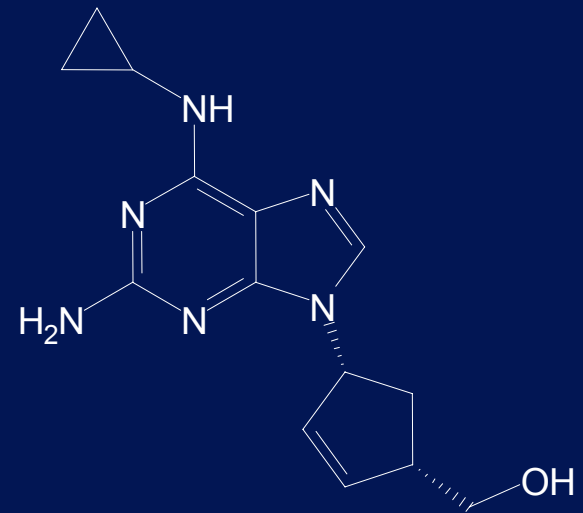
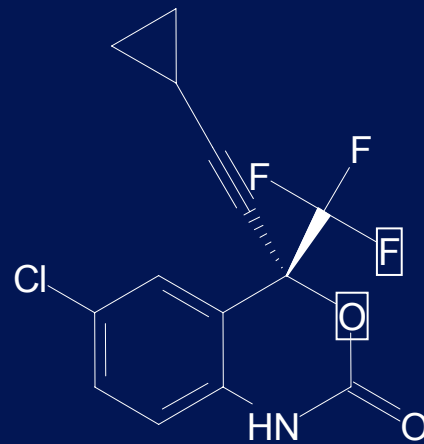
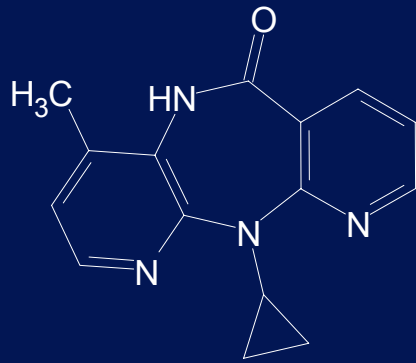


# SWITCHING PROTEASE INHIBITORS TO NEVIRAPINE, EFAVIRENZ OR ABACAVIR: A RANDOMIZED, MULTICENTER, OPEN-LABEL, SIMPLIFICATION TRIAL

(NEV/EFA/ABA Trial)



Results after 18 months of follow-up

# Objective

To compare the virological response when switching protease inhibitors (PI) to either nevirapine, efavirenz or abacavir in HIV-1 infected adults responding (VL<200 copies/mL) to two NRTIs and at least one PI

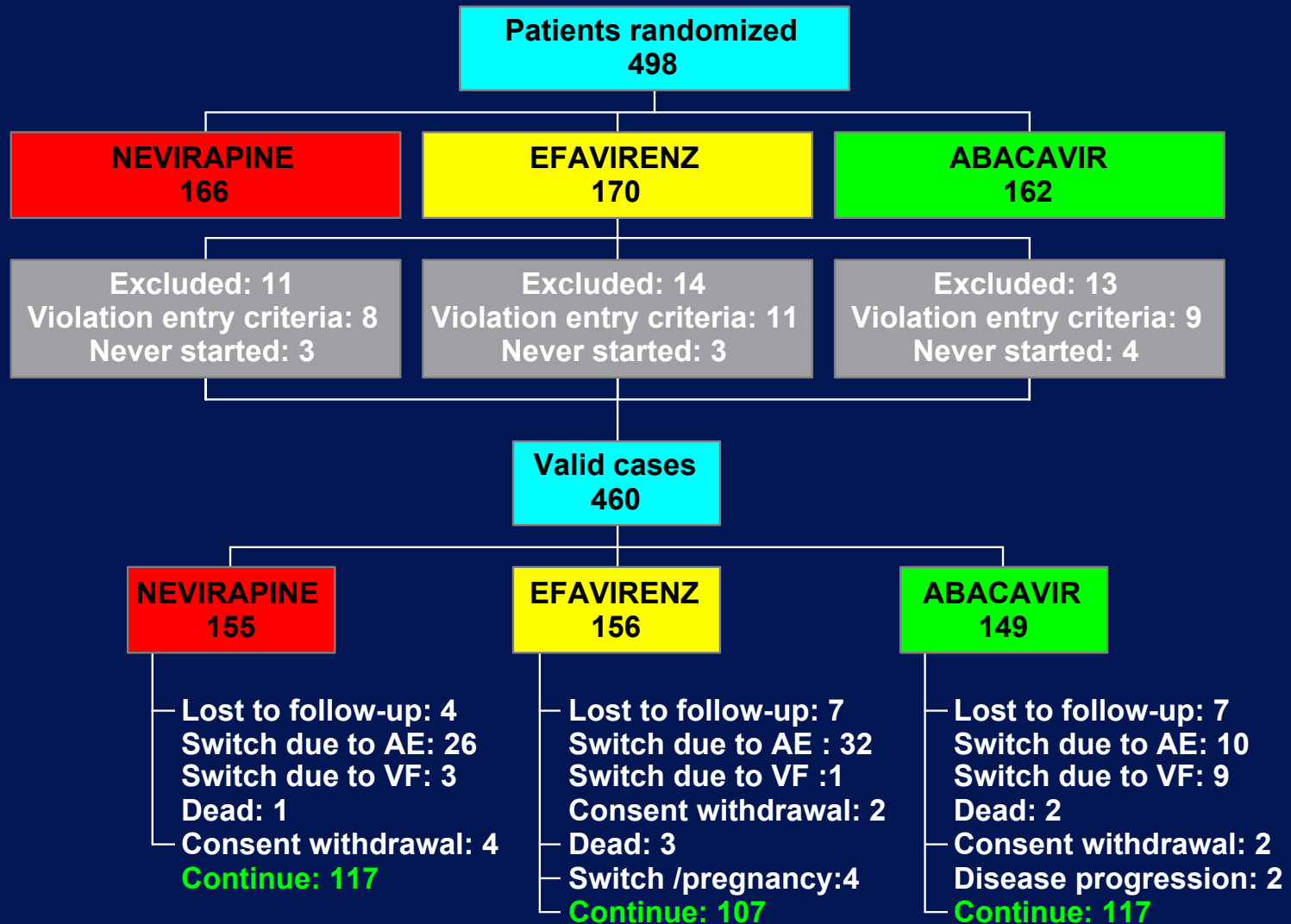
# Methods

- Design: randomized, multicenter (15 sites), 3-arm, parallel, open-label, clinical trial.
- Randomization: Blocks, balanced by site
  - Sample size: 148 per arm (to conclude equivalence [ $\pm 15\%$ ], with 90% power and two-sided  $\alpha = 5\%$ , assuming 90% success rate)
  - Enrollment: Dec 1999-Jan 2001
  - Intervention: Switching the PI component of the HAART combination to either NEV, EFA or ABA

# Methods

- **Visits:** baseline, every 3 months until 24
- **Lab tests:** HIV-RNA (VL), CD4+ cell count, blood chemistry including fasting lipids , and viral genotype if failure
- **Primary endpoint:** Proportion with VL below 200 copies (month 12) (Equivalence hypothesis)
- **Secondary endpoints:** CD4, side effects, metabolic parameters and body fat abnormalities.

# Trial flow chart



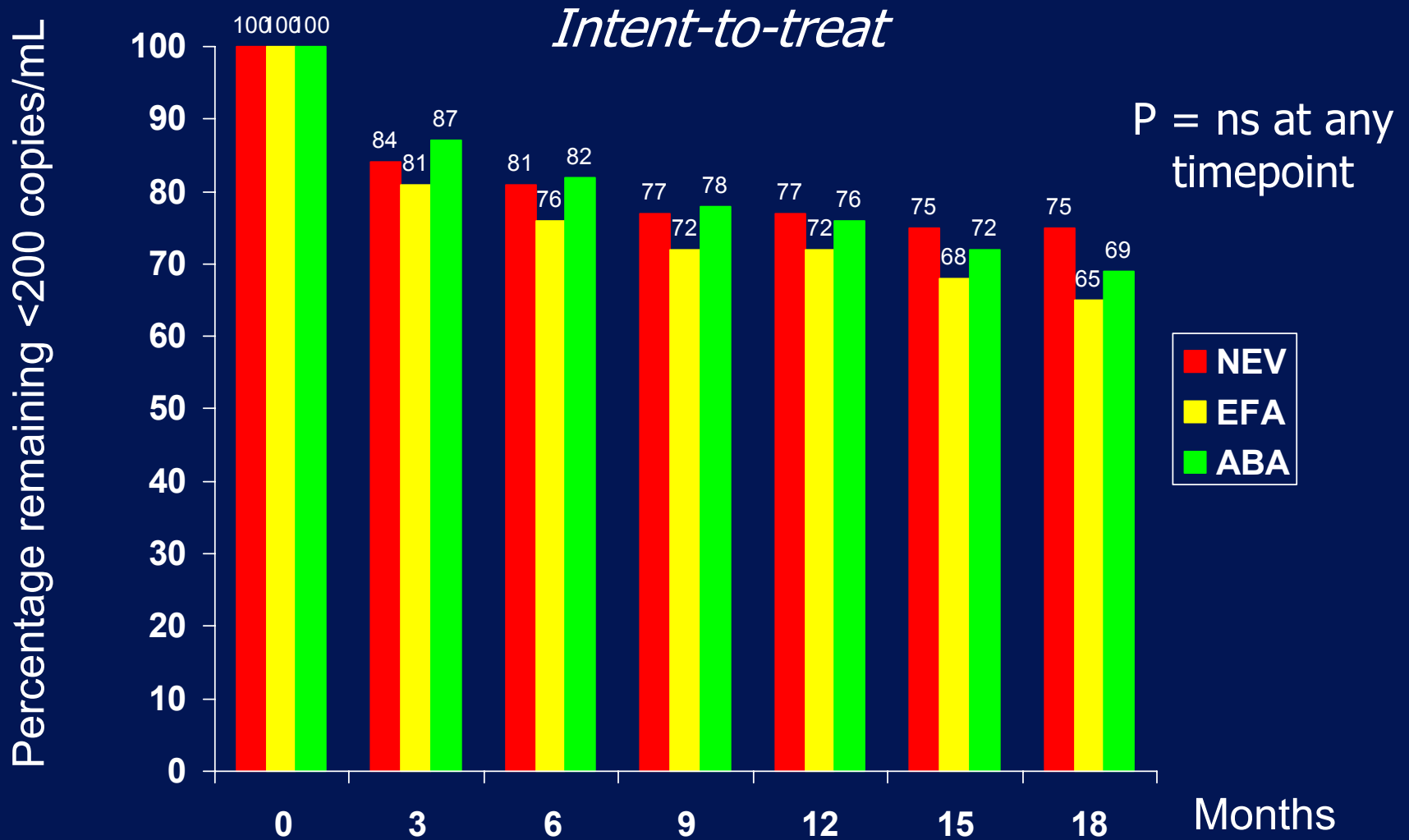
# Baseline characteristics

	<b>NEV</b> N = 155	<b>EFA</b> N = 156	<b>ABA</b> N = 149
<b>Age, years, median (range)</b>	39 (23-73)	38 (21-69)	40 (24-71)
<b>Gender M, n (%)</b>	119 (76)	117 (75)	113 (76)
<b>Risk for HIV, n (%)</b>			
Homo/bisexual	43 (28)	46 (29)	37 (25)
Heterosexual	42 (27)	49 (31)	45 (30)
IVDU	65 (42)	53 (34)	53 (36)
Hemophilia/Transfusion	1 (<1)	3 (2)	2 (1)
Unknown	5 (3)	5 (3)	12 (8)
<b>AIDS, n (%)</b>	55 (35)	52 (33)	56 (38)
<b>CD4+ cell count median (IQ range)</b>	508 (332-755)	558 (356-751)	544 (366-688)

# Baseline characteristics

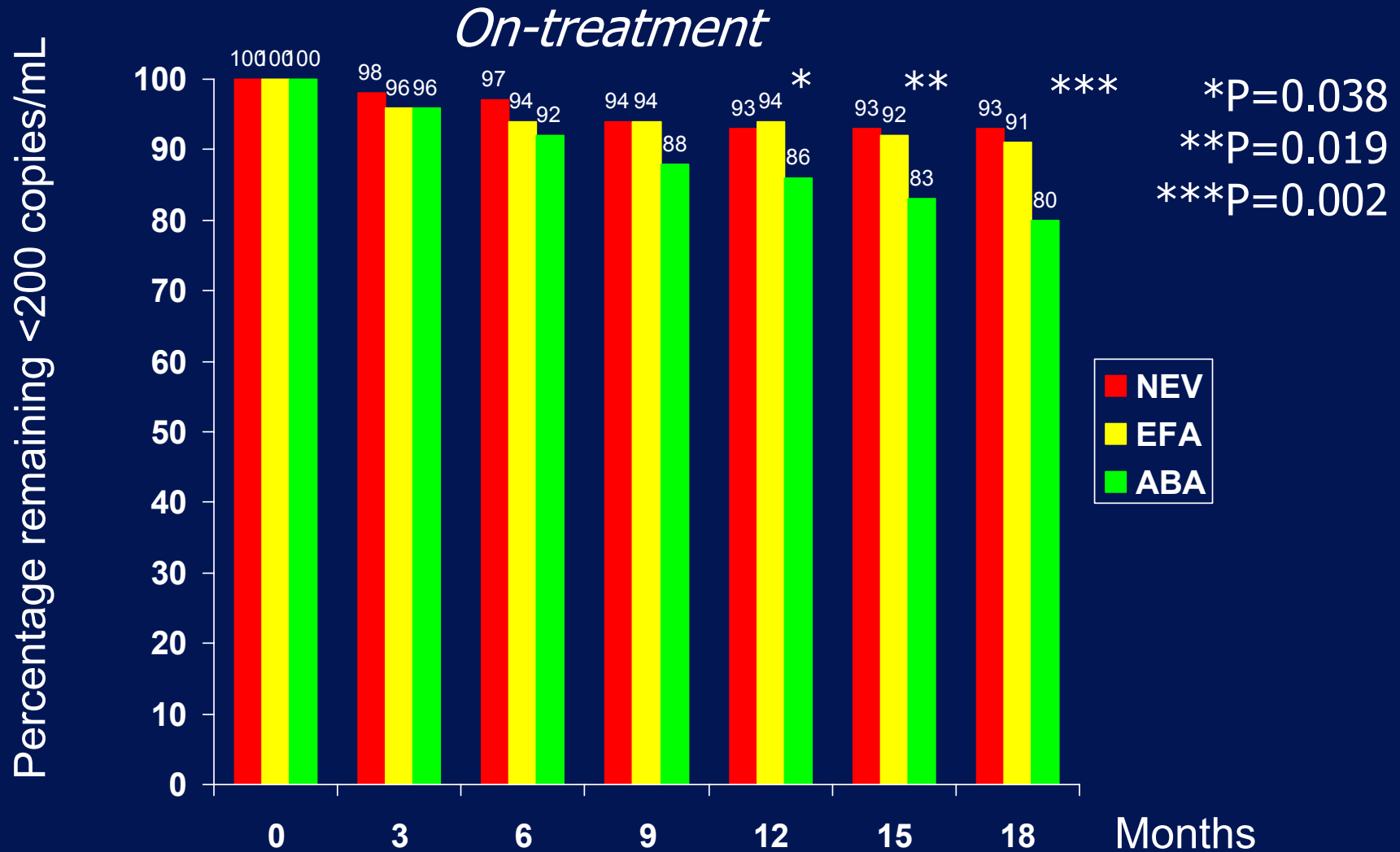
	<b>NEV</b> N = 155	<b>EFA</b> N = 156	<b>ABA</b> N = 149
<b>Current antiretroviral treatment (%)</b>			
d4T+3TC+IDV	31	30	28
AZT+3TC+IDV	22	15	18
d4T+3TC+NFV	15	13	19
AZT+3TC+NFV	7	7	7
d4T+ddI+IDV	5	4	8
Other	20	31	20
<b>Duration of HAART (months), median (range)</b>	29 (6-53)	31 (6-69)	30 (10-64)
<b>Prior NRTI mono-bi therapy, n (%)</b>	79 (51)	90 (58)	69 (46)

# Proportion of non-failing patients



NEV	155	155	155	155	155	155	155
EFA	156	156	156	156	156	156	156
ABA	149	149	149	149	149	149	149

# Proportion of non-failing patients



NEV	155	132	130	128	128	125	125
EFA	156	132	125	123	119	115	111
ABA	149	135	133	132	132	132	132

# Treatment failure

	<b>NEV</b> N = 155	<b>EFA</b> N = 156	<b>ABA</b> N = 149
N patients			
<b>Viral load &gt;200 *</b>	8	7	23
<b>Drop-outs</b>	4	7	8
<b>Switch due to AE **</b>	26	32	10
<b>Switch / physician decisn.</b>	1	1	1
<b>Switch / pregnancy</b>	0	4	0
<b>Disease progression</b>	0	0	2
<b>Dead</b>	1	3	2
<b>Total</b>	<b>40</b>	<b>54</b>	<b>46</b>

\* P < 0.001

\*\* P < 0.01

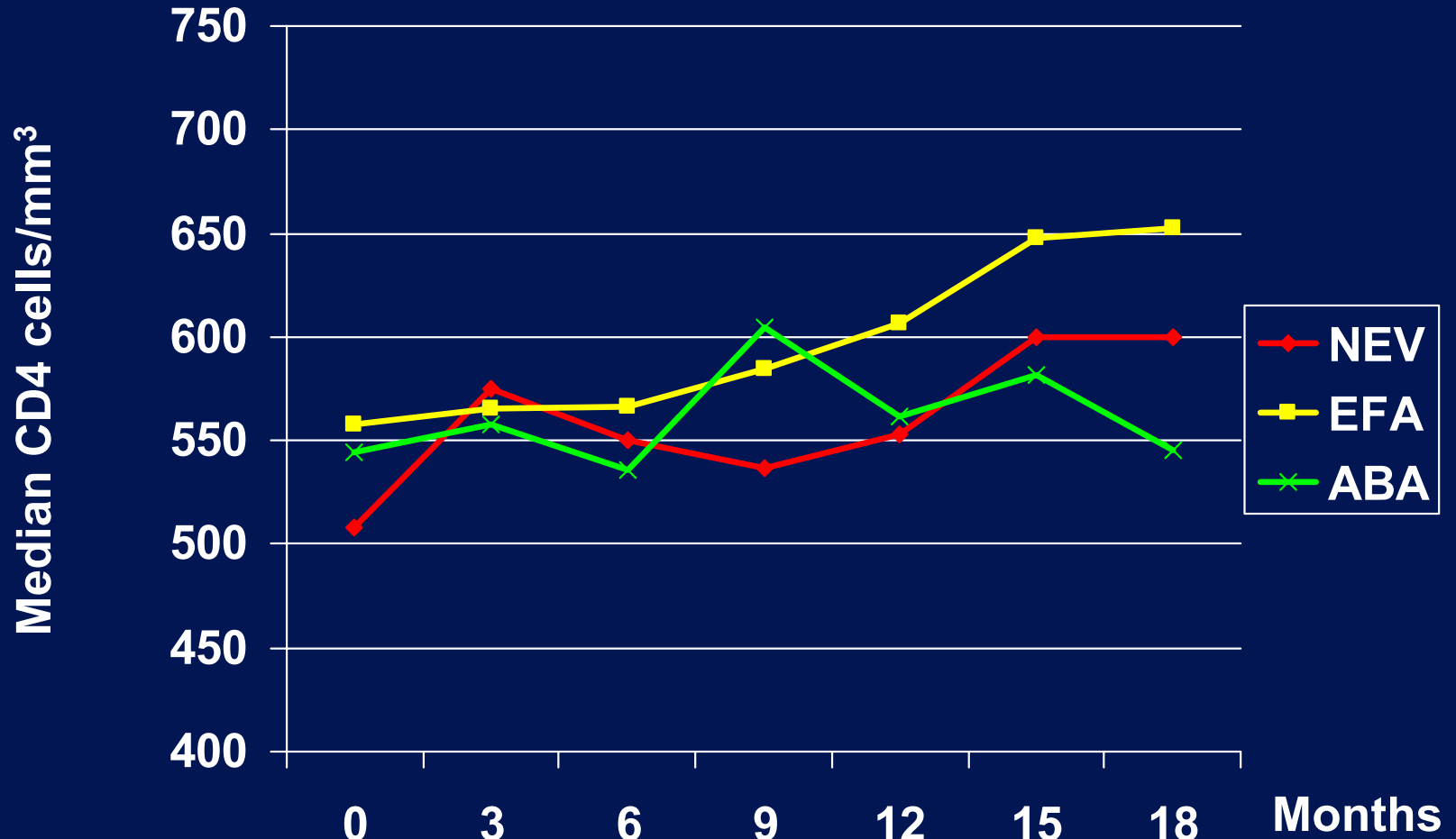
# Virological failure by prior therapy

	<b>NEV</b> N = 155	<b>EFA</b> N = 156	<b>ABA</b> N = 149
N patients			
<b>Suboptimal Rx + HAART</b> (n=238)	5	6	21
<b>Only HAART</b> (n=222)	3	1	2
<b>Total VF</b>	8	7	23

# Genotypic resistance

N patients	<b>NEV</b> N = 155	<b>EFA</b> N = 156	<b>ABA</b> N = 149
<b>Virological failure</b>	8	7	23
<b>Amplified</b>	4	1	12
<b>NAMs</b>	4	1	12
<b>NNRTI mutations</b>	4	1	2
<b>PI mutations</b>	0	1	0
<b>No mutations</b>	0	0	0

# CD4+ cell count

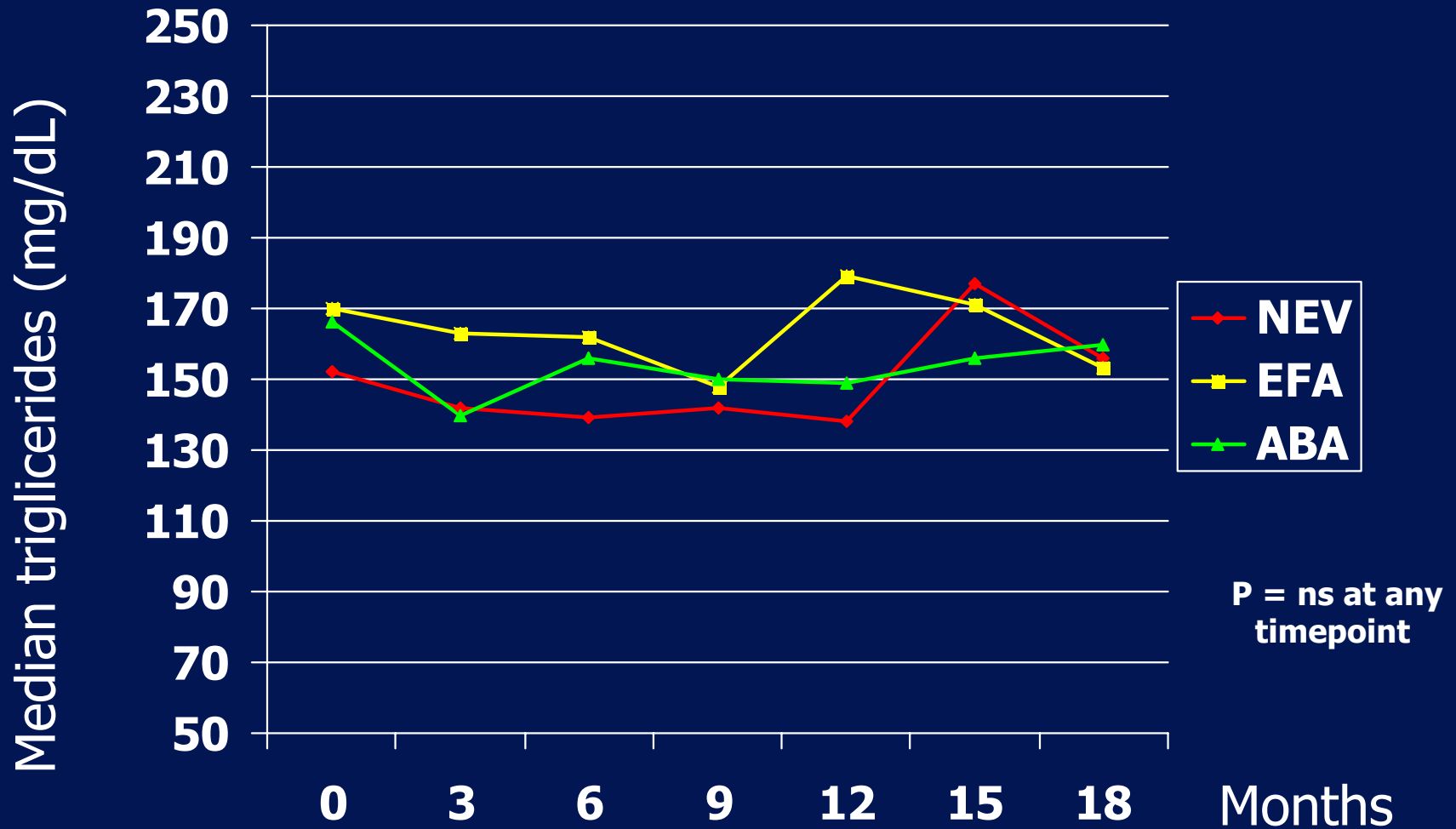


<b>NEV</b>	<b>155</b>	<b>145</b>	<b>122</b>	<b>116</b>	<b>113</b>	<b>87</b>	<b>74</b>
<b>EFA</b>	<b>156</b>	<b>147</b>	<b>124</b>	<b>104</b>	<b>110</b>	<b>78</b>	<b>65</b>
<b>ABA</b>	<b>149</b>	<b>137</b>	<b>123</b>	<b>105</b>	<b>107</b>	<b>89</b>	<b>71</b>

# Adverse events leading to switch treatment

n	<b>NEV</b> N = 155	<b>EFA</b> N = 156	<b>ABA</b> N = 149
<b>Neuropsychiatric</b>	4	23	1
<b>Rash</b>	13	2	0
<b>GI toxicity</b>	2	4	5
<b>Hypersensitivity</b>	1	1	4
<b>Liver toxicity</b>	4	0	0
<b>Rash + liver tox.</b>	2	0	0
<b>Triglycerides ↑</b>	0	1	0
<b>Unknown</b>	0	1	0
<b>Total</b>	<b>26</b>	<b>32</b>	<b>10</b>

# Fasting plasma triglycerides



**NEV**

**155**

**142**

**122**

**110**

**108**

**73**

**68**

**EFA**

**156**

**148**

**119**

**96**

**103**

**71**

**63**

**ABA**

**149**

**134**

**122**

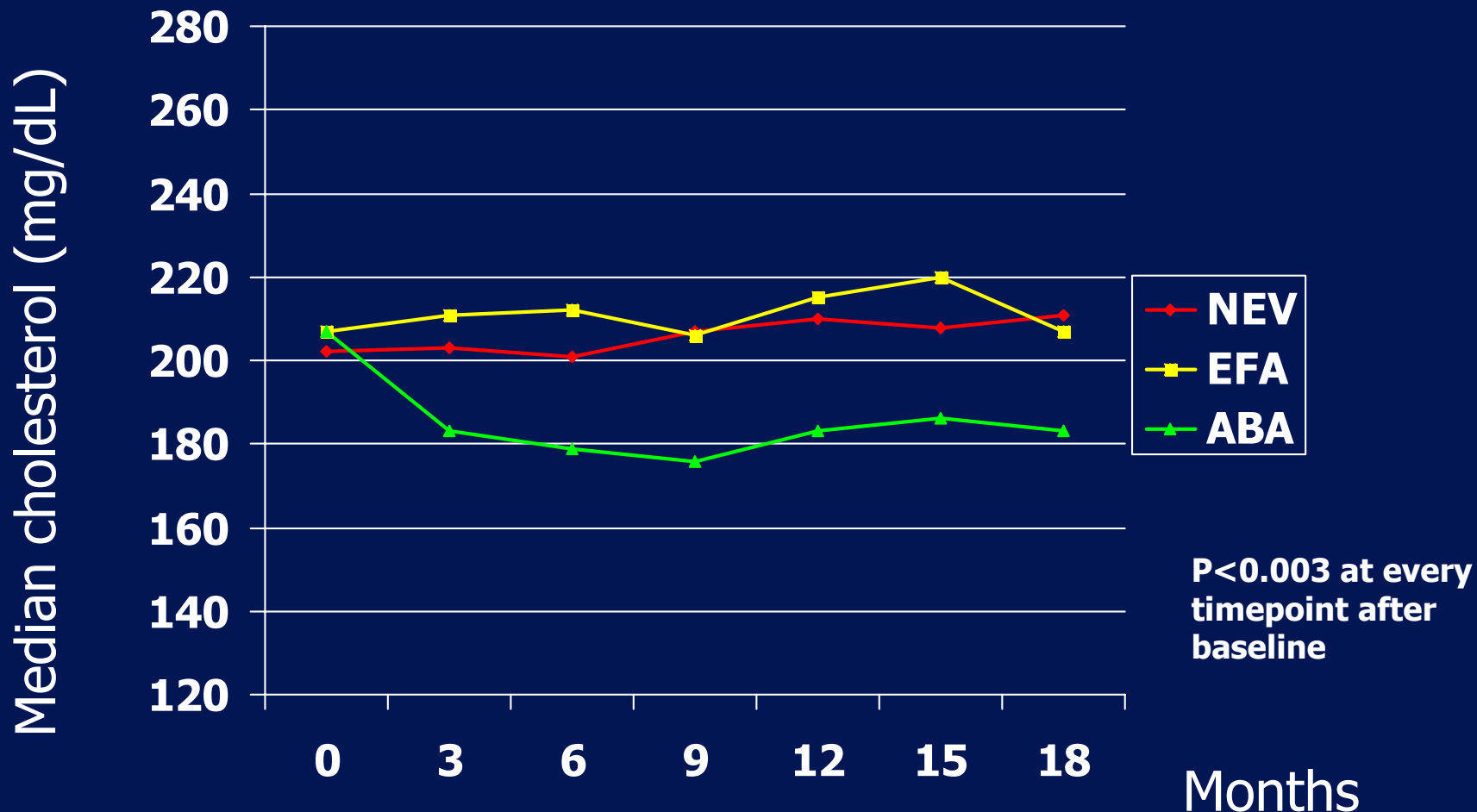
**105**

**100**

**81**

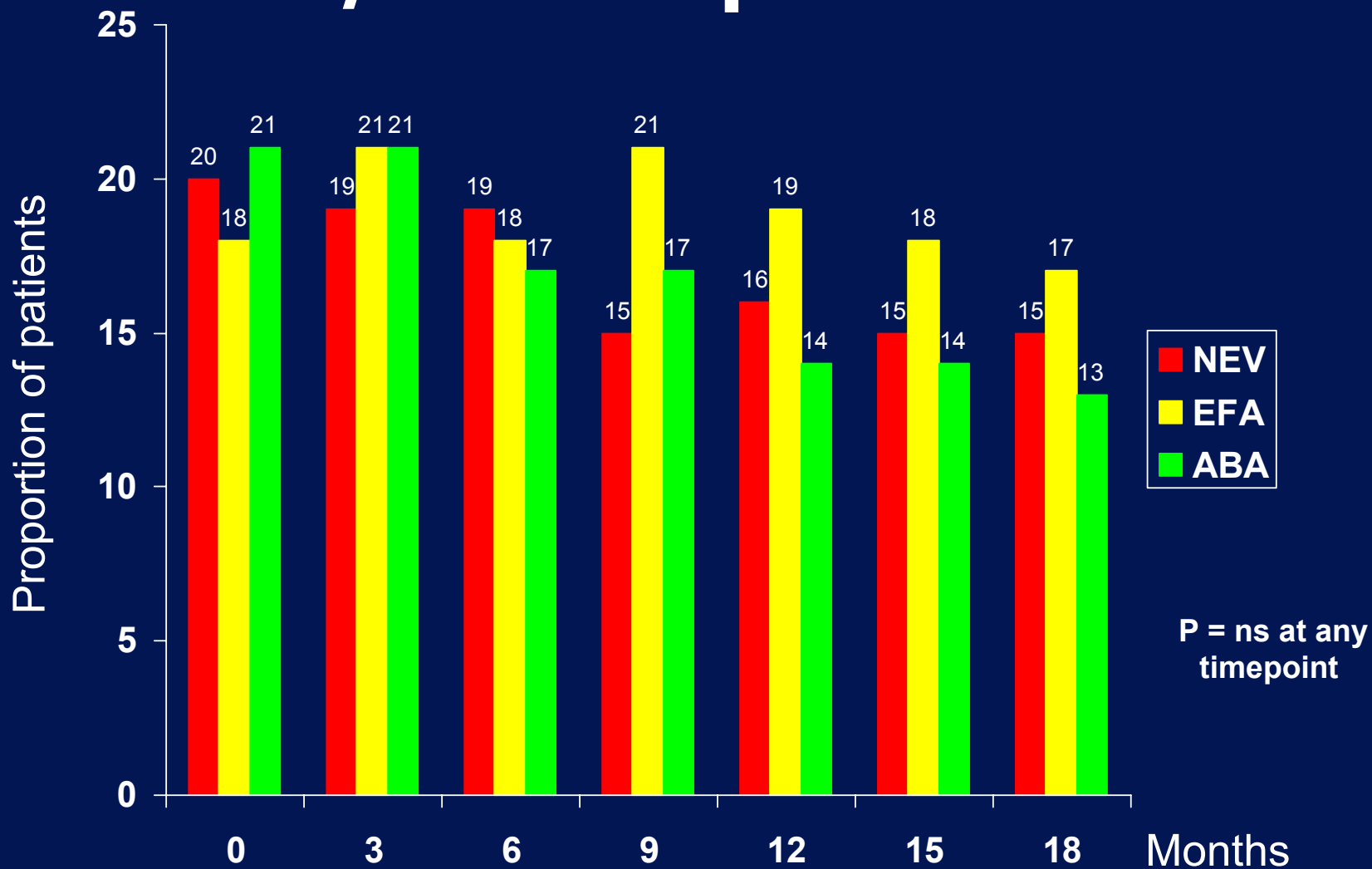
**67**

# Fasting plasma cholesterol



<b>NEV</b>	<b>155</b>	<b>145</b>	<b>125</b>	<b>112</b>	<b>109</b>	<b>75</b>	<b>67</b>
<b>EFA</b>	<b>156</b>	<b>148</b>	<b>119</b>	<b>100</b>	<b>105</b>	<b>70</b>	<b>65</b>
<b>ABA</b>	<b>149</b>	<b>134</b>	<b>123</b>	<b>105</b>	<b>101</b>	<b>82</b>	<b>69</b>

# Moderate/severe lipoaccumulation



**NEV**

**155**

**145**

**122**

**116**

**113**

**87**

**74**

**EFA**

**156**

**147**

**124**

**104**

**110**

**78**

**65**

**ABA**

**149**

**137**

**123**

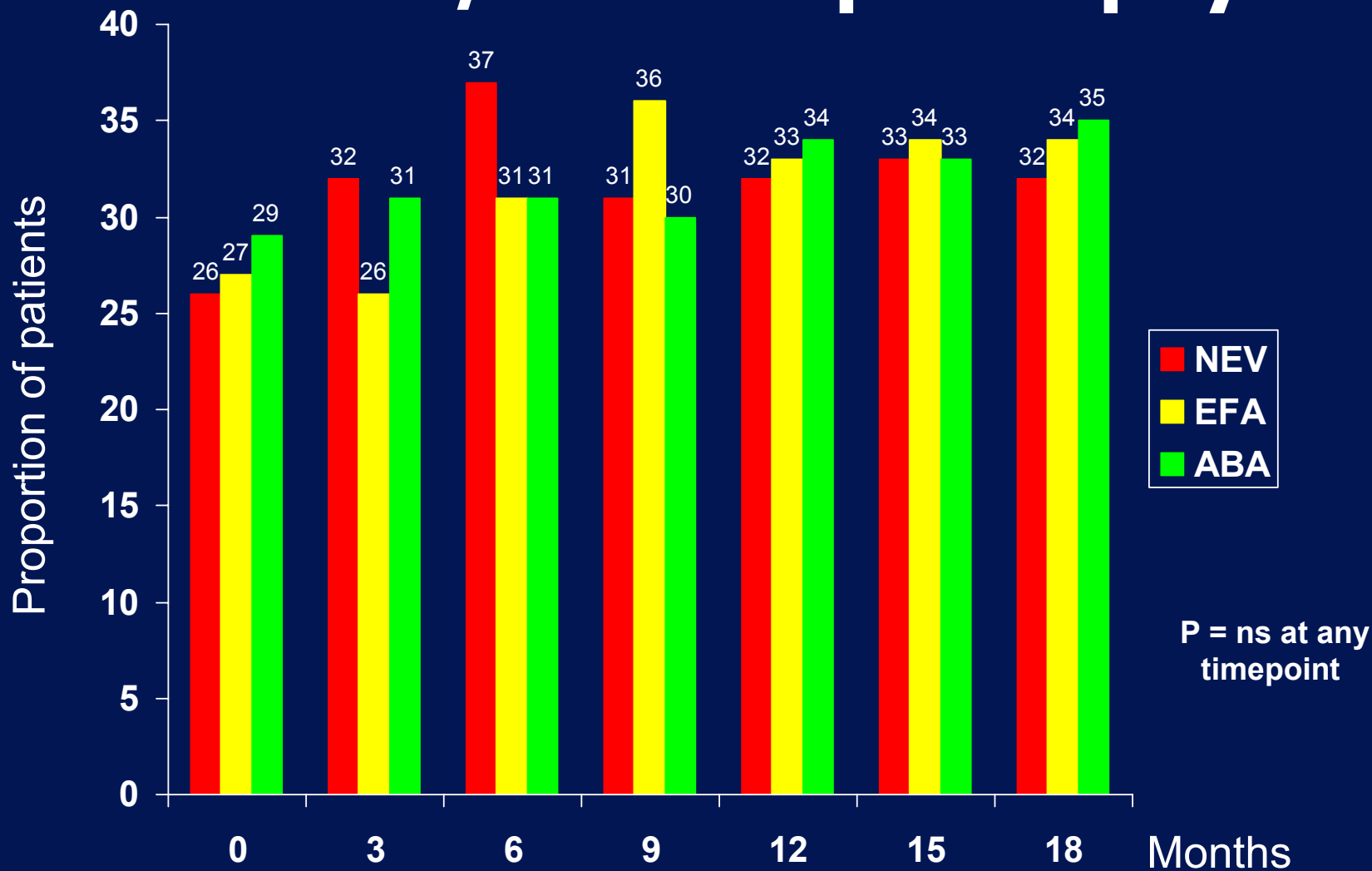
**105**

**107**

**89**

**71**

# Moderate/severe lipoatrophy



	0	3	6	9	12	15	18
<b>NEV</b>	<b>155</b>	<b>145</b>	<b>122</b>	<b>116</b>	<b>113</b>	<b>87</b>	<b>74</b>
<b>EFA</b>	<b>156</b>	<b>147</b>	<b>124</b>	<b>104</b>	<b>110</b>	<b>78</b>	<b>65</b>
<b>ABA</b>	<b>149</b>	<b>137</b>	<b>123</b>	<b>105</b>	<b>107</b>	<b>89</b>	<b>71</b>

# Conclusions

- The simplification of PI-containing HAART in patients with sustained virological suppression had a higher probability of maintaining the virologic control in the NEV or EFA arms as compared with the ABA arm. This consideration was particularly true for patients with a history of suboptimal NRTI therapy. However, the rates of viral suppression for patients switching from first-line PI-based regimens were similar with the three drugs.
- Adverse effects leading to discontinuation of study drugs were those expected and they were more common for NEV and EFA than for ABA.
- The impact on plasma total cholesterol was significantly higher for ABA than for NEV or EFA, although its clinical relevance is unknown because most of the patients in each arm had normal cholesterol values.
- The PI switch strategy was not able to decrease the proportion of patients with clinically evident body fat abnormalities.

# NEV/EFA/ABA Trial

## Team members

E Martínez, A Milinkovic, JB Pérez-Cuevas, JL Blanco, J Mallolas, J Gatell, Hosp Clínic, Barcelona, Spain

D Podzamczar, B Rosón, Hosp Bellvitge, L'Hospitalet, Spain

E Ribera, M Crespo, Hospitals Vall d'Hebron, Barcelona, Spain

P Domingo, M Barceló, F Montero, Hosp de Sant Pau, Barcelona, Spain

H Knobel, A González, Hospital del Mar, Barcelona, Spain

D Dalmau, A Ochoa, Hosp de Mútua de Terrassa, Terrassa, Spain

M Riera, M Leyes, Hosp Son Dureta, Palma de Mallorca, Spain

E Pedrol, M Font, Hosp General Granollers, Granollers, Spain

L Force, P Barrufet, Hosp de Mataró, Mataró, Spain

J Llibre, Hosp Sant Jaume, Calella, Spain

F Segura, E Antón, C H Parc Taulí, Sabadell, Spain

C Richart, J Peraire, C Viladés, F Vidal, Hosp Joan XXIII, Tarragona, Spain

C Cortés, I García, Hosp Creu Roja, L'Hospitalet, Spain

M Javaloyas, Hosp de Viladecans, Viladecans, Spain

M Aranda, Hosp de Terrassa, Terrassa, Spain

JA Arnaiz, A Cruceta, J Pich, S Varea, Coordinating Center

E de Lazzari, Statistician