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**EPZICOM[®] Virologic Response in
ART-Naïve Patients with Baseline
Viral Loads Above and Below
100,000c/mL Using the A5202
Endpoint**

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17th IAC 2008;Oral:THAB0304.

Background

- **Primary endpoints utilized in A5202 are unique**
- **The A5202 interim results:**
 - are unexpected
 - not consistent with prior clinical experience
 - raise the question of whether the two nucleoside backbones have comparable efficacy and safety

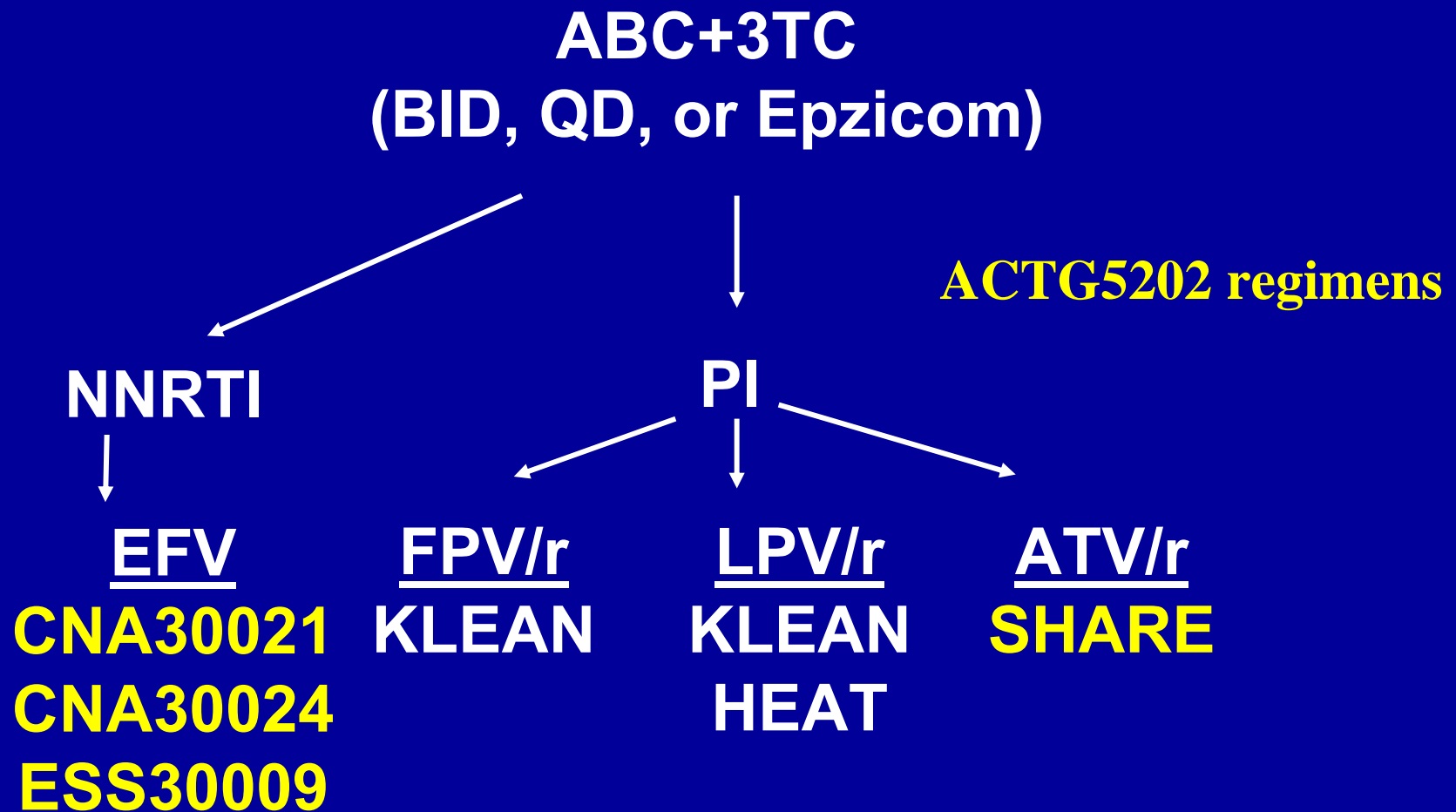
Outline

- **Is ABC/3TC really less effective in $\geq 100,000$ c/mL?**
 - Review of data from six trials using A5202 endpoints
 - Review of 96 week HEAT data
- **Is ABC/3TC really less tolerable than TDF/FTC?**
 - HEAT Data:
 - A5202 safety endpoint
 - Adverse experiences → discontinuation
 - Lipid changes (NCEP guidelines)

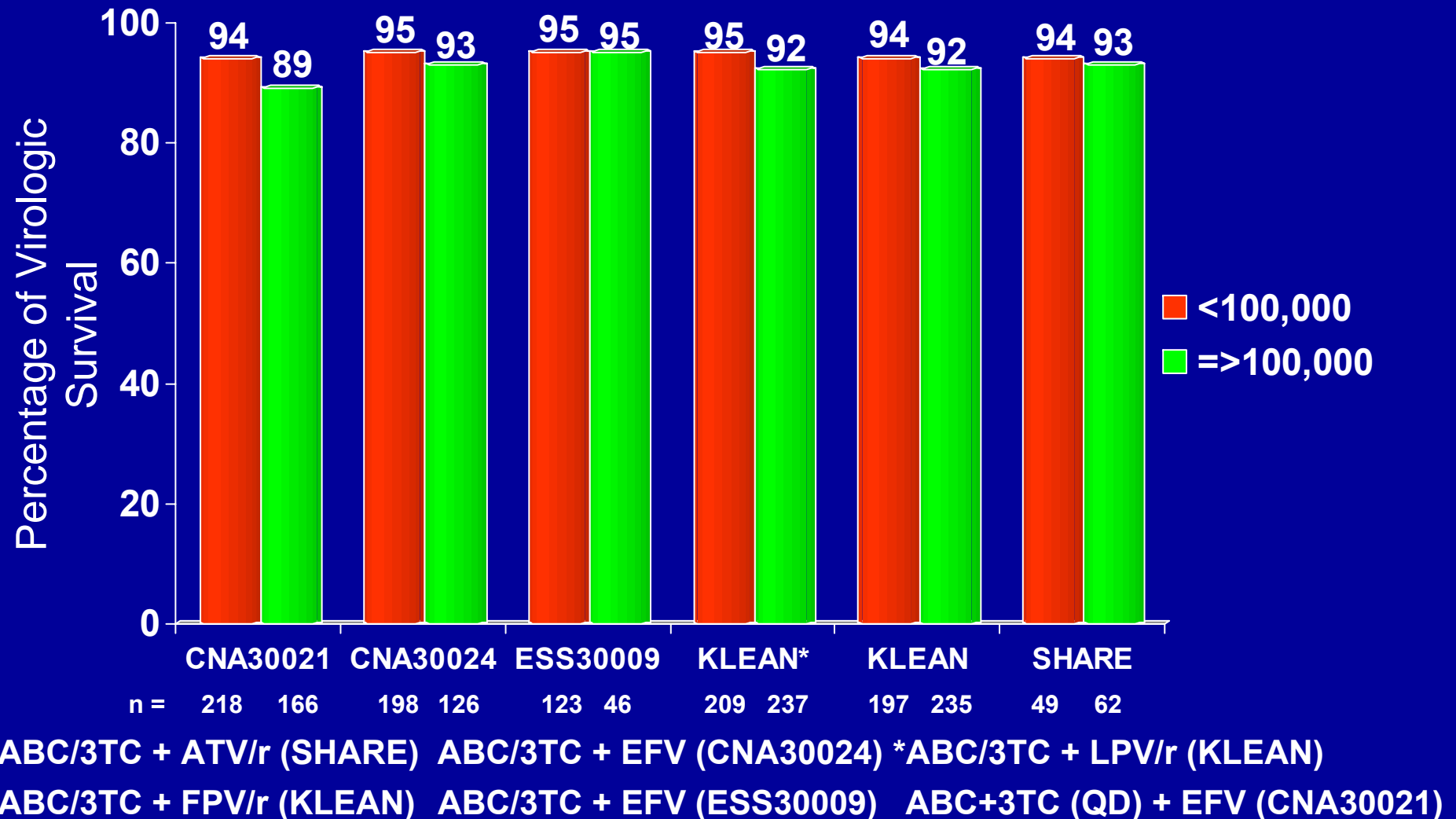
A5202 Primary Efficacy Endpoint

- Time to virologic failure (VF)
- VF: confirmed VL ≥ 1000 c/mL at or after 16 weeks and before 24 weeks or ≥ 200 c/mL at or after 24 weeks

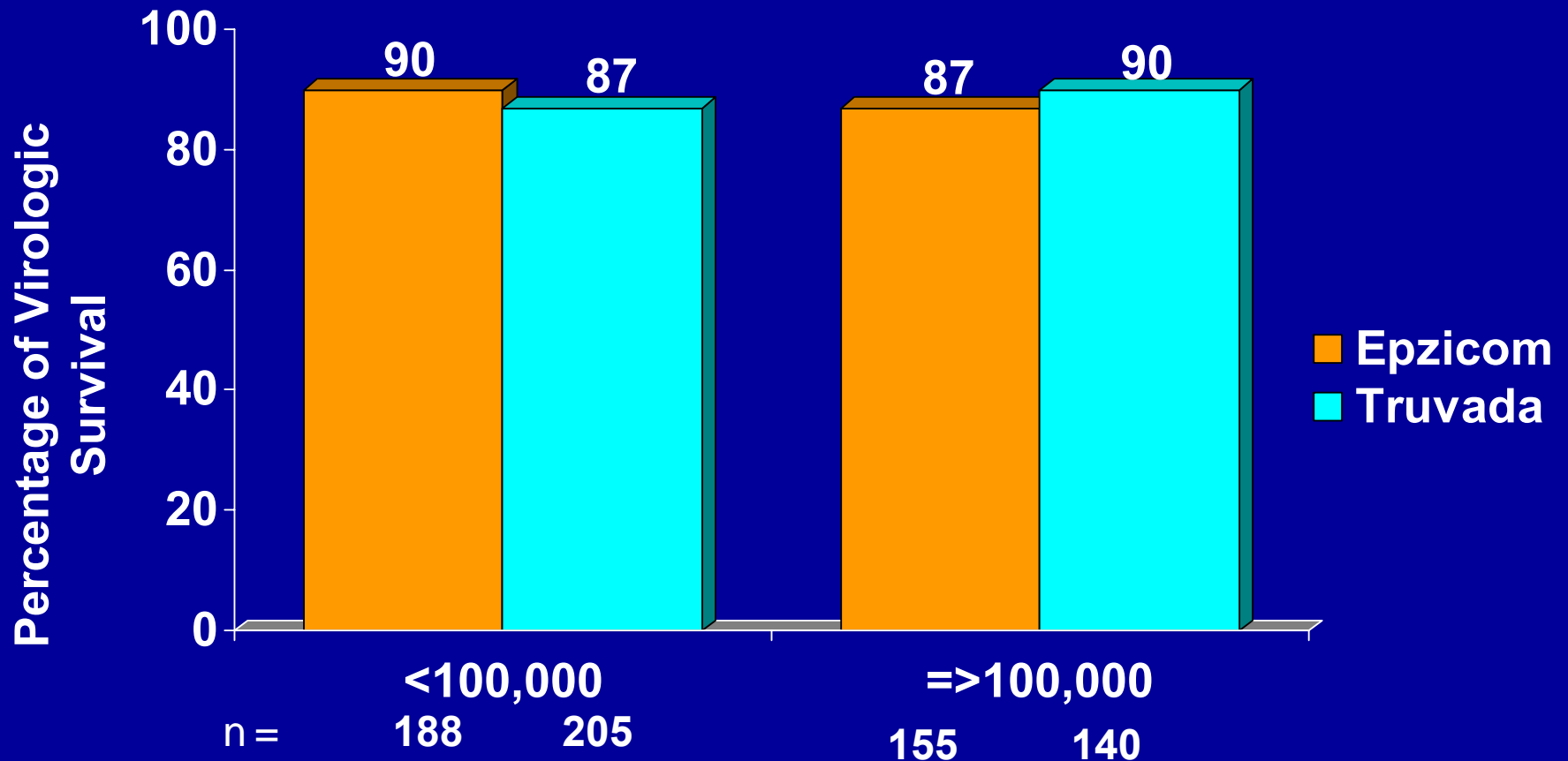
Clinical Trials with Third Drugs ($N \geq 100$)



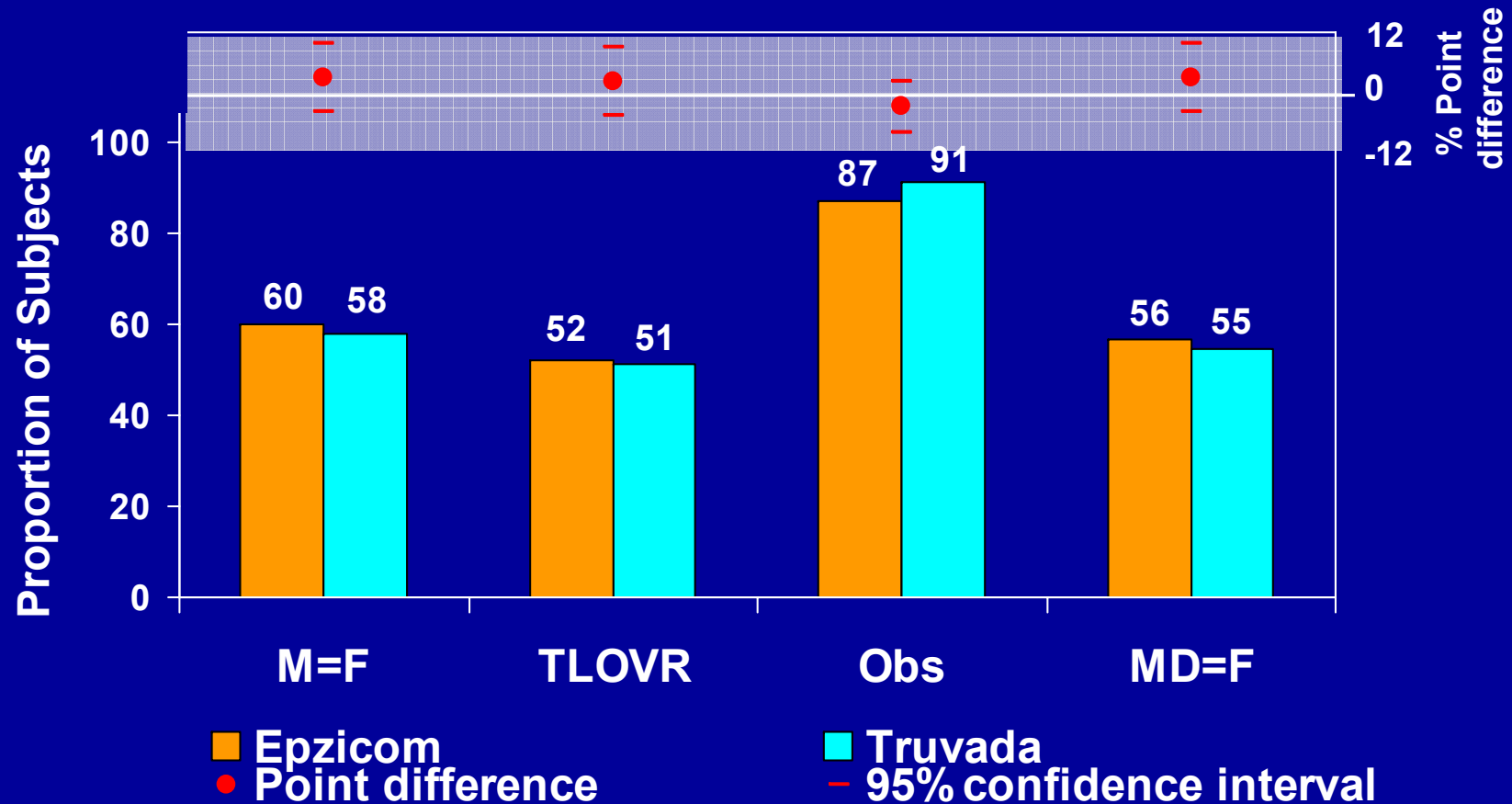
Probability of Protocol-Defined Virologic Survival by Week 48 by BL Viral Load Using the A5202 Efficacy Endpoint¹



HEAT: Probability of Protocol-Defined Virologic Survival by Week 48 by BL Viral Load Using the A5202 Efficacy Endpoint¹



HEAT: HIV-1 RNA <50 c/mL at Week 96



Efficacy Summary

- **Data from six clinical trials using A5202 endpoints indicates consistency in efficacy between low and high VL strata**
- **HEAT 96 week data confirm non-inferiority of ABC/3TC with TDF/FTC**

A5202 Primary Safety Endpoint Component

- Time from treatment dispensation to the first development of Grade 3 or 4 sign, symptom or laboratory abnormality that is at least one grade higher than at baseline*
- CK and bilirubin laboratory values were **excluded**

*HLA-B*5701 screening was not standard of care at study initiation

HEAT 48 Week: Grade 3-4 Sign, Symptom, or Lab Toxicity \geq 1 Grade Higher than BL for Patients with BL VL \geq 100,000 c/mL¹

| | Epzicom (N=155) | Truvada (N=140) |
|-----------------------|--------------------|--------------------|
| GFR decreased | 3(2%) | 3(2%) |
| Diarrhea | 2(1%) | 3(2%) |
| Drug hypersensitivity | 3(2%) | 1(<1%) |
| Pneumonia | 3(2%) | 1(<1%) |
| Phosphorus | 5(3%) | 3(2%) |
| Neutrophils | 3(2%) | 4(3%) |
| Triglycerides | 5 (3%) | 1(<1%) |
| Cholesterol | 5(3%) | 0 / 0 |
| Glucose | 1(1%) | 3(2%) |
| ALT | 4(3%) | 1(<1%) |
| AST | 1(<1%) | 3(2%) |

HEAT Trial - 96 Week: AEs in ≥ 2 Subjects Leading to Study Discontinuation for Subjects with BL HIV-1 RNA $\geq 100,000$ c/mL

| | Epzicom (N=155) | Truvada (N=140) |
|---------------------------------------|--------------------|--------------------|
| Subjects with any event | 8 (5%) | 11 (8%) |
| Blood triglycerides increased | 2 (1%) | 1 (<1%) |
| Mycobacterium avium complex infection | 0 | 2 (1%) |

HEAT Trial- 96 Week: AEs in ≥ 2 Subjects Leading to Study Discontinuation

| | Epzicom (N=343) | Truvada (N=345) |
|---------------------------------------|--------------------|--------------------|
| Subjects with any event | 19 (6%) | 22 (6%) |
| Diarrhea | 1 (<1%) | 2 (<1%) |
| Vomiting | 1 (<1%) | 2 (<1%) |
| Nausea | 0 | 2 (<1%) |
| Blood triglycerides increased | 3 (<1%) | 2 (<1%) |
| Hypercholesterolemia | 1 (<1%) | 1 (<1%) |
| AST increased | 2 (<1%) | 1 (<1%) |
| ALT increased | 1 (<1%) | 1 (<1%) |
| Mycobacterium avium complex infection | 0 | 2 (<1%) |
| Pneumonia | 1 (<1%) | 1 (<1%) |
| Hyperlipidaemia | 2 (<1%) | 1 (<1%) |
| Drug hypersensitivity | 2 (<1%) | 0 |
| Renal Failure | 0 | 2 (<1%) |

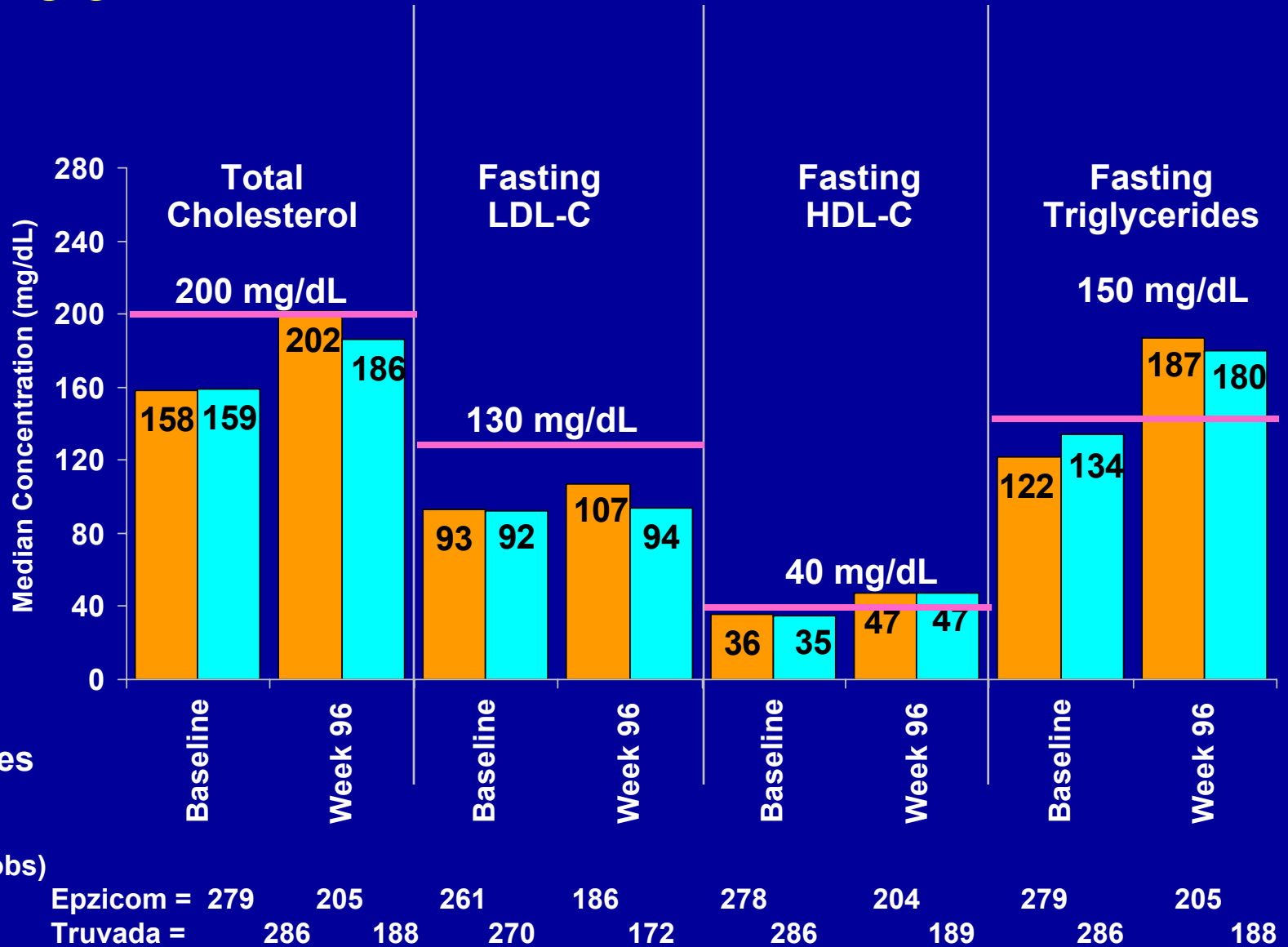
HEAT Study: Fasting Lipid Changes to Week 96

Epzicom

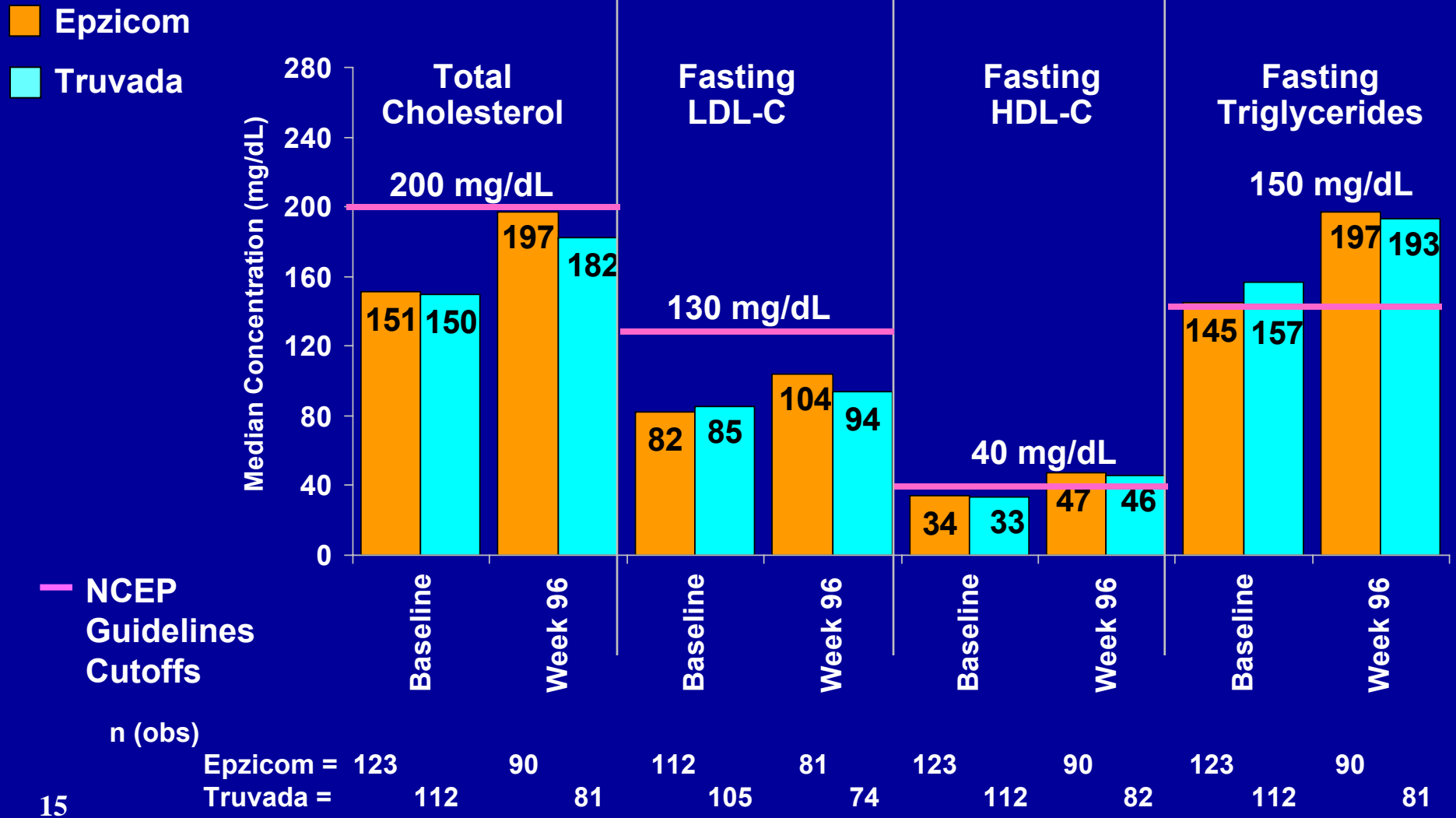
Truvada

NCEP Guidelines Cutoffs

n (obs)



HEAT data: Fasting Lipid Changes to Week 96 for Subjects with Baseline HIV-1 RNA $\geq 100,000$ c/mL



Safety Summary

- **HEAT data utilizing the A5202 endpoint and typical safety endpoints indicate both ABC/3TC & TDF/FTC regimens are:**
 - well-tolerated
 - have comparable safety
 - few study discontinuations due to AEs

Conclusions

- **Recent A5202 findings:**
 - are unexpected
 - different from clinical experience
- **A5202 primary efficacy & safety endpoints are unique**
- **Using A5202 endpoints, analysis of 6 other clinical studies utilizing an ABC/3TC regimen demonstrates robust results irrespective of baseline viral loads**

Conclusions (cont.)

- **96 week HEAT data:**
 - **confirms non-inferiority of ABC/3TC & TDF/FTC**
 - **both regimens are:**
 - **well-tolerated**
 - **comparable safety**
 - **few study discontinuations due to AEs**
 - **no increase in hs-CRP and IL-6 from baseline to weeks 48/96 with ABC/3TC or TDF/FTC. No significant differences between the treatment groups¹**

A5202 Questions Still to be Addressed

- **Study is still ongoing**
- **What is the impact of:**
 - **Baseline resistance**
 - **Treatment interruptions**
 - **Adherence data**
 - **Lipid changes using NCEP guidelines**
 - **Stratifying by screening VL using local labs**
 - **Differences in endpoints**



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