NORTHWEST AIDS EDUCATION AND TRAINING CENTER

STRIBILD (aka. The Quad Pill)

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Stribild: EVG-COBI-TDF-FTC

- Approved by FDA on August 27, 2012
- One pill daily, smaller in size than Atripla
- Taken with food, ≥2 hrs apart from antacids
- Components:
  - **Elvitegravir**: once-daily integrase inhibitor
  - **Cobicistat**: CYP 3A4 inhibitor, no HIV activity
  - **Emtricitabine, Tenofovir:** NRTI's

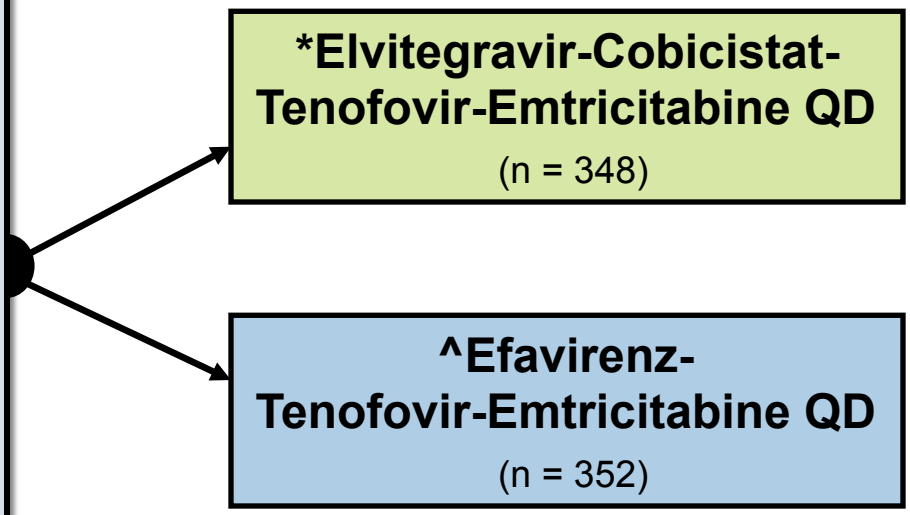
Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC

Study 102: Phase 3, Treatment Naive

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
Study 102: Design

Study Design

Protocol
- N = 700 HIV-infected
- Age ≥ 18
- Randomized, Double-blind
- Phase 3 trial at 130 study sites
- Conducted in U.S. and Puerto Rico
- Antiretroviral naive
- No baseline NRTI, NNRTI mutations
- Baseline HIV RNA ≥ 5,000 copies/ml
- Creatinine Clearance ≥ 70 ml/min
- No AIDS condition in previous 30 days



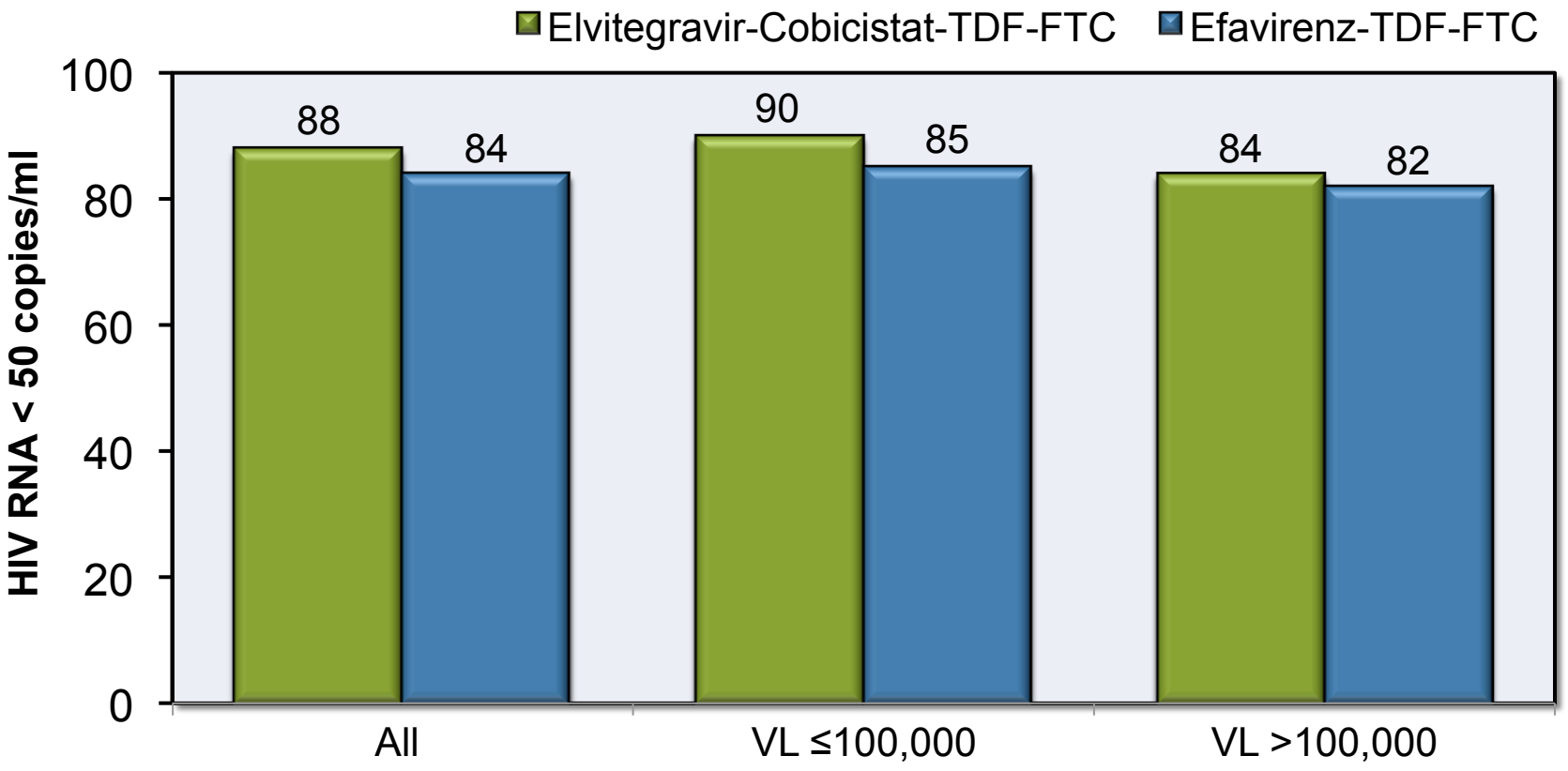
*Dosing: Elvitegravir 150 mg; Cobicistat 150 mg; Tenofovir 300 mg; Emtricitabine 200 mg

^Dosing: Efavirenz 600 mg; Tenofovir 300 mg; Emtricitabine 200mg

Source: Sax PE, et al. Lancet. 2012;379:2439-48.

Elvitegravir-Cobicistat-TDF-FTC vs Efavirenz-TDF-FTC
Study 102: Results

Week 48: Virologic Response (Intent to Treat)



Source: Sax PE, et al. Lancet. 2012;379:2439-48.
Sax P, et al. 19th CROI; Abstract 101.

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC

Common Adverse Events

Treatment Emergent Adverse Events in ≥ 10% of Subjects		
	EVG-COBI-TDF-FTC (n = 348)	**EFV-TDF-FTC (n= 352)**
Diarrhea	23%	19%
Nausea*	**21%**	14%
Abnormal Dreams^	15%	27%
Upper Respiratory Tract Infection	14%	11%
Headache	14%	10%
Fatigue	12%	13%
Depression	9%	11%
Insomnia&	9%	**14%**
Dizziness^	7%	**24%**
Rash#	6%	**12%**

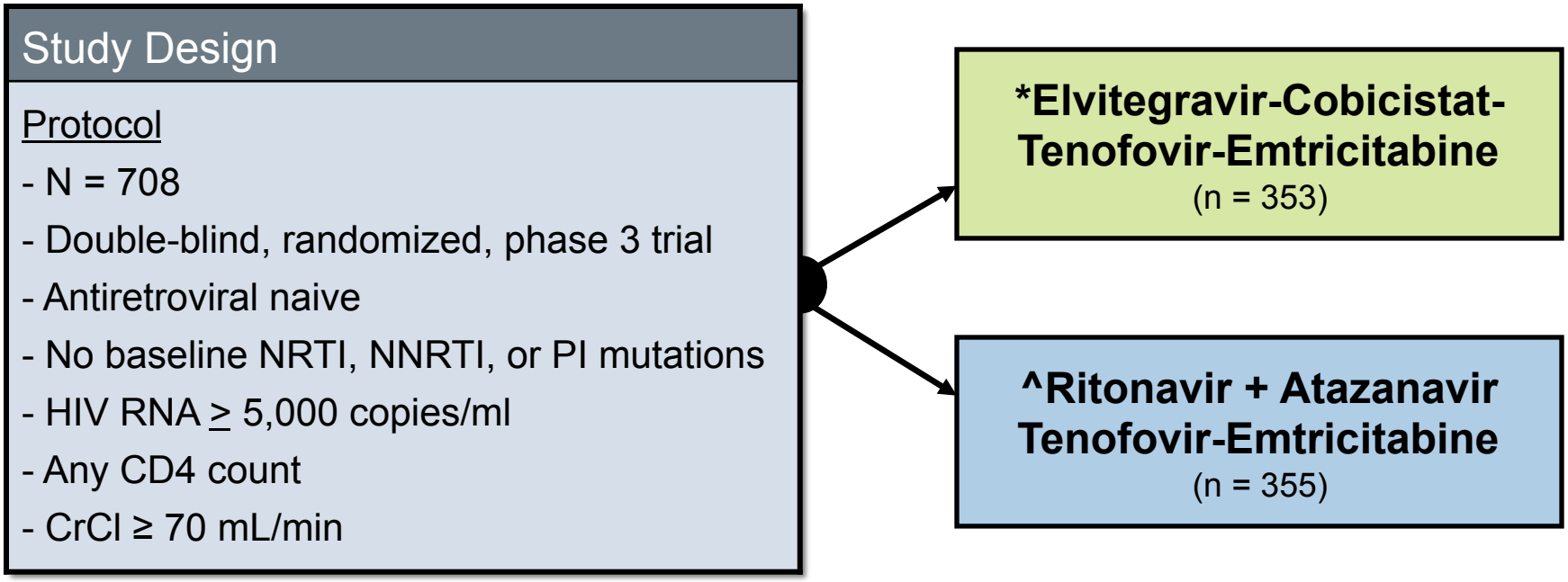
*$p < 0.016$; ^$p < 0.001$; &$p < 0.031$; #$p = 0.009$

Source: Sax PE, et al. Lancet. 2012;379:2439-48.

Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + RTV+ TDF-FTC

Study 103: Phase 3, Treatment Naive

Elvitegravir-Cobicistat-TDF-FTC versus +Atazanavir + RTV + TDF-FTC
Study 103: Design



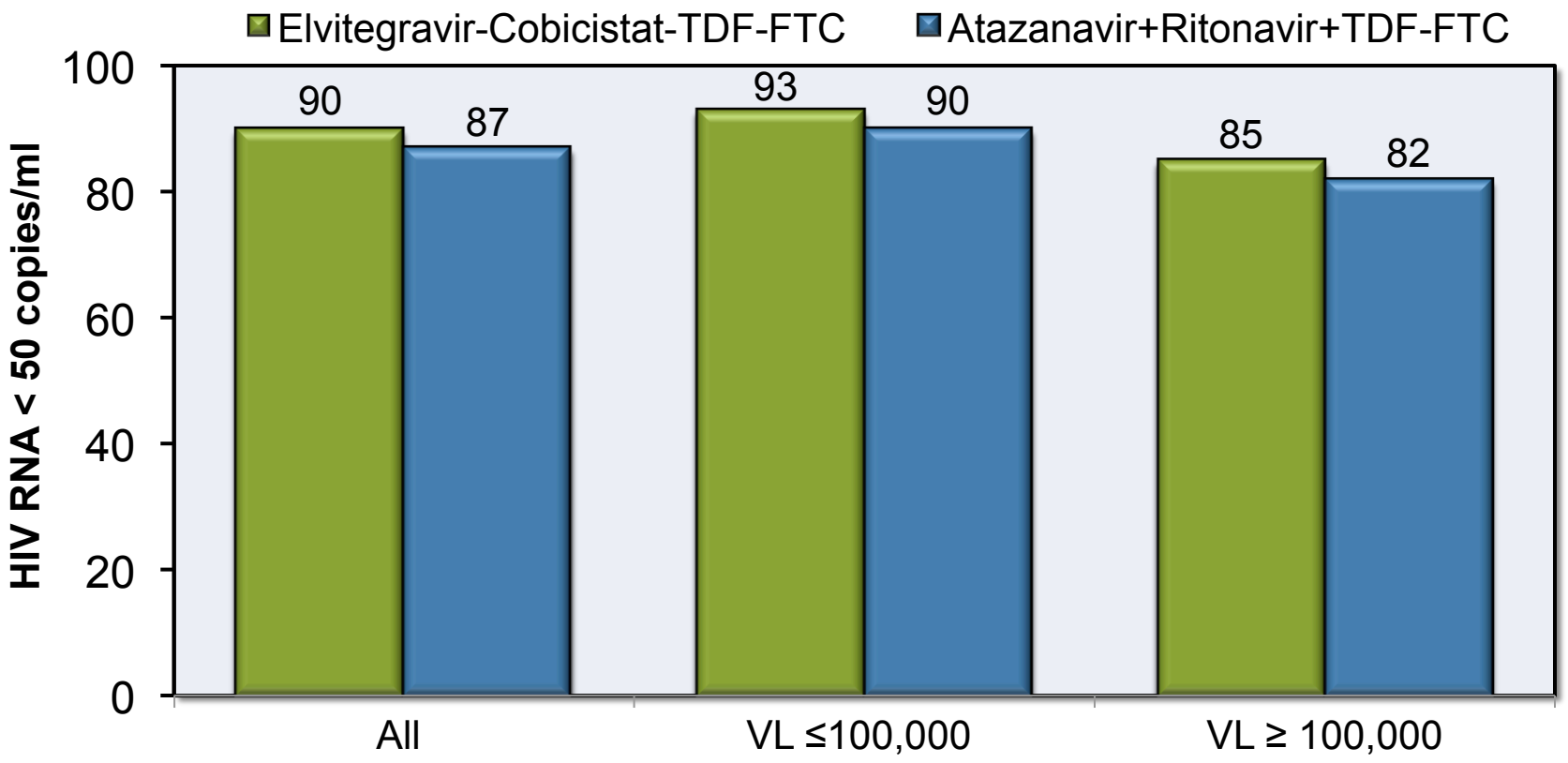
*Dosing (QD): Elvitegravir (150 mg); Cobicistat (150 mg); Tenofovir (300 mg); Emtricitabine (200mg)

^Dosing (QD): Ritonavir (100 mg); Atazanavir (300 mg); Tenofovir (300 mg); Emtricitabine (200mg)

Source: DeJesus E, et al. Lancet. 2012;379:2429-38.

Elvitegravir-Cobicistat-TDF-FTC versus ATZ + RTV+ TDF-FTC
Study 103: Results

Week 48: Virologic Response (Intent to Treat)



Source: DeJesus E, et al. Lancet. 2012;379:2429-38.
DeJesus, et al. 19th IAC. 2012; Abstract TUPE43.

Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + RTV + TDF-FTC
Study 103: Common Adverse Events

Treatment Emergent Adverse Events in ≥ 10% of Subjects		
	EVG-COBI-TDF-FTC (n = 348)	**RTV-ATV-TDF-FTC (n= 352)**
Diarrhea	22%	27%
Nausea	20%	19%
Upper Respiratory Tract Infection	15%	16%
Headache	15%	12%
Fatigue	14%	13%
Ocular Icterus*	1%	**14%**

*$p < 0.001$

Source: DeJesus E, et al. Lancet. 2012;379:2429-38.

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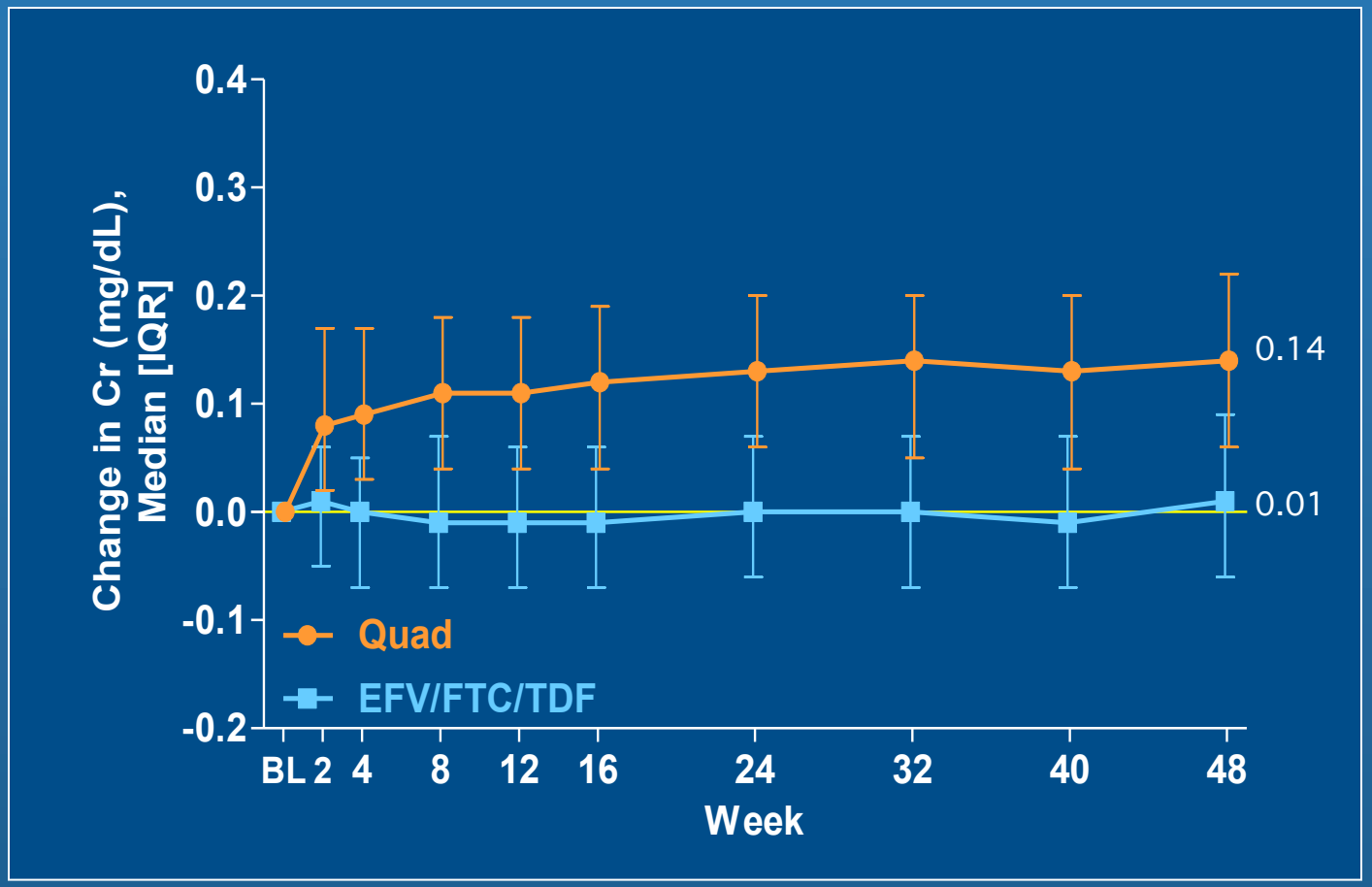
Other Adverse Event Data

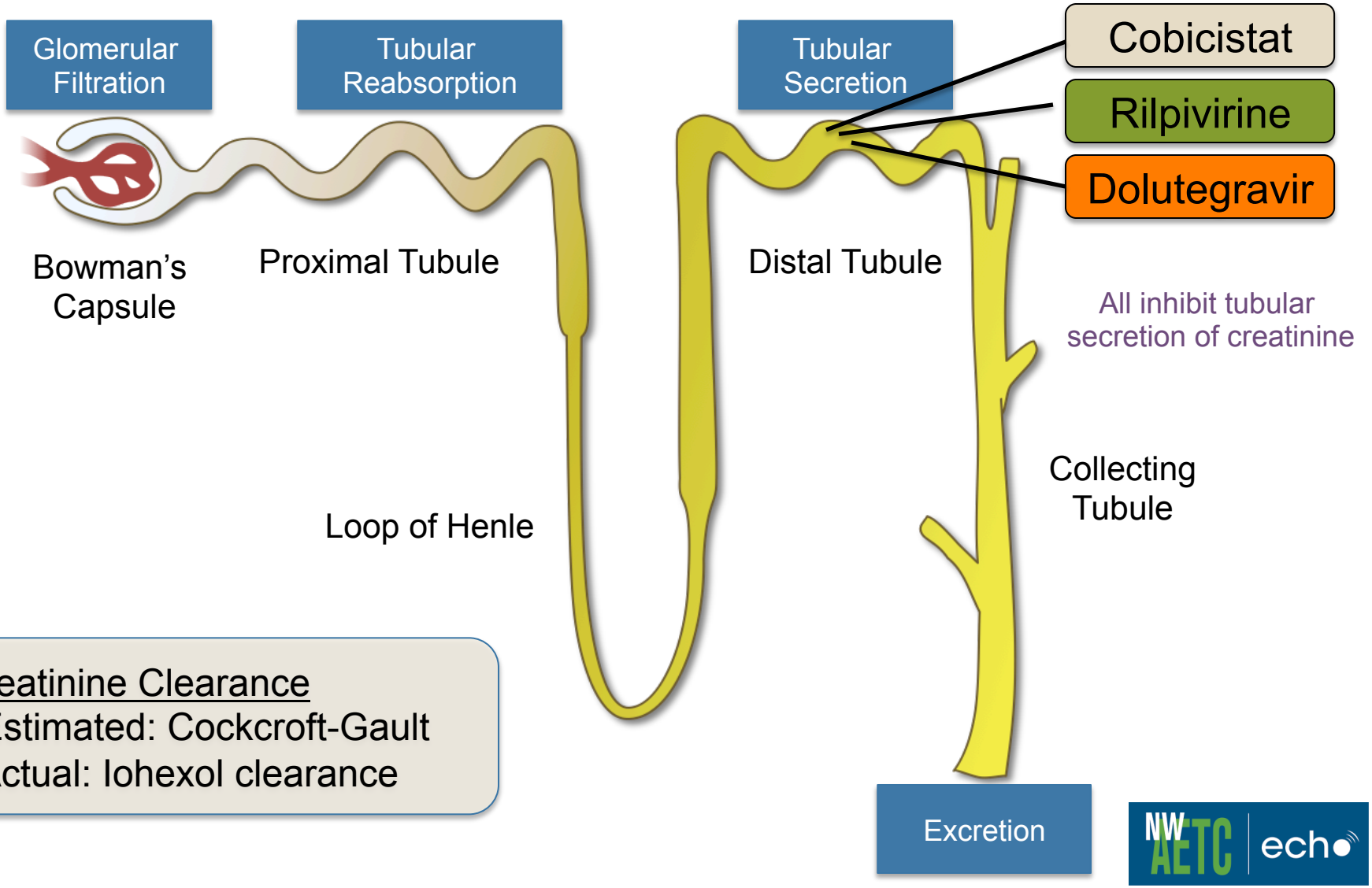
- **Lipids:**
  - Study 102: TC, LDL and HDL changes worse in EFV-arm
  - Study 103: TG changes slightly worse in ATZ-RTV-arm
- **Renal:**
  - Study 102: 1.4% treatment discontinuations in Stribild arm
    - ↑ in sCr of 0.1-0.2 mg/dL (median 0.14 at wk 48)
    - ↓ in eGFR of -14.3 in EVG-COBI-arm vs. -3.0 in EFV
    - Tenofovir toxicity: sCr ↑ was at least **0.4** mg/dL

Change in Serum Creatinine from Baseline

Study 102



Effect of new ARV's on Creatinine Clearance



Creatinine Clearance
- Estimated: Cockcroft-Gault
- Actual: Iohexol clearance

Studies 102 and 103: RESISTANCE

n (%)	Study-102 EVG-COBI (n=348)	Study-102 EFV (n=352)	Study-103 EVG-COBI (n=353)	Study-103 ATV+RTV (n=355)
Subjects Analyzed for Resistance*	14 (4%)	17 (5%)	12 (3%)	8 (2%)
Subjects with Resistance	8 (2%)	8 (2%)	5 (1%)	0
Integrase Resistance -E92Q, T66I, Q148R, N155H	7 (2%)	-	4 (1%)	-
NNRTI or PI Resistance -K103N and others	-	8 (2%)	-	-
NRTI Resistance -M184V/I -K65R	8 (2%) 8 3	2 (0.6%) 2 2	4 (1%) 4 1	-

Summary

- Stribild is non-inferior to two 1st-line regimens
- Fewer CNS and lipid side effects than EFV, similar GI side effects to boosted ATZ
- 0.1-0.2 mg/dL increase in sCr may be seen; if greater, need work-up for tenofovir toxicity
  - Avoid initiation if CrCl <70 ml/min
  - Discontinue if CrCl drops to <50 ml/min
- Remember: taken with food, ≥2 hrs apart from antacids, low resistance barrier

On The Horizon…

- Elvitegravir: NDA submitted 6/27/12
- Cobicistat: NDA submitted 6/28/12
- Dolutegravir: in Phase 3
- PI/NNRTI/RAL switch to Stribild
- Stribild in pts with renal insufficiency and women
- EVG/COBI/FTC/7340