Body Fat Effects of Atazanavir (ATV) and Efavirenz (EFV) Each Combined With Fixed-Dose Zidovudine (ZDV) and Lamivudine (3TC)

48-Week Results From the Metabolic Substudy of BMS-034

JG Jemsek, E Arathoon, M Arlotti, C Perez, N Sosa, V Pokrovskiy, M Giordano, A Thiry, M Soccodato

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HIV and Body Fat Changes: Background

- **Effects of Current PI Treatment**
  - Treatment with existing PIs is associated with changes in body composition
    - IDV associated with accumulation of intra-abdominal (visceral) fat [1]
    - NFV associated with significant reduction in limb fat [2]
  - Significant increases in cholesterol and triglycerides observed across existing PI class
- **FRAM Study [3]**
  - HIV+ patients have less limb and visceral fat compared to HIV- controls

[1] Miller KD *et al*. *Lancet* 1998; 351:871-875
[2] Dubé *et al*. Abstract 27. *4th Lipodystrophy Workshop*, San Diego, Sept 2002
[3] Grunfeld C *et al*. XIV IAC, Barcelona, July 2002. TuOr158

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Atazanavir Background

- **Once-daily azapeptide PI**
  - C_{min} > protein-binding adjusted EC_{90} for > 36 hr
- **Low pill burden (2 capsules/day, 400 mg)**
- **Efficacy in naïve and experienced patients**
- **Favorable lipid profile (TC, fasting LDL-C, fasting TG)**
- **Does not inhibit insulin-mediated glucose transport via GLUT-4**

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BMS-034 Metabolic Substudy

Objectives

- To assess the effect of ATV on body composition by measuring the change from baseline through week 48 in:
  - Visceral adipose tissue (VAT)
  - Subcutaneous adipose tissue (SAT)
  - Total adipose tissue (TAT)
  - Appendicular, truncal, total body fat
- To assess changes in serum lipid levels, fasting glucose and insulin levels

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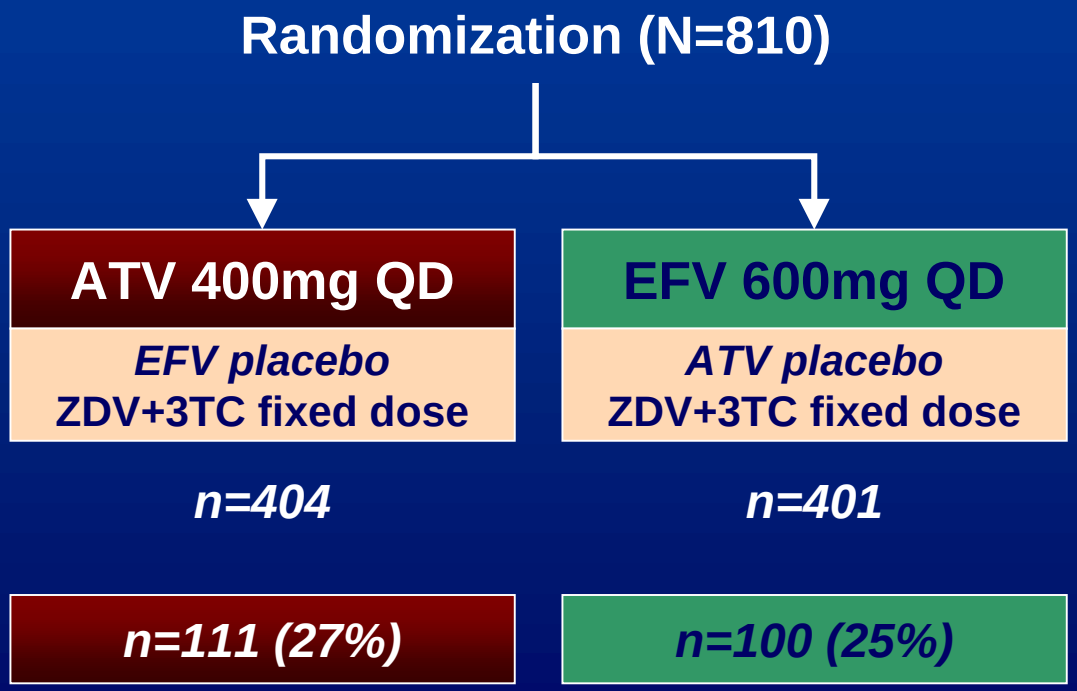
Study Design

Randomized, double-blind, double-dummy, active-controlled

Treatment-naïve patients: HIV RNA ≥2000 c/mL, CD4 ≥100 cells/mm^3



*At time of initial randomization

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Exclusion Criteria

- Uncontrolled hypercholesterolemia
- History of cardiac disease
- Triglyceride level >750 mg/dL
- Untreated hypogonadism
- Receipt of agents with metabolic changes

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BMS-034 Metabolic Substudy

Assessments

L4/L5 Cross Section Computerized Tomography *(CT)*

- Visceral Adipose Tissue (VAT)
- Subcutaneous Adipose Tissue (SAT)
- Total Adipose Tissue (TAT)

Dual Energy X-Ray Absorptiometry *(DEXA)*

- Appendicular fat
- Truncal fat
- Total body fat

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Analyses

- Analyses included all patients with assessments prior to dosing initiation and after Week 24
- Patients discontinued after Week 24: LOCF to Week 48 (n=2 [approx 4%] per group)
- Centralized readings performed at Tufts University

BMS-034 Metabolic Substudy

Patient Baseline Characteristics

	ATV N=111	EFV N=100	*Total 034 N=805*
Age, median, yr	30	29	33
Female, %	26	29	35
Race, %			
Hispanic/Latino	49	48	37
White	45	45	33
Other	6	7	30
IDU, %	8	14	6
AIDS, %	3	4	5
HIV RNA, median, $\log_{10}$ c/mL	4.84	4.69	4.88
CD4 count, median, cells/mm^3	328	323	282
BMI, median, kg/m^2	23.5	23.2	23.5

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Baseline Body Fat

	ATV	EFV
Adipose tissue, median (cm^2)	N=75	N=69
VAT	45.3	46.9*
SAT	136.9	125.9
TAT	188.9	183.8
Body fat, median (kg)	N=90	N=80
Appendicular	5.1	5.4
Truncal	6.9	6.5
Total body	13.0	13.0†

*N=68, †N=79

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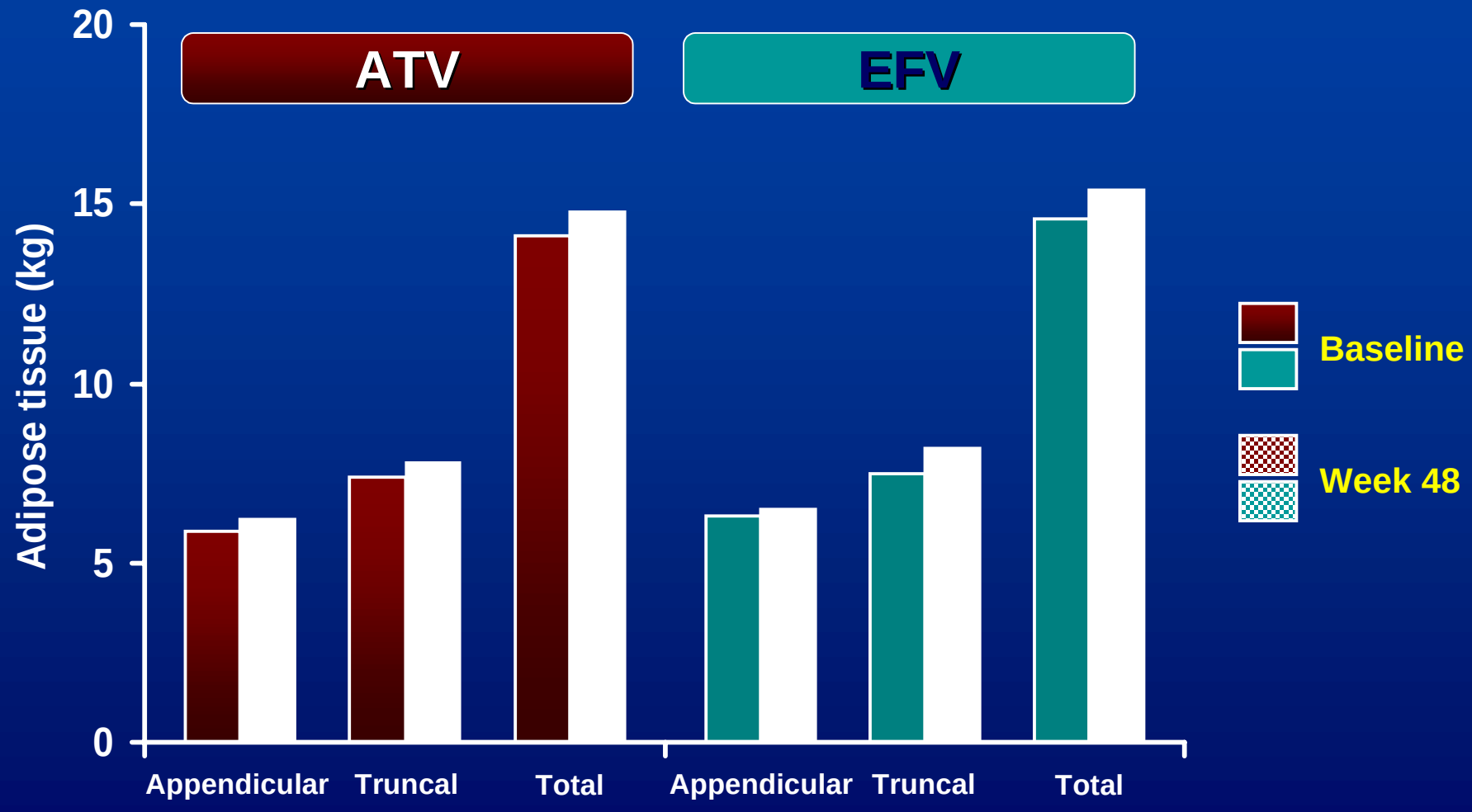
DEXA Results: Baseline and Week 48 (Mean)



No significant difference for change from Baseline within treatment arms and between treatment arms for all compartments

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DEXA Mean Ratios: Baseline and Week 48

	ATV		EFV	
	Baseline	Week 48	Baseline	Week 48
Appendicular:TBF	0.42	0.42	0.43	0.42
Truncal:TBF	0.52	0.52	0.51	0.53

TBF = total body fat

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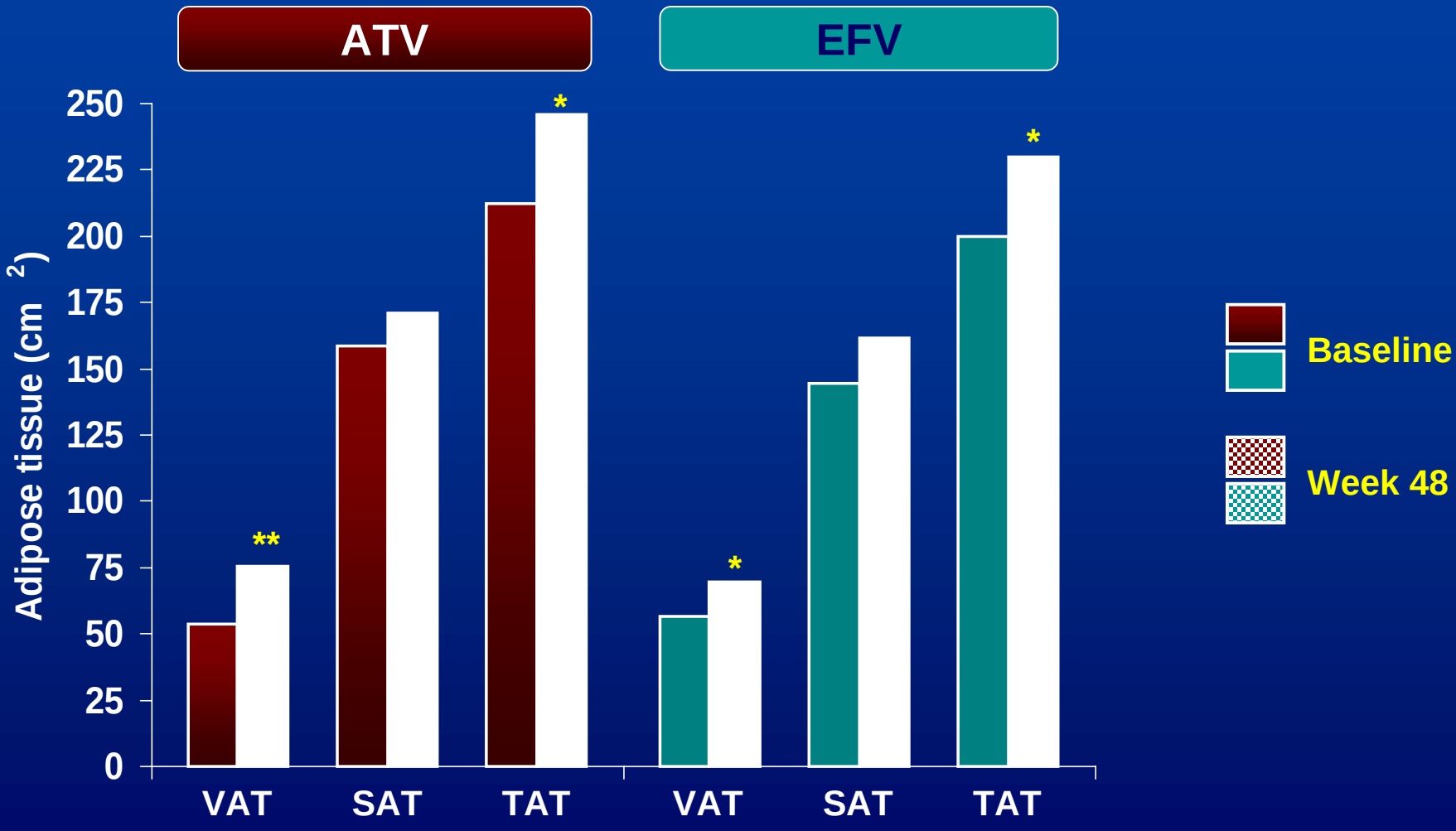
CT Results: Baseline and Week 48 (Mean)



No significant differences between treatment arms

** p<0.001, change from baseline within treatment

* p<0.05, change from baseline within treatment

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CT Mean Ratios: Baseline and Week 48

	ATV		EFV	
	Baseline	Week 48	Baseline	Week 48
VAT:TAT	0.28	0.31	0.28	0.30
VAT:SAT	0.44	0.50	0.42	0.46
SAT:TAT	0.72	0.69	0.72	0.70

Mean weight gain from baseline at Week 48: ATV, 2 kg; EFV, 0 kg

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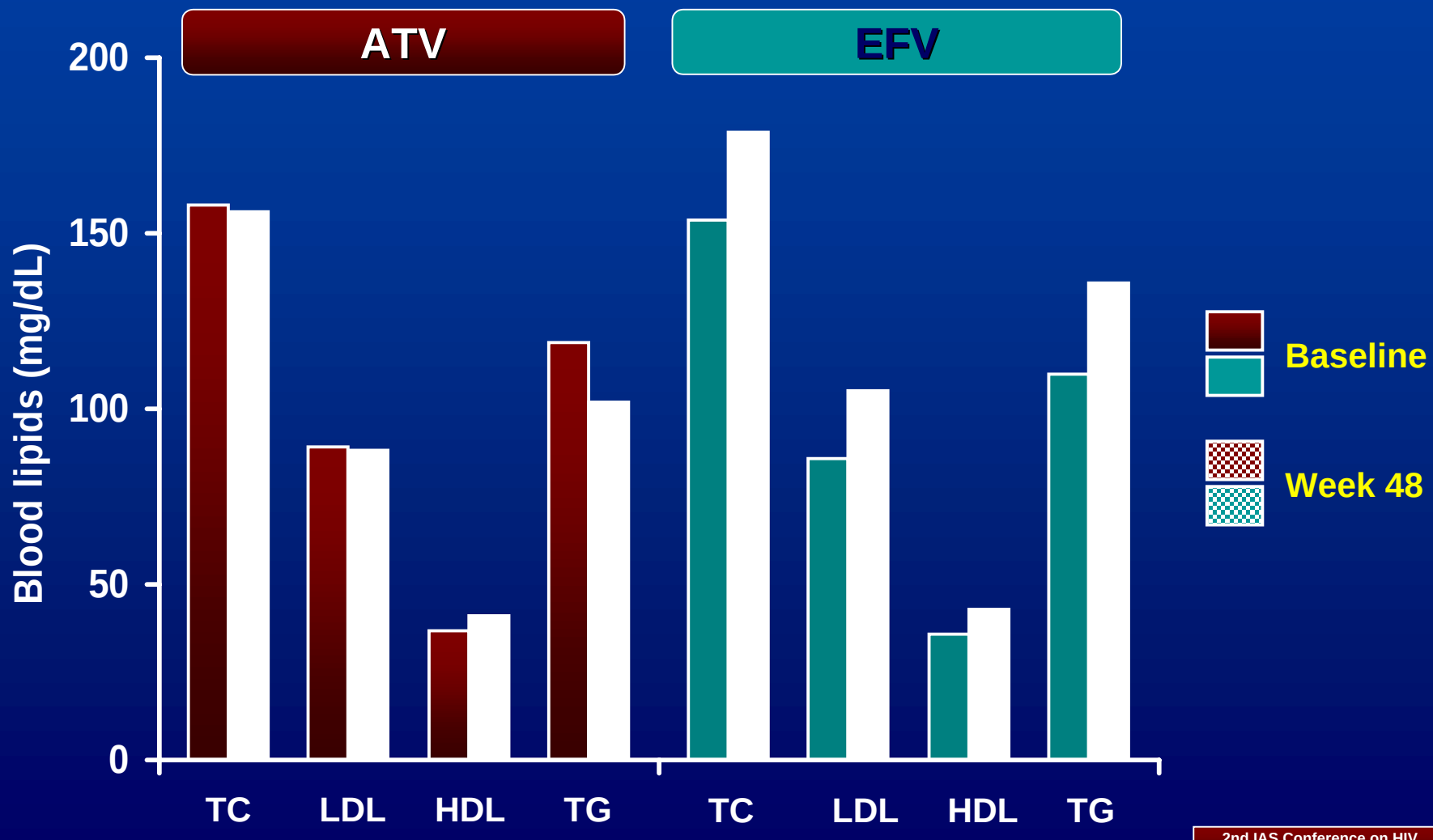
Lipids: Baseline and Week 48 (Median)



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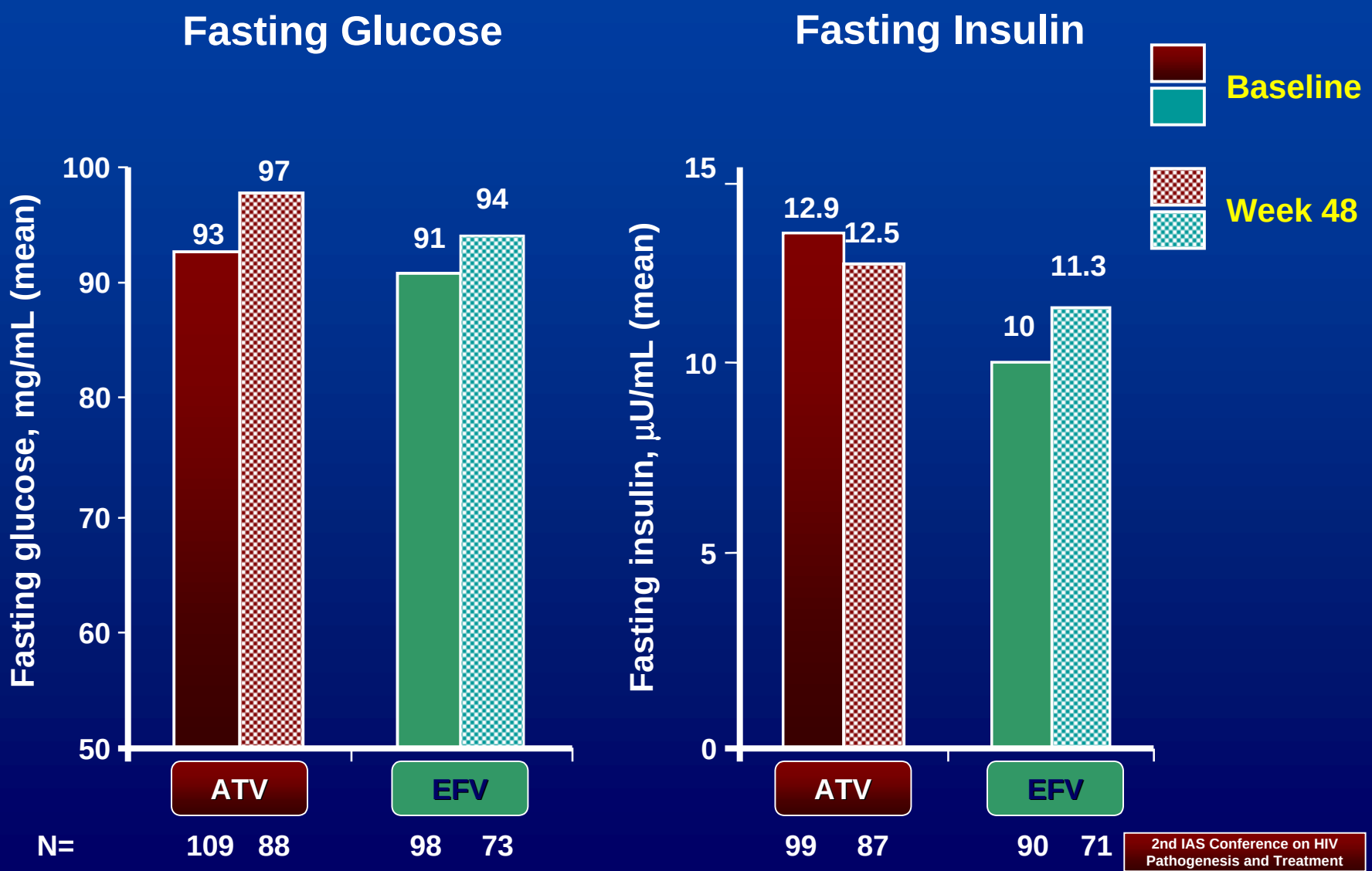
Fasting Glucose and Insulin: Baseline and Week 48



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Conclusions

- **ATV and EFV are associated with comparable and proportional effects in body fat distribution through Week 48**
  - Modest fat increases were consistently noted in both groups (in all compartments)
  - There was no evidence of central adiposity by VAT to TAT ratios
  - There was no evidence of lipoatrophy
- **The pattern of fat increase was consistent with successful disease treatment**
- **ATV treatment did not result in increases in TC, fasting LDL, or fasting TG**
- **Neither ATV nor EFV resulted in increases in insulin resistance indices**

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Acknowledgments

TO ALL THE PATIENTS AND STUDY CENTER PARTICIPANTS

JG Jemsek,[1] E Arathoon,[2] M Arlotti,[3] C Perez,[4] N Sosa,[5] V Pokrovskiy,[6] M Giordano,[7] A Thiry,[7] M Soccodato[7]

[1]Jemsek Clinic PLLC, Huntersville NC, USA, [2]Hospital General San Juan de Dios, Guatemala, Guatemala, [3]Ospedale degli Infermi, Rimini, Italy, [4]Hospital Clínico de La Pontificia Universidad Católica, Santiago, Chile, [5]Consultorio Royal Center, Panama City, Panama, [6]Federal AIDS Center, Moscow, Russia, [7]Bristol Myers Squibb Company, Wallingford, CT, USA

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