ART Guidelines Session - ASHM 2015

What to Start: A look from the Australian perspective

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Disclosures

Benefit to institution:
• Bristol-Myers Squibb - clinical trial PI
• Gilead - clinical trial PI, advisory board, grants
• Merck - clinical trial PI
• Viiv Healthcare - clinical trial PI, advisory board

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DHHS Category Changes

• Recommended, Alternative, Not recommended

• New Category → ‘Other’
  - Comparing with Recommended and Alternative may have:
    • Decreased efficacy or supporting data,
    • Increased toxicity, pill burden or potential drug interactions

• ‘Alternative’ or ‘other’ regimen may be preferred for some patients
  - Table 7 (F-6 to F-8) or arv.ashm.org.au
    • Details different clinical scenarios or patient preferences and their impact on regimen choice

EFV vs IDV^1  EFV vs LPV/rr^2

Intention to Treat at 48 weeks
EFV 70%
IDV 48%

On Treatment at 96 weeks
EFV 89%
LPV/rr 77%

Time to regimen failure (EFV vs LPV/rr)
HR 0.75 (95% CI 0.57 - 0.98)

1 NEJM 1999 341:1865-1873
2 NEJM 2008 358:2095-2106

NRTI backbone 3rd drug DHHS April 2015 DHHS May 2014


Notes
* Only if pre-ART HIV RNA <100,000 c/ml
# Only if pre-ART < 100,000 c/ml and CD4 > 200
EFV vs NVP  
Lancet 2004; 363:1253-1263

ITT - Difference between NVP BD and EFV daily 5.9% (95% CI 0.9 – 12.8)  
2 deaths attributed to NVP  
Equivalence if 95% CI of the difference was within 10% of zero  
"...we could not show equivalence"  
But conclude ‘similar efficacy and recommended for first line treatment’ (in 2004)

On treatment outcomes in figure

EFV vs ATV/ r Ann Intern Med 2011; 154:445-456 (ACTG 5202)

1st virological efficacy similar for ATV/r and EFV, not differing by NRTI backbone  
Hazard ratios for time to virologic failure (EFV as reference):  
1.13 for ABC/3TC (95% CI 0.82-1.56) and 1.01 for TDF/FTC (95% CI 0.70-1.46)

EFV vs RPV  
JAIDS 2012; 60:33-42  
(Combined ECHO and THRIVE)

Intention to treat at 48 weeks  
EFV 82% (561/682)  
RPV 84% (578/686)  
Difference of 2.0% (95% CI 2.0-6.0%)

Baseline HIV RNA  
< 100,000 c/mL  
> 100,000 c/mL  
Rilpivirine (n=368)  
Efavirenz (n=330)  
Rilpivirine (n=318)  
Efavirenz (n=352)  
Virological Failure  
15 (4%)  
10 (3%)  
47 (15%)  
22 (6%)  
Discontinuation  
22 (6%)  
43 (13%)  
26 (8%)  
46 (13%)

Treatment-related AEs ≥ Grade 2  
Rilpivirine (n=686)  
Efavirenz (n=682)  
Rash  
7 (1%)  
56 (8%)  
Dizziness  
4 (1%)  
43 (6%)  
Abnormal dreams/nightmares  
9 (1%)  
25 (4%)  
Headache  
11 (2%)  
15 (2%)  
Insomnia  
12 (2%)  
16 (2%)  

EFV adverse events  
Lancet 2012; 379:2439-2448  

EFV and Suicidality

- Meta-analysis of 4 randomised ACTG studies comparing EFV-containing to EFV-free regimens
- Suicidal ideation or attempted or completed suicide in EFV regimens had HR 2.28 [95% CI 1.27-4.10]; p=.006  
- Attempted or completed suicide HR was 2.58 [CI 0.94 to 7.06]; p=.065  
- 32% participants had a psychiatric history

1 Ann Intern Med 2014 Aug 19;161(4):308
EFV and Suicidality

- Observational studies don’t show same increased risk\(^1\)\(^-\)\(^2\)\.
  - D:A:D, 675 of 4420 deaths had suicide or psychiatric condition reported as the underlying or associated cause of death.
  - FDA adverse event reporting system, 457 reports of ideation, attempt and completed suicide on ART.
- No association with EFV use.
- May reflect appropriate prescribing to people at risk of suicide.

1. JIAS 2014; 17(Suppl 3):19512. 2. JIAS 2014; 17:19214.

Protease Inhibitors

- TDF/FTC + ritonavir boosted DRV is the only non-InSTI based regimen recommended for initial therapy in this update.
- DRV not currently reimbursed for initial therapy in Australia.

ACTG 5257 - VF and combined VF and Tolerability endpoint

- Decreased number of DHHS recommended regimens (EFV, RPV, ATV/r left recommended category).
- Not always in line with PBS.
- ‘Alternative’ or ‘other’ regimen may be preferred for some patients.
  - Different clinical scenarios, patient preferences.