HIV infection: epidemiology, pathogenesis, treatment, and prevention
Gary Maartens, et al
Lancet 2014; 384: 258–71

HIV prevalence is increasing worldwide because people on antiretroviral therapy are living longer, although new infections decreased from 3·3 million in 2002, to 2·3 million in 2012. Global AIDS-related deaths peaked at 2·3 million in 2005, and decreased to 1·6 million by 2012. An estimated 9·7 million people in low-income and middle-income countries had started antiretroviral therapy by 2012. New insights into the mechanisms of latent infection and the importance of reservoirs of infection might eventually lead to a cure. The role of immune activation in the pathogenesis of non-AIDS clinical events (major causes of morbidity and mortality in people on antiretroviral therapy) is receiving increased recognition. Breakthroughs in the prevention of HIV important to public health include male medical circumcision, antiretrovirals to prevent mother-to-child transmission, antiretroviral therapy in people with HIV to prevent transmission, and antiretrovirals for pre-exposure prophylaxis. Research into other prevention interventions, notably vaccines and vaginal microbicides, is in progress.
ASPECTOS GENERALES

HCV Genotype 3 Is Associated With an Increased Risk of Cirrhosis and Hepatocellular Cancer in a National Sample of U.S. Veterans with HCV
Fasiha Kanwal, et al.

Fig. 1. Cumulative incidence of cirrhosis (A) and HCC (B) in patients with HCV genotypes 1, 2, 3 and 4. We used the log rank test to test the differences among these rates. HCC, hepatocellular cancer

Fig. 2. Prevalence of cirrhosis and HCC at the time of HCV diagnosis stratified by HCV genotypes (1-4).
Foxp3$^+$ T Cells Regulate Immunoglobulin A Selection and Facilitate Diversification of Bacterial Species Responsible for Immune Homeostasis
Shimpei Kawamoto, et al
Immunity, 2014 DOI: http://dx.doi.org/10.1016/j.immuni.2014.05.016

Enlace

Foxp3$^+$ T cells play a critical role for the maintenance of immune tolerance. Here we show that in mice, Foxp3$^+$ T cells contributed to diversification of gut microbiota, particularly of species belonging to Firmicutes. The control of indigenous bacteria by Foxp3$^+$ T cells involved regulatory functions both outside and inside germinal centers (GCs), consisting of suppression of inflammation and regulation of immunoglobulin A (IgA) selection in Peyer’s patches, respectively. Diversified and selected IgAs contributed to maintenance of diversified and balanced microbiota, which in turn facilitated the expansion of Foxp3$^+$ T cells, induction of GCs, and IgA responses in the gut through a symbiotic regulatory loop. Thus, the adaptive immune system, through cellular and molecular components that are required for immune tolerance and through the diversification as well as selection of antibody repertoire, mediates host-microbial symbiosis by controlling the richness and balance of bacterial communities required for homeostasis.
**BACTERIAS**

**Whipple’s disease: an unexpected finding in a peripheral lymph node biopsy**
Sarah Walters, et al
Lancet 2014; 383: 2268

![Figure: Whipple's disease](image)

CT at the level of the renal artery showing retroperitoneal lymphadenopathy (A). Lymph node histology showing T whipplei bacteria (B). Diastase periodic acid-Schiff PAS staining of the duodenum showing villous atrophy with lamina propria filled with PAS positive macrophages (C).

**Vancomycin, Metronidazole, or Tolevamer for Clostridium difficile Infection: Results From Two Multinational, Randomized, Controlled Trials**
Stuart Johnson, et al
Clin Infect Dis 2014 59: 345-354 ([enlace](#))

![Figure 1. Kaplan-Meier graphs of time to resolution of diarrhea (A) and time to resolution after resolution of *Clostridium difficile* infection (B)](image)

In a pooled analysis of data from 2 large, randomized, controlled trials of patients with *Clostridium difficile* infection, the toxin-binding polymer tolevamer was inferior to both metronidazole and vancomycin with regard to clinical success, and metronidazole was inferior to vancomycin.
Comparative Evaluation of the Tolerability of Cefazolin and Nafcillin for Treatment of Methicillin-Susceptible Staphylococcus aureus Infections in the Outpatient Setting

Ilan Youngster, et al
Clin Infect Dis 2014 59: 369-375 (enlace)

Nafcillin and cefazolin are commonly used to treat infections with methicillin-susceptible Staphylococcus aureus. Nafcillin treatment was associated with lower rates of treatment completion and higher rates of drug-emergent events compared with cefazolin in our outpatient parenteral antimicrobial treatment program.
VIRUS

Sexual Risk Behaviour and Viral Suppression Among HIV-Infected Adults Receiving Medical Care in the United States


Figure 1. Prevalence of vaginal or anal sex and viral suppression among adults with HIV diagnosis for at least 12 months and receiving medical care in the United States, by sexual behaviour, Medical Monitoring Project, 2009. There were no statistically significant differences between MSM, MSW and WSM in engaging in anal or vaginal sex. More MSM (30%) had unprotected sex than MSW (14%) and WSM (22%). More WSM (22%) had unprotected sex than MSW (14%). More WSM (15%) had unprotected sex with an HIV-negative or unknown stats partner than MSW (9%). aAll viral load measurements in the 12 months before interview undetectable or <200 copies/ml; bMSM, men who have sex with men; cMSW, men who have sex with women; dWSM, women who have sex with men.

Conclusion: The majority of HIV-infected adults receiving medical care in the U.S. did not engage in sexual risk behaviours that have the potential to transmit HIV, and of the 12% who did, approximately half were not virally suppressed. Persons who were virally suppressed were less likely than persons who were not suppressed to engage in sexual risk behaviours.
Lipid Levels and Changes in Body Fat Distribution in Treatment-Naive, HIV-1–Infected Adults Treated With Rilpivirine or Efavirenz for 96 Weeks in the ECHO and THRIVE Trials
Pablo Tebas, et al
Clin Infect Dis 2014 59: 425-434 (enlace)

In treatment-naive adults infected with human immunodeficiency virus type 1, once-daily rilpivirine with a background regimen was associated with fewer lipid changes and comparable body fat changes than efavirenz during 96 weeks of treatment. The background nucleoside/nucleotide reverse transcriptase inhibitor regimen affected lipid levels and body fat distribution changes.
Incomplete Reversibility of Estimated Glomerular Filtration Rate Decline Following Tenofovir Disoproxil Fumarate Exposure
Sophie Jose, et al

<table>
<thead>
<tr>
<th>Table 2. Estimated Glomerular Filtration Rate (eGFR) Slopes Before Initiation of, During, and After Discontinuation of Tenofovir Disoproxil Fumarate (TDF) Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval, Relative to TDF Exposure</td>
</tr>
<tr>
<td>Before initiation</td>
</tr>
<tr>
<td>During</td>
</tr>
<tr>
<td>≤3 mo</td>
</tr>
<tr>
<td>&gt;3 mo</td>
</tr>
<tr>
<td>After discontinuation</td>
</tr>
<tr>
<td>≤3 mo</td>
</tr>
<tr>
<td>&gt;3 mo</td>
</tr>
</tbody>
</table>

Data are mean values (95% confidence intervals) from a piecewise linear regression model.

![Figure 2. Kaplan-Meier plot showing the cumulative proportion of individuals discontinuing tenofovir disoproxil fumarate (TDF) therapy following a decline in the estimated glomerular filtration rate (eGFR) who experienced eGFR recovery following discontinuation.](image-url)
Very Low Levels of 25-Hydroxyvitamin D Are Not Associated With Immunologic Changes or Clinical Outcome in South African Patients With HIV-Associated Cryptococcal Meningitis
Joseph N. Jarvis, et al
Clin Infect Dis 2014 59: 493-500 (enlace)

Vitamin D deficiency may increase susceptibility to opportunistic infections in HIV-infected individuals. We found no evidence that vitamin D deficiency increases risk of cryptococcal meningitis or leads to impaired immune responses or microbiological clearance in HIV-infected patients with cryptococcal meningitis.

Dependence on the CCR5 Coreceptor for Viral Replication Explains the Lack of Rebound of CXCR4-Predicted HIV Variants in the Berlin Patient
Jori Symons, et al
Clin Infect Dis 2014 59: 596-600 (enlace)

The “Berlin patient” is the first patient cured of HIV-1 infection after allogeneic transplantation with nonfunctional CCR5 coreceptor stem cells. We demonstrate that CXCR4-predicted minority viruses present prior to transplant were unable to rebound after transplant due to dependence on CCR5.
Translational challenges in targeting latent HIV infection and the CNS reservoir problem
Carolina Garrido & David M. Margolis
J. Neurovirol. DOI 10.1007/s13365-014-0269-z

Abstract
Too controversial to discuss only a short time ago, achieving a cure for HIV infection has become a priority in HIV research. However, substantial challenges must be overcome. Among key hurdles to be surmounted is the definition of a reliable, validated model in which to test latency reversal agents (LRAs), as current primary cell models differ in their response to such agents. Animal models such as the HIV-infected humanized BLT mouse and SIV-infected macaque will be essential to study LRAs and to quantify their effects in anatomic reservoirs. Of several potential anatomic reservoirs, the central nervous system presents a significant obstacle, as it is known to harbor persistent HIV infection and is difficult to access for study and therapeutic intervention.

RNA-directed gene editing specifically eradicates latent and prevents new HIV-1 infection
Wenhui Hu, et al
www.pnas.org/cgi/doi/10.1073/pnas.1405186111

Significance
For more than three decades since the discovery of HIV-1, AIDS remains a major public health problem affecting greater than 35.3 million people worldwide. Current antiretroviral therapy has failed to eradicate HIV-1, partly due to the persistence of viral reservoirs. RNA-guided HIV-1 genome cleavage by the Cas9 technology has shown promising efficacy in disrupting the HIV-1 genome in latently infected cells, suppressing viral gene expression and replication, and immunizing uninfected cells against HIV-1 infection. These properties may provide a viable path toward a permanent cure for AIDS, and provide a means to vaccinate against other pathogenic viruses. Given the ease and rapidity of Cas9/guide RNA development, personalized therapies for individual patients with HIV-1 variants can be developed instantly.
Simeprevir plus sofosbuvir, with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naive patients: the COSMOS randomised study

Eric Lawitz, et al
Lancet Published Online July 28, 2014
All-oral daclatasvir plus asunaprevir for hepatitis C virus genotype 1b: a multinational, phase 3, multicohort study
Michael Manns, et al
The Lancet, Early Online Publication, 28 July 2014

Table 2: Virological responses
Early treatment may not be early enough
Kai Deng and Robert F. Siliciano
Nature, doi:10.1038/nature13647

Figure 1 | SIV eradication strategies. a, Activation of naïve CD4+ T cells renders the cells highly susceptible to infection with simian immunodeficiency virus (SIV), which becomes integrated into the host-cell genome to allow viral replication. Most CD4+ T cells die rapidly after infection, but a small fraction survives and reverts back to a resting memory state, in which SIV gene expression is turned off, resulting in a latent reservoir of the virus. Subsequent activation of these cells can restart virus production. b, Antiretroviral therapy (ART) soon after infection can stop more cells from becoming infected, but does not affect the fate of already infected cells, and some survive to seed the latent reservoir. Whitney et al. show that a viral reservoir is established within days of SIV infection. c, In vaccinated animals, SIV-specific cytotoxic T cells that are generated in response to the vaccine can kill infected cells before they revert back to the resting state, thereby preventing the establishment of a latent reservoir.
PARASITOS

Efficacy of combined antiparasitic therapy with praziquantel and albendazole for neurocysticercosis: a double-blind, randomised controlled trial

Hector H Garcia, et al

Lancet Infect Dis 2014; 14 (8): 687 – 695 (enlace)
Severe Malarial Anemia is Associated With Long-term Neurocognitive Impairment
Paul Bangirana, et al

One year after illness, children with severe malarial anemia demonstrated significantly lower scores in cognitive ability than community children. Severe malarial anemia may contribute to long-term cognitive impairment in children in sub-Saharan Africa.

Helminth therapy or elimination: epidemiological, immunological, and clinical considerations
Linda J Wammes, et al
Lancet Infect Dis 2014 Published Online June 27, 2014
http://dx.doi.org/10.1016/S1473-3099(14)70771-6

Deworming is rightly advocated to prevent helminth-induced morbidity. Nevertheless, in affluent countries, the deliberate infection of patients with worms is being explored as a possible treatment for inflammatory diseases. Several clinical trials are currently registered, for example, to assess the safety or efficacy of *Trichuris suis* ova in allergies, inflammatory bowel diseases, multiple sclerosis, rheumatoid arthritis, psoriasis, and autism, and the *Necator americanus* larvae for allergic rhinitis, asthma, coeliac disease, and multiple sclerosis. Studies in animals provide strong evidence that helminths can not only downregulate parasite-specific immune responses, but also modulate autoimmune and allergic inflammatory responses and improve metabolic homeostasis. This finding suggests that deworming could lead to the emergence of inflammatory and metabolic conditions in countries that are not prepared for these new epidemics. Further studies in endemic countries are needed to assess this risk and to enhance understanding of how helminths modulate inflammatory and metabolic pathways. Studies are similarly needed in non-endemic countries to move helminth-related interventions that show promise in animals, and in phase 1 and 2 studies in human beings, into the therapeutic development pipeline.
Figure 2: Polarity of T-cell responses to incoming pathogens and environmental factors
At mucosal surfaces, epithelial and immune cells detect changes or danger in the environment. Depending on the nature of the insult, cytokines are produced, which can drive the expansion of group 1, 2, or 3 innate lymphoid cells (ILC-1, ILC-2, and ILC-3) that in turn are associated with the induction of T-helper cells (Th1, Th2, and Th17) with distinct roles. The different T-helper cells combat invading microorganisms. However, when uncontrolled, similar T-cell responses can lead to pathological conditions (shown by broken arrows). DC = dendritic cell, IL-17 = interleukin, TGFβ = transforming growth factor beta.
20th International AIDS Conference, July 20-25, 2014, Melbourne; lo que vamos conociendo ...

TURQUOISE-I: SAFETY AND EFFICACY OF ABT-450/R/OMBITASVIR, DASABUVIR, AND RIBAVIRIN IN PATIENTS CO-INFECTED WITH HEPATITIS C AND HIV-1

Mark S. Sulkowski, et al.

3 Direct-Acting Antiviral Regimen (3D)

The multi-targeted 3D regimen includes:

- **ABT-450**, a potent NS3/4A protease inhibitor (identified by AbbVie and Enanta) co-dosed with low-dose ritonavir* (ABT-450/r) to increase the peak, trough, and overall drug exposures of ABT-450, enabling once daily dosing.

- **Ombitasvir** (ABT-267), a potent NS5A inhibitor

- **Dasabuvir** (ABT-333), a non-nucleoside NS5B RNA polymerase inhibitor

ABT-450, ritonavir, and ombitasvir are co-formulated as a single tablet.

Extensive phase 1 drug-drug interaction studies in healthy volunteers with tenofovir, emtricitabine, atazanavir, and raltegravir indicated no clinically meaningful alterations in HCV or HIV drug exposures.

*Ritonavir does not have antiviral activity against HCV.

TURQUOISE-I: Part 1 Study Design (N = 63)

Open-label Treatment  

<table>
<thead>
<tr>
<th>Open-label Treatment</th>
<th>SVR12</th>
<th>All patients will be followed for 48 weeks after HCV treatment end</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D + RBV (N = 31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3D + RBV (N = 32)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3D: coformulated ABT-450/r/ombitasvir, 150 mg/100 mg/25 mg QD; dasabuvir, 250 mg BID

RBV: 1000 or 1200 mg daily according to body weight in 2 divided doses (<75 kg and ≥75 kg, respectively)
**TURQUOISE-I Results: ITT Virologic Response Rates**

- **RVR (Week 4)**: 100, 31, 31, 32, 31, 32
- **EOTR (Week 12 or 24)**: 96.8, 31, 31, 32, 96.9, 31, 32
- **SVR4**: 93.5, 29, 31, 32
- **SVR12**: 93.5, 29

**TURQUOISE-I: Reasons for Non-Response**

Virologic failure occurred in 2 patients; both were prior null responders with HCV genotype 1a infection and had compensated cirrhosis.

- Each had resistance-associated variants in at least 2 targets at the time of virologic failure not present at baseline.

<table>
<thead>
<tr>
<th>Patient</th>
<th>HCV GT</th>
<th>IL 28B</th>
<th>Regimen</th>
<th>Duration</th>
<th>Type of Virologic Failure</th>
<th>Variants at Time of Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>T/T</td>
<td>12 wks</td>
<td>Relapse at PT Week 2</td>
<td>D168V, M28T</td>
<td>S556G</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>T/T</td>
<td>24 wks</td>
<td>Breakthrough at Week 16</td>
<td>None</td>
<td>Q30R, S556G</td>
</tr>
</tbody>
</table>

1 patient (12-week Arm) withdrew consent but had an undetectable HCV RNA at last study visit (week 10).

No patient discontinued due to adverse events.
Low Frequency of Anemia in Phase 3 Trials of ABT-450/r/ABT-267 and ABT-333 With Ribavirin in Treatment-naïve (SAPPHIRE-I) and Treatment-experienced (SAPPHIRE-II) Patients
Mark S Sulkowski, et al

SUMMARY

- Among non-cirrhotic treatment-naïve and treatment-experienced patients receiving 12 weeks of 3D + RBV, hemoglobin declines to <10 g/dl were infrequent (5.4%) and were managed by RBV dose reduction
- SVR12 rates were not affected by RBV dose modification
- Higher baseline BMI, low baseline CrCl and a lower baseline hemoglobin concentration were significantly associated with a hemoglobin decline to <10 g/dl during treatment or up to 4 weeks post-treatment
- Ribavirin administration was associated with a brisk reticulocytosis, including in the 45.2% of patients who did not develop anemia

CONCLUSIONS

- Low anemia rates observed with this RBV-containing regimen may be related to the following:
  - Absence of interferon and its bone-marrow suppressive effects on reticulocytosis, and
  - The specific drug classes included in the all oral antiviral regimen used in these placebo-controlled trials
- The risk of clinically significant hemoglobin declines may be related to baseline host factors

Prenatal Exposure to Zidovudine and Risk for Ventricular Septal Defects and Congenital Heart Defects: Data From the Antiretroviral Pregnancy Registry (APR)
V Vannappagari et al.

**Results**

<table>
<thead>
<tr>
<th>Regimen Containing ZDV</th>
<th>Overall Total Exposed Live Births</th>
<th>VSD (CHD) Cases</th>
<th>Total Exposed Live Births</th>
<th>Rate</th>
<th>Second/Third Trimester Earliest Exposure</th>
<th>Total Exposed Live Births</th>
<th>Rate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>31073</td>
<td>9</td>
<td>4010</td>
<td>0.23</td>
<td>(0.55)</td>
<td>22</td>
<td>5047</td>
<td>0.24</td>
<td>1.00</td>
</tr>
<tr>
<td>2378</td>
<td>2</td>
<td>1397</td>
<td>0.11</td>
<td>(0.83)</td>
<td>3</td>
<td>538</td>
<td>0.56</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**Conclusions**

- Prevalence of and risk for VSD and CHD among infants exposed to ZDV-containing regimens is no different from infants exposed to non-ZDV ARV regimens
- Among those exposed to ZDV-containing regimens there is no difference in rate of VSD or CHD by trimester of earliest exposure.
All-Oral Therapy with Sofosbuvir Plus Ribavirin for the Treatment of HCV Genotype 1, 2, 3 and 4 Infection in Patients Coinfected with HIV (PHOTON-2)

Jean-Michel Molina et al

Study Design

<table>
<thead>
<tr>
<th>GT 1-4 HIV-HCV (PHOTON-2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GT 2 TN SOF + RBV (n=19)</td>
</tr>
<tr>
<td>GT 2, 3 TE SOF + RBV (n=55)</td>
</tr>
<tr>
<td>GT 1, 3, 4 TN SOF + RBV (n=208)</td>
</tr>
</tbody>
</table>

- GT 1, 2, 3, 4 patients in Europe and Australia
- Broad inclusion criteria
  - Targeted 20% enrollment of patients with compensated cirrhosis, no platelet cutoff
  - Hemoglobin: >12 mg/dL (males), >11 mg/dL (females)
- Wide range of ART regimens allowed
  - Undetectable HIV RNA for > 8 weeks, on stable ART regimen
- Baseline CD4 count
  - ART treated: >200 cells/mm³
  - ART untreated: >500 cells/mm³

Demographics: ART regimens

GT 1-4 HIV-HCV (PHOTON-2)

Patients on ART (n=265)

Tenofovir DF/emtricitabine plus

- Other (n=27)
- Raltegravir (n=61)
- Darunavir (n=66)
- Tipranavir (n=12)
- Elvirez (n=65)
- Atazanavir (n=44)
Results: SVR12
GT1-4 HIV-HCV (PHOTON-2)

Results: SVR12 in GT 1
Cirrhosis vs No Cirrhosis (PHOTON-2)

Results: SVR12 in GT 2, GT 3 and GT 4
Cirrhosis vs No Cirrhosis (PHOTON-2)
Predictors of impaired neurocognitive performance during follow-up among ART-naive individuals initiating ART in ACTG clinical trials.

Smurzynski M, et al

Summary: During Longitudinal Follow-up...

- Longer duration of ART protective with respect to neurocognitive function
- Continuing CD4 recovery linked to protection
  - Prior studies: Starting ART before prolonged immunosuppression enhances CD4 recovery
  - Cross-sectionally, CD4 nadir linked to prevalent impairment
- Specific comorbidities confer increased risk of poor outcomes
  - Stroke: marker of vascular risk?
  - Vascular risk factors highly prevalent in aging HIV+ (metabolic syndrome)

Longer ART, Better CD4 Gain Protect From Neurocognitive Decline in ACTG Analysis

Kuhn L, et al

Background

- HIV antibody tests usually are considered diagnostic
- Anecdotal reports of treated HIV-infected children having negative HIV antibody tests
- Can lead to confusion in the clinical setting
- Frequency in clinical populations is unknown

Conclusions

- ~30% HIV Ab neg if ART start <3 months of age
- ~5% HIV Ab neg if ART start 4-6 months of age
- Use of standard Ab tests in early treated children can lead to confusion
- Early ART may influence ontogeny of Ab response
  — consequences for viral reservoir needs further research
- Earlier ART may have several advantages necessitating earlier infant diagnosis than is currently routine
Maraviroc (MVC) Once Daily With Darunavir/Ritonavir (DRV/r) Compared to Tenofovir/Emtricitabine (TDF/FTC) With DRV/r: 48-Week Results From MODERN (Study A4001095)

H.-J. Stellbrink, et al

**Summary and Conclusions**

- MVC 150 mg QD in 2-drug therapy regimen demonstrated statistically lower rates of viral suppression when compared to a 3-drug regimen of TDF/FTC + DRV/r in antiretroviral-naïve subjects over 48 weeks
  - IDMC recommended that the study be terminated in October 2013
- Within each arm, there was comparable efficacy by tropism assay used for screening
- The majority of PDFTs failed with HIV-1 viral load <400 copies/mL
- There was no treatment-emergent resistance in either arm
- There was comparable safety and no unexpected safety findings
- The efficacy of MVC + PI/r as stable switch therapy is under evaluation in the ongoing MARCH study
HARNESS study: ritonavir-boosted atazanavir (ATV/r)+raltegravir (RAL) switch study in virologically suppressed, HIV-1-infected patients

J. van Lunzen, et al

Figure 1. Study Design

Primary outcome – Efficacy at Week 24
- At week 24, the proportions of patients with stable HIV-1 RNA levels of <40 copies/mL (primary endpoint) were 80.6% in the experimental group and 94.6% in the reference group, by ITT analysis (Figure 2).
- At the Week 24 assessment, CD4+ cell counts had increased from baseline levels to 618 (SD 259) and 661 (SD 232) cells/mm³ in the ATV/r+RAL and ATV/r+TDF/FTC treatment groups, respectively; corresponding absolute increases from baseline in CD4+ counts were 30 and 30 cells/mm³, respectively.

Figure 2. Proportions of Patients with HIV-1 RNA levels of <40 copies/mL (primary endpoint) at Week 24

CONCLUSIONS
- In virologically suppressed patients on a triple-drug ARV regimen, switching to ATV/r+RAL was well tolerated but resulted in a higher incidence of virologic rebound than in the ATV/r+TDF/FTC group at Week 24 and Week 48.
- Overall, at week 24, 5 of the 7 patients who had experienced virologic rebound in the ATV/r+RAL arm had low-level viremia (between 40 and 500 copies/mL) and 2 of the 5 patients had subsequent undetectable HIV-1 RNA levels at week 24 after experiencing low-level viremia.
- Major INSTI drug resistance mutations occurred in one patient treated with the ATV/r+RAL regimen.
Efficacy and Safety of Dolutegravir Relative to Commonly-Used 3rd-Agents at 96 Weeks in Treatment-Naive HIV-1-Infected Patients: A Systematic Review and Network Meta-analysis

Dipen A. Patel, et al

Discussion
- Estimates derived from this meta-analysis may differ from that of any single RCT, due to statistical aggregation of data from several trials and linkage methodology.
- Results were sensitive to statistical model selection, which can be expected because a small sample of studies would result in greater uncertainty with random effects model.

Conclusion
- Indirect comparisons demonstrated sustained and favorable virologic suppression rates, CD4 increases, and lipid changes, and fewer discontinuations for DTG over many commonly used first-line treatments through 96 weeks.
Measuring Patient Views of HIV Treatments: Comparing Dolutegravir With Darunavir/r in the FLAMINGO Study

Murray M, et al

Table 1. Total Score of HIVTSQ by Week Comparing DTG With DRV/r

<table>
<thead>
<tr>
<th></th>
<th>DTG 50 mg once daily Mean N=214 (SD)</th>
<th>DRV/r 800 mg/100 mg once daily Mean N=206 (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>54.1 (6.44)</td>
<td>52.4 (7.94)</td>
<td>0.055</td>
</tr>
<tr>
<td>Week 24</td>
<td>56.1 (5.15)</td>
<td>54.3 (6.94)</td>
<td>0.003</td>
</tr>
<tr>
<td>Week 48</td>
<td>56.2 (4.60)</td>
<td>54.5 (6.78)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

LOCF = Last observation carried forward

Note: Individual item scores ranged from 6 (very satisfied) to 0 (very dissatisfied). The Treatment Satisfaction Score (range: 0-60) was the sum of the individual items.

Note: This table includes subjects from USA, France, Germany, Italy, and Spain for whom valid translations were available.

DTG vs DRV/r P values at each time point based on Wilcoxon rank sum test.

- The HIVTSQ lifestyle/ease subscore showed differences consistent with the total scores, although differences between treatment groups were significant at both Week 24 (P=0.017) and Week 48 (P=0.044).

Conclusions

- DTG 50 mg once daily in combination therapy represents a new treatment option for ART-naïve patients.
- In addition to showing improvement in treatment efficacy, DTG showed improvements in treatment satisfaction over DRV/r in the FLAMINGO study.
Week 144 Renal Safety of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir DF (STB) from Two Phase 3 Randomized Controlled Trials
C Cohen, et al

Figure 1. Study Design

Randomized, double-blind, double dummy, active-controlled study
Treatment naïve Patients with HIV-1 RNA > 5000 c/mL
(CFIR criteria: > 7500 copies/mL)

Study 102 (n=700)
- ATG Placebo QD
- ATR QDS
- STB Placebo QD

Study 193 (n=700)
- ATV + RTV + TDF QD
- ATV + RTV + TDF QD (Placebo QD)

Figure 3. Efficacy Endpoint: HIV-1 RNA <50 c/mL

<table>
<thead>
<tr>
<th>Week</th>
<th>Virologic Success (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>W0</td>
<td>89</td>
</tr>
<tr>
<td>W06</td>
<td>84</td>
</tr>
<tr>
<td>W144</td>
<td>82</td>
</tr>
</tbody>
</table>

*Virologic success (HIV-1 RNA <50 copies/mL) as defined by FDA Snapshot algorithm.

Figure 4. Change from Baseline in CD4 Cells

Figure 5. Changes in Creatinine from Baseline and from Week 4

- Changes in serum creatinine occurred mostly within the first 4 weeks, then stabilized
- COBI, like cilostazol, trihexyphenid, riboflavin, lurasidone, and dolasetron, increases serum creatinine by blocking its tubular secretion without affecting actual GFR
Conclusions

- **STB** had robust and durable efficacy through Week 144
  - Comparable to **ATR** and **ATV+RTV+TVD**
- **STB** was associated with low rates of resistance
- **STB** was well-tolerated through Week 144
- Renal discontinuation in **STB** was low and similar to **ATV+RTV+TVD**, and consistent with historical rates
  - No new cases of proximal tubulopathy occurred after Week 24
- No further increases in serum creatinine after Week 4
- Rates of proteinuria by visit generally comparable between treatment groups
- Renal safety was similar regardless of baseline eGFR
STaR Study: Single-Tablet Regimen Rilpivirine/Emtricitabine/Tenofovir DF Maintains Non-Inferiority to Efavirenz/Emtricitabine/Tenofovir DF in ART-Naïve Adults through Week 96 with a Favorable Safety Profile for Abnormal Dreams and Dizziness

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Figure 2. Virologic Outcomes by Snapshot Analysis and CD4 Change at Weeks 48 & 96

Figure 3. Virologic Suppression at Weeks 48 & 96 by Baseline HIV-1 RNA Stratified by 100,000 c/mL

Table 2. Resistance Analysis Through Week 96

*No multiplicity adjustment was done for comparisons within subgroups
STRATEGY Studies (GS-115 and GS-121): Safety Analysis of Switching to STB from a RTV-Boosted PI or NNRTI Plus TVD Regimen

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Figure 1. STRATEGY – PI and NNRTI: Study Design

Figure 2A. Primary Endpoint: HIV-1 RNA < 50 c/mL

Table 2A. Treatment-emergent Adverse Events Occurring in ≥5% of Subjects in Either Treatment Arm

No subject in either treatment arm developed treatment-emergent resistance

Table 2A.

<table>
<thead>
<tr>
<th></th>
<th>STB (n=293)</th>
<th>PI + RTV + TVD (n=814)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>11.9%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>6.2%</td>
<td>4.3%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7.2%</td>
<td>7.9%</td>
</tr>
<tr>
<td>Nausea</td>
<td>7.2%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Headache</td>
<td>6.0%</td>
<td>6.4%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>5.8%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Back pain</td>
<td>5.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Cough</td>
<td>5.1%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Depression</td>
<td>4.1%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>3.4%</td>
<td>5.0%</td>
</tr>
</tbody>
</table>

Rates of AEs described above were similar between treatment group; differences in AE rates were all less than 5% between treatment groups

- Grade 3 or 4 AEs occurred in 4% STB and 9% PI + RTV + TVD
- AEs leading to DC of study drug 2% STB and 3% PI + RTV + TVD
- AEs were consistent with known safety profile of STB

*Nauna, myalgia, headache (1 subject), major depression, suicide attempt (1), reduced visual acuity (1), Hodgkin’s disease (1), arthralgia (1), depression (1)

**Severe i disorder (1); decreased HIV-RNA (1); diarrhea (1); bronchial carcinoma with liver metastases, not related to study drug (1)
Figure 2B. Primary Endpoint: HIV-1 RNA < 50 c/mL

<table>
<thead>
<tr>
<th>Category</th>
<th>STB (n=291)</th>
<th>NNRTI + TVD (n=143)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory infection</td>
<td>0.6%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Headache</td>
<td>0.6%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>0.3%</td>
<td>6.5%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7.5%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>7.5%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Cough</td>
<td>6.5%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>6.5%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5.5%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>5.2%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

Rates of AEs described above were similar between treatment groups except for headache (p=0.03) and nausea (p=0.05) with differences in AE rates of at least 5% between treatment groups.

- Grade 3 or 4 AEs occurred in 7% STB and 6% NNRTI + TVD
- AEs leading to DC of study drug 2% STB and 1% NNRTI + TVD
- AEs were consistent with known safety profile of STB

† Dyspepsia (1); increased serum creatinine without hyperphosphatemia, glycosuria, or pruritus; associated with CMV post myocardial infarction and pericarditis (1); subdural (1); pruritus (1); acquired Fanconi syndrome (1); arthralgia, coccidiomycosis, paresthesia, muscle atrophy, hypoaesthesia (in 1 subject); ‡ Altered ment (1)
EVENTOS RECENTES

Se han publicado recientemente en JAMA las nuevas recomendaciones de la International Antiviral Society-USA Panel

Tratamiento de la infección por VIH

Prevención de la infección por VIH en centros asistenciales

SOS. Se busca o buscan...

Socio/a o grupo de socios/as para colaborar o dirigir en el futuro esta publicación de la SEICV... La actual Junta Directiva ha continuado una idea de juntas anteriores y se ha mantenido la frecuencia prevista, pero se requiere un recambio para seguir...