the GOOD
the BAD
and the CLASSY
MOVEMBER IS BACK.
STARTS EVERYWHERE NOV. 1
World AIDS Day
December 1st
### Available Antiretrovirals 2013

<table>
<thead>
<tr>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>Protease Inhibitors</th>
<th>Other Classes</th>
<th>STR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>Efavirenz</td>
<td>Atazanavir</td>
<td>Fusion inhibitors</td>
<td>Atripla</td>
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<tr>
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<td>Nevirapine</td>
<td>Darunavir</td>
<td>R5 Inhibitors</td>
<td>Eviplera</td>
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<td>Fos-Amprenavir</td>
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<td>Rilpivirine</td>
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### NRTIs
- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

### NNRTIs
- Efavirenz
- Nevirapine
- Etravirine
- Rilpivirine

### Protease Inhibitors
- Atazanavir
- Darunavir
- Fos-Amprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

### Other Classes
- **Fusion inhibitors**
  - Enfuvirtide
- **R5 Inhibitors**
  - Maraviroc
- **Integrase Inhibitors**
  - Raltegravir
  - Elvitegravir

### STR
- Atripla
- Eviplera
- Stribild
Survival  Efficacy  Tolerability
Mortality among persons 25–44 years old, USA, 1982–1995


Unintentional injury
Cancer
Heart disease
Suicide
HIV infection
Homicide
Chronic liver disease
Stroke
Diabetes

Introduction of PIs

* Preliminary 1998 data

Improved clinical outcomes: ACTG 320

Percentage of patients (%)

- AIDS/death
- Death
- AIDS/death
- Death
- AIDS/death
- Death

AZT (or d4T) + 3TC (n=579)
IDV + AZT (or d4T) + 3TC (n=577)

Adapted from Hammer SM et al. NEJM 1997;337:725–33
...a potent armamentarium

Up to 90% of treatment-naive patients can now achieve undetectable HIV-1 RNA$^{1-16}$

Large head to head study
Small head to head study

Evolution of virological failure rates at 48 weeks in recent studies

- Virological failure rates have generally decreased over time in recent studies

<table>
<thead>
<tr>
<th>Study</th>
<th>ATV/r vs LPV</th>
<th>LPV vs DRV</th>
<th>EFV vs RAL</th>
<th>EFV vs RVP</th>
<th>EFV vs RPV</th>
<th>EFV vs EVG/c</th>
<th>EFV vs DTG</th>
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</tbody>
</table>

Continuum of care
Persons living with HIV in the UK 2011

HIV and AIDS Reporting System
HIV and STI Department, Health Protection Agency - Colindale

- Total: n=96,000
- Diagnosed: n=72,950
- On treatment: n=62,400
- Undetectable VL: n=55,650

- 100%: 76%
- 90%: 84%
- 80%: 89%
- 70%: 76%
- 60%: 84%
- 50%: 89%
- 40%: 76%
- 30%: 84%
- 20%: 89%
- 10%: 76%
- 0%: 84%
Life expectancy by CD4 count compared with UK population

Life expectancy at exact age 20 years:
- 1996-2008
- UK women: 61.6 yrs
- UK men: 57.8 yrs
- HIV+ women: 50.2 yrs
- HIV+ men: 39.5 yrs

Impact on life expectancy of late diagnosis and treatment of HIV-1 infected individuals:
- Start triple ART post 2000
- CD4 200–350: 53.4 yrs
- CD4 100–199: 41.0 yrs
- CD4 <100: 37.9 yrs

Impact on life expectancy of late diagnosis and treatment of HIV-1 infected individuals:
UK CHIC M May, M Gompels, C Sabin for UK CHIC. HIV10 Glasgow abstract 1629596
Survival

Efficacy

Tolerability
Toxicity of first generation PIs

- Nausea
- Diarrhoea
- Metabolic disturbances
- Body shape changes
- Paraesthesia
- Dysgeusia
And nucleosides were associated with......
Resulting in.....
Discontinuations due to toxicity over time

Guideline recommendations for first-line treatment of naïve patients

<table>
<thead>
<tr>
<th>NRTI</th>
<th>TDF/FTC or 3TC</th>
<th>ABC/3TC</th>
<th>EFV</th>
<th>RPV*</th>
<th>ATV/r</th>
<th>DRV/r</th>
<th>RAL</th>
<th>DTG**</th>
<th>EVG/COBI</th>
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<td>DRV/r</td>
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Efavirenz
Efavirenz
EFV: Cross-study comparison of the overall incidence of neuropsychiatric adverse events

Post-approval, EFV-associated CNS toxicity has been consistently reported in both randomized clinical trials and cohort studies.
Evolution of ARV therapy
Persistent neuropsychiatric AEs lead to late discontinuation of EFV/FTC/TDF STR

The majority of cases of CNS toxicity leading to treatment modification occurred after having been established on EFV/FTC/TDF STR for more than 3 months

Time to Switch in those with CNS Toxicity
Time to suicidality, primary analysis

Hazard ratio (95% CI) 2.28 (1.27 to 4.10), $p=0.006$

As-treated HR 2.16 (1.16–4.00)

A new era in HIV treatment

Efficacy: newer treatments outperform EFV

**Newer ARVs have demonstrated higher rates of virologic suppression compared to EFV-based regimens in HIV-1 infected ART-naïve patients**

# Tolerability: Newer ARVs outperform EFV

Incidence of specific AEs of interest (%)

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparator</th>
<th>EFV Pts, n</th>
<th>Dizziness</th>
<th>Insomnia</th>
<th>Abnormal Dreams</th>
<th>Rash</th>
<th>FU Weeks</th>
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<td>EVG/COBI</td>
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<td>24</td>
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<td>27</td>
<td>12</td>
<td>48</td>
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<td>RPV</td>
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<td>22</td>
<td>14</td>
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<td>12</td>
<td>48</td>
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<td>RAL</td>
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<td>13</td>
<td>8</td>
<td>240</td>
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<td>DTG</td>
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<td>17</td>
<td>14</td>
<td>48</td>
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<td>13</td>
<td>14</td>
<td>48</td>
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</table>

Randomized, controlled trials in ART-naïve patients have shown newer ARVs to be associated with a lower incidence of neuropsychiatric symptoms and rash compared with EFV.
Drug-drug interactions

ATV/r

Jaundice

Renal stones

Diarrhoea

‡
Drug-drug interactions

LOP/r

Diarrhoea
RAL

Twice daily

Dress
Dyslipidaemia
Hepatic steatosis
Abnormalities of body composition
CVD
Bone & Kidney disease
HAND
Body image alterations
Glucose metabolism impairment
Depression
Hypertension
Vitamin D
Type 2 diabetes
Cancer
Sexual Dysfunction
## Toxicities: delayed recognition

<table>
<thead>
<tr>
<th>Drug / class</th>
<th>FDA approval</th>
<th>Toxicity</th>
<th>Strong signal</th>
<th>Delay (years)</th>
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<td>lipoatrophy</td>
<td>1999</td>
<td>12</td>
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<td>Stavudine</td>
<td>1994</td>
<td>lipoatrophy</td>
<td>1999</td>
<td>5</td>
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<tr>
<td>Nevirapine</td>
<td>1996</td>
<td>hepatitis / rash at higher CD4</td>
<td>2005</td>
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<td>1996-</td>
<td>heart attack</td>
<td>2003</td>
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<td>1998</td>
<td>suicidality</td>
<td>2013</td>
<td>15</td>
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<td>heart attack</td>
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<td>myopathy</td>
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Tolerability drives adherence, which drives efficacy
Tolerability drives adherence, which drives efficacy
Tolerability drives adherence, which drives efficacy.
Toxicity drives non-adherence, which drives failure
Toxicity drives non-adherence, which drives failure
Toxicity drives non-adherence, which drives failure.
Adherence
Efficacy
Tolerability
“Drugs don’t work if people don’t take them”

Former US Surgeon
General C. Everett Koop
• “Drugs do work if people do take them”

Mark R. Nelson
UK Surgeon General
Adherence Issues: ZDV + ddI + IDV

- Take ddl (2 tablets), no food
- Take IDV (2 pills), drink 12 oz. water, no food
- Drink 12 oz. water
- Take IDV (2 pills), drink 12 oz. water, no food
- Wake up, take IDV (2 pills), drink 12 oz. water, no food
- AM
- Midnight
- Noon
- Lunch
- Dinner + ZDV (1 pill)
- Just before bed
- Take ddl (2 tablets), no food

The Complexity of Adherence

- Dietary Restrictions
- Dosing Frequency
- Injection
- Drug/Alcohol Use
- Lifestyle
- Toxicity
- Mental States
- Adverse Events
- Aging
- Host Variables

Regimen
# Pooled adherence ART-naïve patients

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Once-daily</th>
<th>Twice-daily</th>
<th>Mean difference IV, Random, 95% CI</th>
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<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
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<tr>
<td>Total (95% CI)</td>
<td>1833</td>
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<td>1537</td>
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Heterogeneity: Tau²=5.96; Chi²=18.93, df=6 (p=0.004); I²=68%
Test for overall effect: Z=3.40 (p=0.0007)

Nachega J et al. EACS 2013. Abstr PS4/5
## Pooled virologic suppression in ART-naïve patients

**Study or subgroup** | **Once-daily** | **Twice-daily** | **Risk ratio** | **Risk ratio** |
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<td>Total</td>
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<td>Gathe 2008 [60]</td>
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<td>128</td>
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<td>443</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
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<td>1076</td>
<td>100.0%</td>
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<tr>
<td><strong>Total events</strong></td>
<td>762</td>
<td>692</td>
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Heterogeneity: $\tau^2=0.00$; $\chi^2=3.04$, df=4 ($p=0.55$); $I^2=0$

Test for overall effect: $Z=1.97$ ($p=0.05$)

Nachega J *et al.* EACS 2013. Abstr PS4/5
Single Tablet Regimens (STRs)

Current
• ATRIPLA (1550 mg)
• EVIPLERA (1150 mg)
• STRIBILD (1350 mg)

Future
• DRV-STR (1550 mg)
  – DRV/COBI/FTC/TAF
• STRIBILD 2.0 (1050 mg)
• DOLUTEGRAVIR/ABACAVIR/LAMIVUDINE

2. Mathias AA, et al. IAC 2010; Vienna. THLBPE17
Rationale for STRs

STRs can have a positive impact on treatment outcomes of interest

• Adherence\textsuperscript{1–2}
  – Improved quality of life
  – No refill misalignment
  – Simultaneous dosing of all ARVs

• Health outcomes & healthcare costs\textsuperscript{3–7}
  – Improved virologic outcomes
  – Few discontinuations
  – Remain undetectable longer, potentially reducing transmission
  – Longer duration of therapy
  – Lower risk of hospitalisation
  – Lower healthcare costs
  – Lower pharmacy costs

• Patient convenience
  – Simple\textsuperscript{1}
  – Single co-pay

LifeLink Database
Partial and complete non-adherence to ART regimens

Retrospective analysis of US healthcare claims for commercially insured population (n=4,588) receiving 2 NRTIs plus NNRTI or PI or INSTI based ART (2009–2011)

Cohen C, et al. ICAAC 2012; San Francisco, CA. #H-211

STR patients had significantly more days with a complete regimen

Cohen C, et al. ICAAC 2012; San Francisco, CA. #H-211
Patient reported outcomes STR enhances patients’ acceptability of HAART and self-reported adherence

230 patients on stable HAART completed questionnaires on their attitude towards HAART, adherence level and the acceptability of their regimen\textsuperscript{1,2}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{Patient reported acceptability of current HAART regimen\textsuperscript{1} and Self-reported non-adherence\textsuperscript{2}}
\end{figure}

Patients receiving a STR reported a higher acceptability of their regimen and better adherence compared with those receiving more complex regimens

\textsuperscript{1} Maggiolo F, et al. HIV-11 2012. Glasgow. P18;
**Study Design**

**Study 102**

Randomized, double-blind, double dummy, active-controlled study
(n=350)

- **STB QD**
  - ATR Placebo QD
  - ATR QD
  - STB Placebo QD

**Treatment Naïve**

- HIV-1 RNA ≥ 5000 c/mL
- Any CD4 cell count
- eGFR ≥ 70 mL/min

1:1* Randomization stratified by screening HIV-1 RNA (≤ vs >100,000 c/mL)

- Week 48
  - Primary Endpoint
  - HIV-1 RNA < 50 c/mL by snapshot analysis (ITT)
  - Non-inferiority margin (Wk48): 12%

- Week 144
  - Secondary Endpoint

Conducted in parallel with Study 103 comparing STB to ATV/r + TVD
Efficacy Endpoint: HIV-1 RNA <50 c/mL*
Study 102 – Primary (Week 48) and Secondary (Week 96 and 144)

Virologic Success

STB (n=348)  ATR (n=352)

W48  W96  W144  W48  W96  W144  W48  W96  W144

Virologic Non-Suppression

No data

95% CI for Difference

Favors ATR  Favors STB

W48  -1.6%  8.8%
W96  -2.9%  8.3%
W144  -1.3%  11.1%

*Virologic success (HIV-1 RNA <50 copies/mL) as defined by FDA Snapshot algorithm
## Difference in Efficacy by Subgroup

### Study 102 – Week 144

<table>
<thead>
<tr>
<th></th>
<th>Favors ATR</th>
<th>Favors STB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OVERALL</strong></td>
<td>80%</td>
<td>75%</td>
</tr>
<tr>
<td><strong>AGE (yrs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>79%</td>
<td>73%</td>
</tr>
<tr>
<td>≥40</td>
<td>82%</td>
<td>78%</td>
</tr>
<tr>
<td><strong>SEX</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>80%</td>
<td>75%</td>
</tr>
<tr>
<td>Female</td>
<td>78%</td>
<td>78%</td>
</tr>
<tr>
<td><strong>RACE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>80%</td>
<td>79%</td>
</tr>
<tr>
<td>Nonwhite</td>
<td>80%</td>
<td>68%</td>
</tr>
<tr>
<td><strong>BL HIV-1 RNA</strong></td>
<td></td>
<td></td>
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<tr>
<td>≤ 100K c/mL</td>
<td>82%</td>
<td>74%</td>
</tr>
<tr>
<td>&gt; 100K c/mL</td>
<td>77%</td>
<td>78%</td>
</tr>
<tr>
<td><strong>BL CD4</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 350 cells/μL</td>
<td>75%</td>
<td>76%</td>
</tr>
<tr>
<td>&gt; 350 cells/μL</td>
<td>84%</td>
<td>75%</td>
</tr>
<tr>
<td><strong>Adherence</strong></td>
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<td></td>
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<tr>
<td>&lt; 95%</td>
<td>66%</td>
<td>52%</td>
</tr>
<tr>
<td>≥ 95%</td>
<td>85%</td>
<td>84%</td>
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</table>

Difference in response rate and 95% CI were calculated based on the MH proportions adjusted by baseline HIV-1 RNA stratum.
Efficacy by Baseline HIV-1 RNA
Study 102 – Week 48, 96, and 144

Baseline HIV-1 RNA, copies/mL

- ≤100,000
- >100,000 – 400,000
- >400,000
# Common Adverse Events (Grade 1-4)

## Study 102 – Week 96 and 144

<table>
<thead>
<tr>
<th>Adverse Event $§$</th>
<th>STB (n=348)</th>
<th></th>
<th>ATR (n=352)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W96</td>
<td>W144</td>
<td>W96</td>
<td>W144</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>25%</td>
<td>+1%</td>
<td>24%</td>
<td>+2%</td>
</tr>
<tr>
<td>Nausea</td>
<td>22%</td>
<td>+1%</td>
<td>15%</td>
<td>+1%</td>
</tr>
<tr>
<td>Upper Respiratory Infection</td>
<td>21%</td>
<td>+4%</td>
<td>17%</td>
<td>+5%</td>
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<tr>
<td>Headache</td>
<td>16%</td>
<td>+2%</td>
<td>11%</td>
<td>+2%</td>
</tr>
<tr>
<td>Abnormal Dreams</td>
<td>15%</td>
<td>+1%</td>
<td>28%</td>
<td>+1%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>13%</td>
<td>+2%</td>
<td>15%</td>
<td>+2%</td>
</tr>
<tr>
<td>Depression</td>
<td>12%</td>
<td>+3%</td>
<td>14%</td>
<td>+3%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>11%</td>
<td>+1%</td>
<td>16%</td>
<td>+1%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>9%</td>
<td>+3%</td>
<td>11%</td>
<td>+1%</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>8%</td>
<td>+3%</td>
<td>7%</td>
<td>+3%</td>
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<tr>
<td>Nasopharyngitis</td>
<td>10%</td>
<td>+1%</td>
<td>8%</td>
<td>+1%</td>
</tr>
<tr>
<td>Cough</td>
<td>8%</td>
<td>+2%</td>
<td>6%</td>
<td>+1%</td>
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<td>Rash</td>
<td>7%</td>
<td>+2%</td>
<td>14%</td>
<td>+1%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>7%</td>
<td>+1%</td>
<td>26%</td>
<td>+0.3%</td>
</tr>
</tbody>
</table>

$§$ $\geq 10\%$ in either treatment group at Week 144
Incidence/Prevalence of Common Neuropsychiatric AEs
Study 102 – Week 144

• Incidence (bar): Patients with new onset AEs at each 4-week window
• Prevalence (line): Patients with AEs at each 4-week window

In both groups, most abnormal dreams (STB 96% vs ATR 86%) and dizziness (93% vs 87%) were Grade 1
Study Design

Study 103

Randomized, double-blind, double dummy, active-controlled, international study

(n=350)

Treatment Naïve

HIV-1 RNA ≥ 5000 c/mL
Any CD4 cell count
eGFR ≥70 mL/min

1:1*

*Randomization stratified by screening HIV-1 RNA (≤ vs >100,000 c/mL)

HIV-1 RNA < 50 c/mL by snapshot analysis (ITT)
Non-inferiority margin (Wk48): 12%

Conducted in parallel with Study 102 comparing STB to ATR

Primary Endpoint

Secondary Endpoint

Week 48

Week 144
Efficacy Endpoint: HIV-1 RNA <50 c/mL
Study 103 – Primary (Wk 48) and Secondary (Wk 96 and 144)

Virologic Success
- W48: 90%
- W96: 87%
- W144: 83%

Virologic Non-Suppression
- W48: 5%
- W96: 5%
- W144: 7%

No data
- W48: 78%
- W96: 83%
- W144: 82%

STB (n=353)
- W48: 75%
- W96: 78%
- W144: 82%

ATV+RTV+TVD (n=355)
- W48: 18%
- W96: 14%
- W144: 10%

95% CI for Difference
- W48: -2.1% - 2.7%
- W96: -4.5% - 1.1%
- W144: -3.2% - 9.4%

*Virologic success (HIV-1 RNA <50 copies/mL) as defined by FDA Snapshot algorithm
### Difference in Efficacy by Subgroup

#### Study 103 – Week 144

<table>
<thead>
<tr>
<th></th>
<th>STB (n=353)</th>
<th>ATV+RTV+TVD (n=355)</th>
<th>Favors ATV+RTV+TVD</th>
<th>Favors STB</th>
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<tbody>
<tr>
<td><strong>OVERALL</strong></td>
<td>78%</td>
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<td></td>
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<td>76%</td>
<td>69%</td>
<td></td>
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<tr>
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<td>80%</td>
<td>81%</td>
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<tr>
<td><strong>SEX</strong></td>
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<tr>
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<td>52%</td>
<td>61%</td>
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</tr>
<tr>
<td><strong>RACE</strong></td>
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<td></td>
</tr>
<tr>
<td>White</td>
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<td>75%</td>
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</tr>
<tr>
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<td>73%</td>
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<tr>
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<td>72%</td>
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<tr>
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<td>74%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 350 cells/μL</td>
<td>80%</td>
<td>75%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adherence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>60%</td>
<td>66%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 95%</td>
<td>85%</td>
<td>79%</td>
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</tbody>
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Differences in response rate and 95% CI were calculated based on the MH proportions adjusted by baseline HIV-1 RNA stratum.
Efficacy by Baseline HIV-1 RNA

Study 103 – Week 48, 96, and 144

Baseline HIV-1 RNA, copies/mL

- ≤100,000
- >100,000 – 400,000
- >400,000

ATV/r + TVD

STB
## Common Adverse Events (Grade 1-4)

**Study 103 – Week 96 and 144**

<table>
<thead>
<tr>
<th>Adverse Event*</th>
<th>STB (n=353)</th>
<th>ATV+RTV+TVD (n=355)</th>
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<td>+2%</td>
</tr>
<tr>
<td>Nausea</td>
<td>21%</td>
<td>+1%</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>20%</td>
<td>+4%</td>
</tr>
<tr>
<td>Headache</td>
<td>17%</td>
<td>+2%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>10%</td>
<td>+3%</td>
</tr>
<tr>
<td>Depression</td>
<td>10%</td>
<td>+2%</td>
</tr>
<tr>
<td>Back pain</td>
<td>12%</td>
<td>+1%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15%</td>
<td>+2%</td>
</tr>
<tr>
<td>Ocular icterus</td>
<td>0.6%</td>
<td>0</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>10%</td>
<td>+3%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>7%</td>
<td>+1%</td>
</tr>
<tr>
<td>Cough</td>
<td>8%</td>
<td>+3%</td>
</tr>
<tr>
<td>Rash</td>
<td>8%</td>
<td>0</td>
</tr>
</tbody>
</table>

* ≥ 10% in either treatment group cumulatively at Week 144
DIARREA
LA DIARREA ES MUY PELIGROSA
DELE A SU NIÑO (A)
SUERO ORAL

MINSA
PCI-NICARAGUA
USAID
Incidence/Prevalence of Common Gastrointestinal AEs
Study 103 – Week 144

**Diarrhea**

- Incidence (bar): Patients with new onset AEs at each 4-week window
- Prevalence (line): Patients with AEs at each 4-week window

Most diarrhea (STB 68% vs ATV+RTV+TVD 69%) and nausea (84% vs 86%) were Grade 1
Preclinical studies indicate that cobicistat blocks a transport pathway used for creatinine secretion from the proximal tubule.

Cobicistat Inhibits Active Tubular Secretion of Creatinine
Resulting in Increased Serum Creatinine
Renal AEs Leading to Study Drug Discontinuation
Study 102 and 103 – Week 96

<table>
<thead>
<tr>
<th></th>
<th>STB (n=701)</th>
<th>ATV/r+TVD (n=355)</th>
<th>ATR (n=352)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Discontinuation*</td>
<td>1.6% (11)</td>
<td>2.0% (7)</td>
<td>0</td>
</tr>
<tr>
<td>PRT</td>
<td>0.6% (4)</td>
<td>0.8% (3)^</td>
<td>0</td>
</tr>
<tr>
<td>Non-PRT</td>
<td>1.0% (7)</td>
<td>1.1% (4)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Data are through 18 Feb 2013 (i.e. after 96-week)

^The abstract includes a 4th subject who was later confirmed to not have PRT

Cases of proximal renal tubulopathy (PRT):

- **STB**
  - All 4 cases occurred prior to Week 24 with no new cases occurring after Week 24

- **ATV/r + TVD**
  - All 3 cases occurred after Week 48

- All 7 cases improved after study drug discontinuation
In STB group, the increase in serum Cr occurred in the first few weeks and then stabilized.
Change from Baseline in Fasting Lipids at Week 144
Study 102 – Week 144

No difference in change in TC to HDL ratio
Changes in Fasting Lipids
Study 103 – Week 144

No difference in change in TC to HDL ratio at Week 144
FAILURE IS NOT FINAL

...unless you give up.

Bonnie Pfiester

#Fitness Motivation • © 2013 Bonnie PFIESTER • PFITblog.com
## Integrase, NNRTI, NRTI Resistance Through Week 144

### Study 102 – Week 96 and 144

<table>
<thead>
<tr>
<th></th>
<th>STB (n=348)</th>
<th>ATR (n=352)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W96</td>
<td>W144</td>
</tr>
<tr>
<td><strong>Resistance Analysis Population, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17 (4.9%)</td>
<td>21 (6.0%)</td>
</tr>
<tr>
<td><strong>Emergent Resistance, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (2.9%)</td>
<td>+0 (+0%)</td>
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<tr>
<td><strong>Primary INSTI-R or NNRTI-R, n (%)</strong></td>
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<tr>
<td>E92Q</td>
<td>7</td>
<td>+0</td>
</tr>
<tr>
<td>N155H</td>
<td>3</td>
<td>+0</td>
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<tr>
<td>Q148R</td>
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<td>+0</td>
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<tr>
<td>T66I</td>
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</tr>
<tr>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td><strong>Primary NRTI-R, n (%)</strong></td>
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</tr>
<tr>
<td>M184V/I</td>
<td>10</td>
<td>+0</td>
</tr>
<tr>
<td>K65R</td>
<td>4</td>
<td>+0</td>
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# Integrase, PI, NRTI Resistance

## Study 103 – Week 96 and 144

<table>
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<th></th>
<th>STB (n=353)</th>
<th>ATV+RTV+TVD (n=355)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W96</td>
<td>W144</td>
</tr>
<tr>
<td>Resistance Analysis Population, n(%)</td>
<td>19 (5.4%)</td>
<td>21 (5.9%)</td>
</tr>
<tr>
<td>Emergent Resistance, n (%)</td>
<td>6 (1.7%)</td>
<td>+2 (+0.6%)</td>
</tr>
<tr>
<td>Primary INSTI-R or PI-R, n (%)</td>
<td>5 (1.4%)</td>
<td>+1 (+0.3%)*</td>
</tr>
<tr>
<td>T66I</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>E92Q</td>
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<td>0</td>
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<tr>
<td>T97A</td>
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<td>+1</td>
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<tr>
<td>N155H</td>
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<td>0</td>
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<tr>
<td>Q148R</td>
<td>2</td>
<td>0</td>
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</table>

<table>
<thead>
<tr>
<th>Primary NRTI-R, n (%)</th>
<th>5 (1.4%)</th>
<th>+2 (+0.6%)</th>
<th>0</th>
<th>+2 (+0.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M184V/I</td>
<td>5</td>
<td>+2</td>
<td>M184V/I</td>
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<tr>
<td>K65R</td>
<td>1</td>
<td>0</td>
<td>K65R</td>
<td>0</td>
</tr>
</tbody>
</table>

*One patient with emergent M184V/I post-Week 96 had assay failure for the IN gene.*
Cross-resistance between EVG and RAL

Figure 5. Correlation of EVG and RAL Susceptibility Among EVG/r 125 mg VF Isolates (n=28)

$R^2 = 0.66$

- G140S/C + Q148H/R/K
- G140S + Q148K mixture
- E138K + S147G + Q148R
- Other IN Mutation Patterns
- No IN Mutation Developed
Baseline (Day 1) Viral IN Mutation Pathways and Phenotypic Susceptibility to S/GSK1349572

- More advanced Q148 pathway genotypes exhibit higher fold change to S/GSK1349572

Fold Change, median (range):
- RAL: 161 (0.6 - >166)
- S/GSK1349572: 1.5 (0.6 - 35)

Mixtures:
- n=1 Q148H + G140S / Y143H
- n=1 Q148H+ E138A+G140S / Y143H

Others:
- n=1 E92Q (screen: E92Q, N155H)
- n=1 none (screen: G140G/S, Q148H/Q)
RAL + TVD Switch to STB
Study 123

Phase 3b, Open-Label, Multicenter, 48-Week Study

N=48

RAL + TVD Multi-Pill BID Regimen

Stribild Single-Tablet Regimen

• Suppressed for 6 months on first ARV regimen
• First ARV regimen RAL + TVD
• HIV-1 RNA < 50 copies/mL at screening
• No historical genotypic resistance
• eGFR > 70 mL/min

Primary Endpoint:
HIV-1 RNA <50 c/mL at Week 12 post switch

Secondary Endpoints:
Efficacy and safety of Stribild over 24 and 48 weeks
Virologic Suppression after Switching
Study 123 – Week 48

• All subjects remained virologically suppressed post-switch
• No change in CD4 in pre and post switch at Week 48
Adults and children estimated to be living with HIV | 2011

North America: 1.4 million (1.1 million – 2.0 million)
Caribbean: 230,000 (200,000 – 250,000)
Latin America: 1.4 million (1.1 million – 1.7 million)
Western & Central Europe: 900,000 (830,000 – 1.0 million)
Eastern Europe & Central Asia: 1.4 million (1.1 million – 1.8 million)
East Asia: 830,000 (590,000 – 1.2 million)
Middle East & North Africa: 300,000 (250,000 – 360,000)
Sub-Saharan Africa: 23.5 million (22.1 million – 24.8 million)
South & South-East Asia: 4.0 million (3.1 million – 5.2 million)
Oceania: 53,000 (47,000 – 60,000)

Total: 34.0 million (31.4 million – 35.9 million)
Estimated adult and child deaths from AIDS | 2011

North America
21,000
[17,000 – 28,000]

Caribbean
10,000
[8,200 – 12,000]

Latin America
54,000
[32,000 – 81,000]

Western & Central Europe
7,000
[6,100 – 7,500]

Eastern Europe & Central Asia
92,000
[63,000 – 120,000]

East Asia
59,000
[41,000 – 82,000]

Middle East & North Africa
23,000
[18,000 – 29,000]

South & South-East Asia
250,000
[190,000 – 340,000]

Sub-Saharan Africa
1.2 million
[1.1 million – 1.3 million]

Oceania
1,300
[<1,000 – 1,800]

Total: 1.7 million
[1.5 million – 1.9 million]
Estimated number of adults and children newly infected with HIV | 2011

- North America: 51,000 [19,000 - 120,000]
- Caribbean: 13,000 [9,600 - 16,000]
- Latin America: 83,000 [51,000 - 140,000]
- Western & Central Europe: 30,000 [21,000 - 40,000]
- Eastern Europe & Central Asia: 140,000 [91,000 - 210,000]
- East Asia: 89,000 [44,000 - 170,000]
- Middle East & North Africa: 37,000 [29,000 - 46,000]
- Sub-Saharan Africa: 1.8 million [1.6 million - 2.0 million]
- South & South-East Asia: 280,000 [170,000 - 460,000]
- Oceania: 2,900 [2,200 - 3,800]

Total: 2.5 million [2.2 million - 2.8 million]
Treatment for Survival

Treatment for Success

Treatment for LIFE