National HIV Curriculum

Atazanavir-Cobicistat (*Evotaz*)

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Last Updated: September 19, 2023

Antiretroviral Therapy: Studies

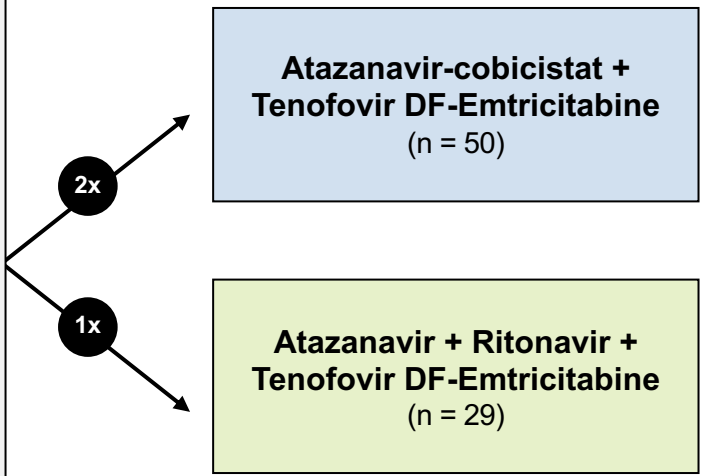
Atazanavir-Cobicistat (*Evotaz*)

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2)

Study 105

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2) Study 105: Study Design

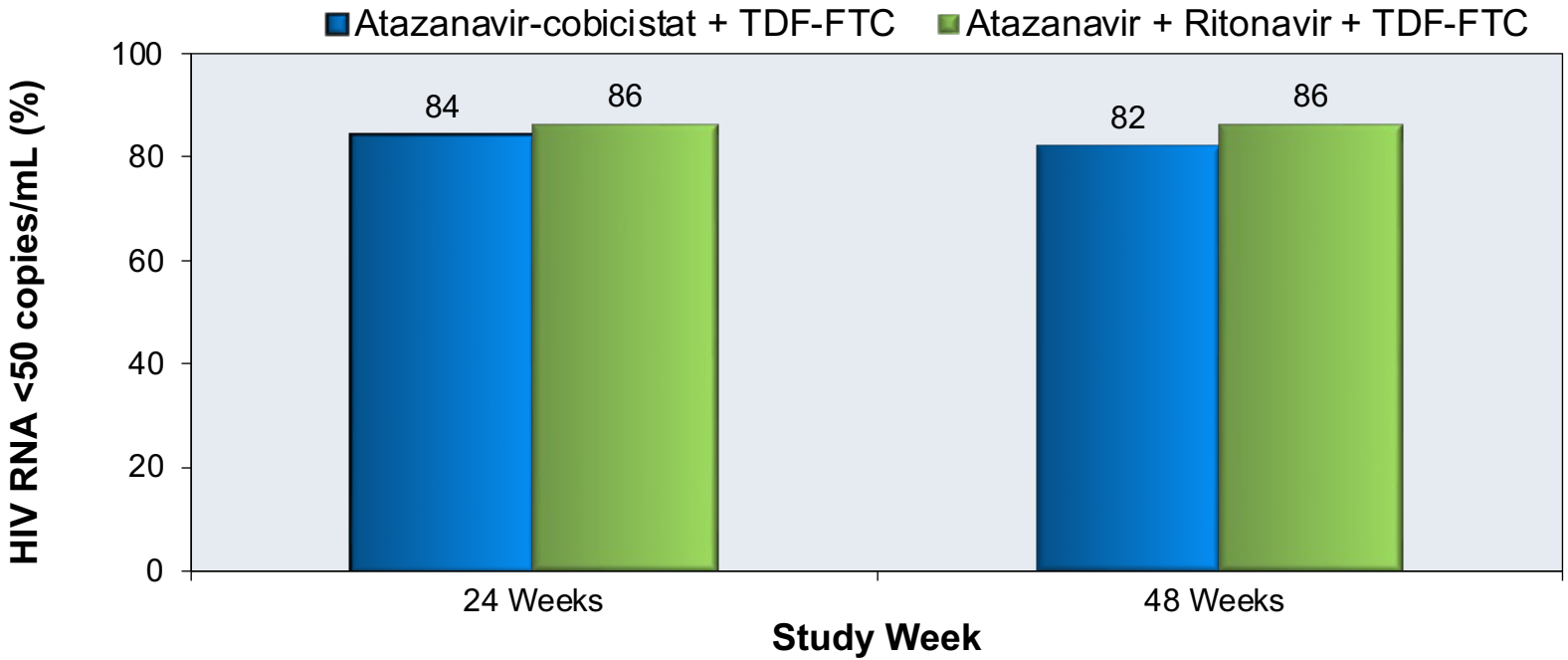
- **Background**: Randomized, partially placebo-controlled, double-blind phase 2 trial to compare the safety and efficacy of cobicistat and ritonavir as pharmacokinetic enhancers administered with atazanavir and fixed-dose tenofovir DF-emtricitabine in treatment-naïve adults with HIV infection
- **Inclusion Criteria** (n = 85)
  - Age ≥18 years
  - Antiretroviral treatment-naïve
  - HIV RNA ≥5000 copies/mL
  - CD4 count >50 cells/mm^3
- **Treatment Arms (all once daily)**
  - Atazanavir-cobicistat (300/150 mg) + TDF-FTC
  - Atazanavir 300 mg + Ritonavir 100 mg + TDF-FTC



Source: Elion R, et al. AIDS. 2011;25:1881-6.

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2) Study 105: Results

Week 24 and 48: Virologic Response (ITT, Missing=Failure)



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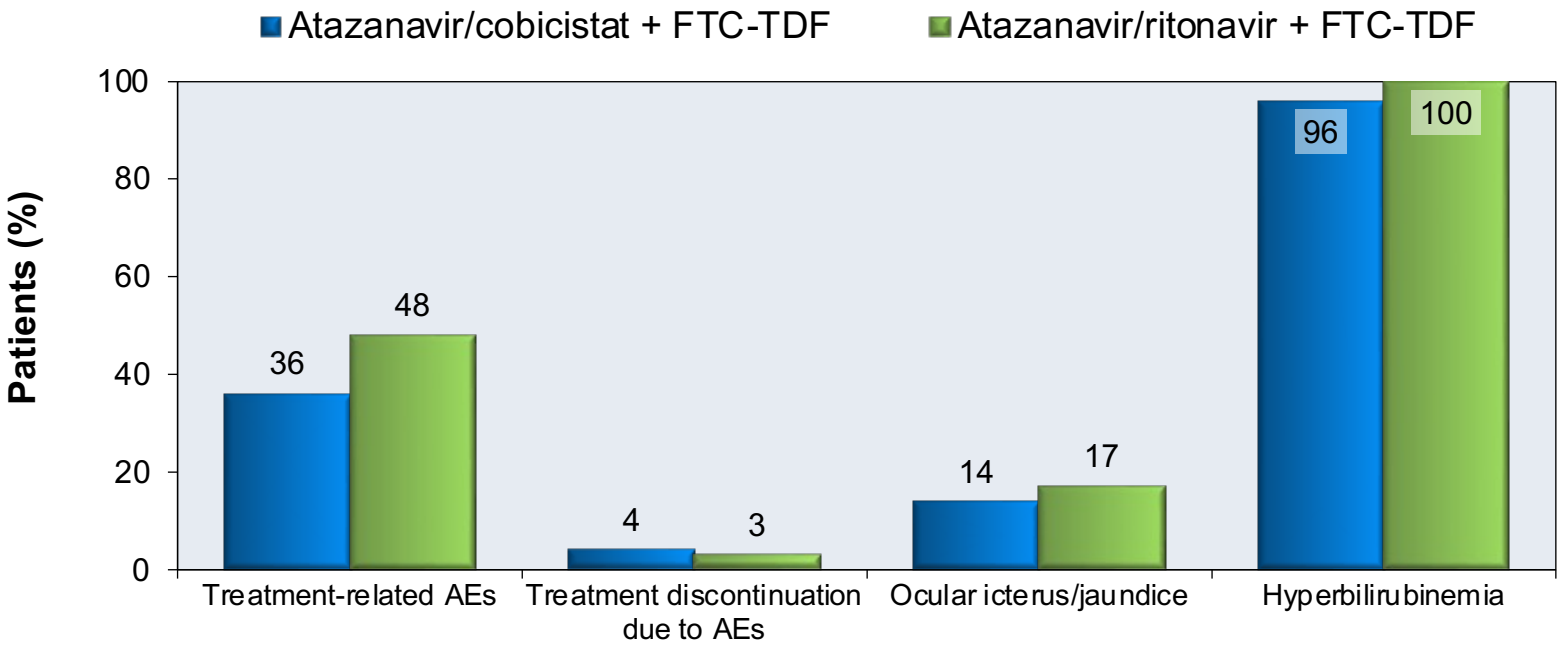
Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2) Study 105: Results

Adverse Events and Treatment Discontinuations



Source: Elion R, et al. AIDS. 2011;25:1881-6.

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 2) Study 105: Conclusions

Conclusion: “Using cobicistat and ritonavir as pharmacoenhancers for atazanavir and administered with emtricitabine/tenofovir DF achieved comparable rates of virologic suppression and CD4 cell count increase with satisfactory safety profiles.”

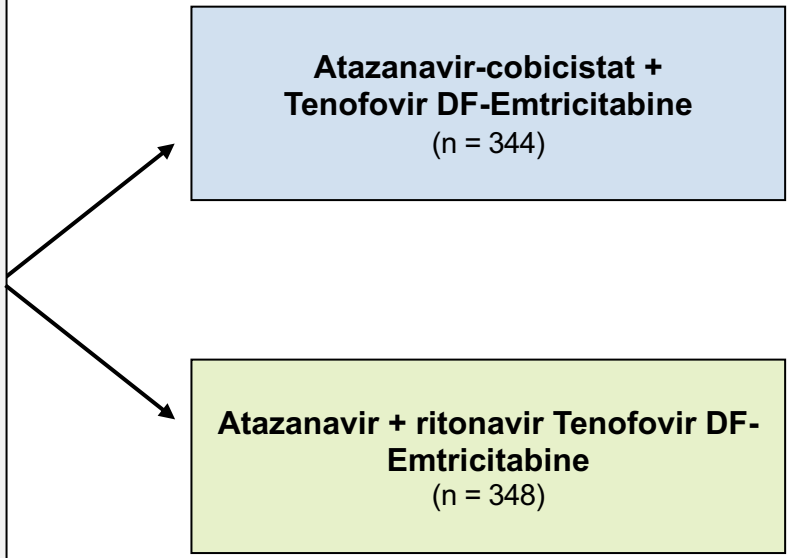
Source: Elion R, et al. AIDS. 2011;25:1881-6.

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3)

Study 114

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3) Study 114: Study Design

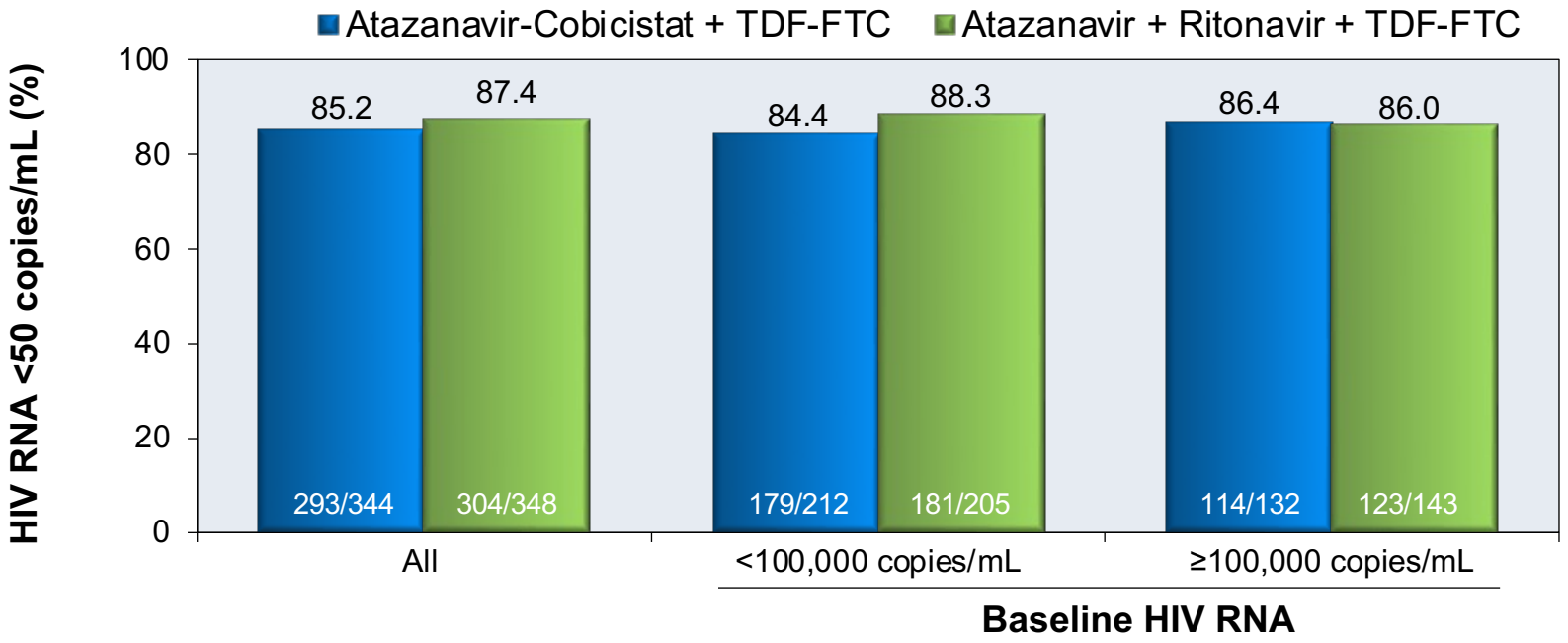
- **Background**: Randomized, double-blind, double-dummy, active controlled phase 3 trial to compare the safety and efficacy of cobicistat and ritonavir as pharmacokinetic enhancers administered with atazanavir and fixed-dose tenofovir DF-emtricitabine in treatment-naïve adults with HIV infection
- **Inclusion Criteria (n = 692)**
  - Age ≥18 years
  - Antiretroviral treatment-naïve
  - Sensitive to atazanavir, tenofovir, and emtricitabine
  - HIV RNA ≥5000 copies/mL
- **Treatment Arms (all once daily)**
  - Atazanavir-cobicistat (300/150 mg) + TDF-FTC
  - Atazanavir 300 mg + Ritonavir 100 mg + TDF-FTC



Source: Gallant JE, et al. J Infect Dis. 2013;208:32-9.

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3) Study 114: Results

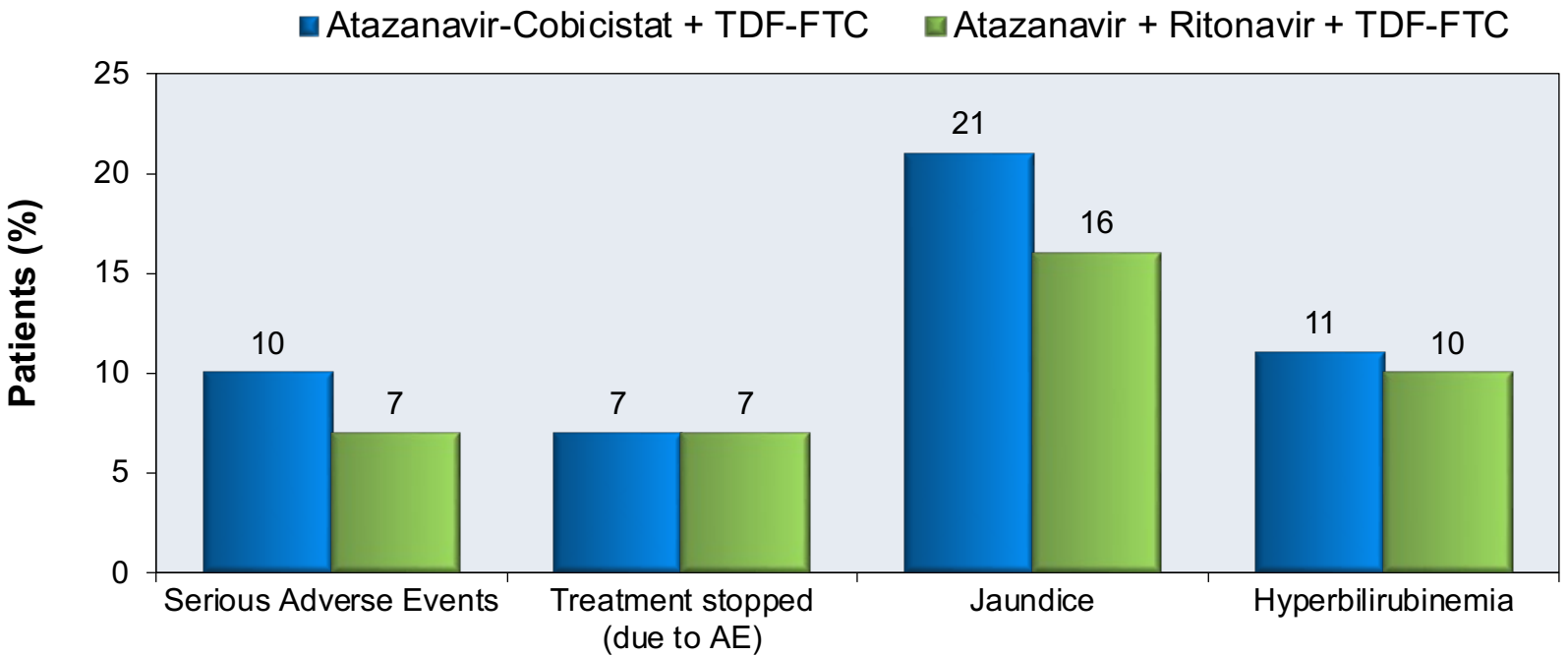
Week 48: Virologic Response (ITT, Missing=Failure)



Source: Gallant JE, et al. J Infect Dis. 2013;208:32-9.

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3) Study 114: Results

Adverse Events (AE) and Treatment Discontinuations



Source: Gallant JE, et al. J Infect Dis. 2013;208:32-9.

Atazanavir + [Cobicistat or Ritonavir] + TDF-FTC (Phase 3) Study 114: Conclusions

Conclusions: “COBI was noninferior to RTV in combination with ATV plus FTC/TDF at week 48. Both regimens achieved high rates of virologic success. Safety and tolerability profiles of the 2 regimens were comparable. Once-daily COBI is a safe and effective pharmacoenhancer of the protease inhibitor ATV.”

Source: Gallant JE, et al. J Infect Dis. 2013;208:32-9.

Cobicistat-Boosted PIs in Patients with Renal Impairment

Study 118

Cobicistat-Boosted PIs in Patients with Renal Impairment
Study 118: Design

- **Background**: Phase 3, non-comparative, open label, 2 cohort study to compare the safety and efficacy of switching ritonavir to cobicistat in virologically suppressed adults with HIV infection and mild to moderate renal impairment
- **Inclusion Criteria (n = 73)***
  - Antiretroviral treatment-experienced
  - HIV RNA undetectable x 6 months
  - On regimen of 2 NRTIs + ATV/r or DRV/r
  - Stable renal function with CrCl 50 to 89 mL/min
- **Treatment Arms**
  - Cobicistat 150 mg QD + [Atazanavir 300 mg QD or Darunavir 800 mg QD] + 2 NRTIs

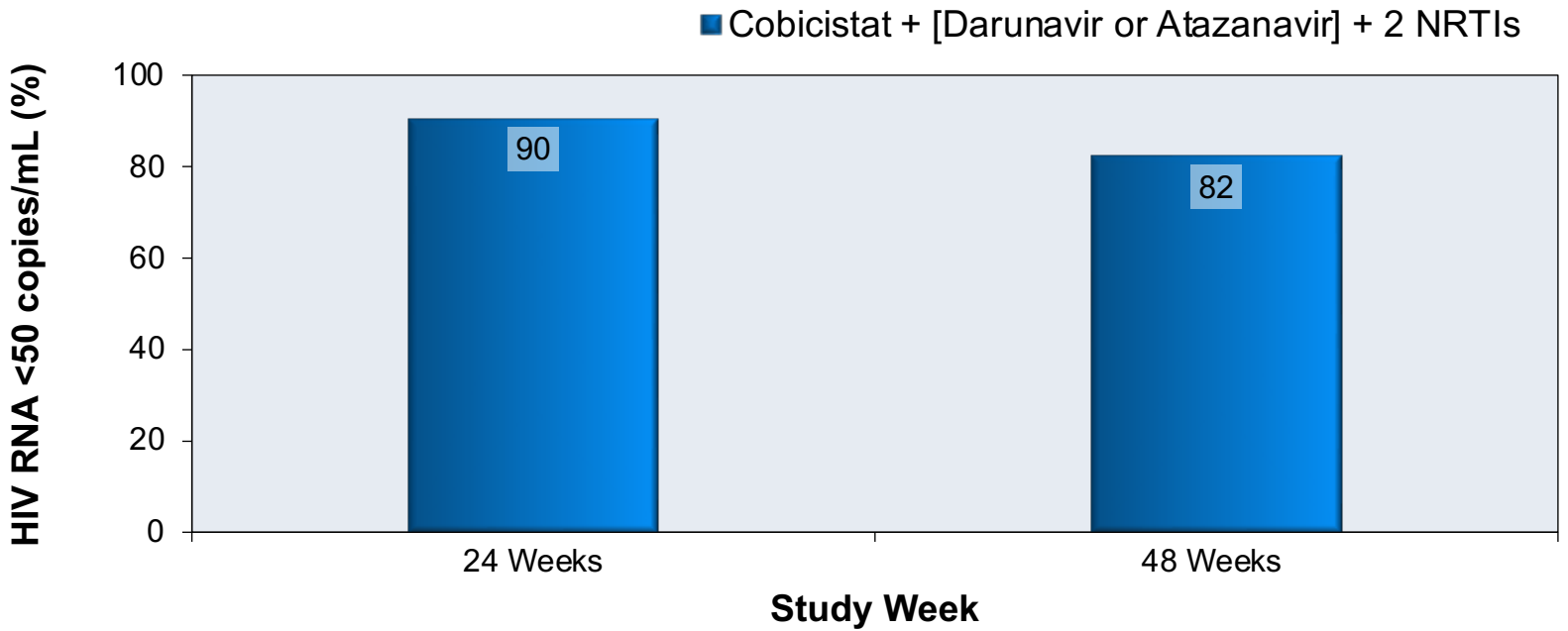
→ **Cobicistat + Atazanavir or Darunavir + 2 NRTIs** (n = 73)

*Note: only ritonavir-to-cobicistat switch cohort presented here

Source: McDonald CK, et al. HIV Clin Trials. 2014;15:269-73.

Cobicistat-Boosted PIs in Patients with Renal Impairment Study 118: Results3

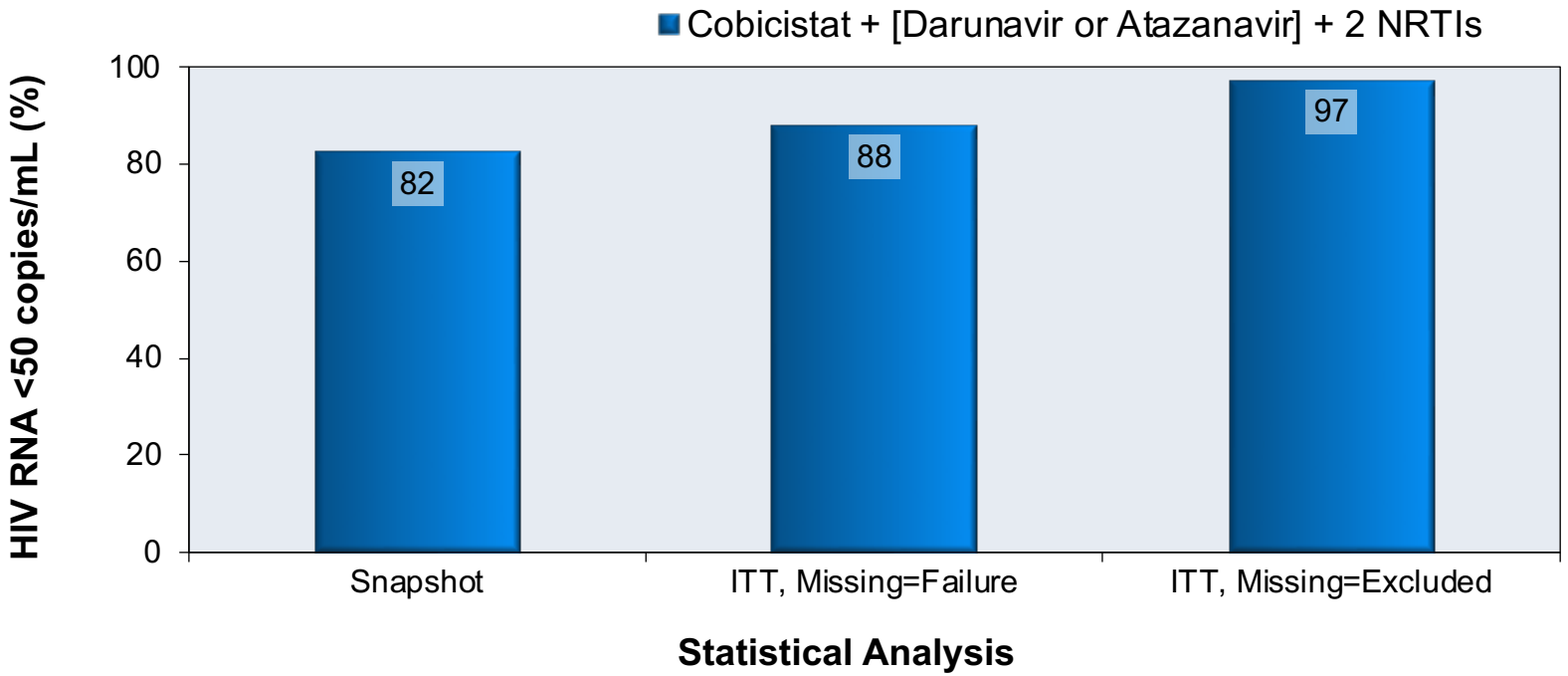
Week 24 and 48: Virologic Response (Snapshot Analysis)



Source: McDonald CK, et al. HIV Clin Trials. 2014;15:269-73.

Cobicistat-Boosted PIs in Patients with Renal Impairment Study 118: Results

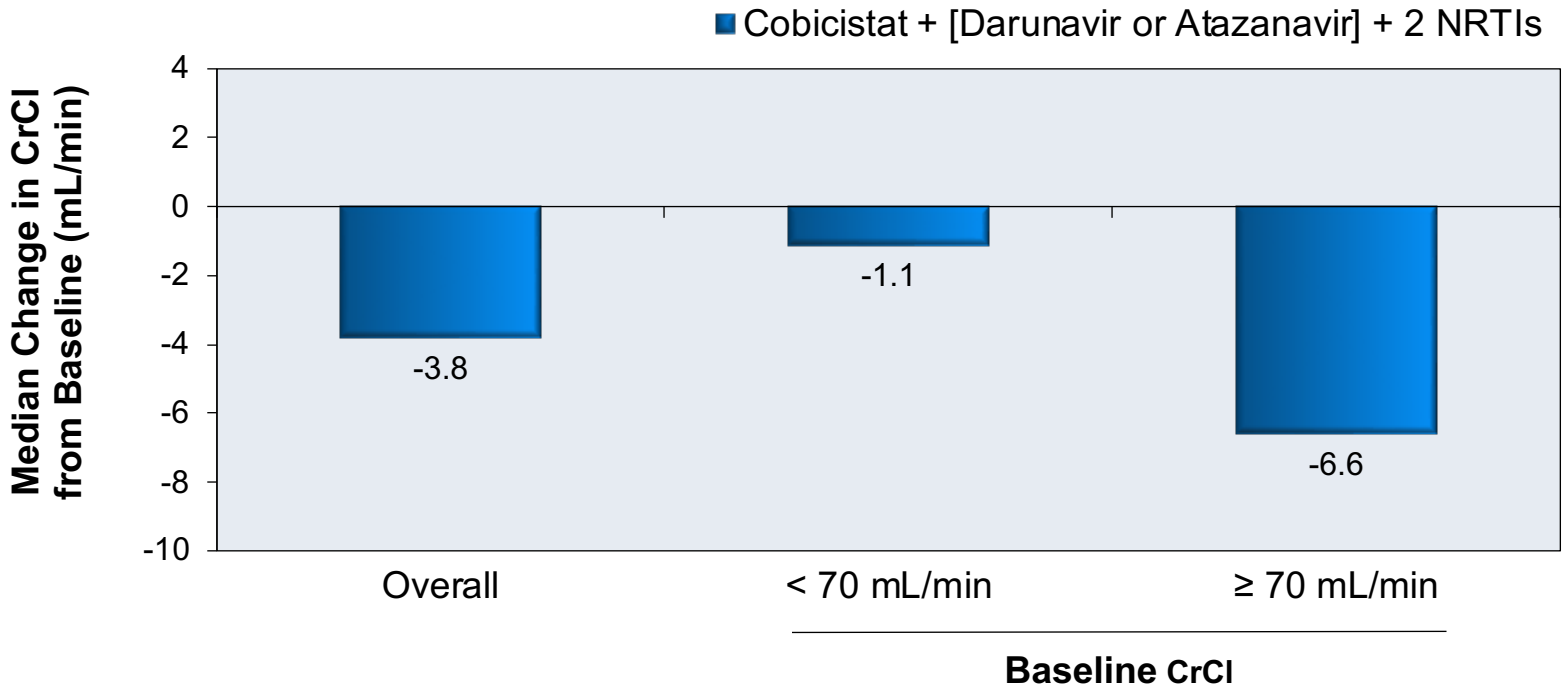
Week 48: Virologic Response, by Different Statistical Analyses



Source: McDonald CK, et al. HIV Clin Trials. 2014;15:269-73.

Cobicistat-Boosted PIs in Patients with Renal Impairment
Study 118: Results

Week 48: Changes in Creatinine Clearance, by Baseline CrCl



Source: McDonald CK, et al. HIV Clin Trials. 2014;15:269-73.

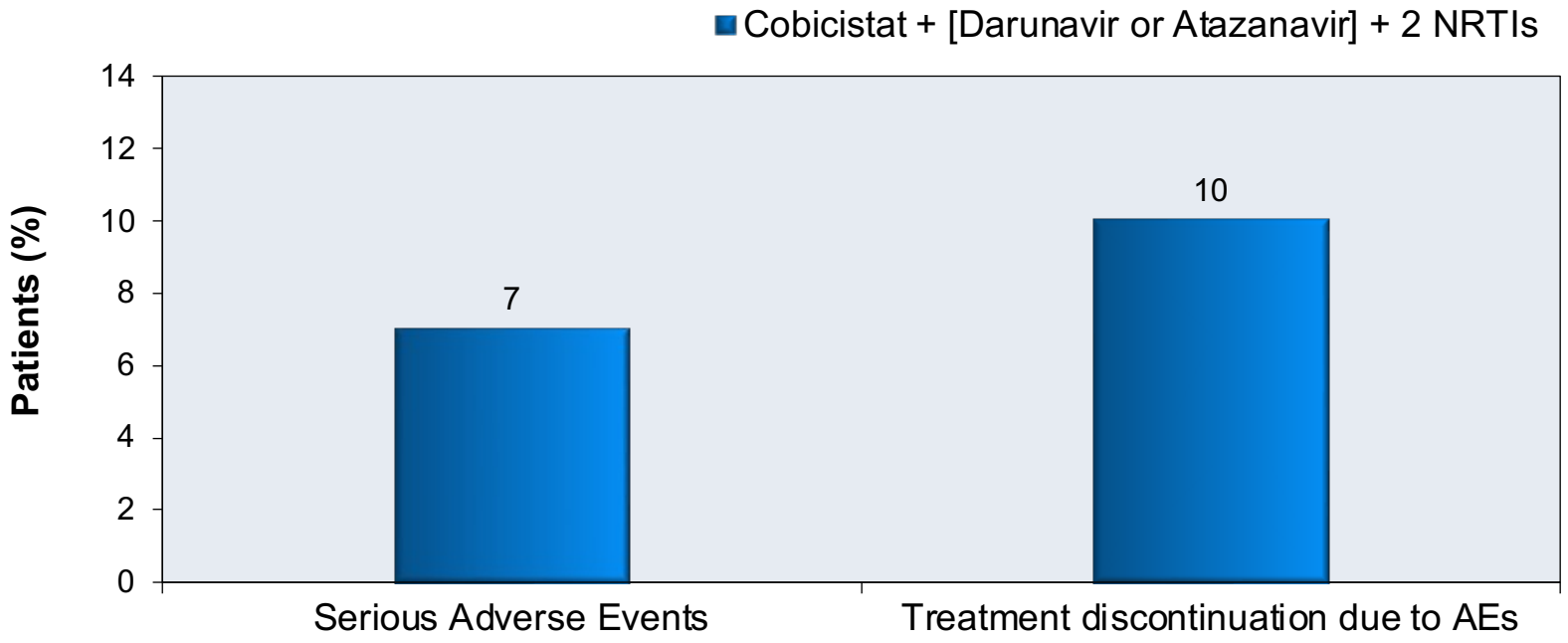
Cobicistat-Boosted PIs in Patients with Renal Impairment
Study 118: Results

Confirmed Renal Laboratory Abnormalities	
Laboratory Value	**Cobicistat + [ATV or DRV] + 2 NRTIs** (n=73)
Serum creatinine increase ≥ 0.4mg/dL	4.1%
Hypophosphatemia (≥ grade 1 increase)	1.4%
Proteinuria (≥ grade 2 increase)	1.4%
Normoglycemic glycosuria (≥ grade 1 increase)	0

Source: McDonald CK, et al. HIV Clin Trials. 2014;15:269-73.

Cobicistat-Boosted PIs in Patients with Renal Impairment Study 118: Results

Adverse Events and Treatment Discontinuations



Source: McDonald CK, et al. HIV Clin Trials. 2014;15:269-73.

Cobicistat-Boosted PIs in Patients with Renal Impairment
Study 118: Conclusions

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Acknowledgments

The **National HIV Curriculum** is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $1,332,044 with 0% financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov. This project is led by the University of Washington's Infectious Diseases Education and Assessment (IDEA) Program.

AETC AIDS Education & Training Center Program

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IDEA INFECTIOUS DISEASES EDUCATION & ASSESSMENT