how it will serve seniors and people with disabilities. Project Inform will be working to ensure that people with HIV are represented in that process. For more detailed budget information and waiver information see www.projectinform.org/XXX.

The work of this last year and the victories we have won together would not have been possible without partners and coalitions but most importantly, people with HIV and their allies who have been strong advocates throughout the process. Unfortunately, California continues to face huge budget challenges, record levels of unemployment, and decreased revenues. Given the unwillingness of California elected officials to raise appropriate revenues and the continued proposed cuts to essential services, our work is far from over.

Activism 2.0: tried and true + new

To save the California ADAP, Project Inform worked with local and state HIV advocacy partners to place pressure on Governor Schwarzenegger and the Legislature to avoid a crisis that could lead to thousands of people losing access to lifesaving drugs. Using Project Inform's Facebook presence, we organized a large attendance and big media presence at our Save California's ADAP press conference on the steps of City Hall in San Francisco at the end of November.

In the weeks after the press conference, using the internet activism platform of *www.change.org*, we secured many signatures on a petition demanding full funding of ADAP. And for Californians signing onto the petition, the website generated emails to the Governor's office, increasing the pressure even more!

Using re-ignited activism from successful earlier campaigns with reinvigorated Web 2.0 activism, Project Inform's constituents were successful! We pressured Governor Schwarzenegger to provide a \$97 million increase for ADAP. The pay off: people living with HIV in California will continue to receive their lifesaving medicines.

Experience Project Inform's expanded social networking presence by visiting:

Facebook: www.facebook.com/projectinform

Twitter: www.twitter.com/projectinform

Youtube: www.youtube.com/projectinform

Change.org: www.change.org/projectinform

PI Action: www.projectinform.org/action.shtml

ATAC's drug company "Report Card"

The number of effective HIV drugs currently approved and on the market is a testament to committed research and treatment advocacy at every stage of development. Ensuring that HIV treatment research and drug development continue has always been a priority at Project Inform. But the HIV pipeline has noticeably shrunk significantly in the last few years and there has been concern over the strength of ongoing HIV drug development.

Several drug companies have merged recently, including Schering-Plough with Merck and the creation of an entirely new entity combining GSK and Pfizer into a new company called ViiV. It is unclear whether these mergers are a result of shrinking drug development, or an indication of pooling resources to continue HIV drug development. Either way, there are big changes occurring in HIV drug companies, yet the epidemic still looms and there are improvements to be made with current drugs including better tolerability, and dosing, and a need for entirely new drug classes.

In order to hold drug companies accountable through activist pressure and media exposure the AIDS Treatment Activist Coalition (ATAC, www.atac-usa.org) — in which Project Inform is a member — issued a drug company report card in September 2009 that rated the 9 largest HIV pharmaceutical companies: Abbott Laboratories, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline, Hoffman La Roche, Merck & Co., Pfizer and Tibotec.

The companies were ranked by the group and an average "grade" was given according to their innovation in drug development, patient access to the drugs, pricing, community relations and

marketing practices. The average company grade for all of the companies was C- which seems indicative of the pace of drug development at this time. Abbott Laboratories received the lowest average grade of F. Merck & Co. and Tibotec received the highest scores of B.

The report card was sent to the individual companies with recommendations for improvements, including the development of newer, safer drugs for people who have run out of options, consultation with the AIDS community earlier in the drug development process and provision for wider access. The entire report can be viewed on the ATAC website, or at www.projectinform.org/pdf/pharma_report_card.pdf.

HIV TREATMENT INFORMATION

New treatment for deep belly fat nearing FDA hearings

Tesamorelin, a synthetic human growth hormone releasing factor, may be approved by the FDA in the first half of 2010 as a way to reduce excess deep belly fat. This visceral fat lies beneath the stomach muscles near the internal organs, and in HIV-negative people it has been shown to increase their risk for heart disease. Although tesamorelin may help some people trim down some of their deep belly fat, it should not be viewed as a weight control product. The drug does not affect subcutaneous fat — the fat in between the stomach muscles and the skin.

About 1 out of 4 people with HIV face a condition called *lipodystrophy*, a complex condition of body shape changes and changes in blood fats and sugars. One of its very visible symptoms in some people is excess belly fat. Some feel uncomfortable or conspicuous with a larger belly. It can also prove painful to some or restrict others from being as active as they once were.

Results from a 52-week study of 816 people showed 18% less deep belly fat in those on tesamorelin compared to those on placebo. Study volunteers took a variety of HIV regimens, with an average time on meds at 4.5 years. Most were men and average age was 48. All had CD4s above 300, and 3 out of 4 had undetectable viral loads. Average time since diagnosis of visceral fat was 4 years.

Side effects were fairly well tolerated and included injection site redness and itchiness as well as joint pain and general aches and pains. At 26 weeks, tesamorelin reduced deep belly fat by 13%. At 52 weeks, for those who continued on the drug, visceral fat reduced by nearly 18%. Those who stopped the drug had their belly fat return.

Tesamorelin also improved triglyceride levels as well as levels of insulin-like growth factor, which aids the body to better use energy that may result in less stored fat. Small increases in lean body mass were also noted, but nowhere near the levels seen with Serostim. However, a person's self image of his/her belly did not significantly change, which may be due to the modest decrease.

Despite the fact that there are no other approved treatment options for this condition, people will need to weigh the pros and cons of using tesamorelin for its modest medical improvements. While it may get rid of some visceral fat to ease the discomfort, pain or immobility that some people face, the modest change may not be enough to feel better about one's belly size. In any case, everyone is faced with an injection every day, which some are not willing or equipped to do. Its costs and therefore reimbursement decisions are expected to be challenging.

For more information, read Project Inform's publication, *Tesamorelin and Excess Belly Fat*, available at www.projectinform.org/info/tesamorelin/.

New heat-stable form of Norvir approved

On February 10, 2010, the FDA approved a new heat-stable form of Norvir (ritonavir) 100mg tablets, which do not need to be refrigerated. The daily dose is 600mg taken twice a day. When used with other protease inhibitors, its dose should be reduced. The tablets are white and oval in shape, with “A NK” on the pill. The soft gel capsule and liquid forms of Norvir are still available.

This new tablet must be taken with meals, unlike the soft gel capsule. It should be swallowed whole to maximize its effectiveness and not chewed, broken or crushed. The prescription label warns that people who switch from the capsule to the tablet may experience more stomach and abdominal side effects, such as nausea, vomiting, pain or diarrhea. These side effects may decrease over time.

Screening for anal cancer better defined but more study is needed

Cases of anal cancer are on the rise in people living with HIV. Part of this is due to more attention being paid to the condition and people with HIV living longer lives. Screening tools are being better defined yet there is controversy over screening recommendations by providers. A recent British study attempted to better define the role of anal Pap smears to screen for anal cancer, similar to the way in which cervical Paps are used to screen for cervical cancer.

The study followed 395 HIV-negative and HIV-positive individuals. More than 9 out of 10 were men, about half were white, and 3 in 4 were men who have sex with men. Three forms of tests were performed on each person: an anal Pap smear (where the doctor swabs an area of the anus to remove surface cells), an anoscopy (where a doctor uses a special microscope to look at the anus), and a biopsy (where the doctor scrapes away an area of the anus to remove surface cells).

The results showed that anal Pap smears accurately detected pre-cancerous skin cells about 70% of the time. The higher the grade of disease, the more likely Pap smears could detect these skin cells. They were also more accurate when there were more pre-cancerous cells present.

Anal Pap smears were also better able to find disease in HIV-positive than HIV-negative people (76% vs. 59%). In addition, anal Pap smears were more likely to find disease when CD4s were below 400, and when two or more areas were swabbed for cells (86%) as opposed to one or more (69%).

Although this is good news for detecting pre-cancerous anal cells earlier, using anal Pap smears still leaves room for errors. These findings still indicate that other tests may need to be used to confirm anal Pap results, such as anoscopy. Medical providers should be encouraged to screen for all cancers related to HIV especially as the population ages. People with HIV should discuss their risk for anal cancer and their screening options and seek out experts in the field if necessary.

For more information on HPV, read Project Inform's publication HPV and HIV disease at www.projectinform.org/info/hpv/. Another online resource for anal cancer is the UCSF Anal Neoplasia Study website at www.analcancerinfo.ucsf.edu.

Case report shows ginkgo may interact with Sustiva

In a Dutch case study of one individual living with HIV, ginkgo biloba appeared to interact with the HIV drug Sustiva (efavirenz), causing it to fail in this person. The data were reported in *AIDS* in June 2009.

The 47-year-old man had been on stable HIV therapy for 10 years. It was reported that he had never missed a single dose, showing a high level of adherence to his regimens, thereby lowering his risk for resistance. During the last two years on therapy he was taking Sustiva + Truvada.

Over 14 months, test results showed that his HIV level had become detectable and continued to rise. At the same time, the amount of Sustiva in his bloodstream continued to decline. His doctor eventually learned that he had been using ginkgo biloba for some time. After careful questioning, he had not started or stopped any other medicine or supplement during this time.

What may help explain this situation is that certain chemicals found in ginkgo biloba products can interfere with the same gene that the liver uses to process many drugs, including Sustiva. It is already known that the herb interacts with aspirin, ibuprofen, omeprazole and warfarin. So it's also possible that an interaction may occur with Sustiva.

This case report does not explain the exact cause for this drug failure, nor should it be interpreted that everyone on Sustiva should avoid ginkgo biloba. However, these data highlight the issue of using herbal products with HIV-related drugs and the potential drug-herb interactions that may result. It is wise to let your doctor know everything you take, from prescription medicines to over-the-counter meds to supplements and herbal products and recreational drugs.

Ginkgo biloba does not improve cognitive health

Data from a randomized study of ginkgo biloba in older adults showed no reversal of cognitive decline when using the herb. Many people use the common herbal product believing it will help improve their memory, attention or mild depression. And as people with HIV are growing older and neuro-cognitive issues are more common, some were hopeful that ginkgo biloba would be a possible complementary therapy.

The large US GEM study followed 3,069 people aged 72 to 96 years from 2000 to 2008. Half were given two daily 120mg doses of ginkgo biloba and the other half took a placebo. People were assessed on issues of memory, attention span, concentration, language and ability to reason through tests that measure the rate of change in these mental qualities over time. The data showed no changes in cognitive function between the two groups.

Despite these conclusive results, people may still choose to use ginkgo biloba as a complementary therapy. There's also a chance that the herb may interact with a common HIV drug, as detailed in the article above.

The lingering debate with abacavir and heart disease

The debate continues on the possible increased risk for heart attacks when using Ziagen (abacavir), a result that was first released about 2 years ago. The D:A:D study, which follows the side effects of HIV drugs, earlier reported that the drugs in general increase a person's risk for heart attack by 26%. Further surprising data from the same study in 2008 found Ziagen itself increased this risk

by 90%. Since Ziagen is still an option, frequently prescribed for those with kidney disease who may not be able to tolerate the often prescribed Viread (tenofovir), more research has been done to settle this finding.

Since then, more than a dozen other studies have also reported on heart disease in HIV with conflicting data. An updated analysis from D:A:D continues to show risk, as do results from a smaller Canadian study. The STEAL study of about 360 treatment-experienced people also found a higher rate of non-AIDS events due to cardiovascular factors.

On the other hand, the HEAT study of about 700 treatment-naïve people found no increased risk when comparing abacavir + 3TC to tenofovir + FTC. A large VA study (19,000 people) supports the HEAT observation after adjusting for typical risk factors like heart disease, kidney disease and hepatitis C.

Similarly, the Spanish BICOMBO study of 80 people showed no increased risk for heart attack. The group who took abacavir did have a higher rate of cholesterol than the tenofovir group, but abacavir did not increase many other markers of heart attack risk, such as inflammation or insulin resistance — the same markers used in the D:A:D. Further, a French study reported that the risk for heart attack was not significant, after adjusting their results for drug use.

In the meantime, as researchers tease out these results, what does this mean for people on therapy? If other cardiovascular risk factors are present at a moderate or high degree, such as smoking or diabetes or hypertension, one might choose not to use Ziagen (or Epzicom or Trizivir) to be on the safe side. For others, with few or no additional risk factors, taking Ziagen may be the right choice given its other proven benefits as an HIV drug. In any case, making decisions of whether to use Ziagen should be made in consultation with a health care professional who understands the latest data and can individualize therapy due to the many HIV drug options.

Two medical groups release new system for treating diabetes

The current system for managing diabetes has become problematic and increasingly outdated for many doctors, especially as newer diabetes drugs have come to market. This may be a concern for some people living with HIV (about 1 in 10) as diabetes is a common co-condition.

Two medical groups released a new system in the second half of 2009 to assist doctors to more accurately diagnose and treat diabetes. The system, *Type 2 Diabetes Mellitus: An Algorithm for Glycemic Control*, is based on the most recent clinical data from a few large studies and several drug approvals by the FDA.

The true mark of whether this new system actually does improve health outcomes would be to compare it to current standard therapy. That will involve more clinical study, and Project Inform hopes that any studies undertaken will also include people living with HIV.

For now, the system may be useful to help guide decisions for treating diabetes when used together with more detailed clinical practice guidelines. The full system can be found at www.project-inform.org/pdf/diabetes_aace.pdf.

New warning of serious Intelence side effect

In August 2009, the FDA announced an updated side effect warning for Intelence (etravirine), the newest approved NNRTI. This comes after reports of severe allergic reactions, usually occurring during the first 6 weeks of taking the drug in a small percent of people. The new drug label warns that those who use the drug and experience these side effects should immediately contact their health providers to discuss whether to stop taking Intelence.

The side effects include severe skin reactions, including the life-threatening rash called *Stevens-Johnson syndrome*. Other hypersensitivity reactions include fever, general ill feeling, extreme tiredness, muscle or joint aches, blisters, oral lesions, eye inflammation, facial swelling and/or signs and symptoms of liver problems.

Smoking nearly triples the risk of death

Results from the FRAM study were presented at CROI in February 2009 and showed that currently smoking, as well as older age, significantly increased the risk of death in people living with HIV. Although the study examined many factors related to disease progression and death, the one that was most notable was smoking.

FRAM followed 922 men and women living with HIV along with 278 HIV-negative individuals. After 5 years, those living with HIV showed a nearly 3-times higher risk of death from causes related to smoking (273%).

It is well documented that HIV-positive people smoke more on average than HIV-negative individuals. However, despite powerful nicotine cravings, people have been able to stop especially with the support of stop-smoking programs, health professionals, friends and family.

This striking result may encourage some people to stop smoking in order to lower their risk of heart disease, cancer and death. Stop-smoking programs can be found at hospitals, community based groups, Nicotine Anonymous and even online at www.ffsonline.org.

CURRENT DRUGS IN CLINICAL STUDY

Most promising pipeline drugs

2009 was not a banner year for HIV drug development, yet over a dozen drugs are in Phase II and III clinical studies. These drugs will be incremental advances, but not exceptional enough to change the current paradigm. Some of these are “me-too” agents from existing drug classes, but there are also new drug classes in research.

It is clear that AIDS activism over the last 20 years has pushed the development of several good options for many people, and competition among the drug companies is fierce. The HIV drug market has become saturated with a few good drugs but includes some older average-to-poor drugs, some no longer recommended by the DHHS Guidelines.

There are important reasons for continued development of safer drugs, newer classes and improved dosing. Many people have suboptimal or discordant responses to current regimens, or they cannot tolerate specific drugs. Twice or even once daily regimens could always be improved upon. In a better scenario, drugs that would only have to be taken once a week or month do exist in other diseases, and this strategy is on the AIDS advocacy agenda.

It has been two years since the last drug, Intelence (etravirine), reached FDA approval. Isentress (raltegravir) and Selzentry (maraviroc), drugs from new drug classes, were approved in late 2007. All these drugs represent change we may be looking for in a few ways.

Intelence provides a new NNRTI for a class that has not seen a drug to overcome resistance. It has taken years to reach this point. Isentress has been an important drug in that it is the first integrase inhibitor, but is potent and long lasting when added to another new drug for those who had few treatment options. It was recently approved as a first line drug as well.

However, we know now that there is a growing number of people who develop Isentress resistance and have blown through the integrase class so far. Many have no other options so they find themselves in salvage therapy. Selzentry is limited because it only impacts CCR5 tropic virus, which is not useful for those who may have dual/mixed tropism or CXCR4 tropism.

There are new approaches and a few strategy studies that seek to improve the current drugs. Better tolerability, higher barrier to resistance, and better dosing are all goals being studied and in some cases proving to be effective so far. The latest drugs nearing approval for treatment experienced individuals are:

- **Elvitegravir:** in late Phase III studies expected to be approved in early 2010 is a new integrase inhibitor that must be boosted and thus be combined in a fixed-dose “quad” pill with a new booster agent and Truvada;
- **Bevirimat:** a maturation inhibitor that may require a resistance test and will only be useful in 60% of the population due to natural occurring mutations in HIV’s gag gene;
- **Vicriviroc:** another CCR5 antagonist, only useful against CCR5 sensitive virus.
- **GSK-572:** a second generation integrase inhibitor showed powerful suppression of 2.5 logs with only 50mg dose in an early 10-day monotherapy study, reported at the IAS meeting in Cape Town. So far it appears to not be cross-resistant to the other integrase inhibitors. It is expected to be co-formulated in a once daily pill with Ziagen (abacavir) and Epivir (3TC).

A new drug nearing approval for treatment-naïve individuals is:

- **Rilpivirine (TMC 278):** a new NNRTI that will most likely be a big competitor to Atripla if studies show it works in a once daily fixed dose combination with Truvada.

IL-7 making its debut

After years of studies and millions of dollars, 2009 saw the death knell for IL-2 (Interleukin-2). A presentation at CROI in February 2009 showed pooled data from ESPRIT and SILCAAT, the two largest and most expensive studies that many hoped would prove effectiveness of the first immune-based therapy for HIV. Despite transient increases in CD4 cells, more side effects were seen in the arms with IL-2 compared to placebo. IL-2 also proved to be highly toxic, resulting in several participants stopping the studies.

Project Inform and others had advocated for development of IL-2 despite several significant setbacks and frustrating pitfalls along the way. In the end, it was a depressing end to one of the brightest hopes for an immune-based therapy for HIV. However, the loss of IL-2 has set the stage for another cytokine therapy, IL-7, waiting in the wings and now making its debut.

As with IL-2, IL-7 is a naturally occurring immune chemical, or cytokine, produced by our bodies. It is important for regulating the thymus, producing important types of T cells and balancing

of the immune system. The rationale for its use in HIV is compelling and several studies are beginning to show it most likely will upstage IL-2. Cytheris, a French biotech company has a patent for the next IL-7 version, now in Phase 2 studies.

An early study has provided proof of concept, dosing and safety information of IL-7 in order to move into larger studies. At the 2009 ICAAC, an interim analysis of a small Phase 2 placebo controlled study was presented. IL-7 showed safety and tolerability in this new version.

This formulation is thought to provide a longer half life and make the drug more stable. A few individuals experienced a small though short-lived increase in their viral loads, yet sustained increases of CD4 cells were reported as well as trends toward higher production of immune cells from the thymus. So far this therapy seems safer than IL-2.

The hope for IL-7 is to restore important and functional CD4 and CD8 cells when there have been wide variations in CD4 gains despite viral control with HIV therapy. And, as people live longer with HIV there becomes more pressing need to restore the immune system. In these people and others, HIV therapy alone is not the answer and immune based therapies will become more important.

New boosting drug looks promising

Norvir (ritonavir) was originally approved as a protease inhibitor in HIV regimens during its first few years on the market. Abbott Laboratories discovered that adding small doses of it to a regimen with the protease inhibitor lopinavir boosted its potency because it kept higher drug levels in the blood. Other companies used the drug with their protease inhibitors to boost those levels, also making them more effective.

However, ritonavir comes with troublesome side effects and drug interactions, especially in the older higher doses. So finding an alternative booster would help ease the stomach and metabolic problems that many people face when using ritonavir. A new drug from Gilead Sciences (GS-9350) looks promising in this boosting role. In order to get approved by the FDA, GS-9350 must be at least equal to ritonavir (*bioequivalent*) and be studied with any HIV drugs it will be used to boost.

In February 2009, early study results presented at CROI showed that GS-9350 performed as well as ritonavir. The booster was combined with the experimental integrase inhibitor elvitegravir and Truvada. Unlike ritonavir, GS-9350 has no anti-HIV effect. Its sole purpose is to enhance the effectiveness of other HIV drugs. It is hoped that GS-9350 will not affect blood fat or sugar levels as ritonavir does, or have as many side effects or drug interactions.

Results from a small study were also presented at ICAAC in September 2009 comparing GS-9350 + Reyataz (atazanavir) to ritonavir + Reyataz in HIV-negative people. GS-9350 performed as well as ritonavir. Another small study in HIV-positive people is underway comparing GS-9350 + Reyataz + Truvada to ritonavir + Reyataz + Truvada.

Should GS-9350 continue to show good results in larger studies, it may become available as early as 2011. Since it is being studied by Gilead to boost their new integrase inhibitor elvitegravir, the company plans to roll it out as a complete regimen with elvitegravir and Truvada, known as the “quad” pill. A second booster called SPI-452 is also under early lab study boosting Prezista (darunavir) and Reyataz and shows promising results similar to those of GS-9350.

Having effective, more tolerable boosting agents can help improve a person’s adherence thereby maintaining better control of HIV. They also provide competition to ritonavir that went through a 400% price increase in 2004. They’re welcomed improvements in treating HIV disease.

Prezista monotherapy may prove effective

Simplifying HIV regimens by using one HIV drug (*monotherapy*) instead of regimens with drugs from different drug classes is seeing more progress. Fewer side effects may be the result with this simplification, as well as less cost and resistance with other drug classes. Proving that monotherapy is once again safe and effective remains difficult, especially since using only one drug to treat HIV disease has been proven much less effective due to resistance ever since the second NRTI came to market in the 80s.

However, there has been great interest in using boosted PIs as monotherapy since they are generally more potent in controlling HIV. More than a dozen monotherapy studies are ongoing or have been completed. Most of the results so far have not been promising, though they have mostly come from using Kaletra (lopinavir/ritonavir). Prezista (darunavir) and Reyataz (atazanavir) are two other PIs now under study.

Early 48-week data from the 144-week international MONET study were released in January 2010 and show relatively good results. MONET followed 256 people who had been on stable regimens for at least 24 weeks (<50 copies viral load) and had never had to change regimens due to drug failure.

Half the participants switched their regimens to boosted Prezista monotherapy while the other half switched to boosted Prezista + 2 NRTIs. Four out of 5 in the study were men and 9 in 10 were white. Average age was 44 years and the average CD4 count was 574. After 48 weeks, both arms controlled HIV below 50 copies equally. CD4 counts remained stable in both groups. Surprisingly, the monotherapy group had a similar level of side effects as those taking 3 drugs. Two of the reasons for these results could be contributed to boosted Prezista's long half-life and its ability to better control HIV than other PIs.

More studies need to be done before HIV monotherapy can be a viable option. PIs generally do not penetrate the central nervous system as well as other HIV drug classes, which may be important for controlling HIV in the brain. Also, using monotherapy as a person's first regimen is now being followed in the MONOI study, though early data differ somewhat from MONET.

Studies in other situations are also needed as people with a serious co-infection like hepatitis C seem to not do as well on HIV monotherapy. The biggest concern, drug resistance, will not be known for some time, so the effectiveness of this type of therapy needs to be confirmed in larger studies with longer-term follow-up.

Vicriviroc fails for the treatment experienced

Unfortunate news was recently released by Merck on their experimental co-receptor antagonist, vicriviroc, which might have provided another option as the second R5 drug, just behind Selzentry (maraviroc). The company will not move forward for FDA approval given the disappointing results from 2 large studies (VICTOR-E3 and -E4) in treatment-experienced people. Complete data will be released at CROI (Conference on Retroviruses and Opportunistic Infections) in February 2010.

Both studies followed people who had been on therapy before. Everyone was on effective HIV therapy (3 or more active drugs) and was then randomly assigned to take vicriviroc or placebo. A press release by the company stated that the studies did not meet their main goal, most likely not keeping HIV under control and below 50 copies over time. Vicriviroc is still being studied in those starting their first HIV regimen.

Disappointing results for a promising microbicide

In December 2009, hopes were dashed when results from a large study revealed that the microbicide PRO 2000 was ineffective at protecting women from getting HIV. Given the modest results highlighted earlier in the year from a smaller US study of the product, some believed that PRO 2000 might become the breakthrough microbicide.

The earlier US study followed nearly 3,100 women using the vaginal microbicide gel to prevent HIV. But in spite of its encouraging results (a 30% decrease in HIV infections), the “relatively” small size of the study needed more follow-up.

The more recent results come from a 4-year British study that followed 9,385 women in Africa. Half the women used PRO 2000 (resulting in 130 infections) while the other half used a placebo gel (resulting in 123 infections).

Another gel, with the HIV drug tenofovir, is also in study. Given the steady rate of new infections worldwide, there is a need to study as many prevention methods as possible, especially for women who face situations in which their partners refuse to wear condoms.

SAVE THE DATE:

Project Inform, Marking 25 Years of TLC+

Sunday, April 25, 2010, 11:00am–2:00pm

On Sunday, April 25, 2010 Project Inform will mark 25 years of leadership in the fight against HIV/AIDS with a wonderful brunch at the very hip and interesting Flora Grubb Gardens in San Francisco. We would love to have you join us as we reflect on 25 years of major achievements and anticipate our continued, effective stewardship to help end the HIV/AIDS epidemic within the next 25 years.

Flora Grubb Gardens, www.floragrubb.com
1634 Jerrold Avenue, San Francisco, CA. 94124

Individual Tickets: \$75, Five Tickets: \$500, Ten Tickets: \$1,000
Sponsorship opportunities are available starting at \$2,500

For more information regarding sponsorship opportunities or to purchase tickets, please contact Henry Lucero, Deputy Executive Director for Development at (415) 558-8669 x211 or hlucero@projectinform.org.