# Switching from ABC/3TC + Efavirenz [EFV] to TDF/FTC/EFV [Atripla, ATR] Reduces Cholesterol in Hypercholesterolemic Subjects: 24-Week Final Results of a Randomised Study

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# 17 UK Sites


Newcastle

Belfast

North Manchester

Leicester

Gloucester

Edinburgh

Bolton

Heartlands

Whittle street

Brighton

Royal Free

Central Middlesex

North Middlesex

Homerton


Barts

C & W

St. Georges

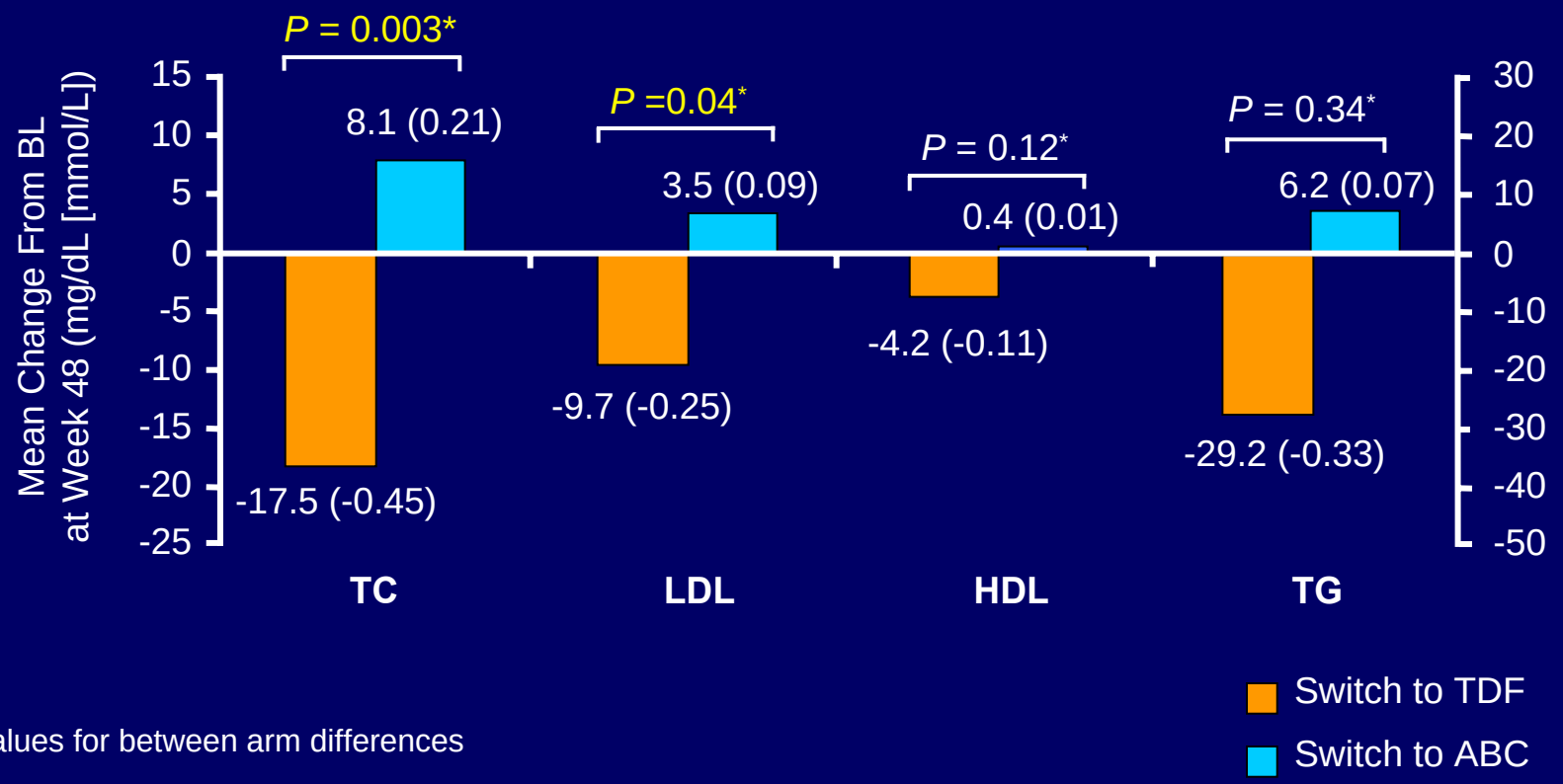
# Background

- **Dyslipidaemia in HIV contributes to CV risk[1]**
- **Higher Triglyceride levels are independently associated with an increased risk of MI in HIV-infected people[2]**
- **Initial therapy[3] and switch[4] studies suggest tenofovir DF-based regimens have less of an impact on lipids relative to abacavir-based regimens**
- **We studied the change in fasting total cholesterol (TC) in hypercholesterolaemic subjects switching from ABC/3TC + EFV to a single tablet regimen (STR) of TDF/FTC/EFV (ATR)**


1. Grover, SA, et al., Am J Cardiol 2005; 95 (5): 586-591
2. Worm, S, et al., CROI 2010, Paper # 127
3. McComsey, G, et al., CROI 2010, Paper # 106LB
4. Moyle, G et al., AIDS 2006; 20 (16): 2043-2050

# RAVE Study
# Lipid Effects of Switching Thymidine Analogues to ABC or TDF

- **Switch to TDF associated with improved lipid parameters**

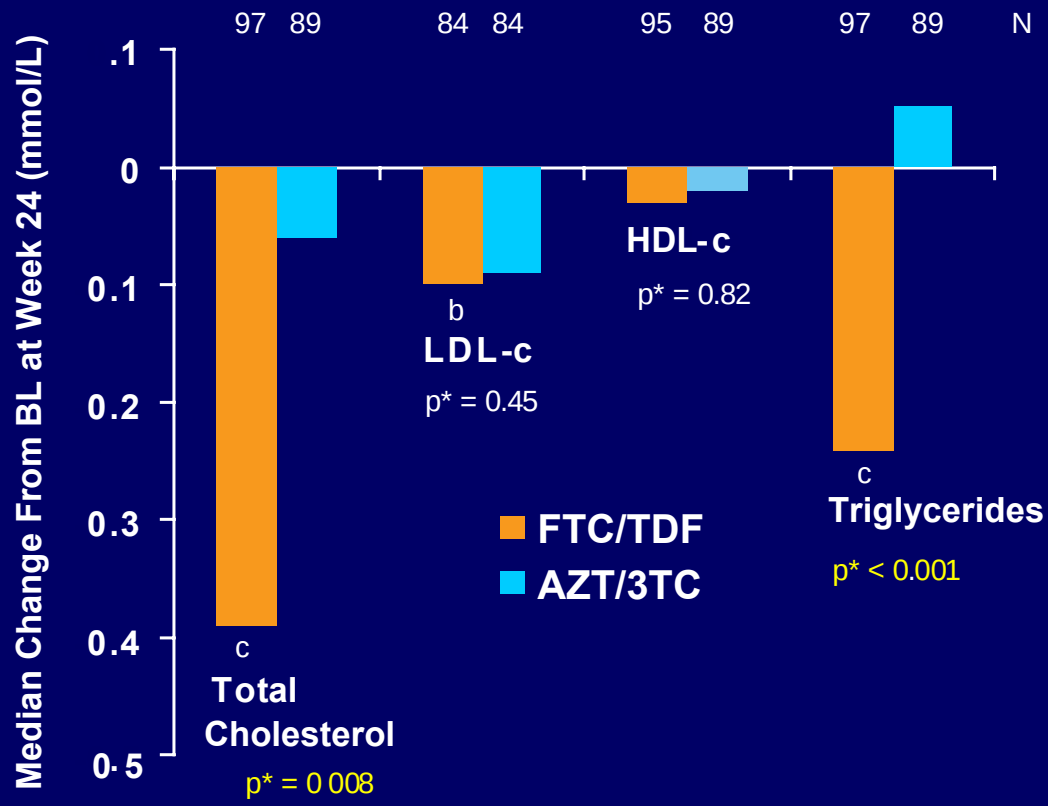



* *P* values for between arm differences

Moyle GJ, et al. AIDS. 2006;20:2043-2050.

# SWEET study
## Lipid Effects of Switching AZT to TDF

- **Switch to TDF associated with improved lipid parameters**

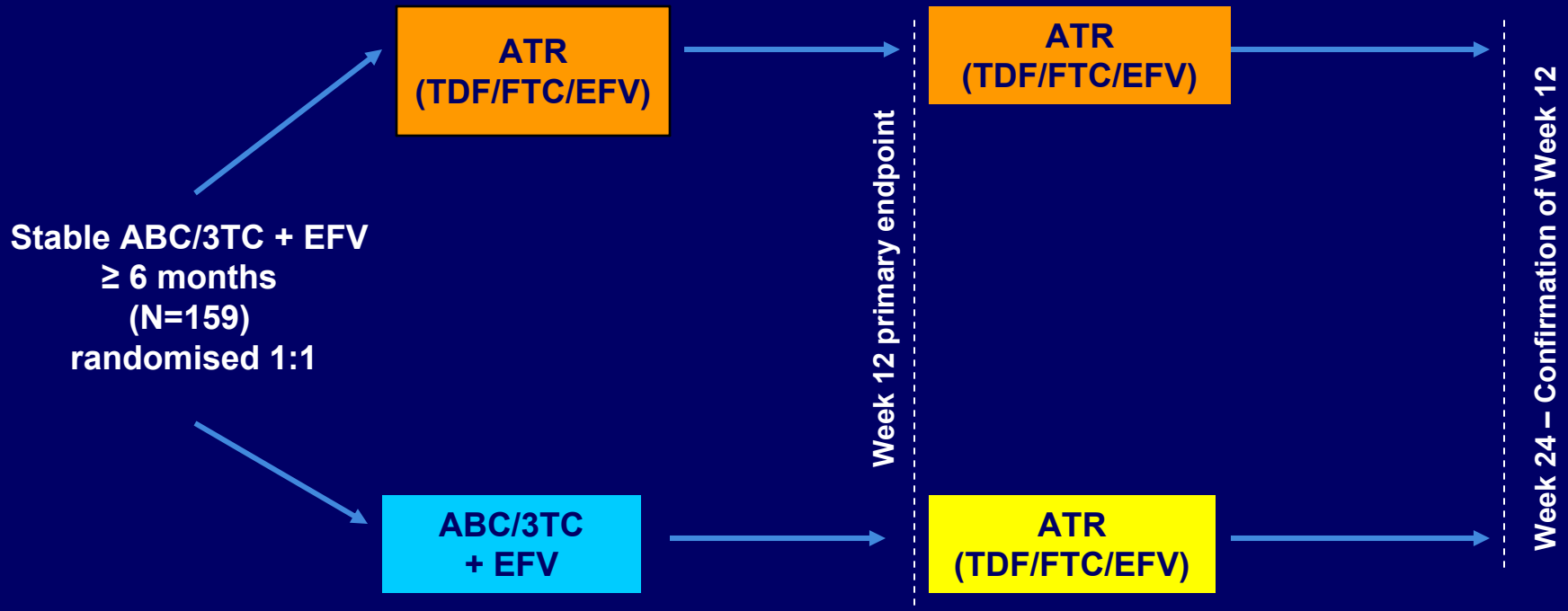



*** TVD vs CBV comparison**
**p-value from Wilcoxon Rank Sum test**

a. Treated Analysis Set, Fasted
b. $p < 0.02$
c. $p < 0.001$ from Wilcoxon sign rank test or significant change from baseline

Fisher et al., JAIDS 2009; 51 (5): 562-568

# ROCKET: Randomised Open Label Switch for Cholesterol on Kivexa Evaluation Trial




- Undetectable viral load (< 50 copies/mL) ≥ 12 weeks
- TC cholesterol ≥ 200 mg/dL at screening
- Adequate Baseline renal (CrCl ≥ 60mL/min) and Hepatic (AST / ALT ≤ 5 x ULN) function
- 157 / 159 subjects enrolled received at least one dose of study drug

# Objectives

- **Primary objective:**
  - **Determine whether switching from ABC/3TC + EFV to QD ATR STR leads to a reduction in total fasting cholesterol at 12 weeks[1]**
- **Secondary objectives:**
  - **Fasting metabolic parameters (i.e., TC, LDL*, HDL, triglycerides, non-HDL cholesterol and cholesterol ratios) to week 24**
  - **Evaluate efficacy and safety**
  - **Outcomes research: patients' satisfaction, adherence and tolerability**

[1] Moyle et al., IAS 2010, poster # THPE0133

* LDL measured directly

# Baseline Characteristics[a]

| | ATR | ABC/3TC + EFV |
|---|---|---|
| Number of subjects | 79 | 78 |
| Median age in yrs (IQR) | 42 (36, 48) | 44 (40, 50) |
| Race<br>White<br>Black<br>Asian<br>Other | <br>45 (57.0%)<br>29 (36.7%)<br>2 (2.5%)<br>3 (3.8%) | <br>48 (61.5%)<br>27 (34.6%)<br>0<br>3 (3.9%) |
| Gender<br>Male | <br>61 (77.2%) | <br>64 (82.1%) |
| HIV RNA[b]<br>< 50 copies/ml<br>< 400 copies/ml | <br>76/79 (96.2%)<br>79/79 (100%) | <br>71/77 (92.2%)<br>77/77 (100%) |
| Median BMI [kg/m$^2$] (IQR) | 25.7 (23.5, 29.3) | 25.8 (23.7, 28.0) |
| Median Fasting Total Cholesterol [mg/dL] (IQR) | 256 (231, 281) | 239 (224, 262) |
| Number of Subjects on Prior Lipid Modifying Agents | 9 (11.4%) | 13 (16.7%) |

a. Treated Analysis Set
b. One subject in ABC/3TC arm did not have a baseline viral load sample

# Subject Disposition at Week 24[a]

| N (%) | ATR (N=79) BL – Wk 24 | ABC/3TC + EFV (N=78) BL – Wk 12 | Delayed ATR* (N=73) Wk 12-Wk 24 |
|---|---|---|---|
| **Subjects completing study treatment** | **72 (91.1%)** | **73 (93.6%)** | **71 (91.0%)** |
| **Early Treatment Discontinuation** | **7 (8.9 %)** | **5 (6.4%)** | **2 (2.7%)** |
| Adverse Events[b] | 3 (3.8%) | 1 (1.3%) | 2 (2.7%) |
| Pregnancy | 2 (2.5%) | 0 | 0 |
| Protocol Violation | 1 (1.3%) | 2 (2.5%) | 0 |
| Withdrew Consent | 1 (1.3%) | 1 (1.3%) | 0 |
| Investigator's Decision | 0 | 1 (1.3%) | 0 |

a. Treated Analysis Set

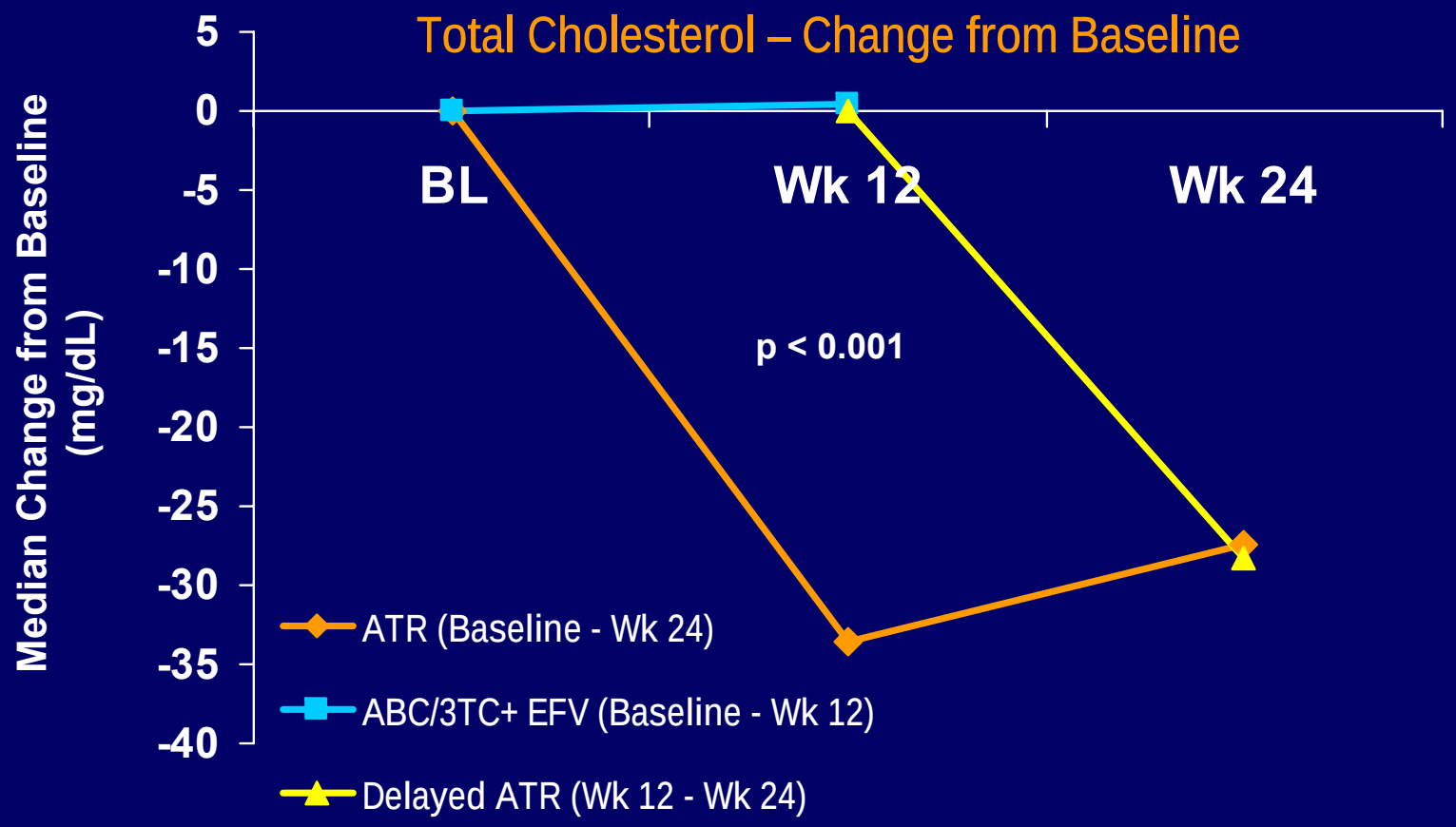
b. Adverse Events leading to study drug discontinuation:

- ATR arm - anxiety; insomnia; night sweats
- ABC/3TC arm - depression
- Delayed ATR – sleep disorder; urticaria

*subjects randomised to ABC/3TC who received at least one dose of ATR after switch

# Fasting Metabolic Parameters: Week 24 – Confirmation of Week 12

**Treated Analysis Set**

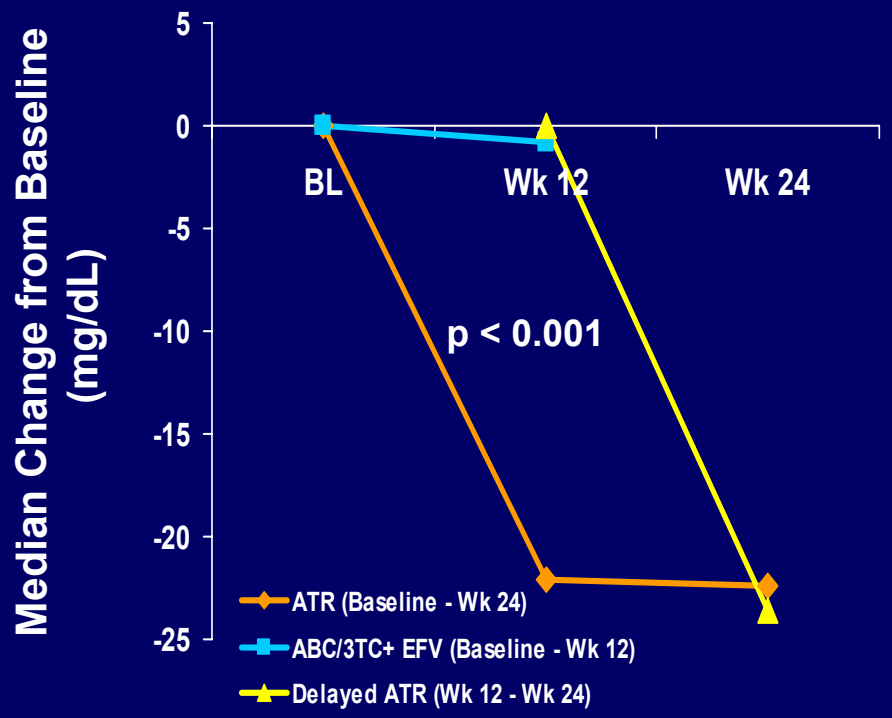



- Baseline for Delayed ATR is reset at Wk 12
- p value for comparison between ATR and ABC/3TC + EFV arms at Week 12

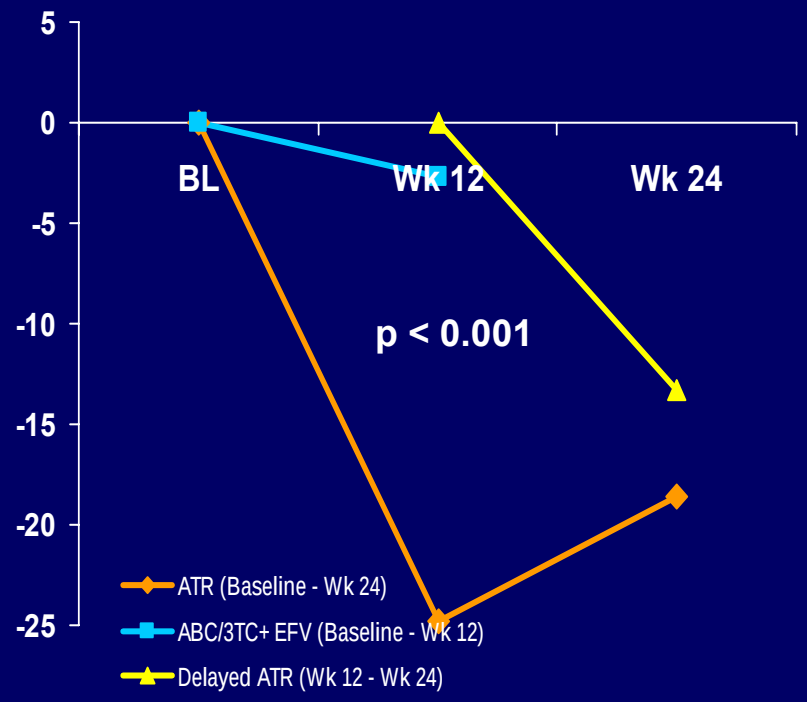
# Fasting Metabolic Parameters: Week 24 – Confirmation of Week 12

**Treated Analysis Set**

## LDL – Change from Baseline




## Triglyceride– Change from Baseline

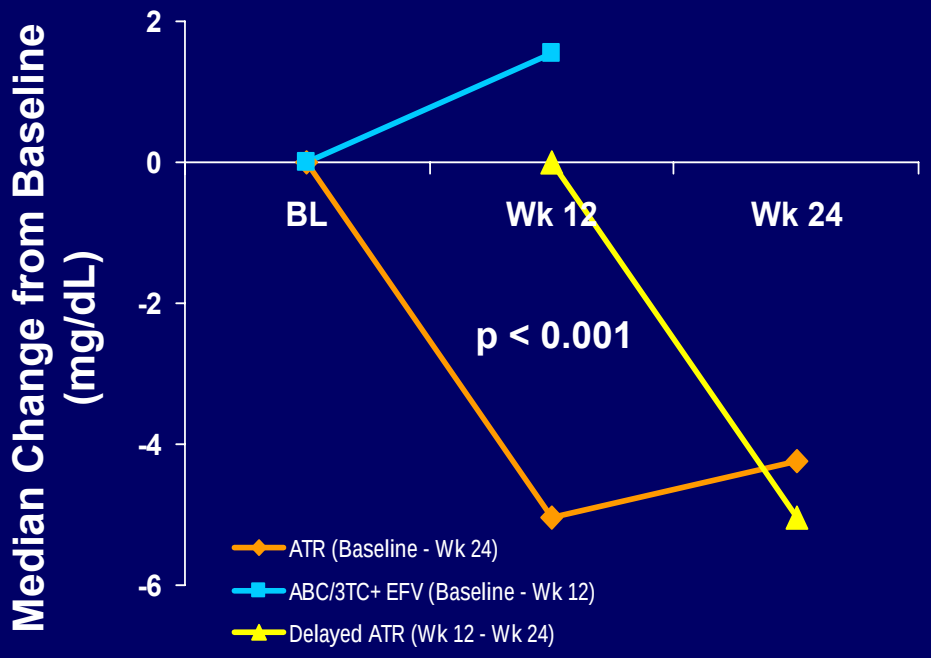



- LDL measured directly.
- Baseline for Delayed ATR is reset at Wk 12
- p value for comparison between ATR and ABC/3TC + EFV arms at Week 12

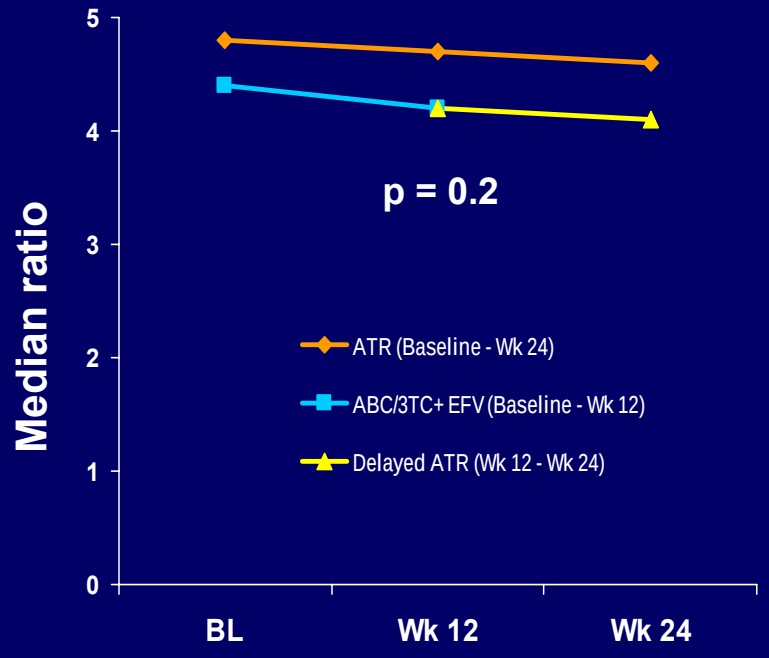
# Fasting Metabolic Parameters: Week 24 – Confirmation of Week 12

**Treated Analysis Set**

## HDL – Change from Baseline



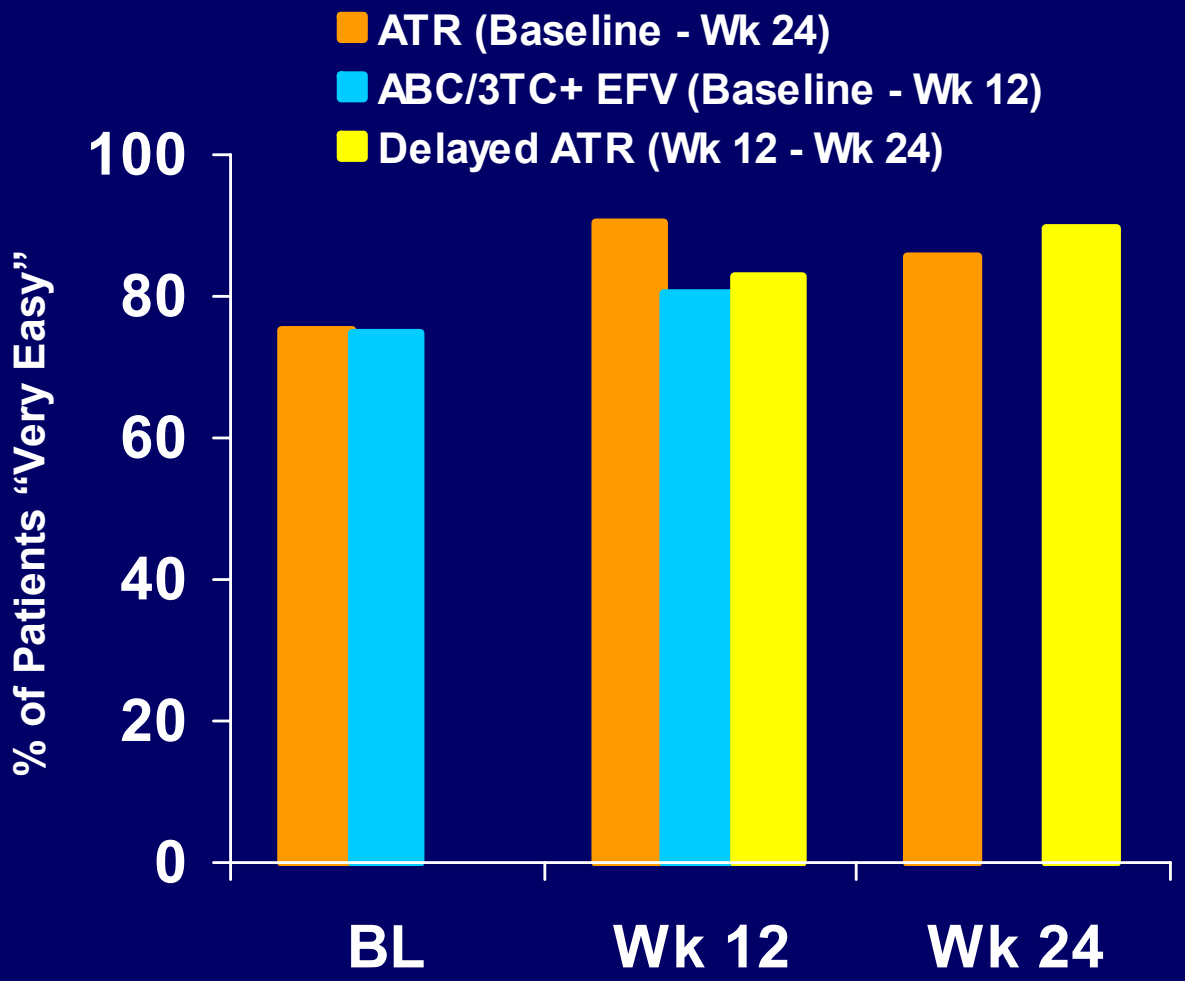

## Ratio of TC/HDL




- Baseline for Delayed ATR is reset at Wk 12
- p value for comparison between ATR and ABC/3TC + EFV arms at Week 12

# Perceived Ease of Regimen[1]

**Treated Analysis Set**

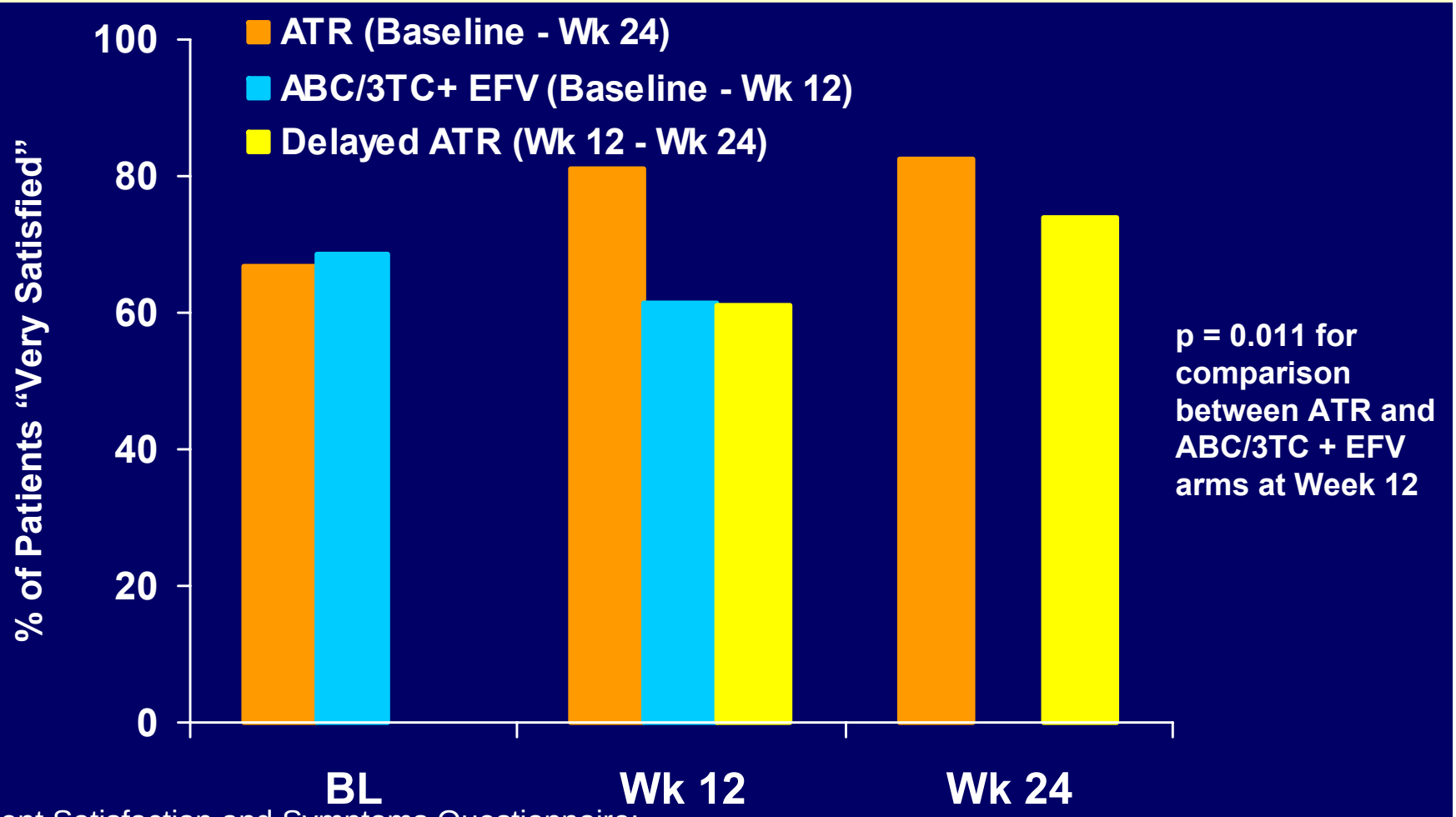



**p = 0.10 for comparison between ATR and ABC/3TC + EFV arms at Week 12**

1. Perceived Ease of Regimen for Condition Questionnaire;
Question: How easy did you find it to follow your current HIV medication regimen?

# Patient Satisfaction - Ability to Tolerate[1]

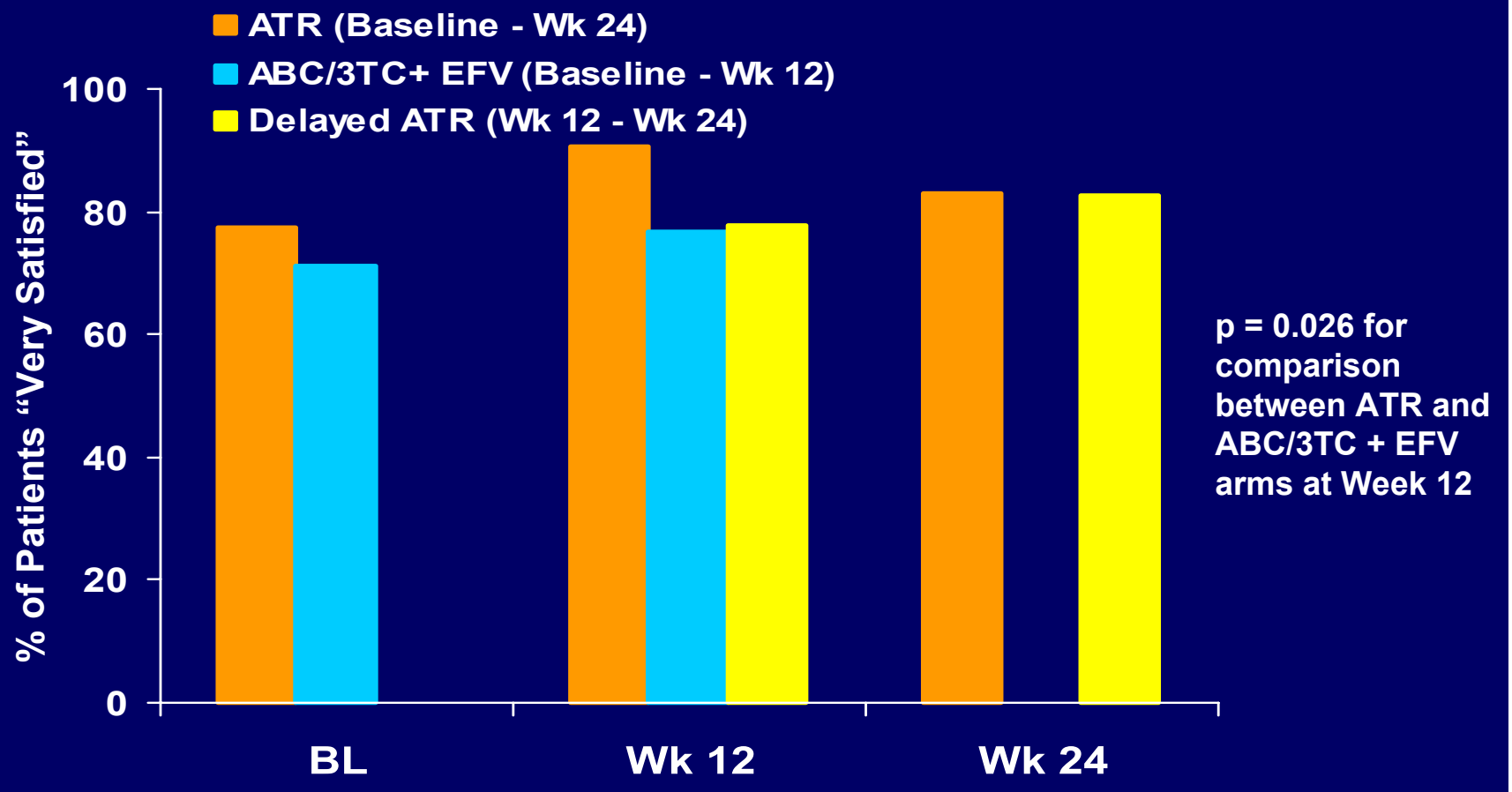
**Treated Analysis Set**




1. Treatment Satisfaction and Symptoms Questionnaire;
Question: In general, how satisfied are you with your ability to tolerate your current treatment regimen?

# Patient Satisfaction - Convenience and Simplicity of Treatment Regimen[1]

**Treated Analysis Set**



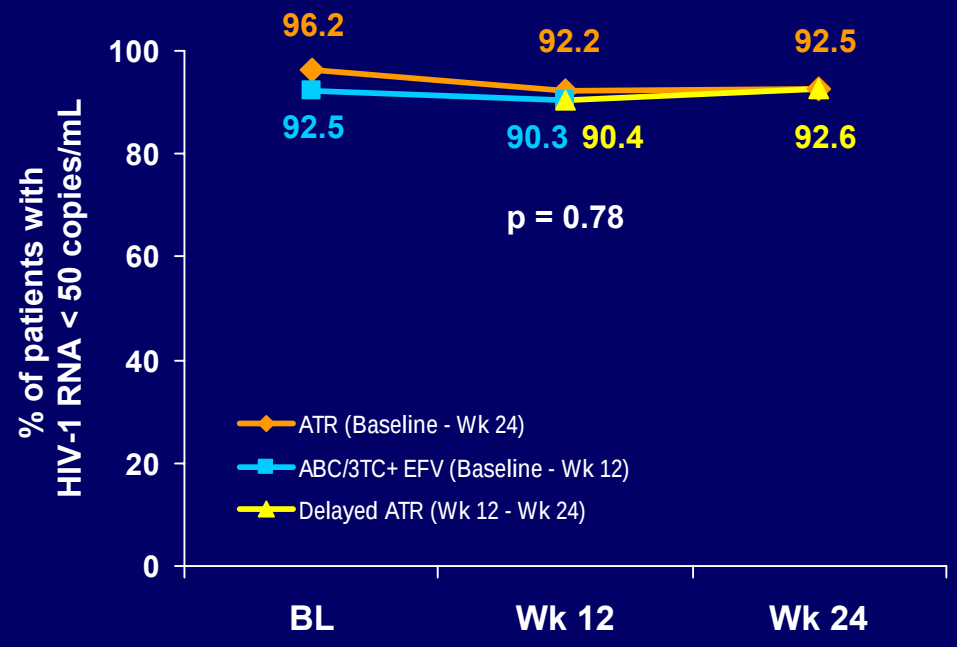

1. Treatment Satisfaction and Symptoms Questionnaire;

Question: In general, how satisfied are you with the convenience and simplicity of your current treatment regimen?

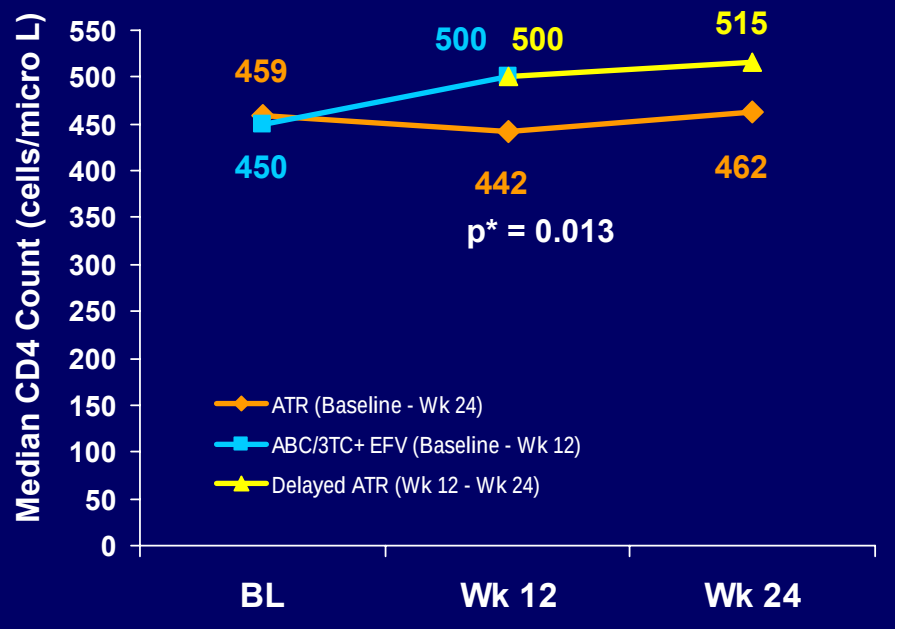
# Viral Suppression and CD4 Count by Visit

## ITT Analysis Set (Missing = Excluded)

### % of Patients HIV-1 RNA < 50 copies/mL




### CD4 Count




Virological failure: No participants met the criteria for virological failure in either arm (2 consecutive post-baseline value ≥ 400 copies/ml)

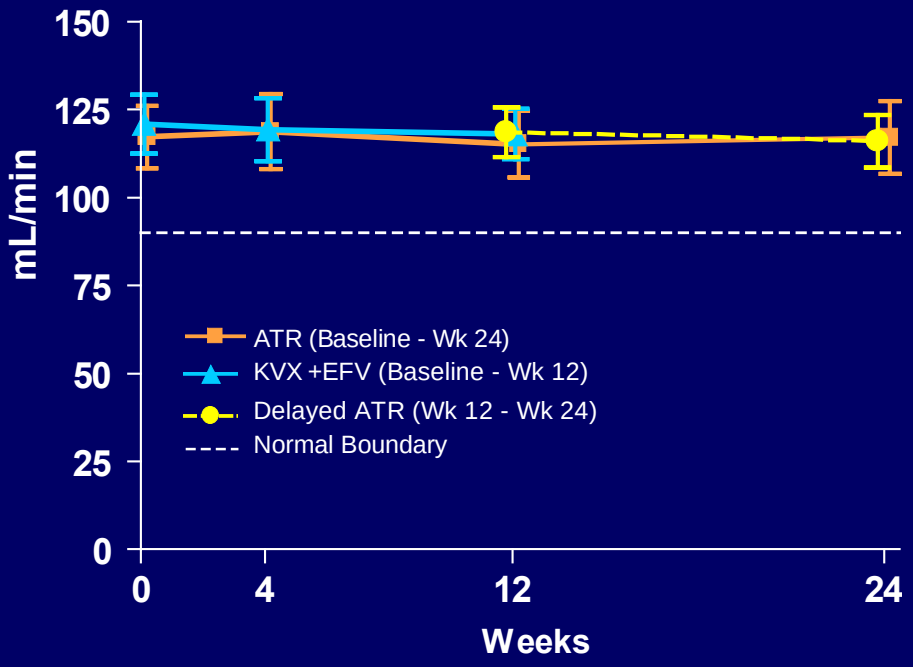
p value for comparison between ATR and ABC/3TC + EFV arms at Week 12.

* Comparison is performed on change from baseline in CD4 count.

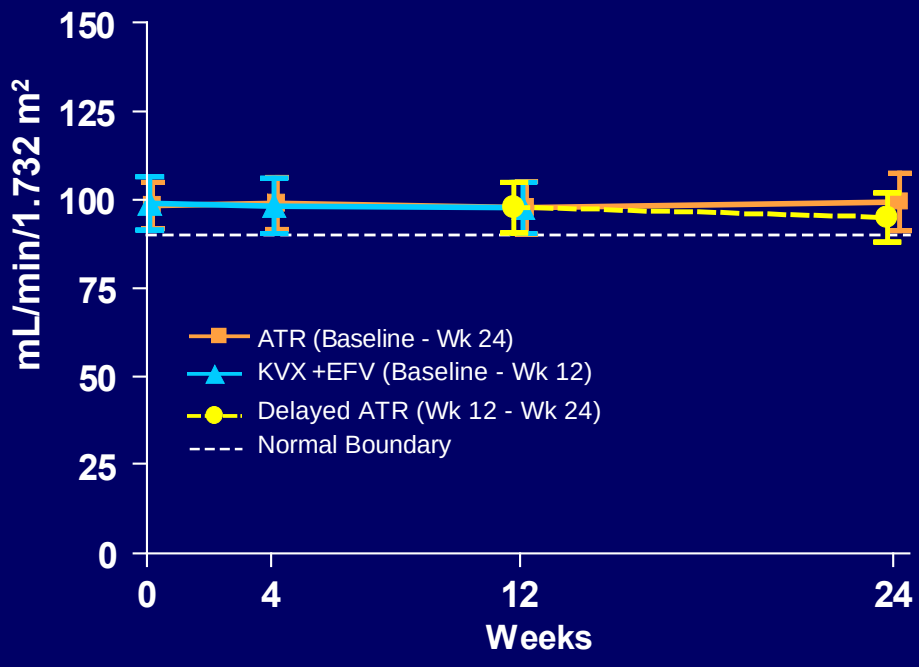
# Renal Function - Creatinine Clearance

## Treated Analysis Set

**Creatinine Clearance:**
**Cockroft Gault (ml/min)- Median (IQR)**




**Estimated GFR:**
**MDRD (ml/min/1.732 m²) - Median (IQR)**




No subject experienced a grade 3 or 4 renal abnormality in either arm

No subject discontinued due to renal adverse events in either arm

# Conclusions

- **Switching from a 2 pill regimen of ABC/3TC + EFV to a Single Tablet Regimen of TDF/FTC/ EFV (ATR):**
  - **Significantly reduces key lipid parameters**
  - **Is well tolerated over 12 and 24 weeks**
  - **Maintains virologic suppression**
  - **Improves patient satisfaction and perceived convenience of administration**

# Acknowledgements


**[4] The ROCKET I Study Group**

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