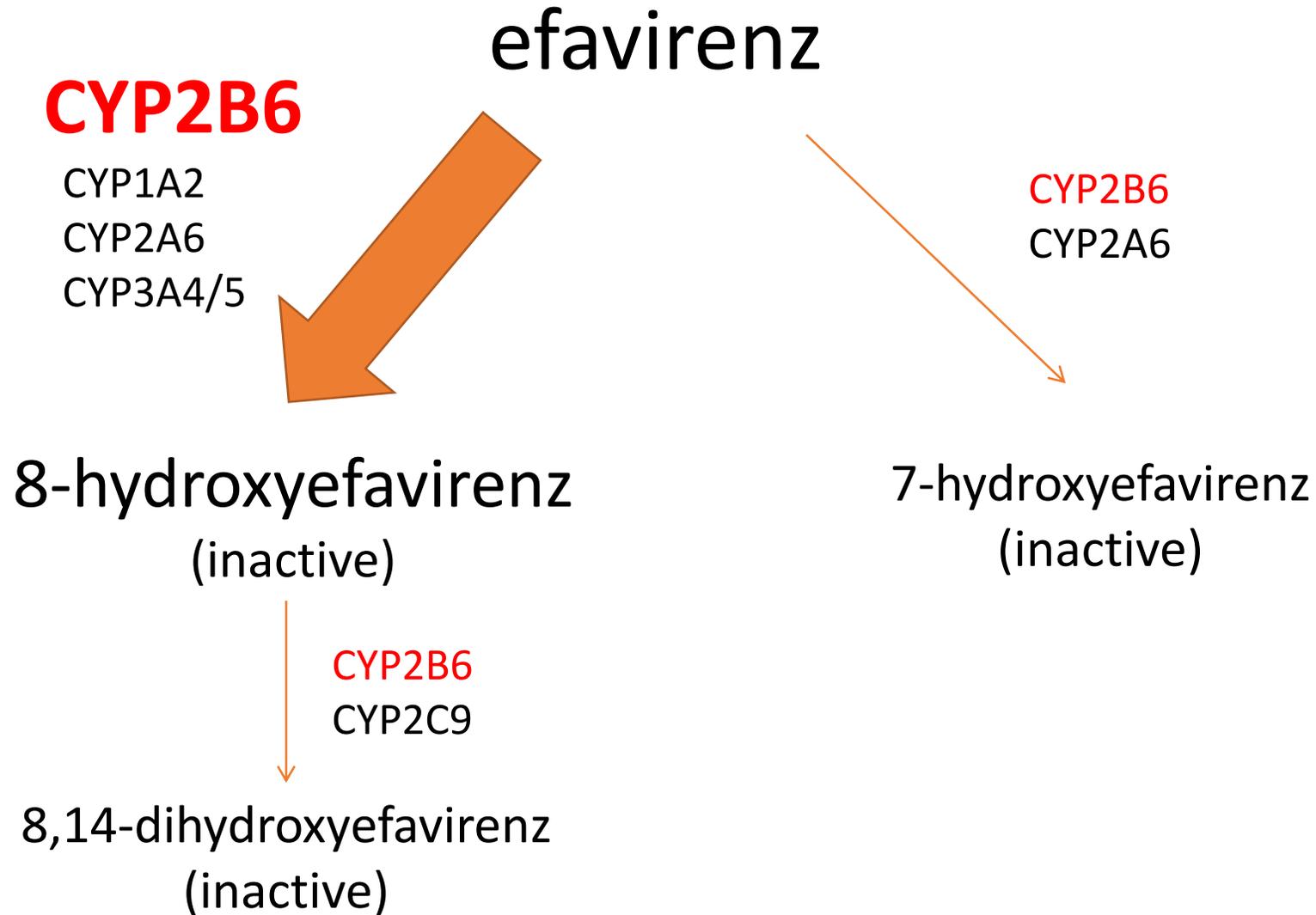


CYP2B6/efavirenz

Efavirenz is metabolized by **CYP2B6**



Efavirenz-associated CNS toxicity affects ~50% of patients



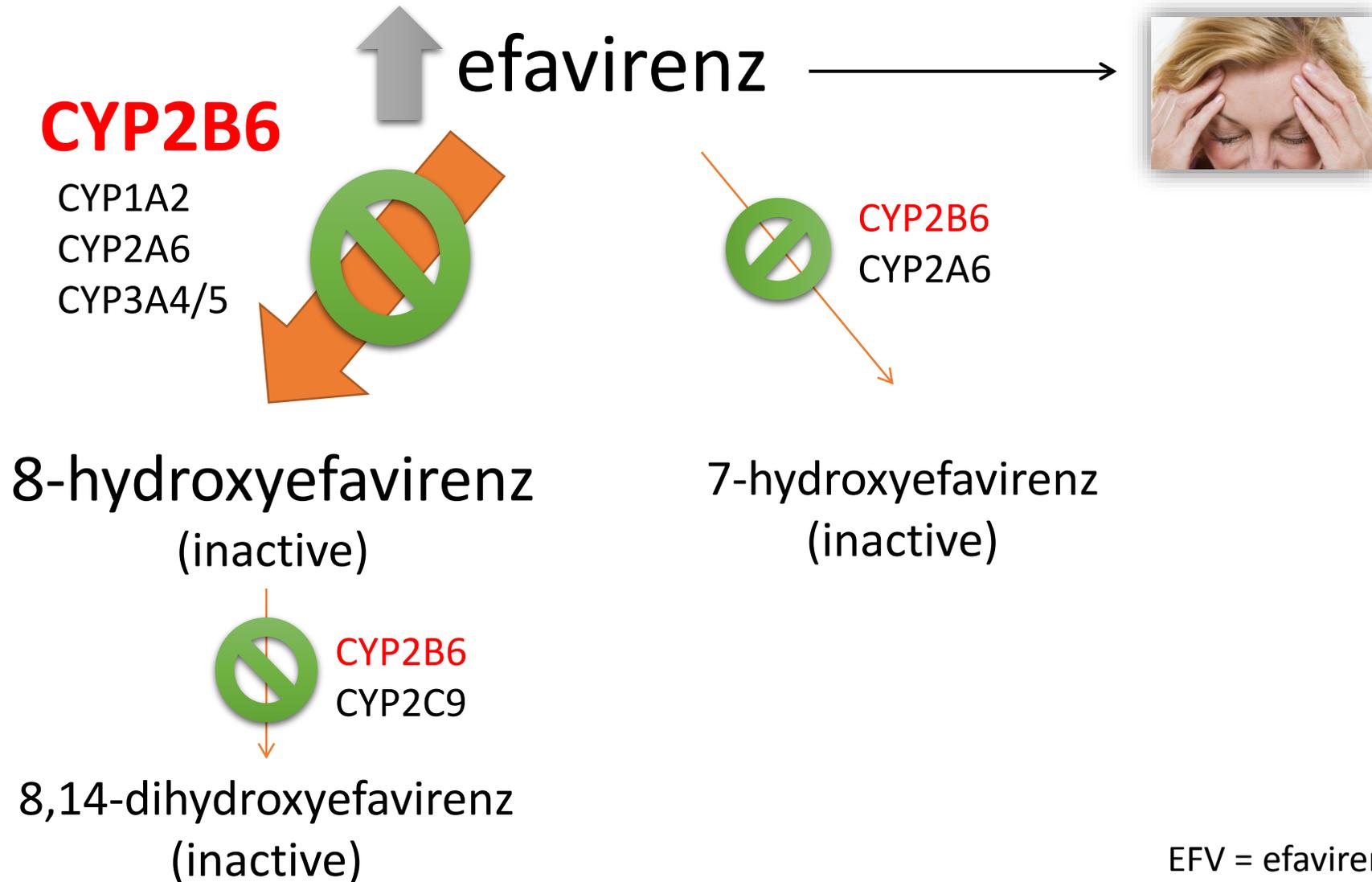
Poor quality of life

Decreased adherence

Treatment discontinuation

Symptoms usually begin within 1 to 2 days after starting efavirenz and **may resolve** within 2 to 4 weeks of continued therapy.

CYP2B6 516 G>T leads to increased EFV concentrations and CNS toxicity



CYP2B6 516 G>T is a component of several star alleles, including:

***6, *6A, *6B, *6C, *7, *7A, *7B, *9,
*13, *13A, *13B, *19, *20, *26,
*34, *36, *37, *38**

Evidence Review

DECREASING EVIDENCE	Study Conclusions	# Adult Studies	# Pediatric Studies	Total
	516 G>T is associated with increased EFV concentrations/decreased EFV clearance.	52	8	60
	516 G>T is associated with CNS toxicity.	16	2	18
	EFV dose reductions may benefit patients with 516 G>T.	11	0	11
	High EFV plasma concentrations are associated with CNS toxicity.	7	1	8
	High EFV plasma concentrations are associated with hepatotoxicity.	2	0	2
	516 G>T is associated with hepatotoxicity.	3	0	3
	516 G>T is associated with treatment discontinuation.	1	0	1

EFV = efavirenz

72 studies total (8 in pediatric patients)

EFV dose reductions may benefit patients with 516 G>T

Prospective study, n = 12 (adults)

Dose reductions based on elevated EFV concentrations (> 6 mg/L)

Table 2. Changes in CNS-related symptoms after reduction of efavirenz dosage.

Symptom	No. (%) of subjects who reported symptom status during efavirenz treatment		
	Present ^a	Improved ^b	Disappeared ^b
Dizziness	8 (57)	8 (100)	4 (50)
Strange dreams	7 (50) ^c	7 (100) ^c	0 (0)
Depression	5 (36)	5 (100)	1 (20)
Irritability	5 (36)	5 (100)	1 (20)
Concentration problem	4 (29)	4 (100)	2 (50)
Sleep difficulty	3 (21)	3 (100)	0 (0)
Any of the above	10 (71) ^c	10 (100) ^c	4 (40)

^a Including the 4 grades "slight," "sometimes," "often," and "always" at the initial dosage. Includes 2 patients whose efavirenz treatment was originally 400 mg and was reduced to 200 mg.

^b Percentage of those who initially reported "present."

^c Including 1 patient whose efavirenz dose was originally 400 mg and was reduced to 200 mg.

EFV dose reductions may benefit patients with 516 G>T, *without compromising efficacy*

