

# Safest NNRTI

Gary Maartens



Rilpivirine

# NNRTI overview

- Nevirapine clearly most toxic with highest potential for severe hypersensitivity reactions, especially with high CD4 counts (poor choice for the test & treat strategy)
- Etravirine is only used in salvage – only small phase 2 study versus EFV done as 1<sup>st</sup> line regimen:
  - Grade 2-4 adverse events 27% ETR vs 42% EFV
- No RCT of etravirine versus rilpivirine
- Efavirenz vs rilpivirine most data – 2 RCTs, ECHO & THRIVE

**TABLE 3. Summary of Treatment-Emergent AEs and Laboratory Abnormalities at the Time of the Week-48 Analysis**

	RPV 25 mg Once Daily, N = 686	EFV 600 mg Once Daily, N = 682
Median (range) treatment duration (wks)	56 (0–87)	56 (0–88)
AE, n (%)		
Any AE	616 (90)	629 (92)
Any treatment-related AE $\geq$ grade 2	109 (16)*	212 (31)
AE leading to permanent discontinuation	23 (3)	52 (8)
Any serious AE (including death)	45 (7)	55 (8)
Death	1 (0.1)	4 (1)
Most common treatment-related AEs $\geq$ grade 2 and occurring in $\geq$ 2% of patients in either group†		
Rash‡	7 (1)*	56 (8)
Dizziness	4 (1)	43 (6)
Abnormal dreams/nightmares	9 (1)	25 (4)
Headache	11 (2)	15 (2)
Insomnia	12 (2)	16 (2)
Nausea	5 (1)	17 (2)
Most common treatment-related AEs of interest (all grades) occurring in $\geq$ 10% of patients in either group†,§		
Any neurologic AE	117 (17)*	258 (38)
Dizziness	55 (8)*	179 (26)
Any psychiatric AE¶	102 (15)#	155 (23)
Abnormal dreams/nightmares	56 (8)**	87 (13)
Rash‡	21 (3)*	93 (14)
Treatment-emergent grade 2–4 laboratory abnormalities occurring in $\geq$ 5% of patients in either group, n (%)		
Any grade 2–4 laboratory abnormality		
Hypophosphatemia	62 (9)	69 (10)
Increased pancreatic amylase	42 (6)	60 (9)
Hyperglycemia (fasted)	37 (5)	30 (4)
Grade 2–3 increased LDL-cholesterol (fasted)††	38 (6)	102 (15)
Grade 2–3 increased total cholesterol (fasted)	34 (5)	122 (18)
Increased aspartate amino transferase	33 (5)	60 (9)
Increased alanine amino transferase	35 (5)	66 (10)

# Adrenal function

- In animals high doses ↑progesterone and ↓cortisol
  - Inhibits steroidogenesis
- In the pooled Phase 3 trials at Week 96:

Cortisol	RPV	EFV
Basal cortisol	-19.1	-0.6
ACTH-stimulated	18.4	54.1

- ?clinical significance (children/adolescents)

# Virological failure ECHO & THRIVE

Baseline VL	RPV	EFV	P
VL ≤100,000	19/368 (5%)	16/330 (5%)	0.987
VL >100,000	53/318 (17%)	23/352 (7%)	<0.0001

Proportion of failures with new resistance mutations:

RAMs	RPV	EFV	P
NNRTI	39/62 (64%)	15/28 (54%)	0.49
NRTI	42/62 (68%)	9/28 (32%)	0.003

# Conclusions

- Rilpivirine is the safest NNRTI for 1<sup>st</sup> line
- EFV is more effective, so this should remain first choice
- Rilpivirine could replace nevirapine as the second choice NNRTI in 1<sup>st</sup> line & could be used in 3<sup>rd</sup> line