National HIV Curriculum

# Darunavir-Cobicistat

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# Darunavir-Cobicistat
# Summary of Key Phase 3 Studies

- **Study 130: Darunavir-cobicistat + 2NRTIs**
- **PROBE 2: Darunavir-cobicistat + Rilpivirine versus 3-Drug Regimen**

**Abbreviations**: NRTIs = nucleoside reverse transcriptase inhibitors

# Darunavir-Cobicistat

Darunavir-Cobicistat + 2 NRTIs

# Study 130

# Darunavir-Cobicistat + 2 NRTIs
# Study 130: Design

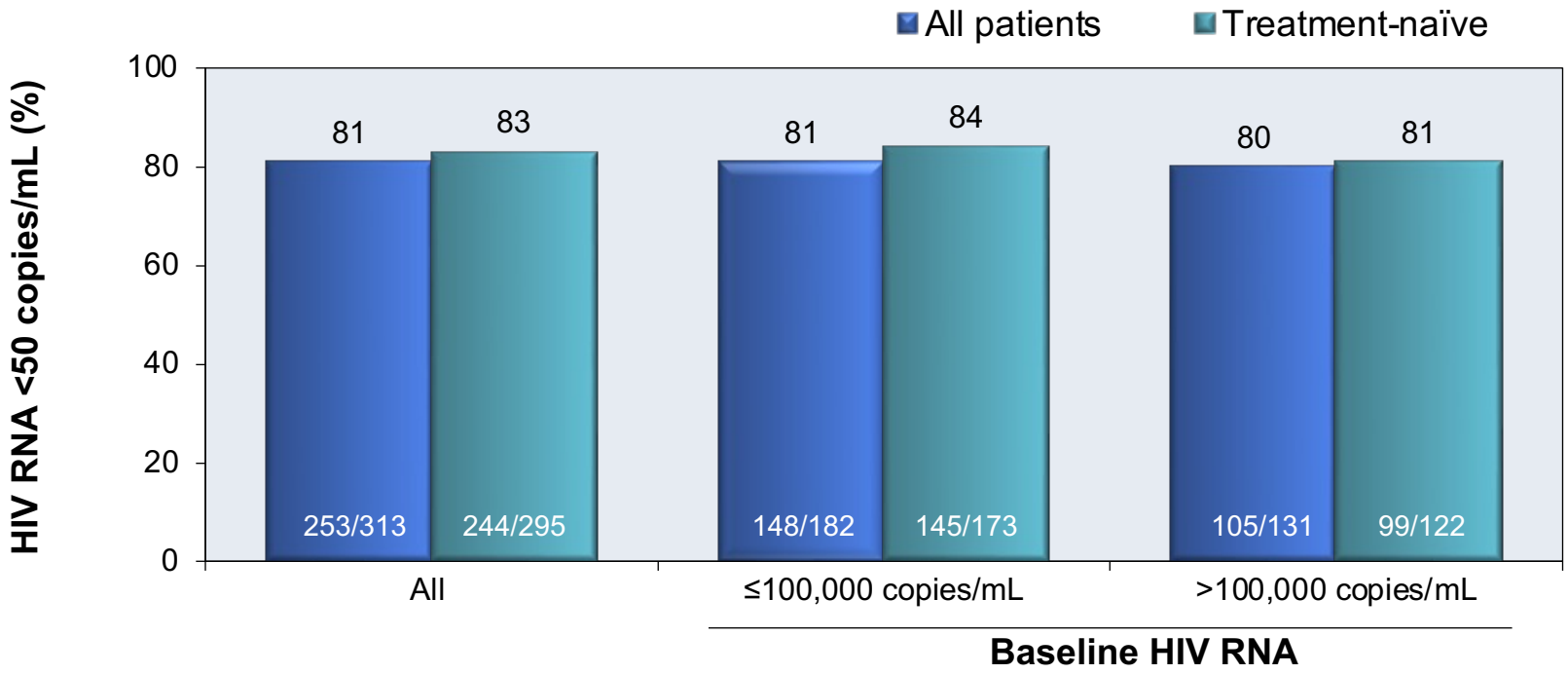
- **Background**: Phase 3b, open label, single-arm study to evaluate the safety and efficacy of cobicistat-boosted darunavir plus two NRTIs in antiretroviral treatment-naïve and treatment-experienced adults with HIV
- **Inclusions Criteria (n = 313)**
  - Antiretroviral treatment-naïve or –experienced
  - On stable ART for ≥12 weeks
  - HIV RNA ≥1000 copies/mL
  - GFR ≥80 mL/min
  - No darunavir-associated resistance mutations
  - Genotypic sensitivity to the two NRTIs
  - No past or current use of darunavir
- **Treatment Arms**
  - Cobicistat 150 mg QD + Darunavir 800 mg QD + 2 investigator-selected NRTIs

→ **Cobicistat + Darunavir + 2 NRTIs**
(n = 313)

Source: Tashima K, et al. AIDS Res Ther. 2014;11:39.

# Darunavir-Cobicistat + 2 NRTIs
# Study 130: Results

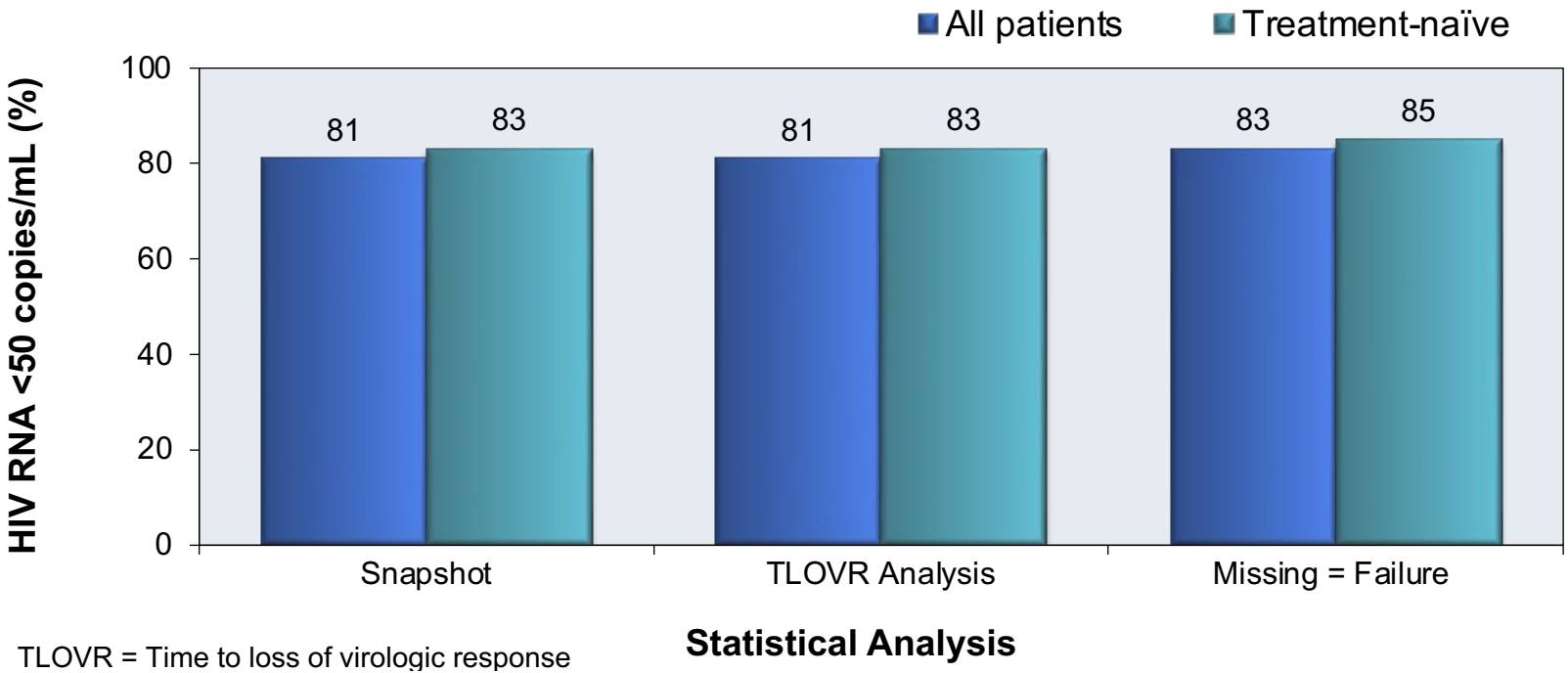
## Week 48: Virologic Response (Intent-to-Treat FDA Snapshot Analysis)




Source: Tashima K, et al. AIDS Res Ther. 2014;11:39.

# Darunavir-Cobicistat + 2 NRTIs
# Study 130: Results

## Week 48: Virologic Response, by Different Statistical Analyses




TLOVR = Time to loss of virologic response

Source: Tashima K, et al. AIDS Res Ther. 2014;11:39.

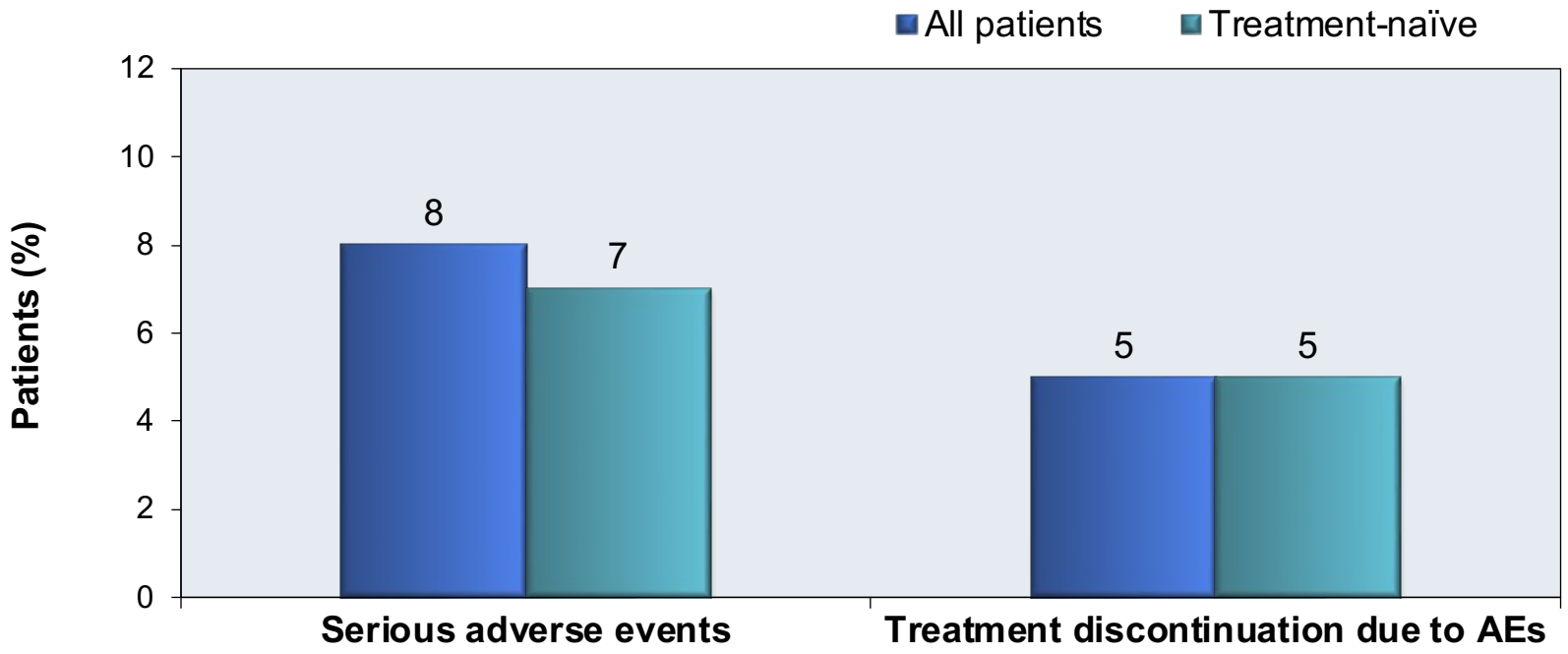
# Darunavir-Cobicistat + 2 NRTIs
# Study 130: Results

| Week 48: Adverse events (any grade), occurring in ≥ 10% of patients | | |
|---|---|---|
| Adverse Event | All Patients (N = 313) | Treatment-Naïve (N = 295) |
| Diarrhea | 27% | 27% |
| Nausea | 23% | 23% |
| Upper respiratory tract infection | 14% | 15% |
| Headache | 12% | 12% |

Source: Tashima K, et al. AIDS Res Ther. 2014;11:39.

# Darunavir-Cobicistat + 2 N(t)RTIs
# Study 130: Results

## Adverse Events and Treatment Discontinuations




Source: Tashima K, et al. AIDS Res Ther. 2014;11:39.

# Darunavir-Cobicistat + 2 NRTIs
# Study 130: Conclusion

**Conclusion**: “Darunavir/cobicistat 800/150 mg once daily was generally well tolerated through Week 48, with no new safety concerns. Pharmacokinetics, virologic and immunologic responses for darunavir/cobicistat were similar to previous data for darunavir/ritonavir 800/100 mg once daily.”

Source: Tashima K, et al. AIDS Res Ther. 2014;11:39.

Rilpivirine + Darunavir-Cobicistat Dual ART as an Alternative to Standard 3-Drug ART

# PROBE 2

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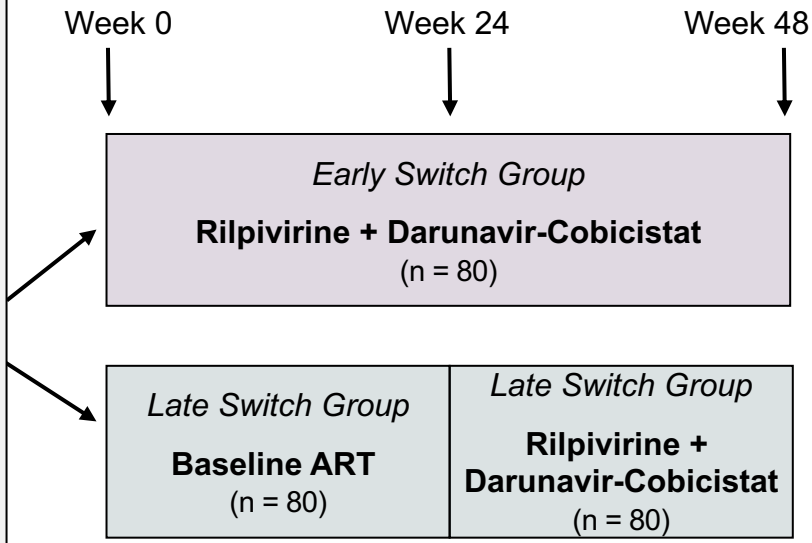
# Rilpivirine + Darunavir-Cobicistat versus Standard 3-Drug ART
# PROBE 2 Trial: Background

- **Background**: Randomized, open label, parallel group, active controlled trial comparing a switch to dual ART maintenance therapy with rilpivirine + darunavir-cobicistat versus continued 3-drug ART for individuals with a suppressed viral load
- **Enrollment Criteria**
  - Age ≥18 years
  - HIV RNA <50 copies/mL for ≥6 months
  - Taking an NNRTI, INSTI, or boosted PI, along with a 2-NRTI backbone
  - No INSTI or PI resistance-associated mutations
  - No chronic hepatitis B
  - Not pregnant or breastfeeding




Source: Maggiolo F, et al. Antivir Ther. 2021;26:51-7.

# Rilpivirine + Darunavir-Cobicistat versus Standard 3-Drug ART PROBE 2 Trial: Baseline Characteristics

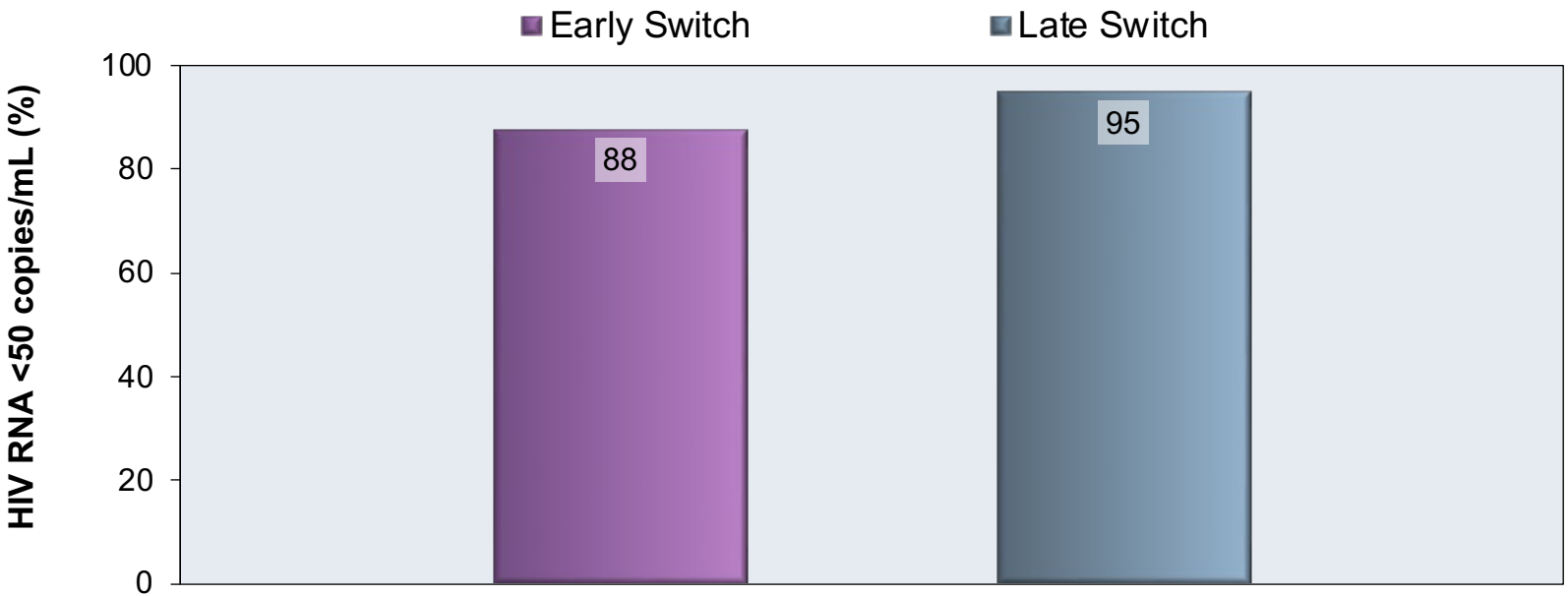
| Baseline Characteristic (%) | Early Switch (n = 80) | Late Switch (n = 80) |
|---|---|---|
| Main NRTI backbone agent | | |
| ABC | 22.5 | 12.5 |
| TAF | 30.0 | 35.0 |
| TDF | 47.5 | 52.5 |
| Core (anchor) agent | | |
| PI | 21.3 | 17.5 |
| NNRTI | 72.4 | 65.0 |
| INSTI | 6.3 | 17.5 |
| Number of pills in regimen | | |
| 1 | 55.0 | 67.5 |
| 2 | 36.3 | 28.8 |
| 3 | 8.8 | 3.8 |

Overall, 82.5% participants were men, 95.6% were white, and median age was 50 years

Source: Maggiolo F, et al. Antivir Ther. 2021;26:51-7.

# Rilpivirine + Darunavir-Cobicistat versus Standard 3-Drug ART PROBE 2 Trial: Baseline Characteristics

## Week 48 Virologic Response (Intention-to-Treat Analysis)




Virologic failure (HIV RNA >50 copies/mL) occurred in zero participants in early switch group and 2 participants in late switch group, though with no emergent drug resistance mutations.

Source: Maggiolo F, et al. Antivir Ther. 2021;26:51-7.

# Rilpivirine + Darunavir-Cobicistat versus Standard 3-Drug ART PROBE 2 Trial: Week 48 Results

| Variable (medians) | Early Switch (n = 80) | | | Late Switch (n = 80) | | |
|---|---|---|---|---|---|---|
| | Baseline | Week 48 | P Value | Baseline | Week 48 | P Value |
| Total cholesterol, mg/dL | 200 | 208 | 0.51 | 188 | 210 | <0.001 |
| HDL, mg/dL | 48 | 48 | 0.32 | 46 | 46 | 0.783 |
| LDL, mg/dL | 125 | 135 | 0.002 | 125 | 139 | <0.001 |
| Triglycerides, mg/dL | 126 | 156 | 0.004 | 125 | 164 | 0.001 |
| Bone stiffness, g/cm$^2$* | 83.9 | 86.0 | 0.017 | 85.4 | 87.1 | 0.894 |
| Body weight, kg | 69.5 | 69.0 | NR | 73.0 | 73.0 | NR |

*Bone stiffness measured by quantitative ultrasound

Source: Maggiolo F, et al. Antivir Ther. 2021;26:51-7.

# Rilpivirine + Darunavir-Cobicistat versus Standard 3-Drug ART
# PROBE 2 Trial: Conclusions

**Conclusions**: “The combination of rilpivirine plus darunavir/cobicistat sustained virological suppression, was associated with a low frequency of virological failure, and had a favorable safety profile, which support its use as a nucleoside reverse transcriptase inhibitor-sparing and integrase inhibitor-sparing alternative to three-drug regimens.”

Source: Maggiolo F, et al. Antivir Ther. 2021;26:51-7.

# Acknowledgments

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AETC AIDS Education & Training Center Program

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