

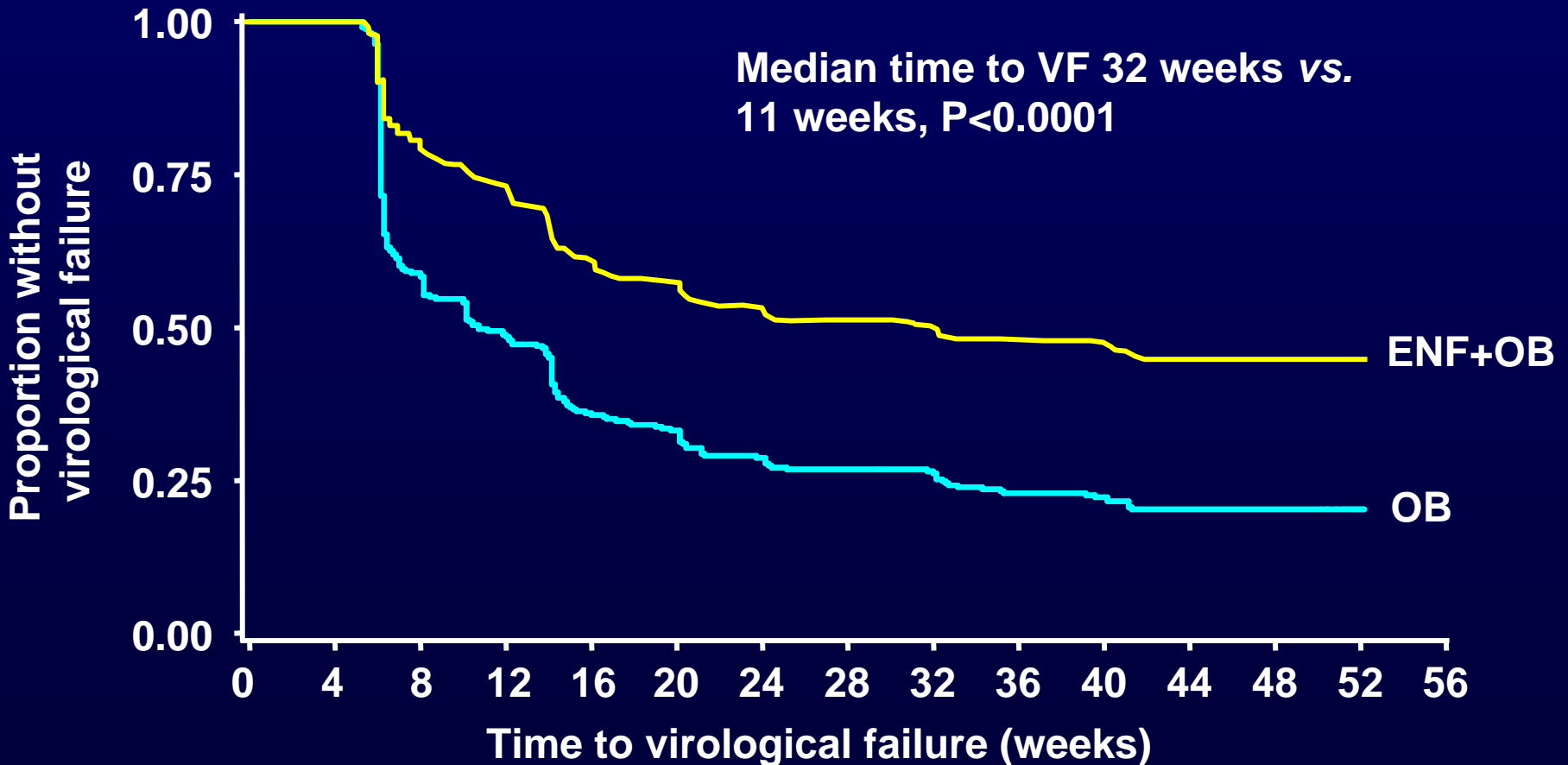
Final analysis of T1249-102: T-1249 Retains Potent Short Term Antiviral Activity in Patients who Have Failed a Regimen Containing Enfuvirtide (ENF)

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TORO studies

Time to virological failure* was longer on ENF+OB compared to OB

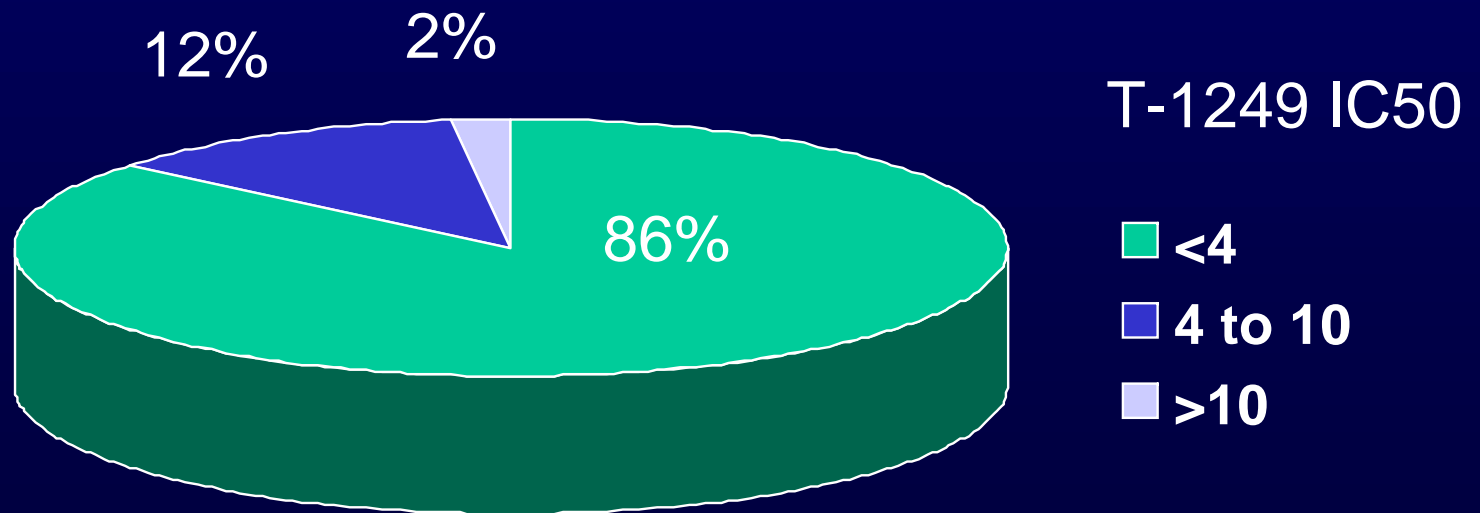


* Protocol defined

D. Cooper, IAS 2003, Paris

TORO studies (24 week analysis) In vitro susceptibility to T-1249 in virus from patients with protocol defined VF

Patients' viral isolates with ENF IC50 > 10 fold from TORO baseline (N=159)*



*out of 206 patients with protocol defined VF and paired samples available

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Objective

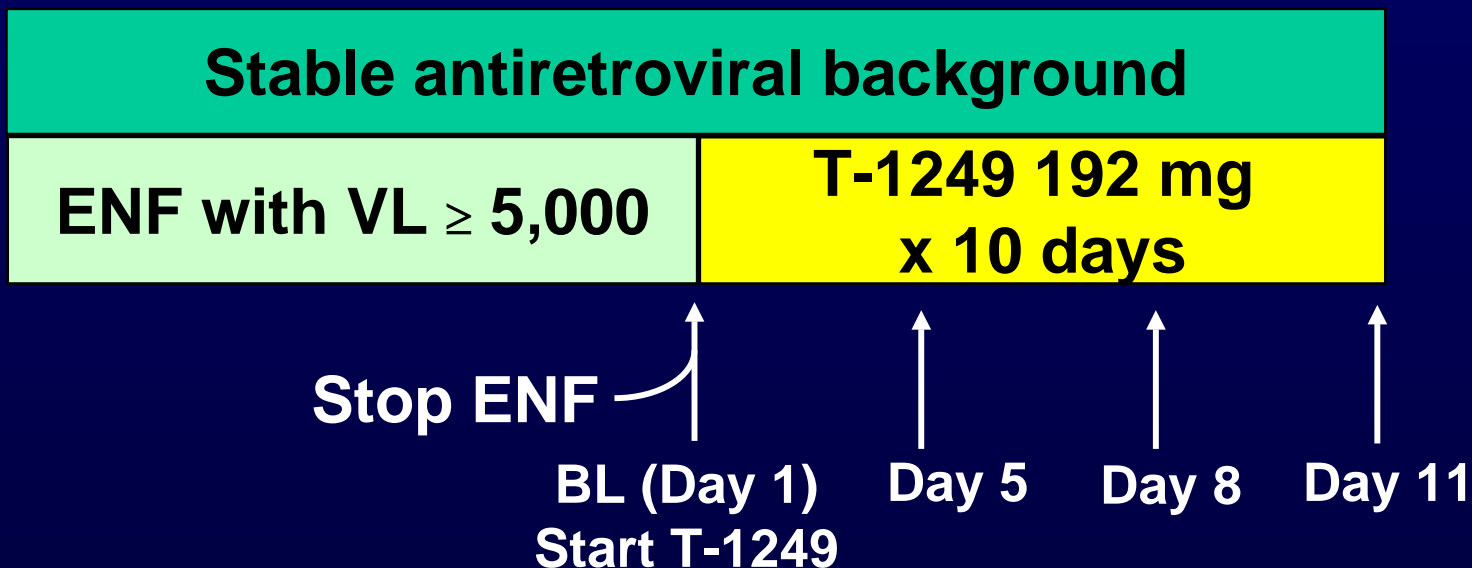
- To evaluate the safety and short term activity of T-1249 on ENF resistant isolates in vivo

Design

- T-1249 (192 mg/day x 10 days) replaces ENF in a failing regimen
- Entry Criteria: Two most recent viral loads $\geq 5,000$ and $\leq 500,000$ copies/mL while on stable ENF-containing ARV regimen.
- Patients derived from ENF phase II, phase III, and EAP

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Study Design



Viral Load taken at BL and each Study visit
GT and PT of gp41 performed at Day 1 and Day 11

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Baseline Patient Characteristics

53 patients were dosed* = Safety Population

- 47 (89%) Males; 6 (11%) Females; Mean age 43.2 years
- Median baseline HIV RNA: 4.9 log₁₀ copies/mL (range 3.5 - 5.6)
- Most recent median CD4 count (prior to first dose): 86 cells/ mm³ (1 - 522)
- Median time on an ENF containing regimen after VL \geq 5,000 : 65 weeks (range 13-165)

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Safety

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Treatment-Emergent Serious Adverse Events (SAE)

Three patients reported at least one SAE

Patient	Preferred Term	Related T-1249
200764	Elevated transaminases (grade 4)	No
202730	Acute Bronchitis	No
200148	Pneumonia/respiratory failure	No

•Safety Population (SAP): n=53

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Treatment Emergent Adverse Events*

Adverse Event	N (%)
At least one ISR	34 (64%)
Arthralgia	2 (4%)
Diarrhea	2 (4%)
Fatigue	2 (4%)
Myalgia	2 (4%)
Pyrexia	2 (4%)

•Occurring in at least 2 subjects

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Treatment Emergent
Grade 3-4 Laboratory Abnormalities*

Laboratory Test	N (%)
Creatinine	2 (4%)
Neutropenia	1 (2%)
Thrombocytopenia	1 (2%)
ALT	1 (2%)
AST	1 (2%)
Calcium	1 (2%)
Random glucose	1 (2%)

*None was assessed related to T-1249

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Antiretroviral activity

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Definition of ITT

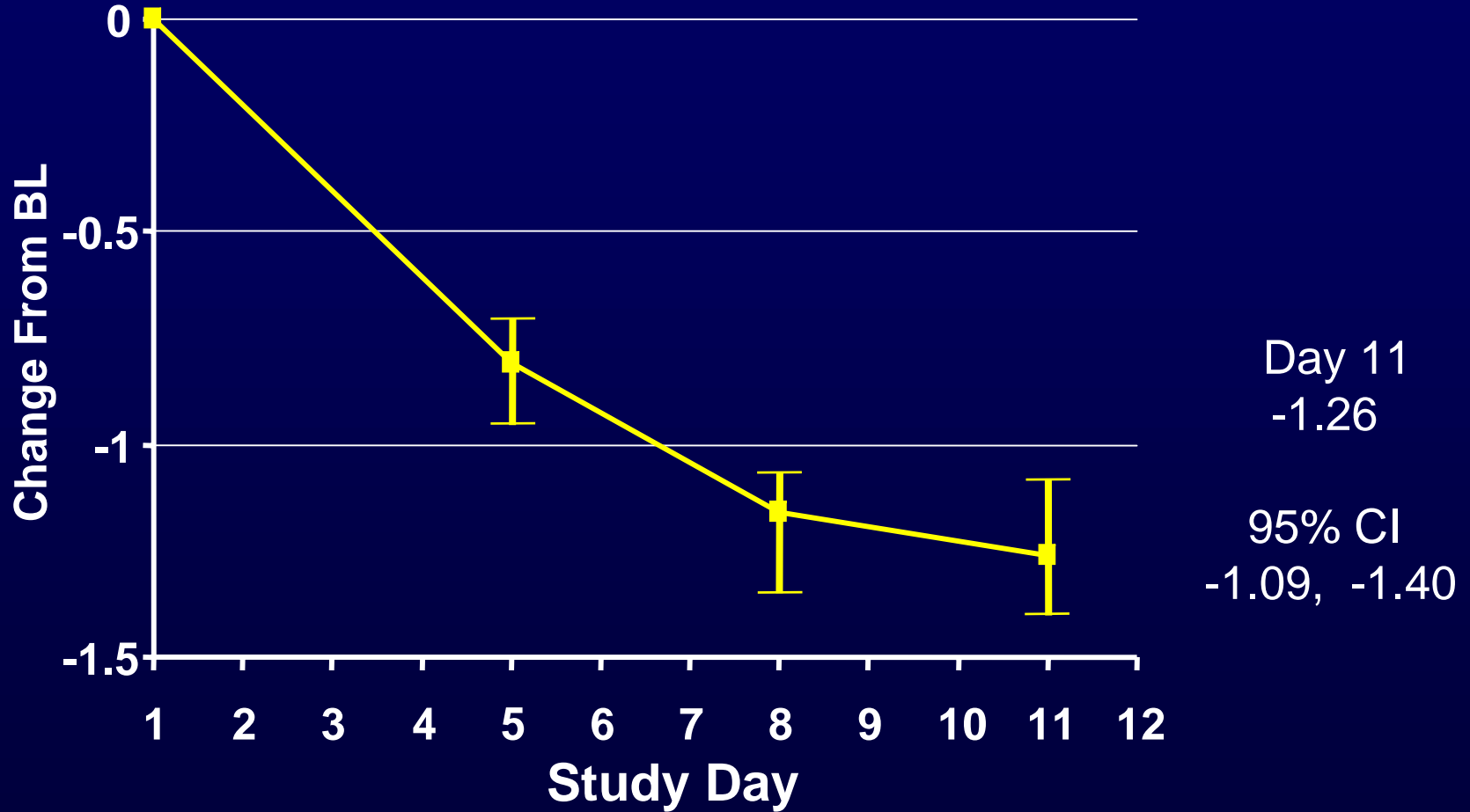
- ITT population N=51

Patients who demonstrated decreased ENF susceptibility or associated GT substitutions.

- Virus from one patient could not be sequenced
- Virus from one patient had no GT or PT evidence of resistance

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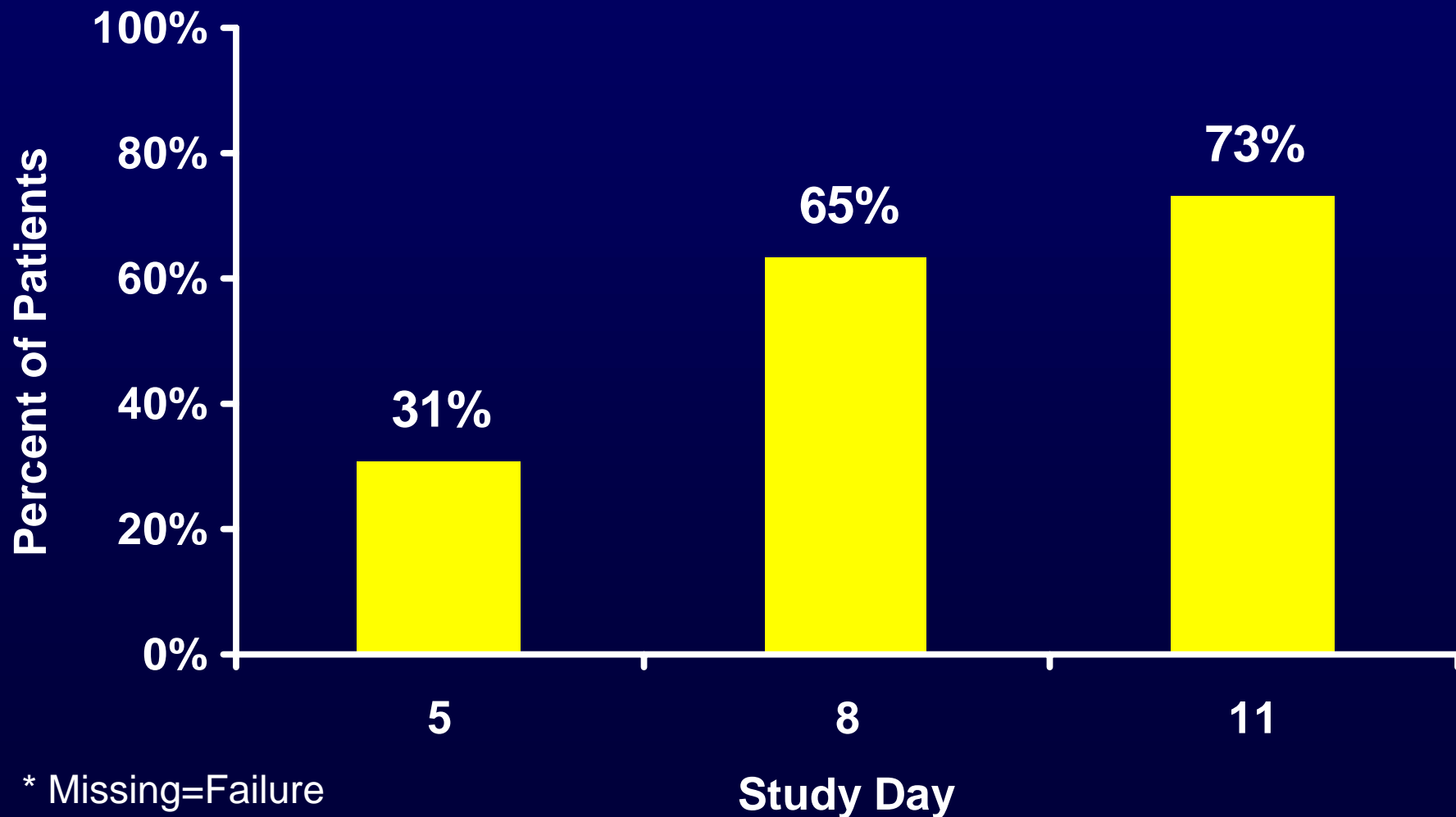
Median Log Change from Baseline



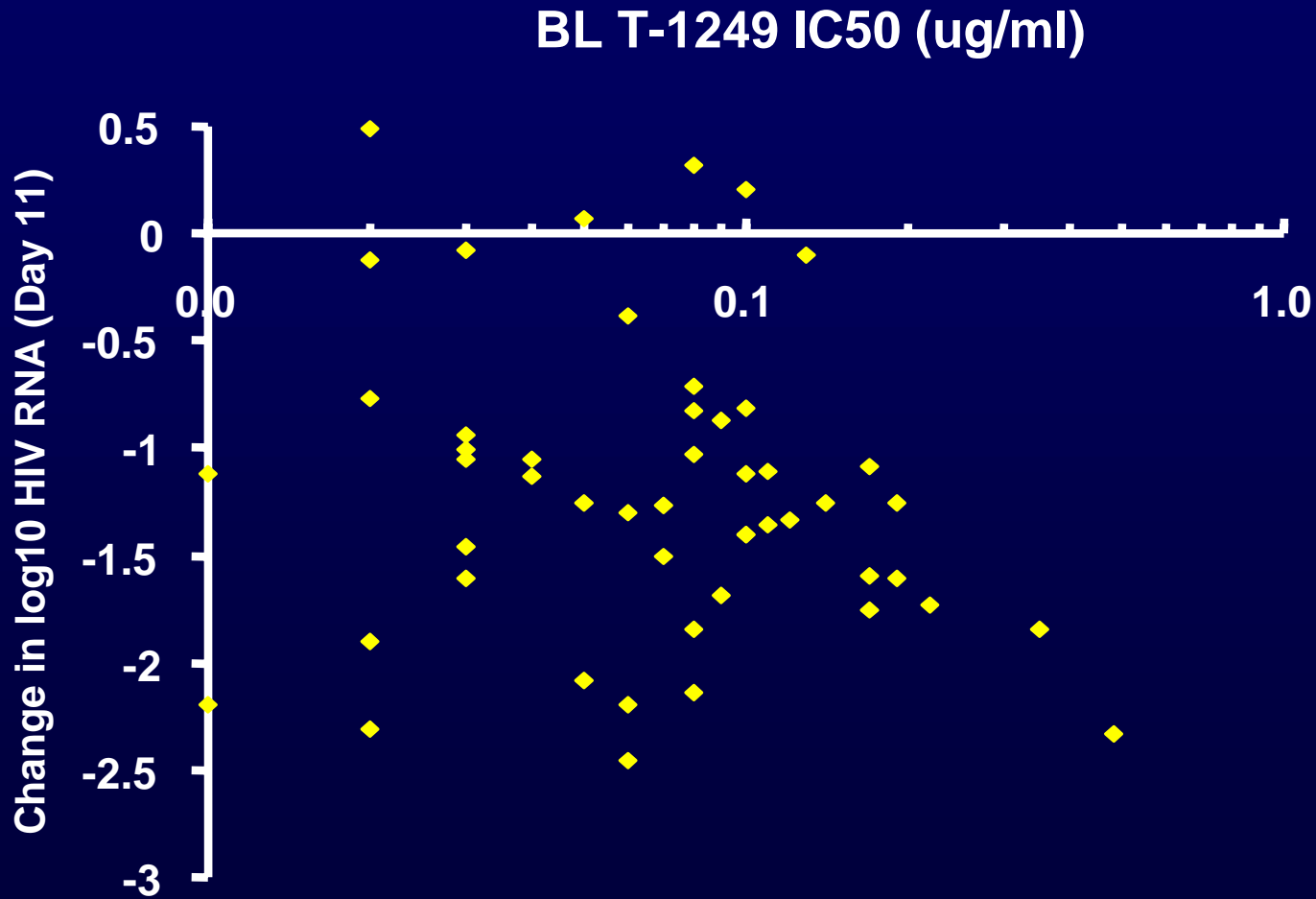
ITT N=51

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Percent of patients with ≥ 1.0 log Decline (ITT*)



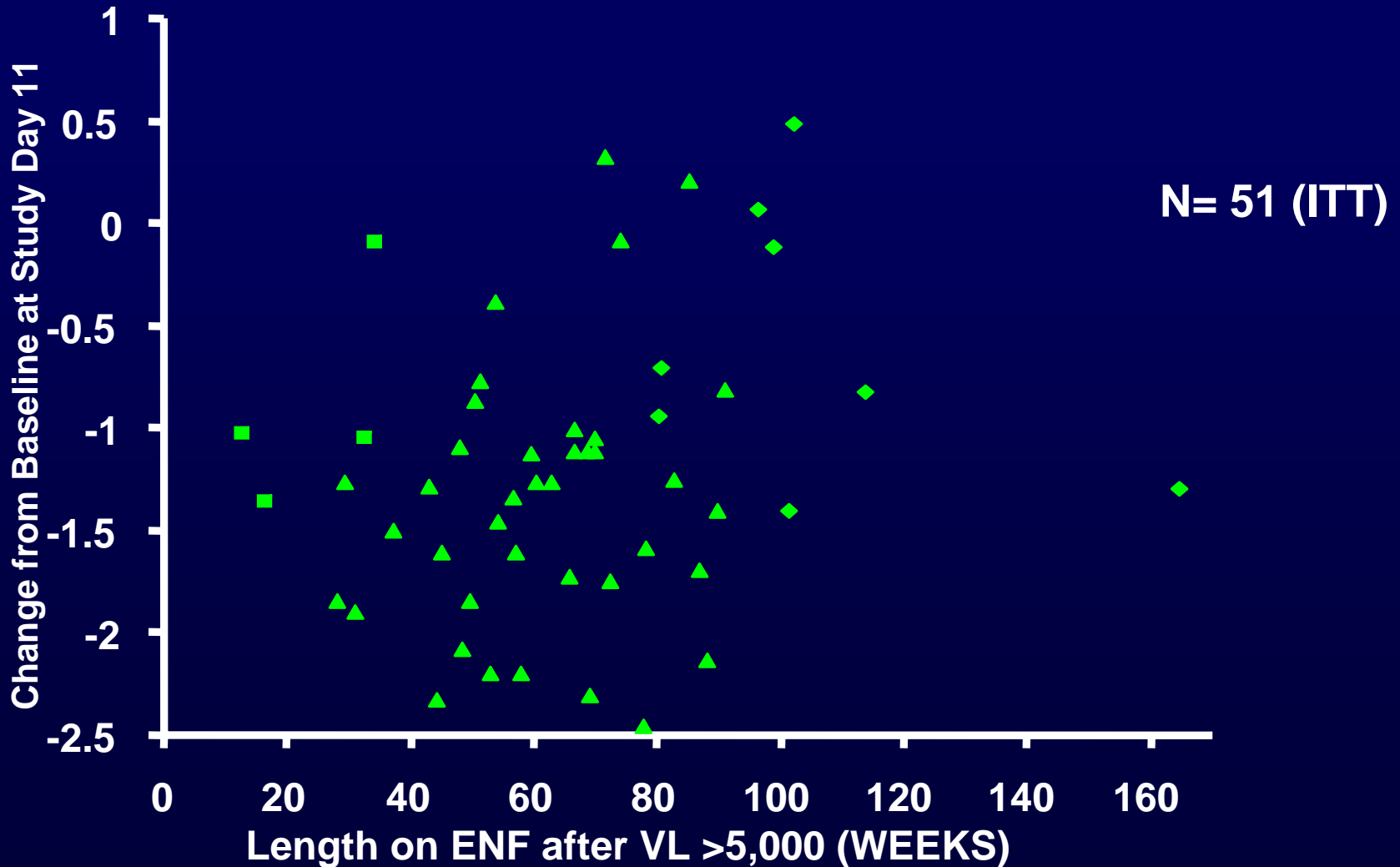
Day 11 change in log₁₀ HIV RNA versus Baseline T-1249 pIC₅₀



Spearman Correlation Coefficient ($r = -0.173$, $p = 0.230$)

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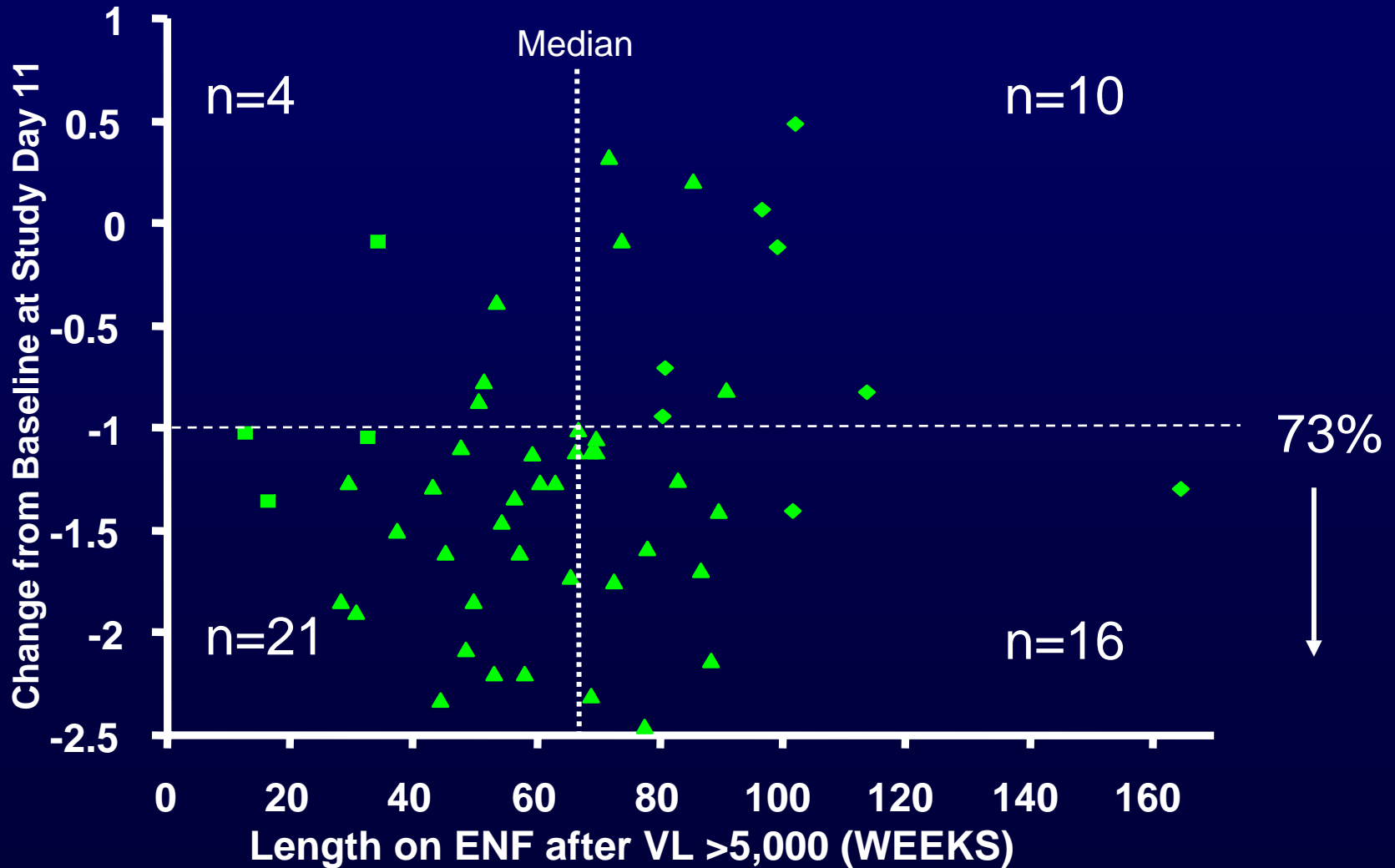
Length of ENF Therapy After VL $\geq 5,000$
versus Log RNA Change from Baseline to Study Day 11



Spearman Correlation Coefficient (r= 0.265, p=0.061)

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Length of ENF Therapy After VL $\geq 5,000$
versus Log RNA Change from Baseline to Study Day 11



Spearman Correlation Coefficient ($r= 0.265$, $p=0.061$)

Conclusions

- T-1249 was well tolerated in this patient population; no grade 3/4 abnormalities related to T-1249 occurred
- T-1249 demonstrates potent short term antiviral activity in most patients failing an ENF containing regimen
- Baseline T-1249 susceptibility does not appear to predict short-term antiviral responses to T-1249
- Studies are needed to establish the long term safety and antiviral efficacy of sequencing the fusion inhibitor class

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