Relationship between combination of baseline viral load and CD4 cell count, and Week 48 or 96 responses to rilpivirine (RPV) or efavirenz (EFV) in treatment-naïve HIV-1-infected adults: pooled analysis from the Phase III ECHO and THRIVE trials

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Pooled ECHO and THRIVE relationship between baseline viral load and CD4 cell count, and Week 48 or 96 responses: introduction

- **RPV was non-inferior to EFV in confirmed response (viral load <50 copies/mL, ITT-TLOVR) at Week 48 (primary objective)[1,2] and Week 96[3], in antiretroviral-naïve HIV-1-infected adults**
- **RPV is approved in the USA, Canada and Europe as a single-agent tablet (EDURANT®)[4,5] and as a qd, single-tablet regimen with TDF/FTC (Complera® [USA][6]; Eviplera® [EU][7])**
- **The European Medicines Agency approval of EDURANT® and Eviplera® is for patients with a viral load ≤100,000 copies/mL[5,7]**
- **Using pooled data from the ECHO and THRIVE trials, the aim of the current post-hoc analysis was to compare Week 48 and 96 responses and virologic outcomes within categories of baseline viral load and CD4 cell count, from a univariate perspective**

[1]Molina JM, et al. Lancet 2011;378:238-46; [2]Cohen CJ, et al. Lancet 2011;378:229-37
[3]Cohen CJ, et al. 6th IAS 2011. Abstract and poster TULBPE032; [4]Prescribing information for EDURANT™ (rilpivirine) tablets. 2011;
[5]EDURANT™ (rilpivirine) tablets Summary of Product Characteristics. Janssen-Cilag, November 2011;
[6]Prescribing information for COMPLERA™ (emtricitabine/rilpivirine/tenofovir DF fixed dose combination) tablets. 2011; [7]EVIPLERA ™
(emtricitabine/rilpivirine/tenofovir DF fixed dose combination) tablets Summary of Product Characteristics Gilead Sciences, November 2011

ITT-TLOVR = intent-to-treat time-to-loss-of-virologic response
TDF = tenofovir disoproxil fumarate; FTC = emtricitabine

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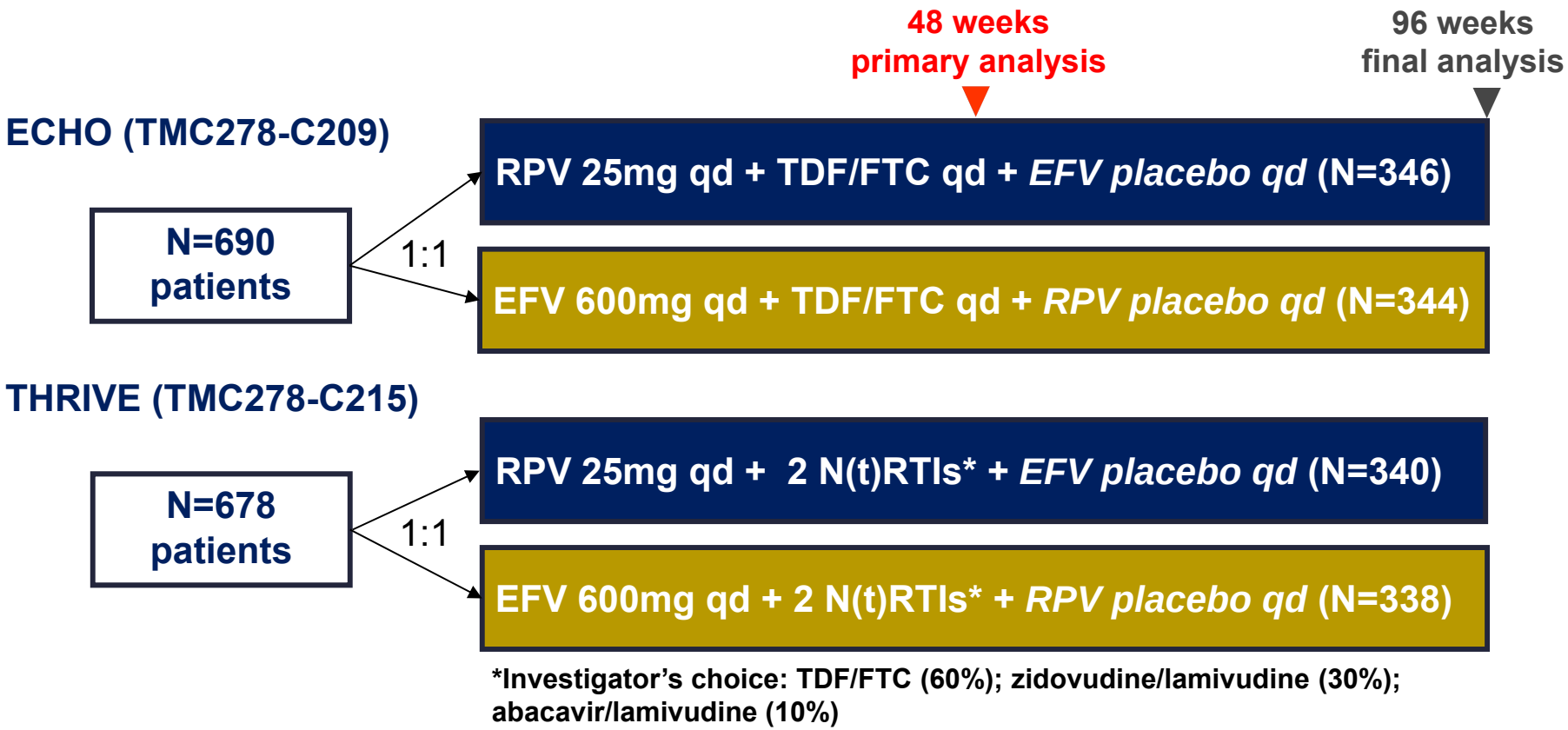
ECHO and THRIVE randomised Phase III double-blind study designs



*Investigator's choice: TDF/FTC (60%); zidovudine/lamivudine (30%); abacavir/lamivudine (10%)

- RPV/RPV placebo taken with food; EFV/EFV placebo taken on an empty stomach, at bedtime
- Randomization was stratified by baseline viral load: ≤100,000; >100,000–≤500,000 and >500,000 c/mL (and by background regimen in THRIVE). Given the small size of the >500,000 c/mL subgroup, data are presented in two subgroups: ≤100,000 c/mL and >100,000 c/mL

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Pooled ECHO and THRIVE analysis: baseline viral load and CD4 cell count

	RPV N=686	EFV N=682
Median $\log_{10}$ baseline viral load, c/mL (range)	5 (2–7)	5 (3–7)
Baseline viral load, % >100,000 c/mL	46	52
Median baseline viral load, c/mL (IQR)		
Median baseline viral load >100,000 c/mL	235,000 (152,000–443,000)	236,000 (150,000–460,000)
Median baseline viral load ≤100,000 c/mL	37,000 (18,000–59,000)	34,000 (16,000–62,000)
Median baseline CD4 cell count, cells/mm^3 (range)	249 (1–888)	260 (1–1137)

IQR=interquartile range

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Pooled ECHO and THRIVE Wk 48 analysis: response by baseline viral load or CD4 cell count

	RPV 25 mg qd N=686		EFV 600 mg qd N=682	
Week 48	N	Response, %	N	Response, %
Baseline viral load, c/mL				
≤100,000	368	90	330	84
>100,000	318	77	352	81
Baseline CD4 cell count, cells/mm^3				
<50	34	59	36	78
≥50–<200	194	80	175	82
≥200–<350	313	87	307	82
≥350	144	90	164	83

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Pooled ECHO and THRIVE Wk 96 analysis: response by baseline viral load or CD4 cell count

	RPV 25 mg qd N=686		EFV 600 mg qd N=682	
Week 96	N	Response, %	N	Response, %
Baseline viral load, c/mL				
≤100,000	368	84	329	80
>100,000	318	70	353	75
Baseline CD4 cell count, cells/mm^3				
<50	34	56	36	69
≥50–<200	194	71	175	75
≥200–<350	313	81	307	79
≥350	144	85	164	79

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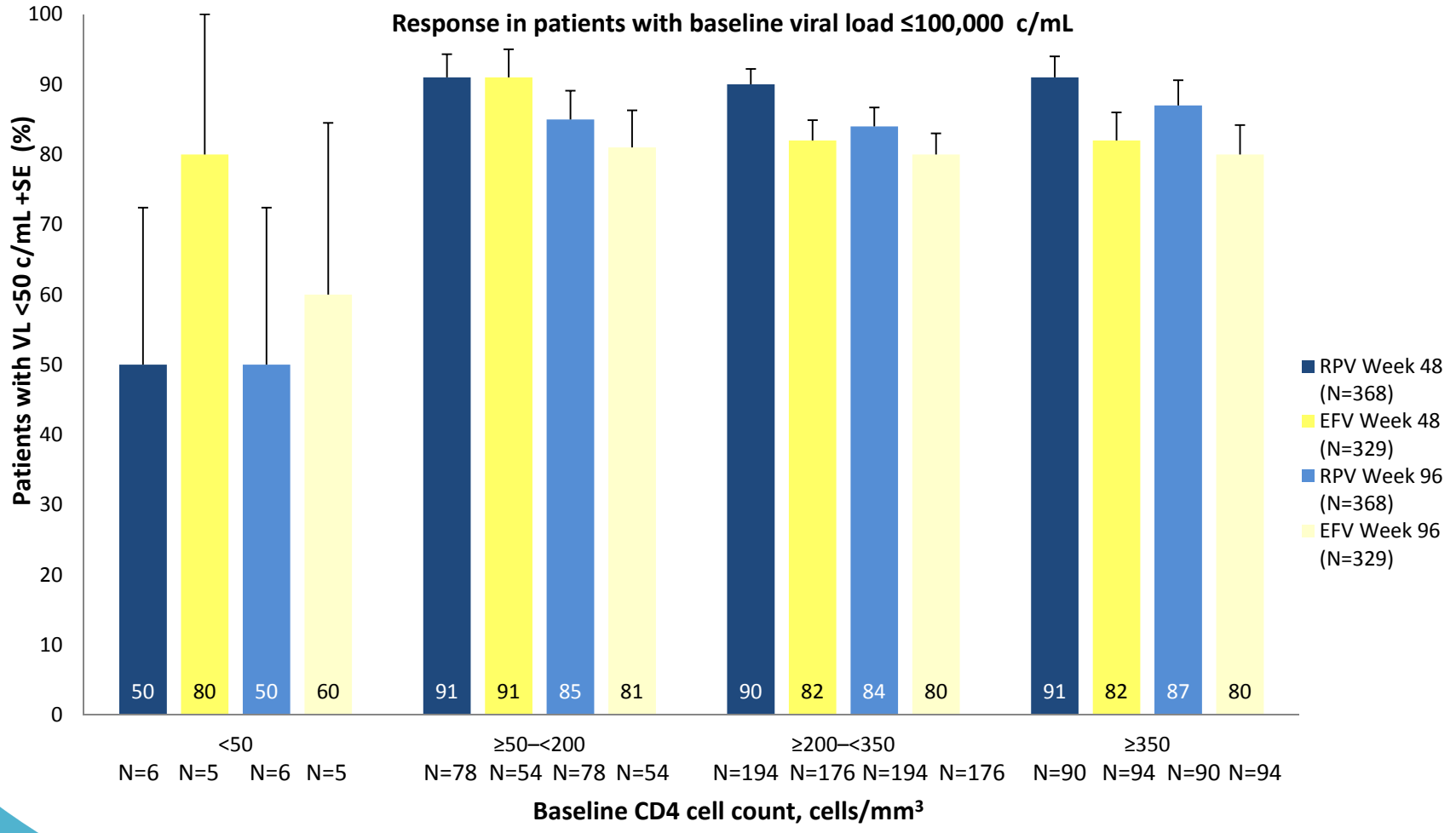
Pooled ECHO and THRIVE: response in patients with baseline viral load ≤100,000 c/mL by baseline CD4 cell count at Weeks 48 and 96



Response = viral load <50 c/mL, ITT-TLOVR; SE = standard error

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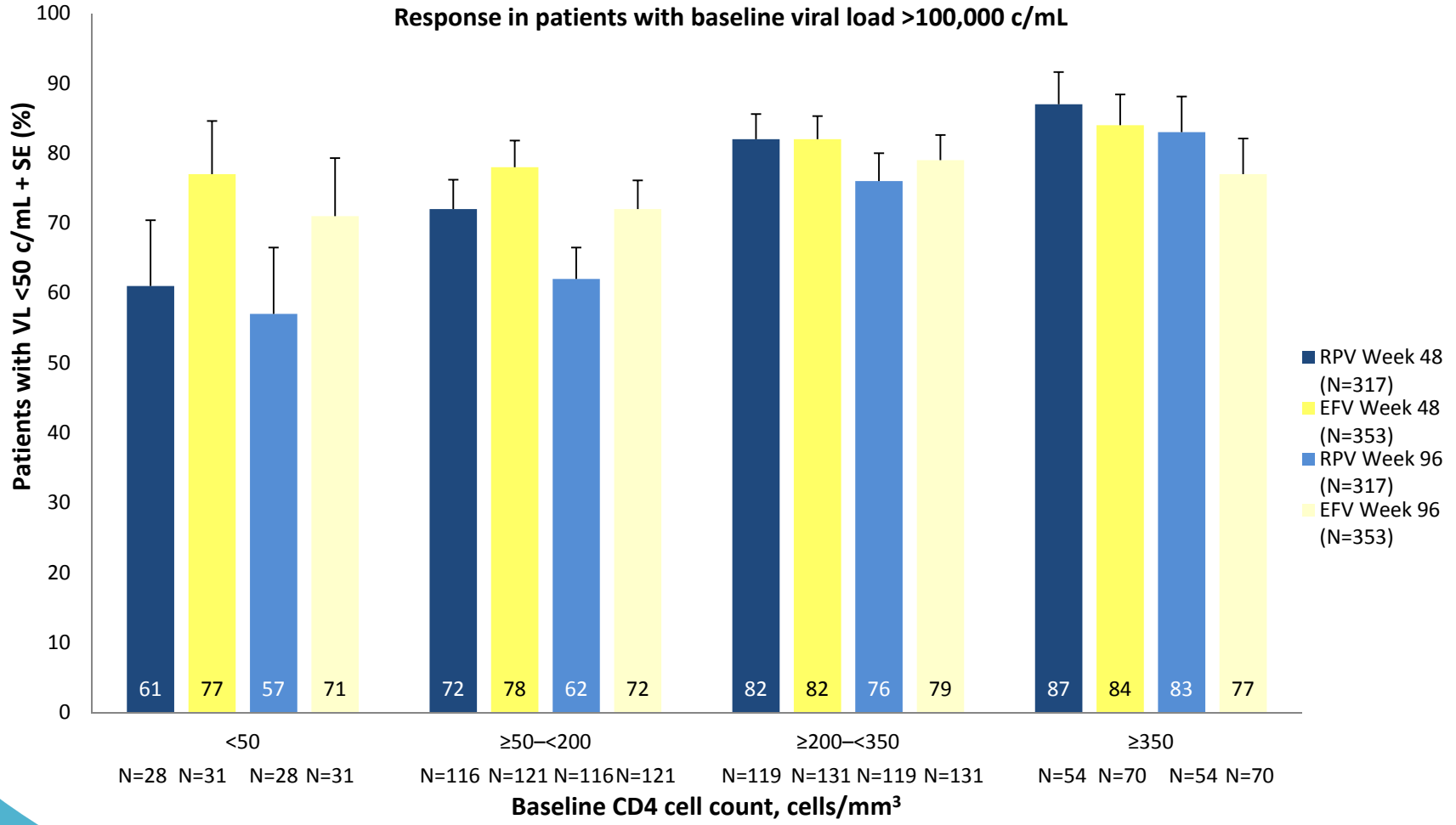
Pooled ECHO and THRIVE: response in patients with baseline viral load >100,000 c/mL by baseline CD4 cell count at Weeks 48 and 96



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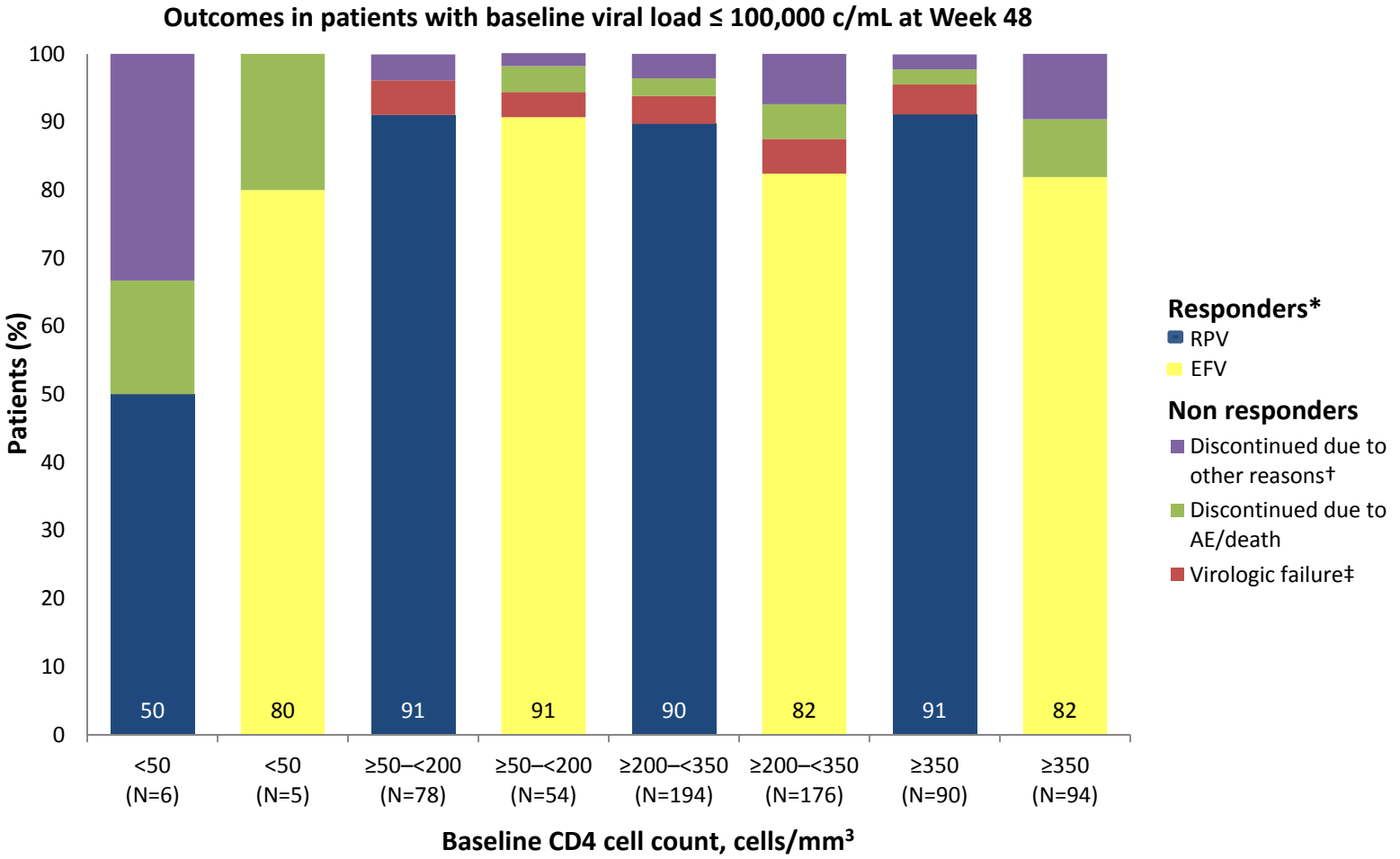
Pooled ECHO and THRIVE: virologic outcomes at Week 48 in patients with baseline viral load ≤100,000 c/mL by baseline CD4 cell count



*Patients with viral load <50 c/mL, ITT-TLOVR; †Lost to follow-up, non-compliance, withdrew consent, ineligible to continue, sponsor's decision; ‡Determined by TLOVR in the ITT population: confirmed response before Week 48 and confirmed rebound at or before Week 48, or no response before Week 48

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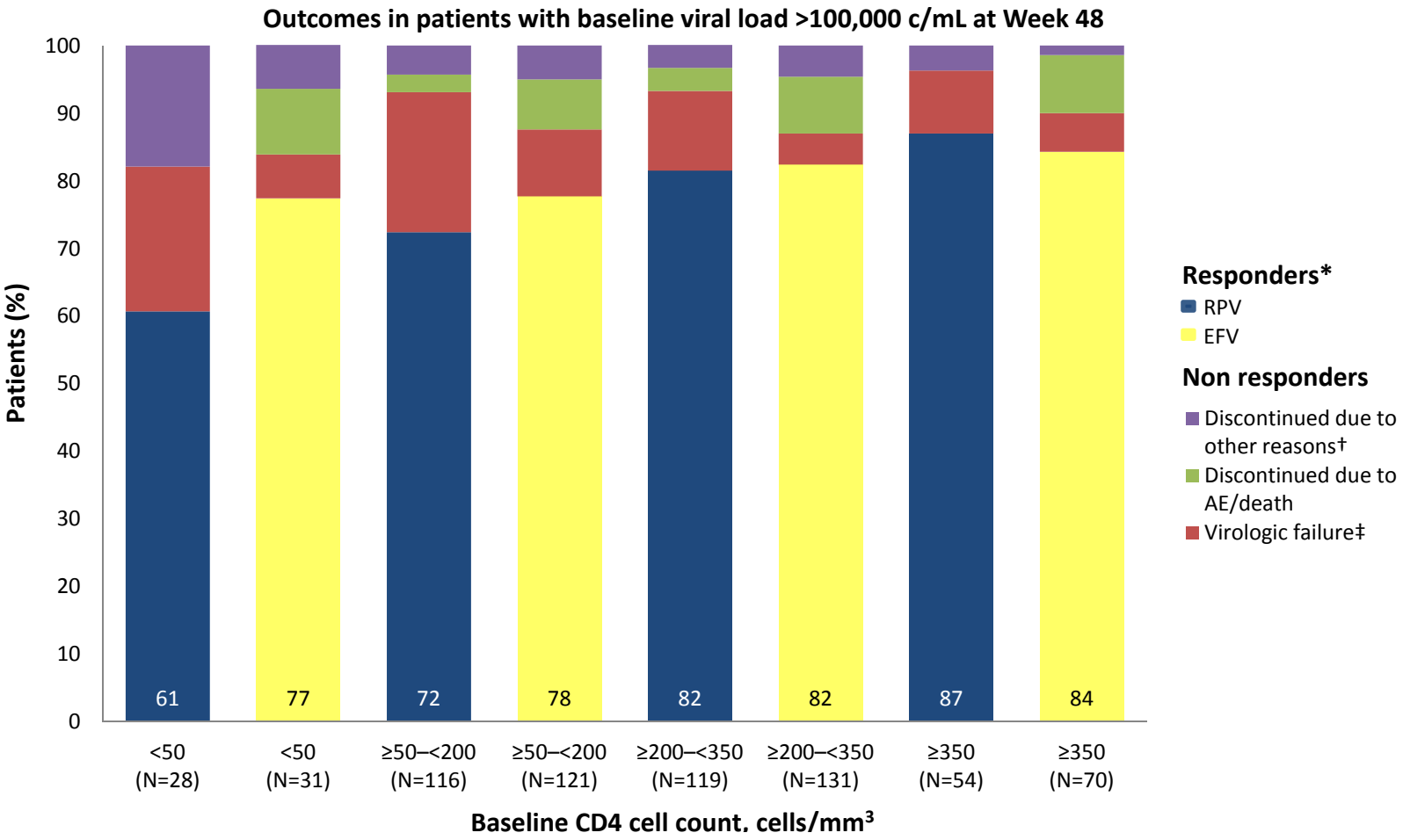
Pooled ECHO and THRIVE: Virologic outcomes at Week 48 in patients with baseline viral load >100,000 c/mL by baseline CD4 cell count



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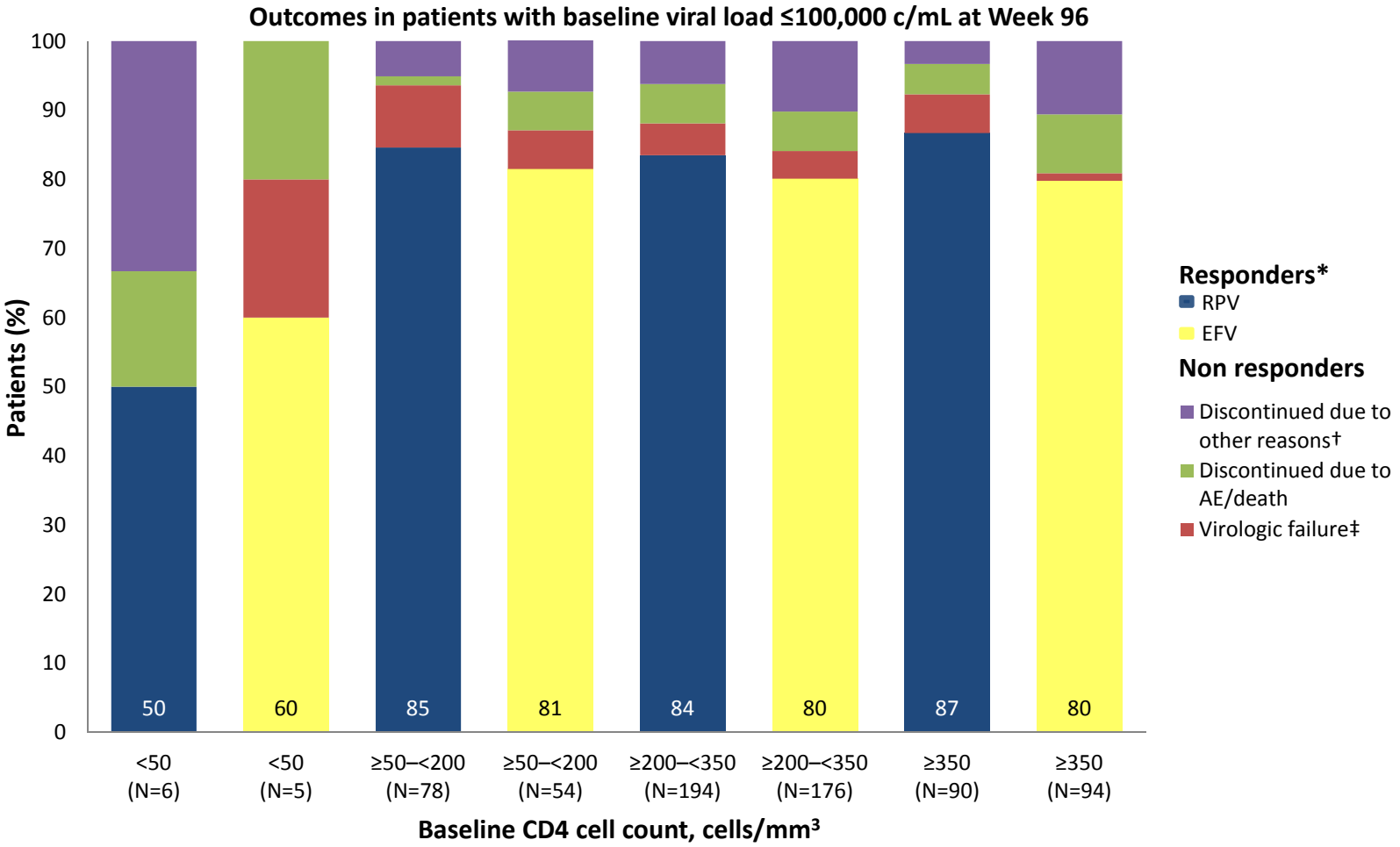

*Patients with viral load <50 c/Ml, ITT-TLOVR; †Lost to follow-up, non-compliance, withdrew consent, ineligible to continue, sponsor's decision; ‡Determined by TLOVR in the ITT population: confirmed response before Week 96 and confirmed rebound at or before Week 96, or no response before Week 96

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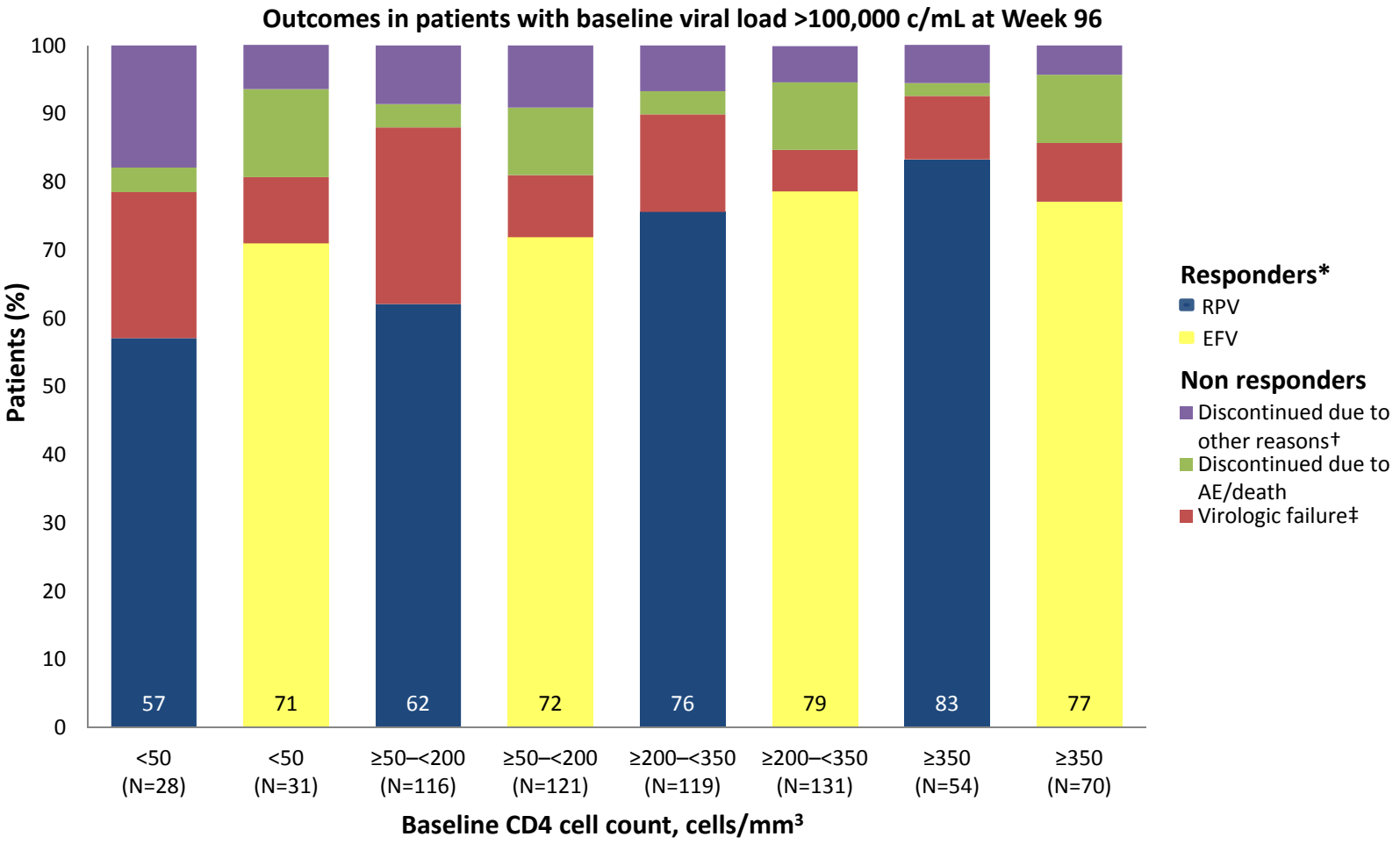
Pooled ECHO and THRIVE: Virologic outcomes at Week 96 in patients with baseline viral load >100,000 c/mL by baseline CD4 cell count



*Patients with viral load <50 c/Ml, ITT-TLOVR; †Lost to follow-up, non-compliance, withdrew consent, ineligible to continue, sponsor's decision; ‡Determined by TLOVR in the ITT population: confirmed response before Week 96 and confirmed rebound at or before Week 96, or no response before Week 96

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Conclusions

- **Responses with RPV were numerically higher than EFV responses in patients with both baseline viral load ≤100,000 c/mL and CD4 cell count ≥200 cells/mm^3**
- **Overall, non-inferiority between groups was met in patients with baseline viral load >100,000 c/mL (any CD4 cell count)**
  - **differences in responses between treatment groups (95% CI) at Week 48 and 96 were –3.4% (–9.6%; 2.7%) and –5.0% (–11.7%; 1.7%), respectively**
- **RPV responses were numerically lower than EFV responses in patients with baseline viral load >100,000 c/mL and CD4 cell count <200 cells/mm^3, but in patients with a CD4 cell count >200 cells/mm^3 and baseline viral load >100,000 c/mL, the response rates were similar**
- **A higher baseline VL or a lower CD4 cell count were partially predictive of response with RPV or EFV at Week 48 and 96 (lower for RPV than EFV)**

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Conclusions (cont'd)

- **The effect of CD4 cell count on treatment response was largely but not completely explained by the effect of baseline viral load (given the low rate of VF in patients with low viral load and low CD4 cell count)**
- **These results demonstrate that in patients with baseline viral load ≤100,000 c/mL and CD4 cell count >50 cells/mm^3 or with baseline viral load >100,000 c/mL and CD4 cell count >200 cells/mm^3, RPV gave good response rates**
  - **More patients on RPV discontinued due to VF and more patients on EFV discontinued due to AEs, especially for those with baseline viral load >100,000 c/mL**
  - **Results in some subgroups should be interpreted with caution because of small sample sizes, in particular CD4 cell count <50 cells/mm^3**

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