Similar Efficacy and Tolerability of Atazanavir Compared to Atazanavir/Ritonavir, each with ABC/3TC after Initial Suppression with ABC/3TC + ATV/r

84 Week Results of the ARIES Trial

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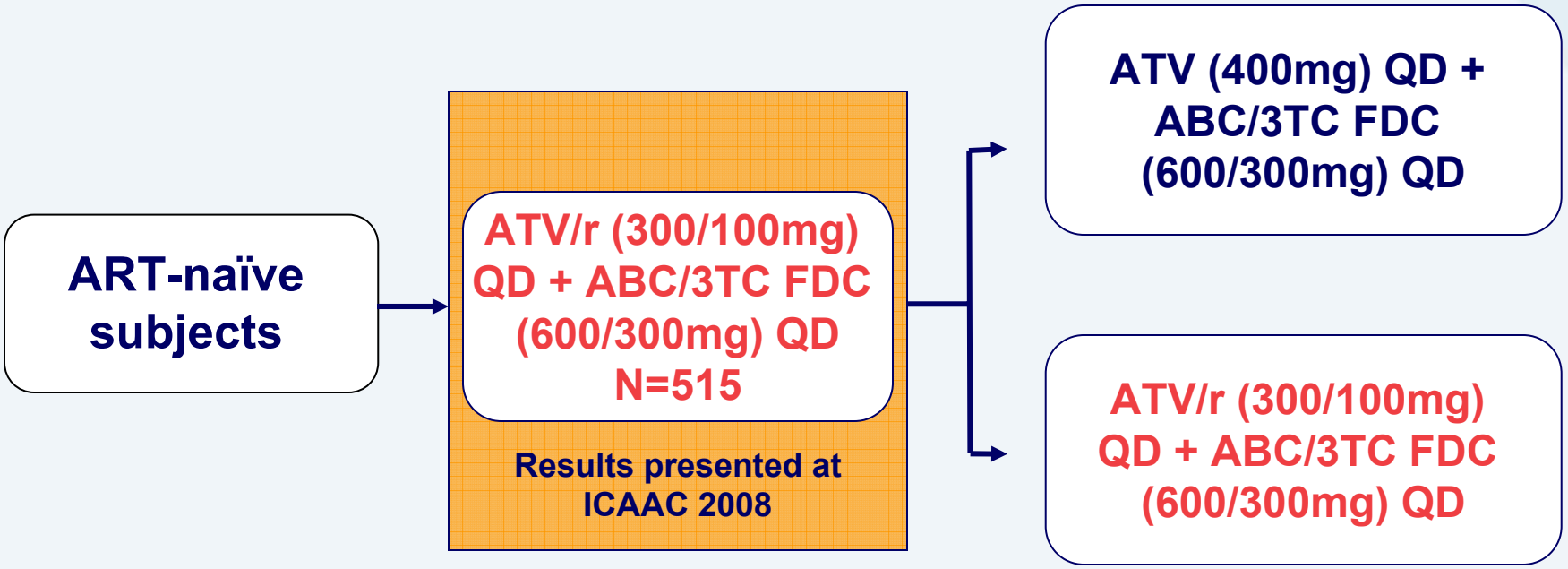
Study Design

Phase IIIb, randomized (1:1), open-label, non-inferiority study



Randomization

48 weeks

Entry criteria:
- HIV-1 RNA ≥1000 c/mL
- No CD4 cell count restrictions
- Appropriate genotype
- HLA-B*5701 negative

Stratified at randomization by baseline HIV-1 RNA < or ≥100,000 c/mL

*Optional treatment extension to Week 144

Study Design

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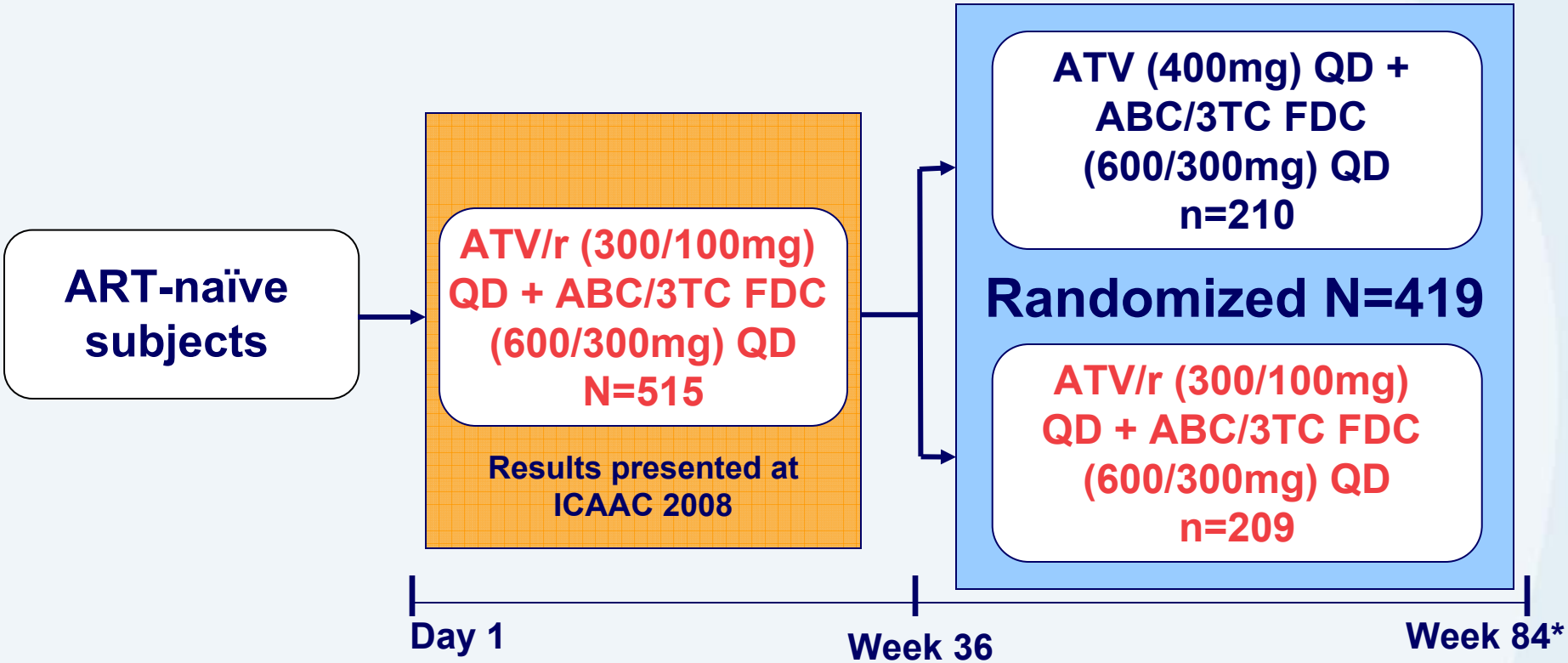


Randomization criteria:

- Confirmed RNA <50 c/mL prior to Week 36
- RNA <50 c/mL immediately preceding Week 36
- No protocol defined virologic failure

*Optional treatment extension to Week 144

Objectives/ Endpoints

Primary Objective

- Evaluate & compare efficacy, safety, tolerability, and durability of antiviral response between the randomized treatment groups over 48 weeks

Endpoints

- Primary
  - Proportion of subjects with HIV RNA <50 c/mL (TLOVR) at Week 84
- Secondary/Exploratory
  - Proportion of subjects with HIV RNA <50 c/mL and <400 c/mL
  - Change from baseline in HIV RNA and CD4+ cell count
  - Resistance in subjects with virologic failure
  - Safety

Baseline Demographics, Randomized Population (ITT-E)

	ATV n=210	ATV/r n=209	Total n=419
Mean age, years	38	40	39
Male	176 (84%)	177 (85%)	353 (84%)
Racial Distribution			
White	133 (63%)	132 (63%)	265 (63%)
Black	67 (32%)	68 (33%)	135 (32%)
Other	10 (5%)	9 (4%)	19 (5%)
CDC Class C	34 (16%)	17 (8%)	51 (12%)
Hepatitis C positive	10 (5%)	13 (6%)	23 (5%)
Framingham Score			
≤ 10 (low risk)	90%	90%	--
10 – 20 (medium risk)	9%	8%	--
≥ 20 (high risk)	2%	2%	--

Baseline Characteristics, Randomized Population (ITT-E)

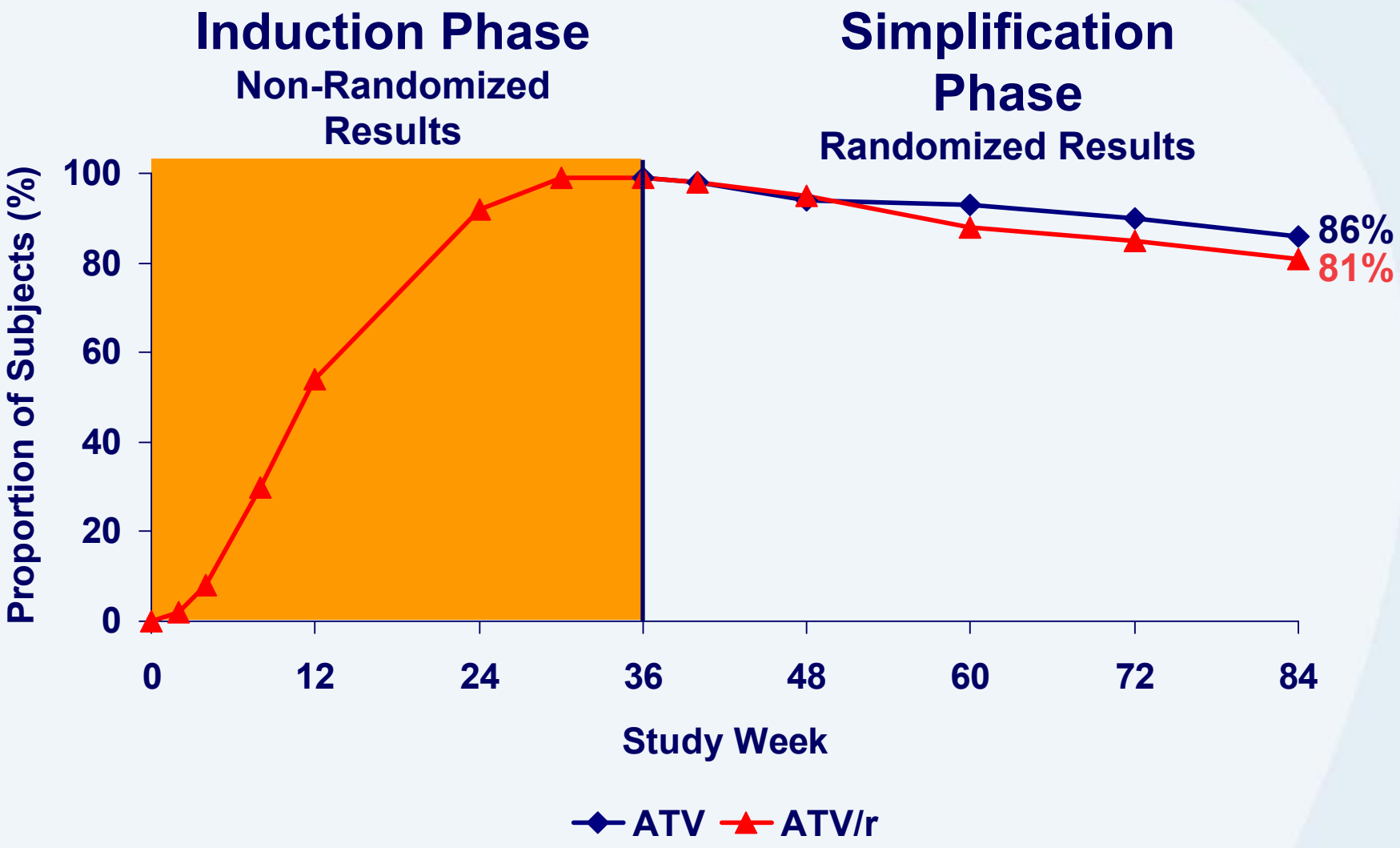
	ATV n=210	ATV/r n=209	Total n=419
Median HIV RNA, log_{10} c/mL	5.05	5.06	5.05
<100,000 c/mL	88 (46%)	83 (47%)	171 (46%)
≥100,000 c/mL	106 (53%)	104 (54%)	210 (53%)
Median CD4+ count, cells/mm^3			
>200	103 (49%)	107 (51%)	210 (50%)
50 - ≤200	70 (33%)	83 (40%)	153 (37%)
<50	37 (18%)	19 (9%)	56 (13%)

Study Outcomes, Randomized Population (ITT-E)

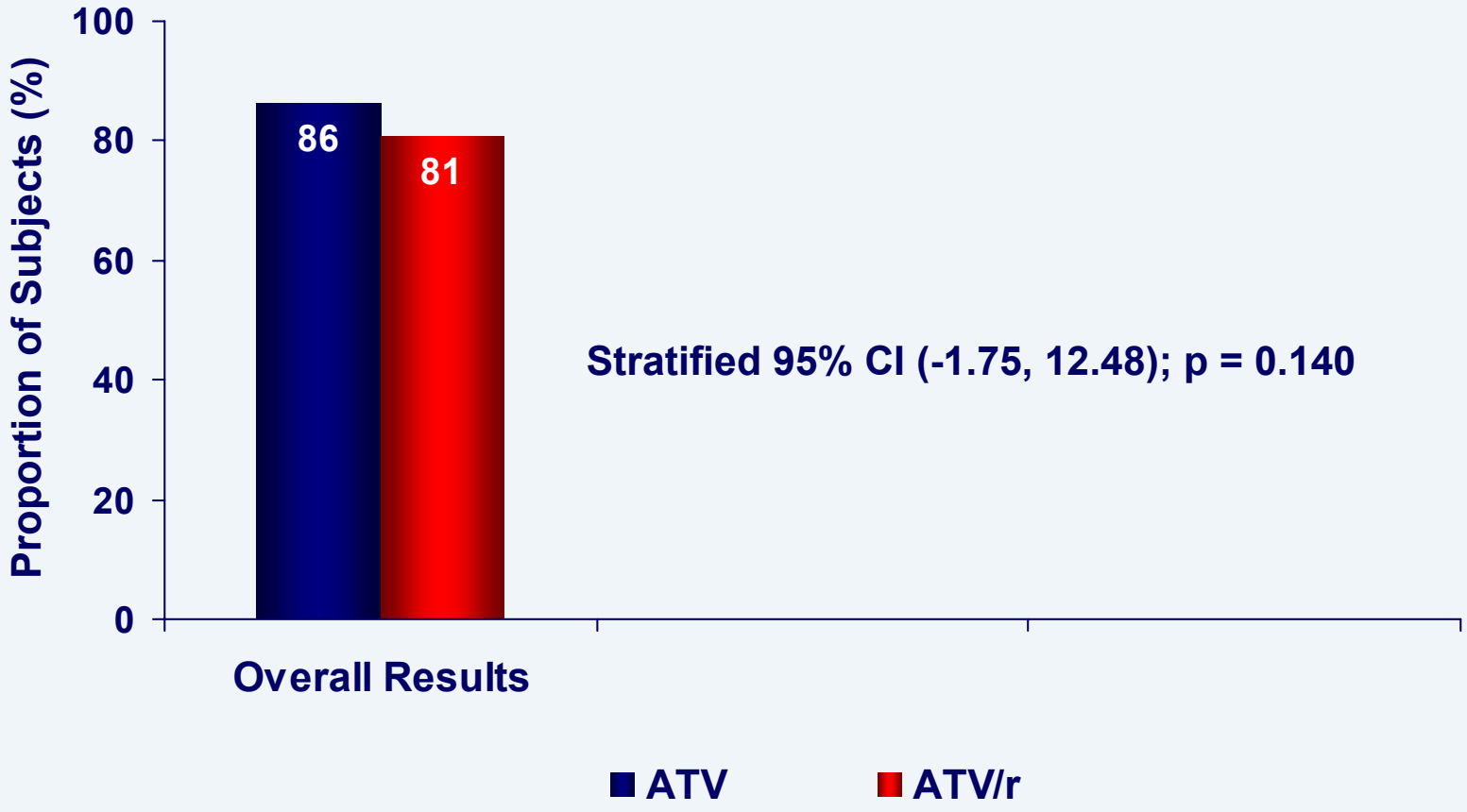
	ATV n=210	ATV/r n=209	Total n=419
Completion Status			
Completed	194 (92%)	185 (89%)	379 (90%)
Prematurely withdrawn	16 (8%)	24 (11%)	40 (10%)
Primary Reason for Withdrawal*			
n	16 (8%)	24 (11%)	40 (10%)
Adverse event	2 (<1%)	5 (2%)	7 (2%)
Protocol violation	0	1 (<1%)	1 (<1%)
Protocol defined virologic failure	1 (<1%)	1 (<1%)	2 (<1%)
Lost to follow-up	2 (1%)	8 (4%)	10 (2%)
Subject decision	2 (1%)	4 (2%)	6 (3%)
Non-compliance	3 (1%)	4 (2%)	7 (2%)

*as noted on the CRF

HIV RNA <50 copies/mL, Randomized Population (ITT-E, TLOVR)

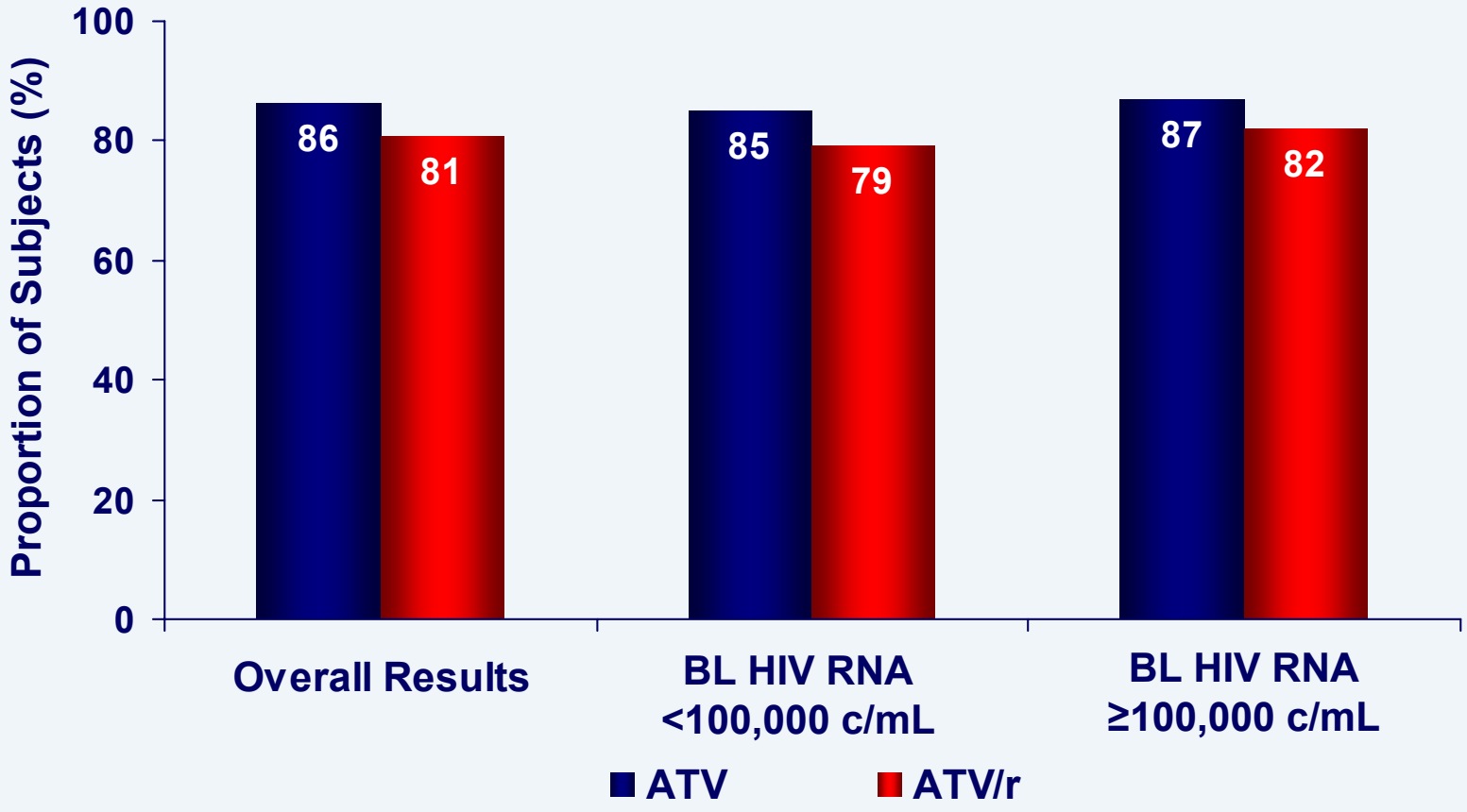


HIV RNA <50 copies/mL at Week 84, Randomized Population (ITT-E, TLOVR)

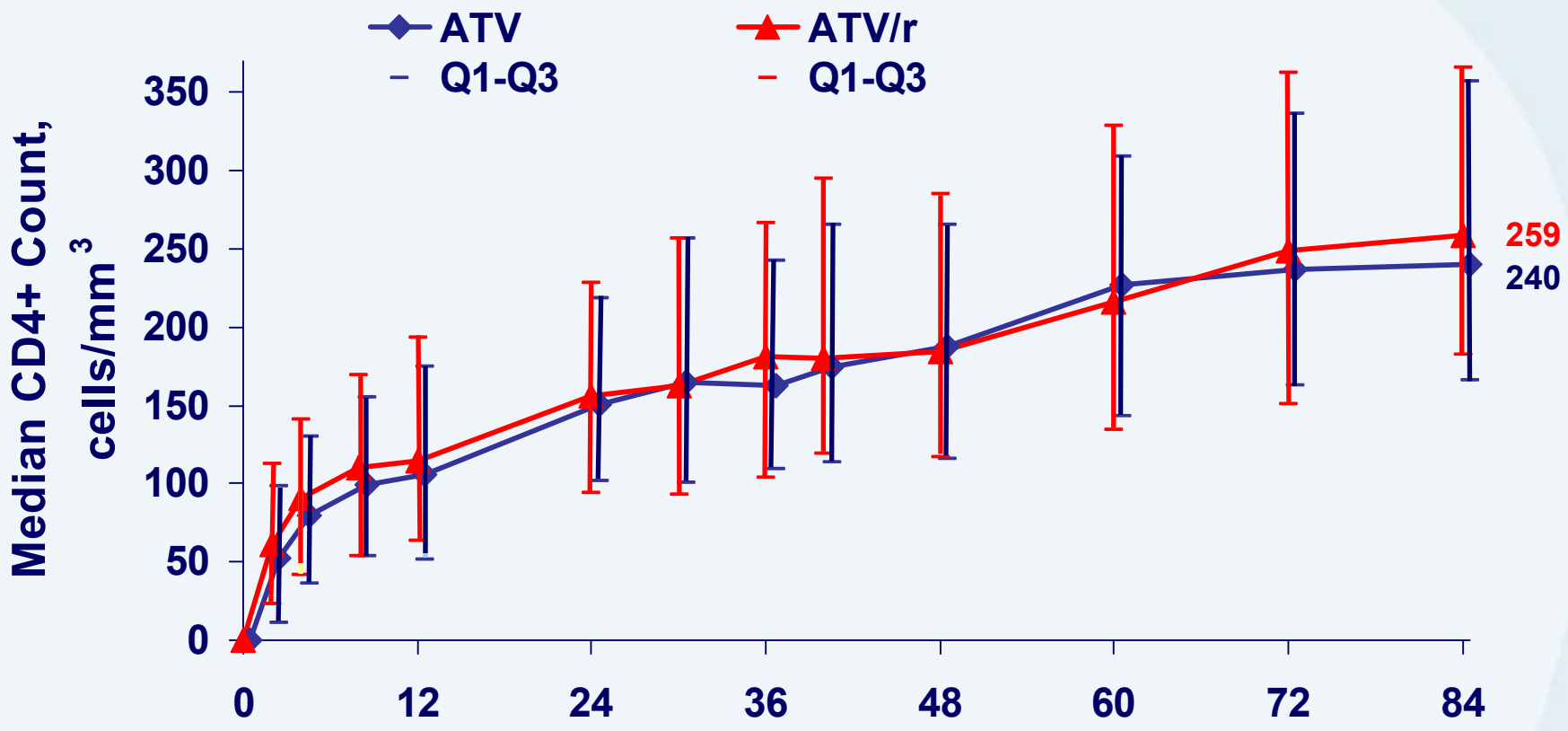


HIV RNA <400 c/mL at Week 84 (TLOVR): ATV 92% vs. ATV/r 86%, 95% CI (0.44, 12.22); p = 0.036

HIV RNA <50 copies/mL at Week 84, Randomized Population (ITT-E, TLOVR)



Change in CD4+ Cell Count from Baseline, Randomized Population (ITT-E, Observed)



Median CD4+	197 204							434 469
n (ATV)=	210	208	204	203	208	201	194	193
n (ATV/r)=	209	209	207	203	204	200	191	187

Protocol Defined Virologic Failure, Randomized Population (ITT-E)

	ATV n=210	ATV/r n=209	Total n=419
Confirmed Virologic Failures	**1 (0.5%)**	**7 (3%)**	**8 (2%)**
Treatment Emergent Mutations	1	2*	3
RT Region			
M184M/I/V	1	0	1
Major PI Mutations	0	0	0

Subject with M184M/I/V did have reduced susceptibility to 3TC at time of failure.
*Two PI polymorphisms, G16G/E and K20K/R, were detected at failure: HIV from these subjects remained susceptible to all PIs.

Definition of Virologic Failure

Baseline to Week 36:

- Failure to achieve HIV RNA <400 c/mL by Week 30
- Confirmed HIV RNA ≥400 c/mL after achieving <400 c/mL

After Week 36:

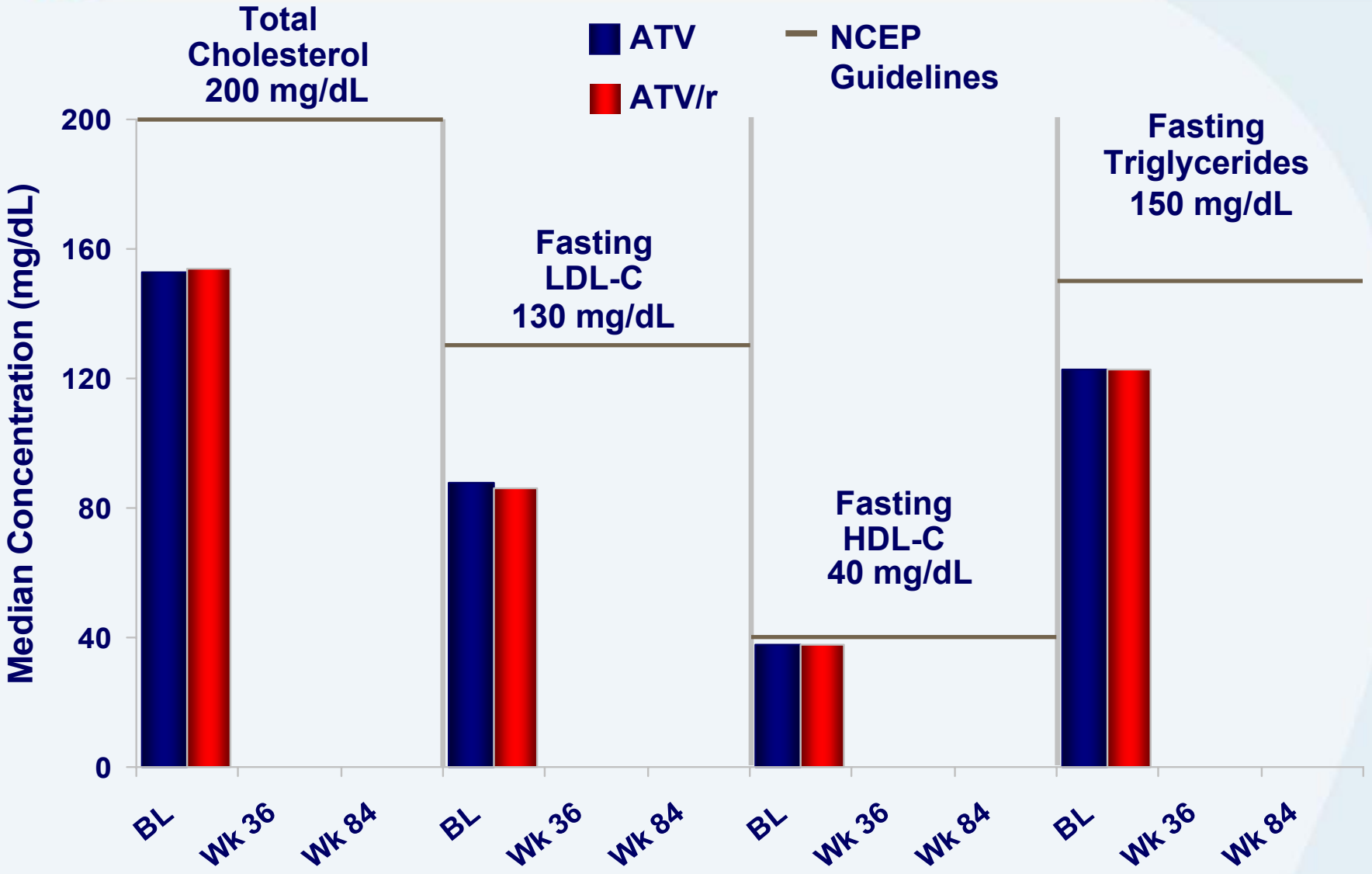
- Confirmed HIV RNA ≥400 c/mL

Treatment-Related Adverse Events (≥5%), Randomized Population (ITT-E)

	ATV n=210	ATV/r n=209
Induction Phase (BL to Week 36)		
Grade 2-4 AEs	54 (26%)	54 (26%)
Hyperbilirubinemia	30 (14%)	25 (12%)
Randomized Phase (Week 36 to 84)		
Grade 2-4 AEs	22 (10%)	29 (14%)
Hyperbilirubinemia	9 (4%)	20 (10%)

Note: No MIs reported to date

Fasting Lipids



Lipid lowering medication usage: ATV 13% vs. ATV/r 16% through 84 weeks

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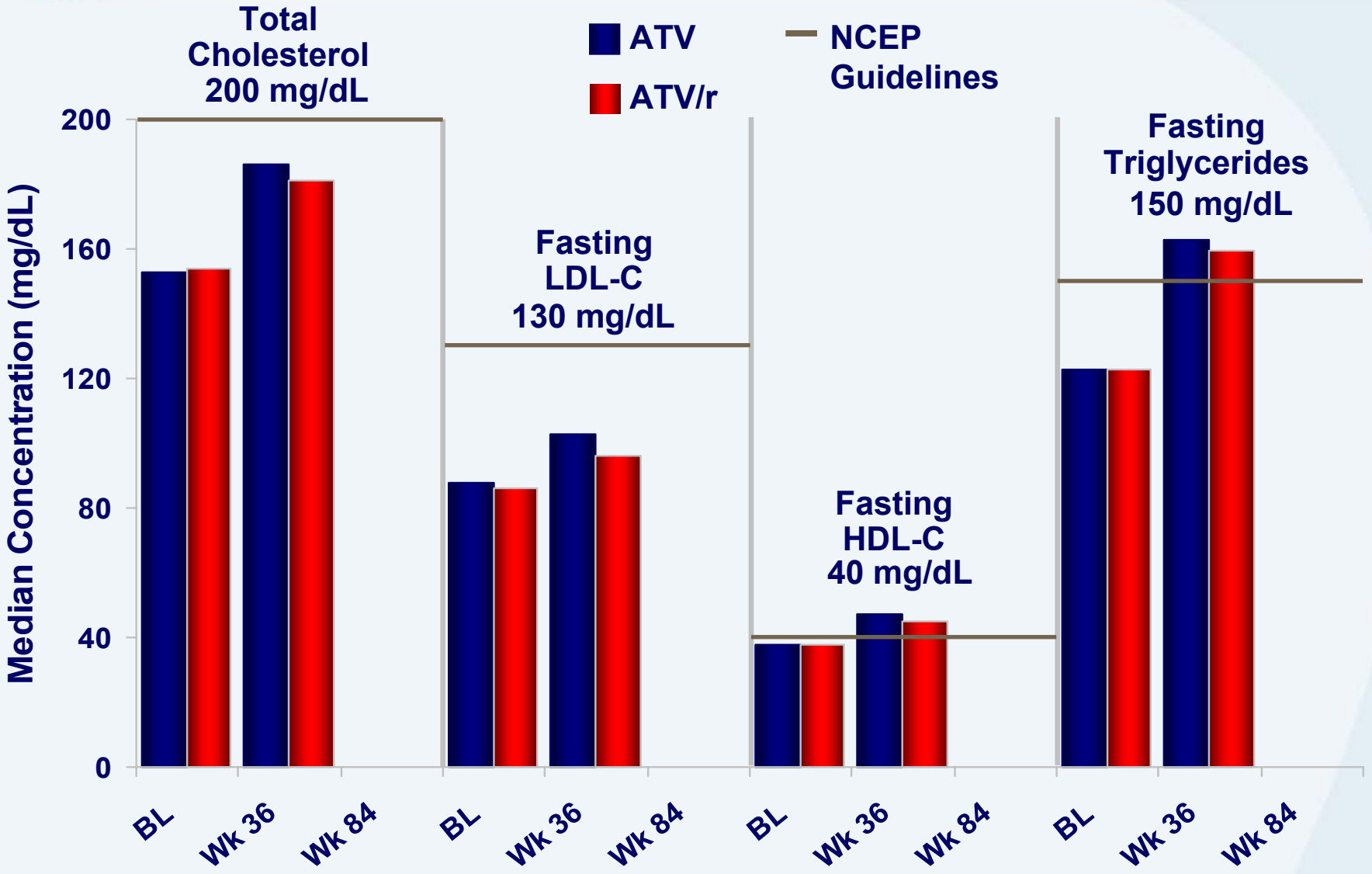

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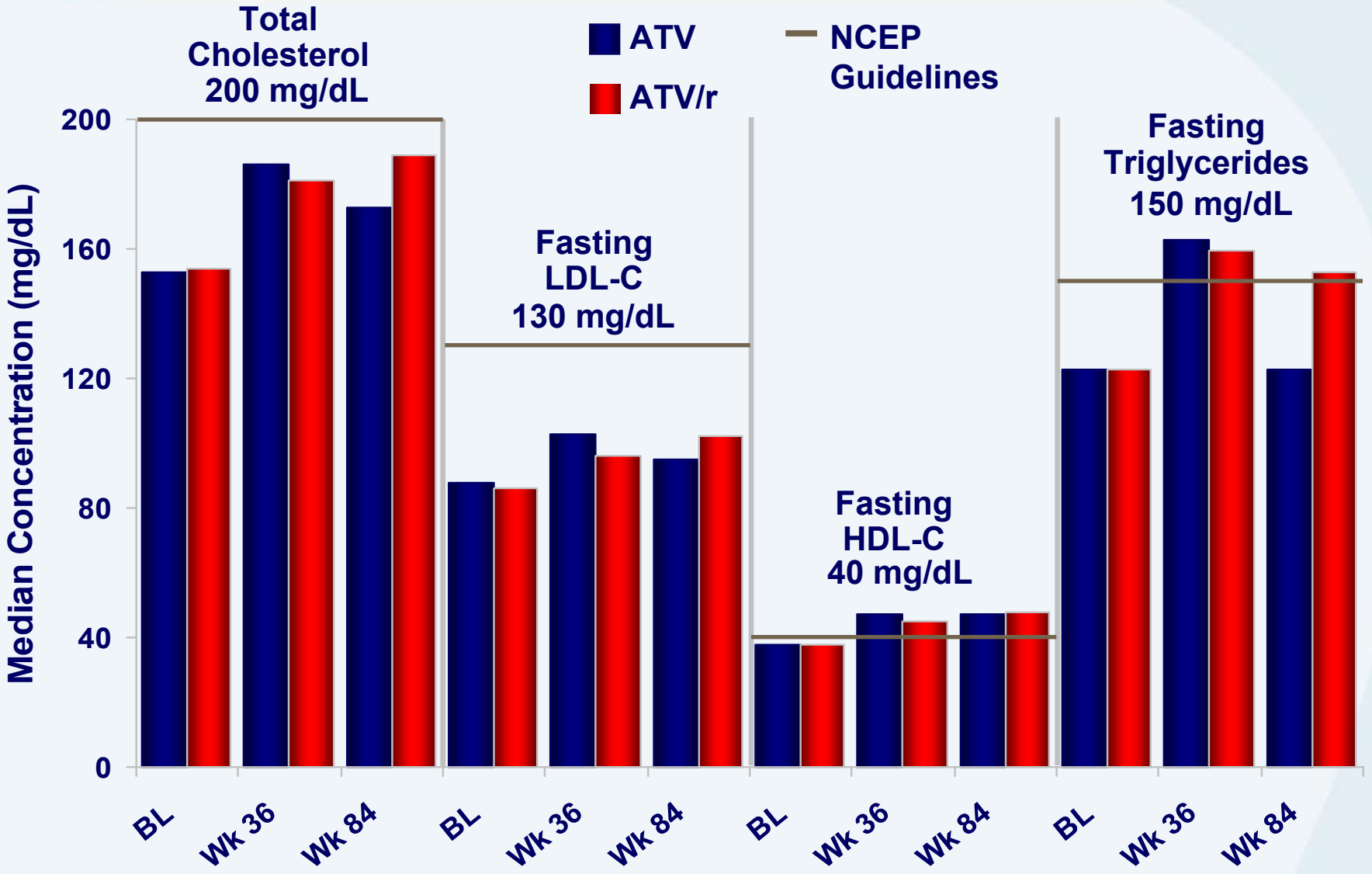

Lipid lowering medication usage: ATV 13% vs. ATV/r 16% through 84 weeks

Conclusions

- ATV demonstrated similar efficacy to ATV/r (non-inferior: TLOVR < 50 c/mL), each in combination with ABC/3TC, regardless of baseline viral load
- Both treatment regimens were generally well tolerated over 84 weeks
- Subjects in the simplification arm demonstrated a more favorable lipid profile and decreased bilirubin levels compared to those in the continuation arm
- Protocol-defined virologic failure was infrequent (2%) from Week 36 to 84
  - There were no major treatment-emergent PI mutations