Novel Antiretrovirals and Salvage Therapy

Jintanat Ananworanich, MD, PhD
Deputy Director in Scientific Affairs,
The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT)
Chief, South East Asia Research Collaboration with Hawaii (SEARCH)
The Thai Red Cross AIDS Research Center
Jintanat.A@hivnat.org; jintanat.a@searchthailand.org
Outline

- Novel antiretrovirals
- Salvage therapy
- Use of novel agents in the pediatric population
- The Thai HIV Vaccine trial
Mechanisms of Action of Novel ARV Classes
HIV Entry

T-20 or enfuvirtide (Fuzeon®)

Chinen and Shearer, JACI 2002: 110 (2): 189-198
Inhibiting HIV Cell Entry by Blocking CCR5

CCR5 INHIBITORS For R5 (M tropic) HIV virus

1. Maraviroc, Vicriviroc
2. CCR5 monoclonal antibody PRO140 (investigational)

Walker. NEJM 1998
Mechanism of Integrase Inhibitors

1. Assembly of PIC on viral DNA in nucleoprotein complex
2. Processing of 3’ ends by PIC
3a. Target DNA binding
3b. Concerted target DNA cleavage and joining

Gap repair
Host DNA
Mature provirus
Nuclear membrane
Viral DNA synthesis
Nuclear entry
Novel Antiretrovirals

• New drugs in old classes
  – Etravirine (NNRTI)
  – Darunavir/r (PI)
  – Tenofovir (NRTI) – for pediatric use

• New drugs in new classes
  – Raltegravir, elvitegravir (integrase inhibitors)
  – Maraviroc (CCR5 inhibitor)

• Non ARV booster
  – GS9350 and QUAD pill
HIV-infected patients with VF on current HAART regimen, history of ≥1 NNRTI resistance mutations, ≥3 primary PI mutations, HIV-1 RNA > 5000 copies/mL

(DUET-1: N = 612; DUET-2: N = 591)

**Week 24**

- **Etravirine 200 mg BID + DRV/RTV-containing OBR**
  - (n = 599)

- **Placebo + DRV/RTV-containing OBR**
  - (n = 604)

*Investigator-selected OBR to consist of DRV/RTV (600/100 mg/mL) + ≥2 NRTIs ± enfuvirtide.

†Planned Week 24 analysis: primary endpoint HIV-1 RNA < 50 copies/mL (TLOVR).

**DUET-1 and -2: Etravirine + DRV/RTV-Containing OBR Phase III Trials**


DUET-1 and -2: Pooled Virologic and Immunologic Responses

<table>
<thead>
<tr>
<th>Outcome at Week 24</th>
<th>Etravirine (n = 599)</th>
<th>Placebo (n = 604)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 RNA &lt; 50 copies/mL, %</td>
<td>59</td>
<td>41</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Mean change in HIV-1 RNA from baseline, log&lt;sub&gt;10&lt;/sub&gt; copies/mL</td>
<td>-2.4</td>
<td>-1.7</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Mean change in CD4+ cell count from baseline, cells/mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>+86</td>
<td>+67</td>
<td>&lt; .0001</td>
</tr>
</tbody>
</table>


DUET-1 and -2: Predictors of ETR Response and Resistance at Failure

- 17 ETR resistance associated mutations, now weighted based on impact on response
  - 3.0: Y181I/V
  - 2.5: L100I, K101P, Y181C, M230L
  - 1.5: V106I, V179F, E138A, G190S
  - 1.0: V90I, A98G, K101E/H, V179D/T, G190A
- K103N does not affect ETR resistance

TITAN: DRV/RTV vs LPV/RTV in Tx-Experienced, LPV-Naive Patients

Stratification by treatment site, use of NNRTI in OBR, and HIV-1 RNA > or < 50,000 copies/mL

Treatment-experienced, LPV-and DRV-naive patients with HIV-1 RNA > 1000 copies/mL  
(N = 595)

Week 48  
Prespecified primary analysis

Week 96

- DRV/RTV 600/100 mg BID + OBR  
  (n = 298)

- LPV/RTV* 400/100 mg† BID + OBR  
  (n = 297)

*Patients started on LPV/RTV 133/33-mg capsules and then some (18%) were switched to 200/50-mg tablets.  
†LPV/RTV increased to 533/133 mg BID (for capsules) or 600/150 mg BID (for tablets) if NNRTI included in OBR.

www.clinicaloptions.com
TITAN: Week 48 Outcomes, Overall and by BL LPV Fold Change


*DRV/RTV-LPV/RTV; estimated from logistic regression model including treatment and stratification factors: baseline log_{10} HIV-1 RNA and use of NNRTIs in the OBR.

†P values for superiority

95% CI* = 11 (3 to 19)  
P value† = .005

10 (2 to 18)  .013

7 (-1 to 16)  .068

HIV-1 RNA < 50 copies/mL, %

Overall (n = 595)  
LPV FC ≤ 40 (n = 569)  
LPV FC ≤ 10 (n = 524)
Potential Uses of Integrase Inhibitors: Multiple Failures

**Advantages**
- Novel mechanism of action
- Well-established data
- Excellent safety and tolerability
- Limited lipid effects
- Limited drug interactions

**Disadvantages**
- Must be used with other active agents
- Does a boosted PI always need to be included?
- Low barrier to resistance
- Cross resistance between RAL and ELV

Patterns associated with high-level resistance to both RAL and ELV:
- G140S/Q148H
- G140S/Q148R
BENCHMARK 1 & 2:
OBR + RAL vs. OBR + Placebo
HIV-1 RNA < 50 c/mL at Week 48 (NC = F)

BENCHMRK-1 & -2: HIV-1 RNA < 50 c/mL at Week 48, Overall and by GSS


<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n</th>
<th>RAL</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>443</td>
<td>228</td>
<td>34</td>
</tr>
<tr>
<td>GSS:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>112</td>
<td>65</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>166</td>
<td>92</td>
<td>37</td>
</tr>
<tr>
<td>2</td>
<td>109</td>
<td>47</td>
<td>62</td>
</tr>
<tr>
<td>≥3</td>
<td>49</td>
<td>21</td>
<td>71</td>
</tr>
</tbody>
</table>

**Patients (%):**
- Total: RAL 64, Placebo 34
- GSS: 0: RAL 67, Placebo 3
- GSS: 1: RAL 77, Placebo 37
- GSS: 2: RAL 62, Placebo 45
- GSS: ≥3: RAL 71, Placebo 52
BENCHMARK 1 & 2: HIV-1 RNA < 50 c/mL by New Agents in OBR, Wk 48

68% of patients who failed (64/94) had RAL resistance
Prevalence of Coreceptor Tropism Using First-Generation Assay

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demarest et al[1]</td>
<td>325</td>
<td></td>
</tr>
<tr>
<td>HOMER[2]</td>
<td>979</td>
<td></td>
</tr>
<tr>
<td>Moyle et al*[3]</td>
<td>402</td>
<td></td>
</tr>
<tr>
<td>Study 1026[4]</td>
<td>1428</td>
<td></td>
</tr>
<tr>
<td>Demarest et al[1]</td>
<td>117</td>
<td></td>
</tr>
<tr>
<td>Moyle et al*[3]</td>
<td>161</td>
<td></td>
</tr>
<tr>
<td>SCOPE[5]</td>
<td>186</td>
<td></td>
</tr>
<tr>
<td>Melby et al[6]</td>
<td>724</td>
<td></td>
</tr>
<tr>
<td>Wilkin et al[7]</td>
<td>391</td>
<td></td>
</tr>
<tr>
<td>MOTIVATE 1 &amp; 2[4]</td>
<td>2560</td>
<td></td>
</tr>
</tbody>
</table>

R5 only  | D/M   | X4 only
---------|-------|---------
325      |       |         |
979      |       |         |
402      |       |         |
1428     |       |         |
117      |       |         |
161      |       |         |
186      |       |         |
724      |       |         |
391      |       |         |
2560     |       |         |

*Tx Experienced

*X4 data NA.

MOTIVATE 1: Maraviroc in Treatment-Experienced Patients With R5 Virus

- Randomized, double-blind, placebo-controlled, phase IIb/III studies

- 2:2:1 randomization; stratified by ENF use and HIV-1 RNA < or ≥ 100,000 c/mL

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Dosage</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVC 150 mg or 300 mg + OBR*</td>
<td>(n = 235)</td>
<td></td>
</tr>
<tr>
<td>MVC 150 mg or 300 mg QD + OBR*</td>
<td>(n = 232)</td>
<td></td>
</tr>
<tr>
<td>Placebo + OBR</td>
<td>(n = 118)</td>
<td></td>
</tr>
</tbody>
</table>

Patients receiving PI (except TPV) or delavirdine received 150 mg; all others received 300 mg.

Week 24 planned endpoint analysis

Week 48

48-week results of MOTIVATE-2 to be presented at EACS
MOTIVATE 1: Virologic and Immunologic Outcomes at Week 48

HIV-1 RNA < 50 copies/mL

- Placebo + OBR (n = 118)
- MVC QD + OBR (n = 232)
- MVC BID + OBR (n = 235)

Mean Change From BL (cells/mm³)

- Placebo + OBR: +54
- MVC QD + OBR: +113*
- MVC BID + OBR: +122*

GS9350

- Boost elvitegravir and PI
- No anti HIV effect; therefore, no risk of resistance
- Potent CYP3A inhibitor
- Less induction of drug metabolizing enzymes and transporters

QUAD pill
- TDF/FTC/Elvitegravir/GS9350
- One pill once daily
- Being studied as first line therapy in adults and adolescents
Salvage Regimen
Drug Resistance Mutations Development

HIV Infection

Homogeneous NSI

Virus turn over $10^{10}$ per day

Mutation rate $10^{-4}$ to $10^{-3}$ bp

Selective Pressures

More Drug resistant

ARV drugs

Acute Early Intermediate Late Stage

More homogeneity More heterogeneity

Selective Pressures

ARV drugs

More Drug resistant

Virus turn over $10^{10}$ per day

Mutation rate $10^{-4}$ to $10^{-3}$ bp

More homogeneity

More heterogeneity
Time after virologic failure

- d4T or AZT /3TC/NVP failure

We will lose more ARV options over time!!!

**NNRTI-R only** + **3TC-R** + **< 4TAMs** + **≥ 4TAMs other MDRs**

- NVP
- EFV

- 3TC
- FTC

- AZT
- d4T

- Other NRTIs

- bPIs

- Other MDRs

- ddl
- d4T
- ABC
- TDF

- New drugs

Modified from the slide collection of Prof. Kiat Ruxrungtham
HIV-NAT 086: Frequent multi NRTI and NNRTI resistance in Thai children failing first line d4T or AZT+ 3TC + NVP or EFV (n=120)

Puthanakit T, CROI 2009, Abstract 878 (MS submitted to JAIDS)
Sequencing Regimens after Triple Class Failure

<table>
<thead>
<tr>
<th>Failure</th>
<th>Options</th>
<th>ARVs</th>
</tr>
</thead>
<tbody>
<tr>
<td>d4T/AZT</td>
<td>NRTI</td>
<td>TDF recycling NRTI</td>
</tr>
<tr>
<td>3TC</td>
<td>NNRTI</td>
<td>Etravirine</td>
</tr>
<tr>
<td>NVP, EFV</td>
<td>PI/r Integrase inhibitor</td>
<td>Darunavir/r</td>
</tr>
<tr>
<td>LPV/r</td>
<td>CCR5 inhibitor</td>
<td>Raltegravir</td>
</tr>
<tr>
<td></td>
<td>Antigp41</td>
<td>Maraviroc</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enfuvirtide (T20)</td>
</tr>
</tbody>
</table>
New Regimen should have at least two but ideally 3 active agents

Goal of undetectable HIV-1 RNA is achievable in most patients with available new agents from existing classes combined with agents from novel classes

Focus on Number of Active Agents

- Highest rate of virologic suppression in patients receiving investigational drug plus OBR containing ≥ 1 other active agent
- Trend toward greater benefit with 3 vs 2 fully active agents
- No added benefit from using 4 vs 3 fully active agents
- Must also consider potential drug-drug interactions, adverse events, pill burden, absence of future options

Sequencing of ARV

First Line
AZT or d4T + 3TC + NVP or EFV

Second Line
TDF + 3TC ± AZT + LPV/r

Third Line
1. Recycle NRTIs + DRV/r
2. RAL + DRV/r + ETR ± NRTI
3. RAL + DRV/r + ETR ± NRTI + MVC (if R5)

Early failure (M184V, few NNRTI mutations, no K65R, no multi NRTI resistance, few TAMs)
- 2 fully active drugs (TDF, LPV/r) + partially active AZT
- 1. 1 fully active drug (DRV/r) + ≥ 2 partially active
- 2. 2 fully active (RAL, DRV/r) + ≥ 2 partially active
- 3. 3 fully active (RAL, MVC, DRV/r) + ≥ 2 partially active

T20 could be added to third line regimens

Routine VL monitoring with capture of early treatment failures
Sequencing of ARV

Targeted VL monitoring or no routine VL monitoring

**First Line**
AZT or d4T + 3TC + NVP or EFV

**Second Line**
TDF + 3TC ± AZT + LPV/r

**Third Line?**
1. Recycle NRTIs + DRV/r
2. RAL + DRV/r + ETR ± NRTI
3. RAL + DRV/r + ETR ± NRTI + MVC (if R5)

T20 could be added to third line regimens

Late failure with multi NRTI/NNRTI resistance, possibly K65R

1. No fully active drugs + ≥ 1 partially active (DRV/r, NRTI)
2. 1 fully active (RAL) + ≥ 2 partially active
3. 2 fully active (RAL, MVC) + ≥ 2 partially active
Sequencing of ARV

New strategies being studied

First Line
AZT or d4T + 3TC + NVP or EFV

Second Line
RAL + LPV/r

Third Line
DRV/r + ETR + NRTI
± T20 ± MVC (if R5)

Early or late failure
2 fully active drugs

Number of active drugs in third line depends on early vs. late failure in first/second line

High chance of VL suppression for second line therapy regardless of resistance in first line therapy but limited third line choices especially with late failures
Use of Novel Agents in Pediatric Patients
<table>
<thead>
<tr>
<th>ARV</th>
<th>US FDA-approved drugs with pediatric labels by age</th>
<th>Commercially-available pediatric-appropriate formulation</th>
<th>Availability of the pediatric formulation as a WHO-prequalified generic ARV</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- LPV/r</td>
<td>Yes, ≥ 2 wks</td>
<td>Yes: liquid, tablet</td>
<td>No</td>
</tr>
<tr>
<td>- ATV</td>
<td>Yes, ≥ 6 yrs for ritonavir-boosted</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>- FPV</td>
<td>Yes, ≥ 2 years for ritonavir-boosted; &gt; 6 years for unboosted</td>
<td>Yes: liquid</td>
<td>No</td>
</tr>
<tr>
<td>- RTV</td>
<td>Yes, &gt; 1 mo</td>
<td>Yes: liquid, capsule</td>
<td>No</td>
</tr>
<tr>
<td>- IND</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>- SQV</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>- NFV</td>
<td>Yes, ≥ 2 yrs</td>
<td>Yes: powder, tablet</td>
<td>No</td>
</tr>
<tr>
<td>- DRV</td>
<td>Yes, ≥ 6 yrs and ≥ 20 kg</td>
<td>Yes: tablet</td>
<td>No</td>
</tr>
<tr>
<td>- TPV</td>
<td>Yes, &gt; 2 yrs</td>
<td>Yes: liquid</td>
<td>No</td>
</tr>
<tr>
<td>Entry inhibitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- T20</td>
<td>Yes, ≥ 6 yrs</td>
<td>Yes: injection</td>
<td>No</td>
</tr>
<tr>
<td>Integrase inhibitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- RAL</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>CCR5 inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- MVC</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
**Tenofovir**

- Not yet approved for age < 18 years

- Pediatric European (PENTA) guidelines recommend TDF for Tanner Stage IV or post-pubertal children only

- Potential toxicities in children
  - Renal tubular diseases
    - 2.2 serious events per 100 child years
  - Bone demineralization
    - Some may not be reversible

TDF trials in children

- Investigational dose in children
  - 2-8 years: 8 mg/kg once daily
  - >8 years: 210 mg/m² once daily
  - Maximum 300mg once daily

- Overdosing/underdosing of TDF was common because of one dosing formulation of 300mg tear drop tablet (Riodan A, PIDJ 2009)

- Results from two phase III randomized studies of TDF are expected in 2010 (sprinkle tasteless formulation)
  - 100 treatment-experienced children ages 12-17 years randomized to optimized background regimen with or without TDF (www.clinicaltrials.gov NCT00352053)
  - 100 virally-suppressed 2-12 year old children randomized to staying on d4T or AZT vs. switching to TDF (www.clinicaltrials.gov NCT00528957)
Etravirine

- Not yet approved in children

- Investigational dose of 5.2 mg/kg/dose twice daily (max 200mg twice daily) showed good PK (Konigs C, CROI 2009, Abs 879)

- Ongoing 48-week phase II trial (PIANO) of 100 treatment-experienced children ages 6 to 17 years of etravirine plus optimized background regimen ([www.Clinicaltrials.gov](http://www.Clinicaltrials.gov) NCT00665847)

- Can request for compassionate use from Tibotec or send to sites to enroll in PIANO
Darunavir/r (DRV/r)

- Approved for use in children ≥ 6 years old
  - Have waiver from FDA to study children < 3 yrs because of seizure/death in young animals
- Dose (75, 150, 300, 600mg tablets)
  - 375/50 mg for 20 to < 30 kg
  - 450/60 mg for 30 to < 40 kg
  - 600/100 mg for ≥ 40 kg
- If RTV liquid is not available, may need to use with 100mg RTV capsule
- The DELPHI study
  - 80 triple class failing children ages 6-17 years old were treated with DRV/r plus optimized background regimen
  - At 24 weeks, 64% with VL < 400 and 50% with VL < 50 and 117 CD4 cell increase (Bologna R, CROI 2008, Abs 78LB)
  - 48 week data will be available in mid 2010 (www.Clinicaltrials.gov NCT00355524)
- Can request compassionate use from Tibotec
Raltegravir

- IMPAACT P1066
  - 5 groups of children, 20 per group
    - 12-18 yrs on adult dose (400mg BID)
    - 6-11 yrs on adult tab
    - 6-11 yrs on chewable tab
    - 2-5 yrs on chewable tab
    - 6mo-2 yrs on granules
    - 4wks-6 mo on granules

- So far the 6-11 yrs + 12-18 yrs groups, 80% had VL < 400 at wk 12.

- Neonate study
  - PK safety in HIV-exposed neonates
  - RAL + standard PMTCT until HIV excluded, PK and 6-month follow up for safety

Wiznia A, CROI 2009 [Abs 874]
A child with triple class failure

- A 13 year-old boy referred to HIV-NAT for treatment failure
- Body weight is 24 kg and his height is 134 cm
- CDC B (pulmonary TB treated with rifampicin-based regimen while on IDV+RTV)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Start-stop date</th>
<th>Reason to stop</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. GPOvir</td>
<td>Uk/uk/2003 - uk/uk/2004</td>
<td></td>
</tr>
<tr>
<td>2. GPOvir</td>
<td>12/07/2005 - 20/07/2005</td>
<td></td>
</tr>
<tr>
<td>3. 3TC+d4T+EFV</td>
<td>20/07/2005 - 5/10/2005</td>
<td></td>
</tr>
<tr>
<td>4. 3TC+IDV+RTV</td>
<td>Uk/01/2006 - 14/07/2009</td>
<td>Virological failure</td>
</tr>
<tr>
<td>5. 3TC</td>
<td>14/07/2009 - present</td>
<td></td>
</tr>
</tbody>
</table>
Interpretation of resistance testing
1. Multi NRTI resistance except TDF (Q151M)
2. 3TC resistance (M184V)
3. Resistance to NVP and EFV (Y181C, G190A)
   and partial resistance to etravirine (≥4 weight score)
4. Partial resistance to all PIs especially IDV/r and LPV/r
   (major PI mutations: V82A, M46I and multiple minor mutations)

<table>
<thead>
<tr>
<th>HIV RNA (copies/ml)</th>
<th>Date 3/04/2007</th>
<th>Date 02/10/2007</th>
<th>Date 6/05/2008</th>
<th>Date 03/03/2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 (cells/ml)</td>
<td>672</td>
<td>715</td>
<td>718</td>
<td>717</td>
</tr>
</tbody>
</table>

His genotypic resistant codons from June 2009 indicate as follows;
NRTI mutation: F116Y, Q151M, M184V
NNRTI mutation: Y181C, G190A
L63P, H69K, A71V, V82A, L89M, I93L
What is the next best regimen?

<table>
<thead>
<tr>
<th>First Line</th>
<th>Second Line</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT or d4T + 3TC + NVP or EFV</td>
<td>TDF + 3TC ± AZT + LPV/r</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Third Line?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Recycle NRTIs + DRV/r</td>
</tr>
</tbody>
</table>

| 2. RAL + DRV/r + ETR ± NRTI |
| 3. RAL + DRV/r + ETR ± NRTI + MVC (if R5) |

Late failure with multi NRTI/NNRTI resistance, possibly K65R

1. No fully active drugs + ≥ 1 partially active (DRV/r, NRTI)
2. 1 fully active (RAL) + ≥ 2 partially active
3. 2 fully active (RAL, MVC) + ≥ 2 partially active

Compared to adults, limited options for pediatric cases
For this pediatric case: TDF, 3TC, ETR, DRV/r
[1 fully active (TDF) + 3 partially active]
HIV trial provides hope
Vaccine effective in a third of volunteers

A breakthrough in the world's largest and long-running HIV vaccine trial has given new hope in the battle against HIV/AIDS.

Thailand wins praise for AIDS vaccine trial

For First Time, AIDS Vaccine Shows Some Success
1990s to 2003
Phase III Antibody-based trials
Recombinant gp120 (AIDSVAX)
in US MSM
and in Thai IDUs (n~2500 to 5000)

2004 to 2007
Phase IIB T cell-based trials
Merck gag/pol/nef, Ad5
STEP and Phambili (N~3000)

2003-2009
Phase III Antibody- and T-cell based trials
RV144 in Thailand
ALVAC/AIDSVAX prime boost
(n~16000)

No difference in HIV incidence in the vaccine vs. placebo arm

Higher HIV incidence in vaccinees with pre-existing Ad5 antibody and/or uncircumcised

Reduction in HIV incidence by 31% in the vaccine arm but no reduction in HIV viral load in those infected with HIV
RV144: Prime Boost Strategy

Prime (T-cell based):
ALVAC (canary pox vector) for subtype B gag/pol; subtype E env

Boost (Antibody-based):
AIDSVAX B/E gp120 (subtype B and E env)

Detailed results will be presented at the AIDS Vaccine meeting in Paris (Oct 2009)
www.hivresearch.org/phase3/phase3pressrelease.html
Summary

- Novel ARVs include new NNRTI (etravirine), new PI (darunavir), integrase inhibitors (raltegravir, elvitegravir), CCR5 inhibitor (maraviroc) and anti-gp41 (enfuvirtide)
- Salvage regimen should include at least 2 but preferably 3 active drugs
- Darunavir/r appears to be more effective than LPV/r in triple class failing patients
- Etravirine and raltegravir are effective when used with boosted PI
- Maraviroc is only effective in patients with R5 virus (approximately 50% of failing patients)
- Early detection of virological failure can preserve future ARV options