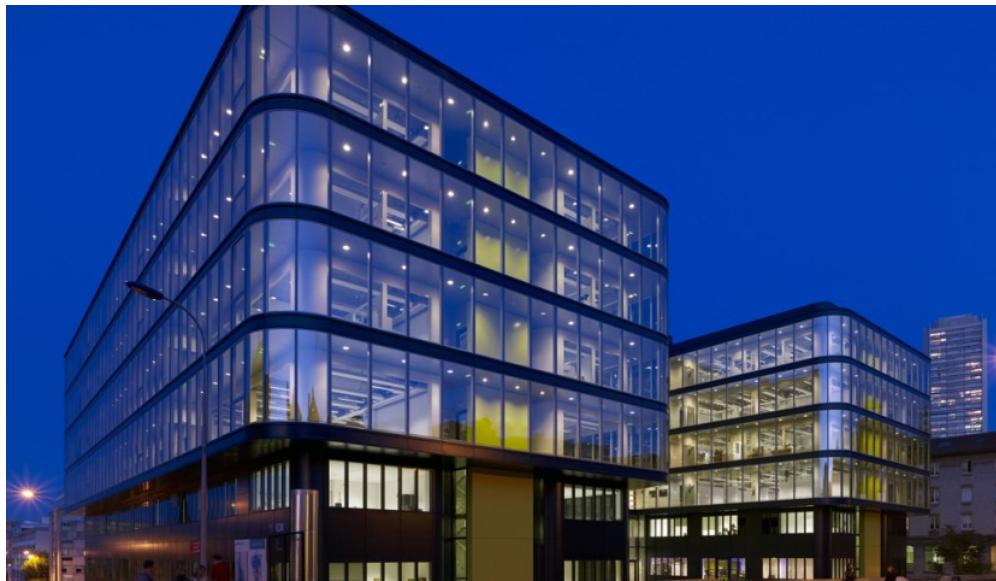


Triheptanoin is associated with clinical stability and decreased caudate atrophy in Huntington disease

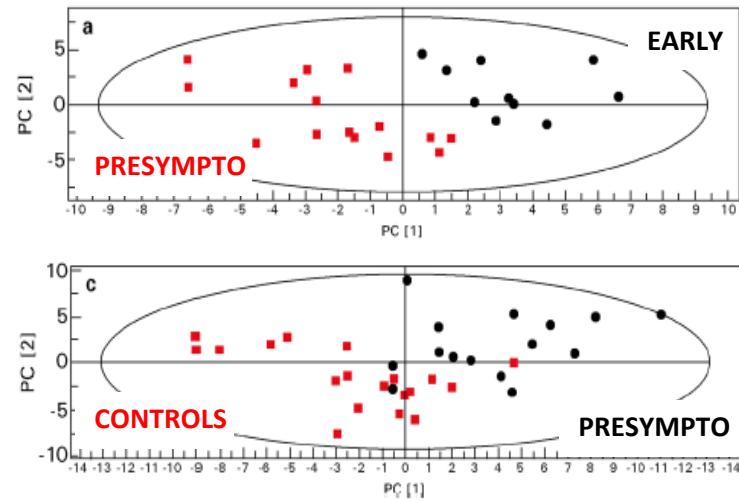
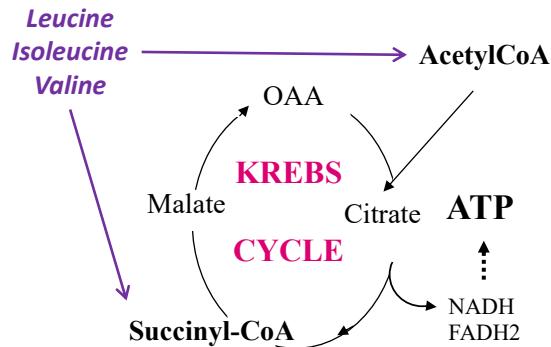
Fanny Mochel, Aurélie Méneret, Isaac Adanyeguh, Camille Giron, Elodie Hainque, Marie-Pierre Luton, Mariana Atencio, Magali Barbier, Milou Jacobs, Fleur C.M. Veldkamp, Emma M. Coppen, Anne Kampstra, Jessica Y. Winder, Kasper F. van der Zwaan, Eric Vicaut, Raymund Roos, Alexandra Durr



Background: Brain energy deficiency in HD

- Decreased levels of branched chain amino acids suggesting a need for Krebs cycle intermediates

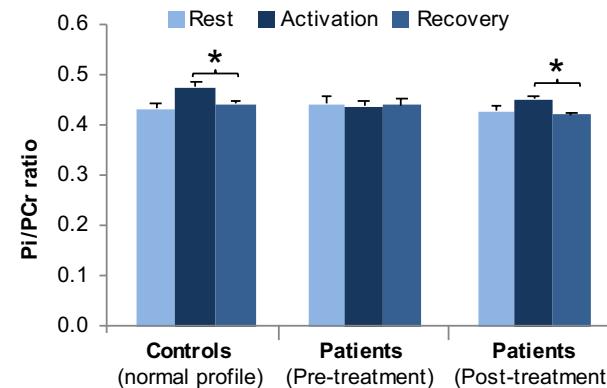
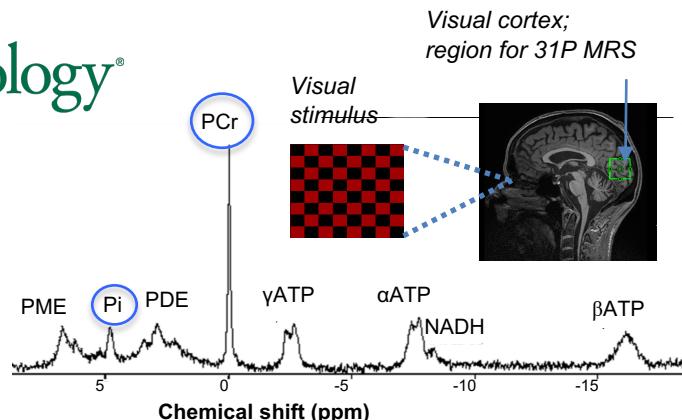
PLOS ONE



Mochel et al, PLoS One 2012

- Correction of abnormal brain energy profile in HD using triheptanoin for one month

Neurology®

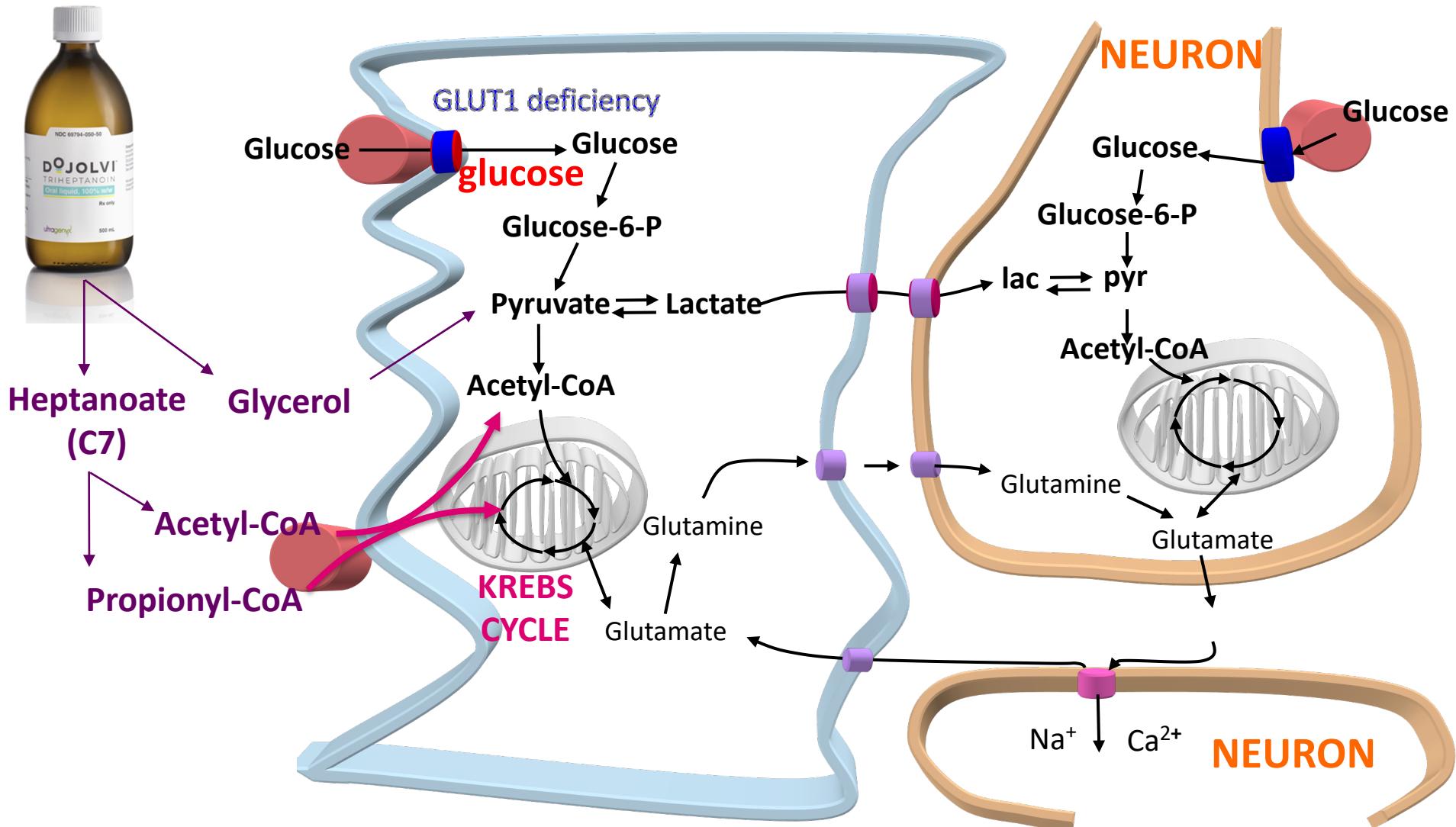


Adanyeguh et al, Neurology 2015

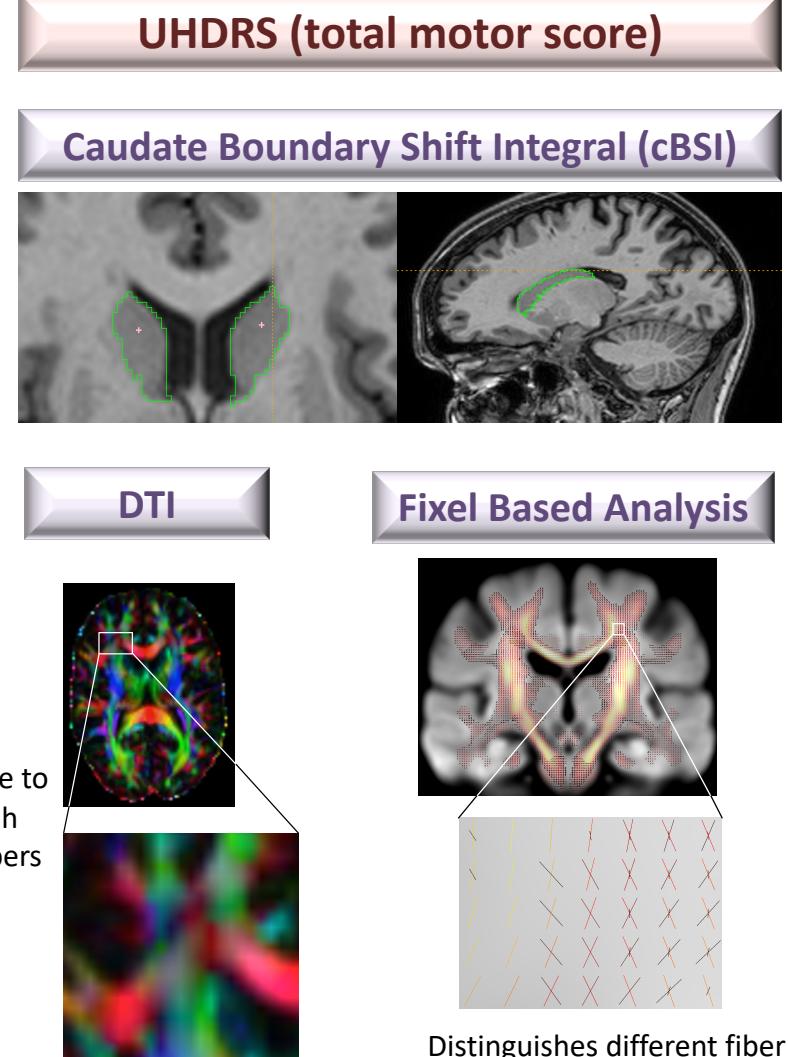
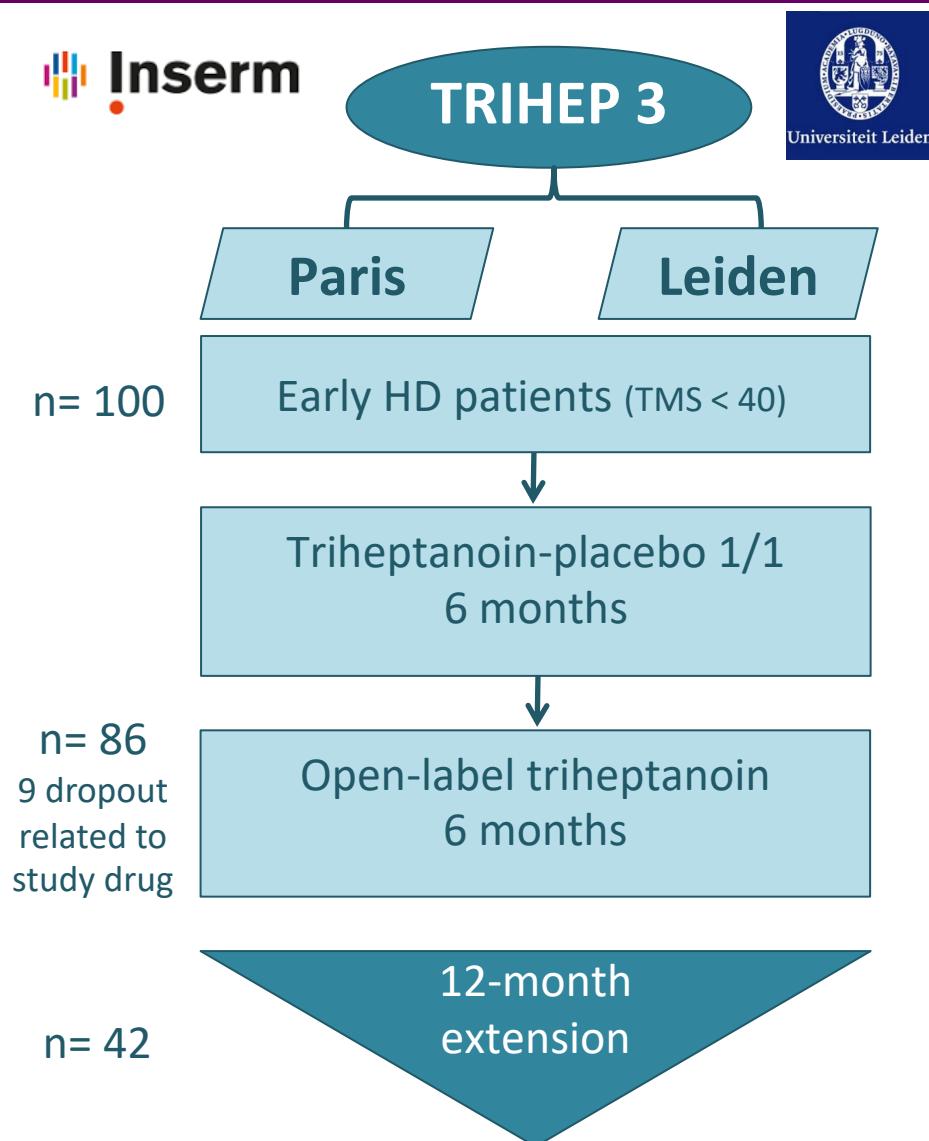
Triheptanoin – an anaplerotic drug (Krebs cycle)

- Major clinical benefit in GLUT1 deficiency

Hainque et al, J Neurol Neurosurg Psychiatry 2019
Mochel et al, J Neurol Neurosurg Psychiatry 2016



TRIHEP3 study



UHDRS-TMS

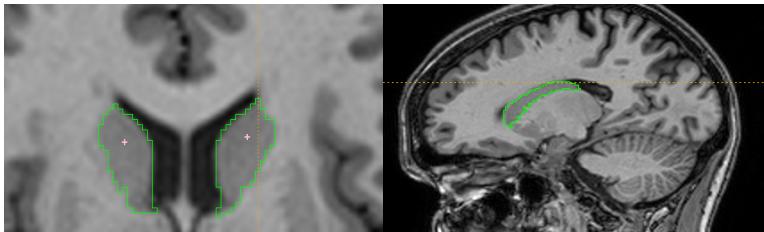
	Placebo N=50	Triheptanoin N=50	Overall Population N=100	p-value
Absolute change (between baseline and month 6) in UHDRS score				
n (miss.)	50(0)	45(5)	95(5)	
Mean ± sd	0.4 ± 4.4	1.6 ± 4.7	0.9 ± 4.5	0.215 ³
Median (Q1;Q3)	0.0 (-2.0;4.0)	1.0 (-1.0;4.0)	1.0 (-1.0;4.0)	
Min, Max	-11.0, 9.0	-11.0, 15.0	-11.0, 15.0	
Absolute change (between baseline and one year) in UHDRS score				
n (miss.)	46(4)	41(9)	87(13)	
Mean ± sd	2.5 ± 4.5	0.6 ± 5.1	1.6 ± 4.8	0.072 ³
Median (Q1;Q3)	2.0 (-1.0;5.0)	0.0 (-2.0;4.0)	1.0 (-1.0;5.0)	
Min, Max	-6.0, 15.0	-15.0, 12.0	-15.0, 15.0	
Absolute change (between month 6 and one year) in UHDRS score				
n (miss.)	46(4)	41(9)	87(13)	
Mean ± sd	1.9 ± 4.7	-0.7 ± 3.9	0.7 ± 4.5	
Median (Q1;Q3)	1.0 (-1.0;4.0)	0.0 (-4.0;2.0)	0.0 (-2.0;3.0)	0.024 ⁴
Min, Max	-7.0, 18.0	-9.0, 8.0	-9.0, 18.0	

⁴Mann Whitney U/Wilcoxon Sum Rank test

³Two-Sample T-test

Neuroimaging data

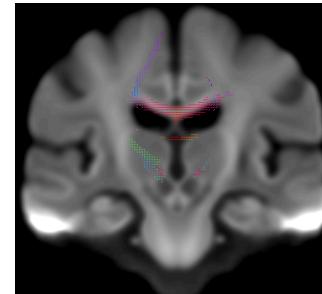
Caudate Boundary Shift Integral (cBSI)



- No difference in cBSI at 6 month

Pixel Based Analysis

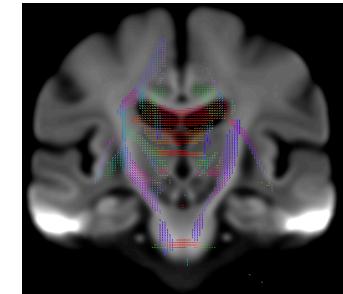
Triheptanoin



M0 > M24

- Greater alterations in placebo group

Placebo 6 months

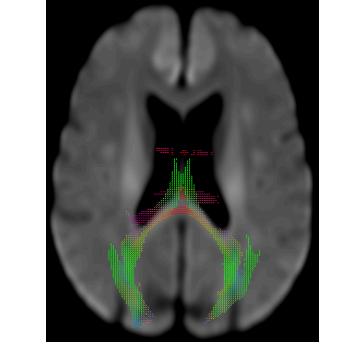
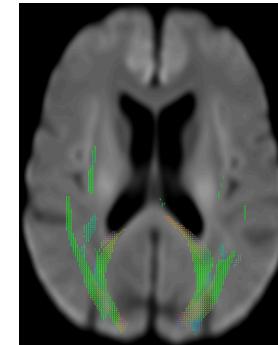


M6 > M24

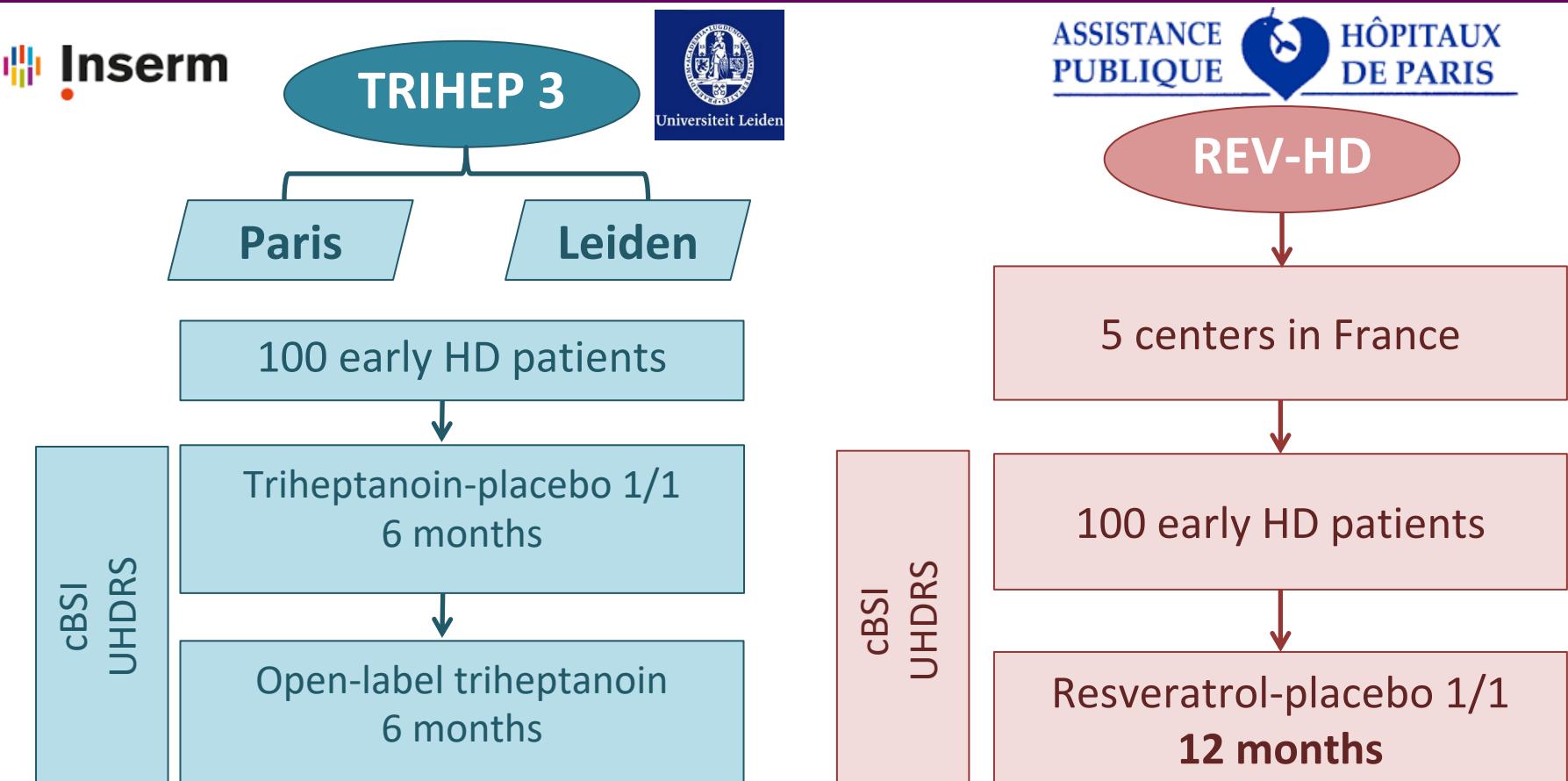
M24 > M0

M24 > M6

- Improved fiber metrics in both at 2y



Comparison with an external parallel placebo group



Age
Disease duration
TFC
UHDRS
CAG repeats



UHDRS-TMS

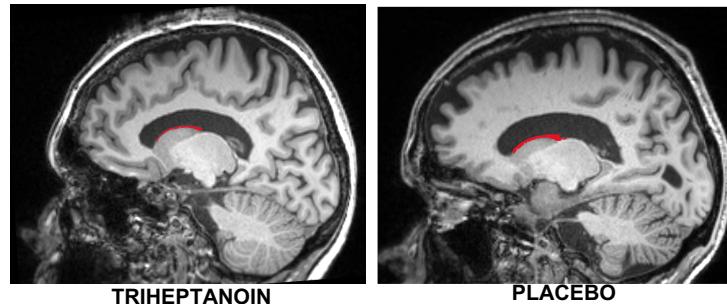
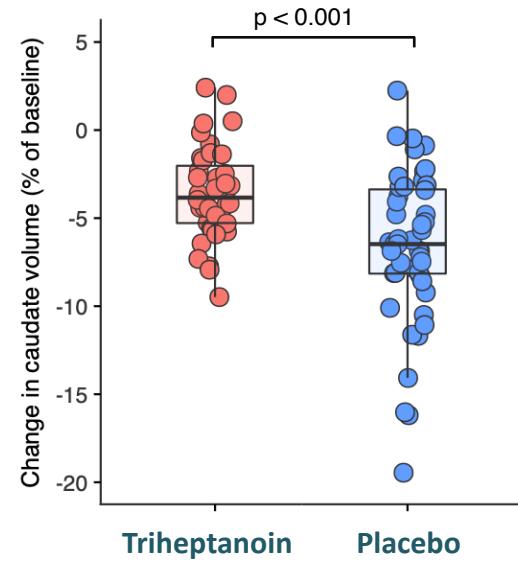
	Overall Population N=101	Triheptanoin N=50	Placebo REV- HD N=51	p-value
UDRS score at baseline				
n (miss.)	101 (0)	50 (0)	50 (0)	
Mean ± sd	20.2 ± 9.3	18.9 ± 9.1	21.5 ± 9.4	
Median (Q1;Q3)	18 (12;27)	16 (12;27)	21 (14;29)	
Min, Max	5, 40	6, 39	5, 40	
UHDRS score at one year				
n (miss.)	87(14)	41(9)	46(5)	
Mean ± sd	22.1 ± 11.0	19.4 ± 9.1	24.5 ± 12.0	
Median (Q1;Q3)	20 (13;31)	18 (13;23)	26 (16;33)	0.0455 ⁴
Min, Max	4, 52	6, 43	4, 52	
Absolute change (from baseline to one year) in UHDRS score				
n (miss.)	87(14)	41(9)	46(5)	
Mean ± sd	1.6 ± 4.9	0.6 ± 5.1	2.6 ± 4.6	0.0576 ³
Median (Q1;Q3)	1 (-1;6)	0 (-2;4)	3 (-1;6)	
Min, Max	-15, 12	-15, 12	-7, 12	

⁴Mann Whitney U/Wilcoxon Sum Rank test

³Two-Sample T-test

Caudate Boundary Shift Integral (cBSI)

	TRIHEP3 Triheptanoin	TRIHEP Placebo	REVHD Placebo	REVHD Resveratrol
6 months	0.021	0.019		
	<i>n=44</i>	<i>n=45</i>		
12 months	0.030	0.038	0.067	0.065
	<i>n=39</i>	<i>n=42</i>	<i>n=50</i>	<i>n=48</i>



Conclusion

- Triheptanoin was associated with clinical stability (UHDRS).
- Triheptanoin decreased the rate of caudate atrophy by 50%.
- Next step: phase 3 study?

THANK YOU

Amazing patients
& family!



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