Conventional (and not-so-conventional) Treatments for Idiopathic Hypersomnia

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List of FDA approved treatments for IH:

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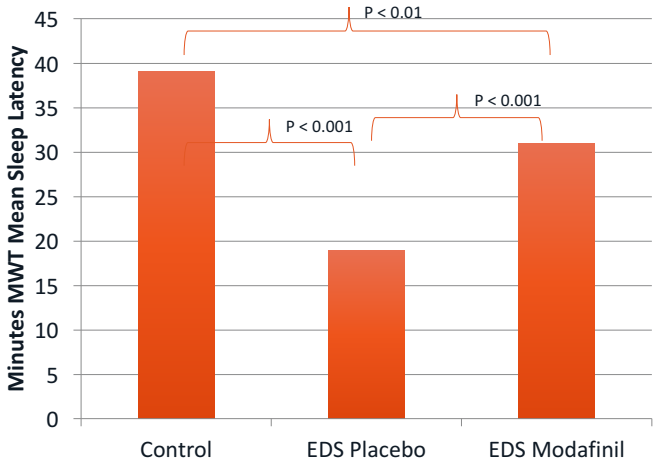
List of FDA approved treatments for narcolepsy:

- Non-amphetamine wake-promoting meds:
  - Provigil (modafinil)
  - Nuvigil (armodafinil)
- Amphetamines and related:
  - Ritalin/Ritalin SR/Metadate ER/Methylin/ (methylphenidate)
  - Adderall (dextroamphetamine/amphetamine)
  - Dexedrine/Dexedrine ER/Procentra/Zenzedi (dextroamphetamine)
- Xyrem (sodium oxybate)

hypersomnia foundation.org

Modafinil for IH or narcolepsy: Easier to stay awake



13 PWN, 14 with IH, 14 controls

Modafinil 200 mg bid vs placebo (RCT cross-over)

Phillip P, Sleep, 2014, 37(3):483-7

Modafinil improves, but doesn't normalize, safety risk

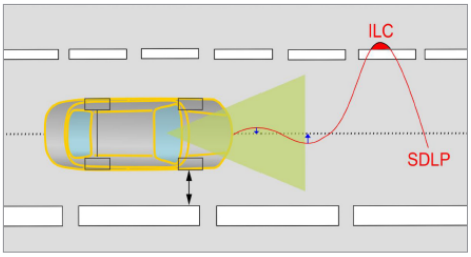


Figure 2—Schematic representation of the on-road driving test. A Continental system continuously records the actual position of the car within the traffic lane by tracking the relative distance of the car from the delineated stripe in the right of the road. Primary outcomes are Inappropriate Line Crossings (ILC) and Standard Deviation of Lateral Position (SDLP) (cm).

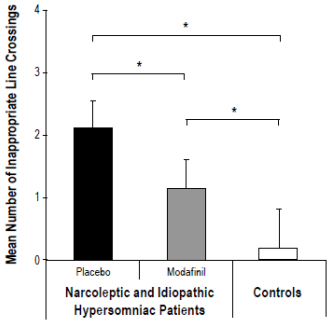
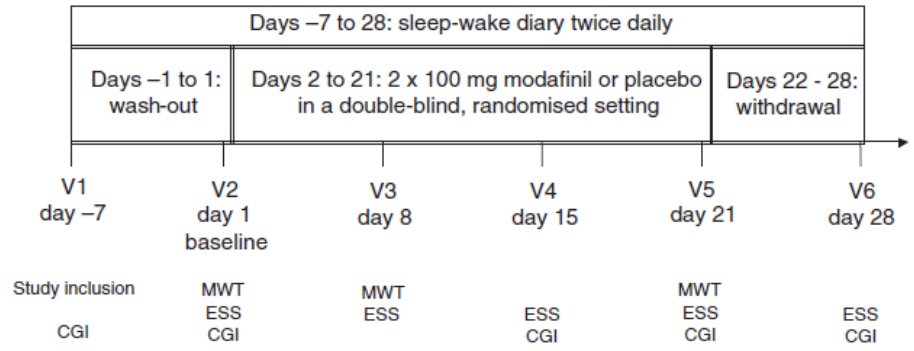


Figure 3—Mean number of Inappropriate Line Crossings (ILC) with on-road driving in patients with narcolepsy and idiopathic hypersomnia (IH) under placebo and modafinil and in healthy controls (mean ± standard error). *P < 0.05.

Phillip P, Sleep, 2014, 37(3):483-7

Modafinil for IH (without long sleep time)



Mayer G, J Sleep Res, 2015; 24(1):74-81

Modafinil for IH (without long sleep time)

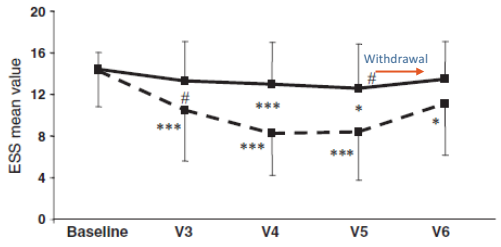


Figure 2. Epworth Sleepiness Scale (ESS) scores for modafinil and placebo. The solid line represents ESS scores for the placebo groups (n = 14) over time, the dashed line modafinil (n = 17). #$P < 0.1$; *$P < 0.05$; ***$P < 0.005$. Signs between the lines indicate group differences, signs above or below a line indicate the comparison with baseline. V = visit.

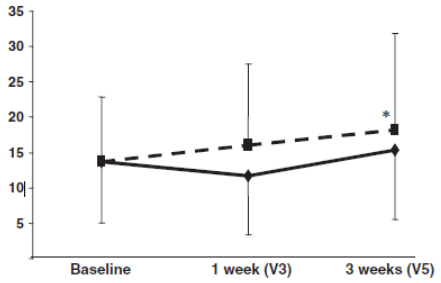
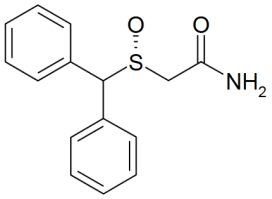
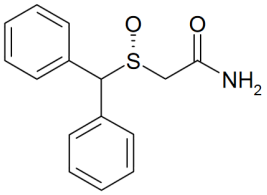


Figure 3. Mean Maintenance of Wakefulness test (MWT) sleep latency. V = visit. *$P < 0.05$ compared to baseline; solid line = placebo; dashed line = modafinil.

Mayer G, J Sleep Res, 2015; 24(1):74-81

Modafinil vs Armodafinil





Clinical series of patients with IH show 63% (124/197) remain on modafinil with good response

Modafinil package insert; Trotti LM, Sleep Med Clinics, 2017

Stimulants for IH

	Clinical series	Sample size	Response rate
Methylphenidate	-Ali 2009	N = 61	-41% remained on methylphenidate with complete response
Amphetamine-Dextroamphetamine	-Ali 2009	N = 8	-25% remained on amphetamine-dextroamphetamine with complete response
Dextroamphetamine	-Ali 2009 -Anderson 2007	N = 15	-33% responded to dextroamphetamine

25% of IH patients are unable to achieve good symptom control with "standard" medications

Trotti LM, Sleep Med Clinics, 2017

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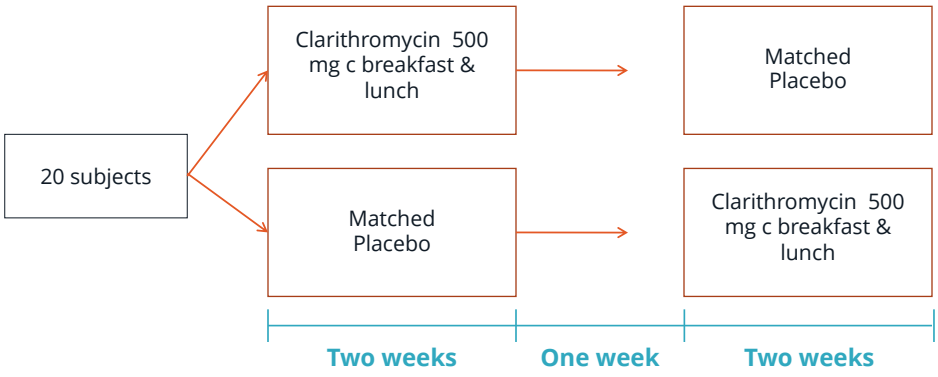
Unconventional (but published) treatments for IH

Sodium oxybate for IH (compared to people with narcolepsy)

	IH (n = 46 ever prescribed; 85% actually took)	NT1 (n ~42)	P-value	
Max total dose (gm/night)	4.3 (+/- 2.2)	6.6 +/- 2.8	0.03	← **IH patients took less**
Single evening dose	66%	21%	<0.01	← **IH patients often took only one dose**
ESS change	-3.5 (+/- 4.5)	-3.2 (+/- 4.2)	NS	← **But sleepiness improved**
Improvement in sleep drunkenness	24/34 (71%)	3/7 (43%)	NS	← **And so did sleep drunkenness**
Continued treatment	47%	32%		

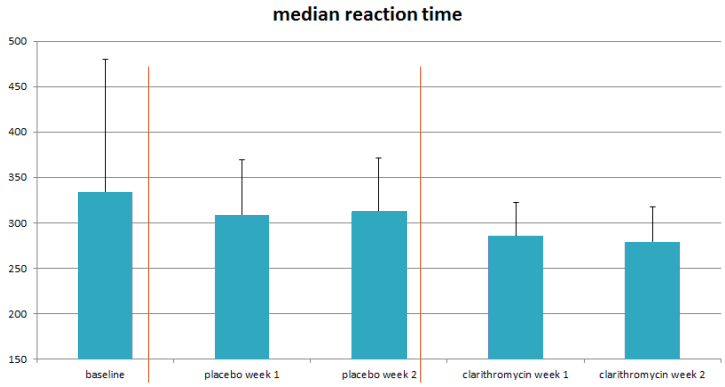
Leu-Semenescu S, 2016, Sleep Medicine

Clarithromycin: A randomized, double blind, placebo controlled trial



Funded by the American Sleep Medicine Foundation

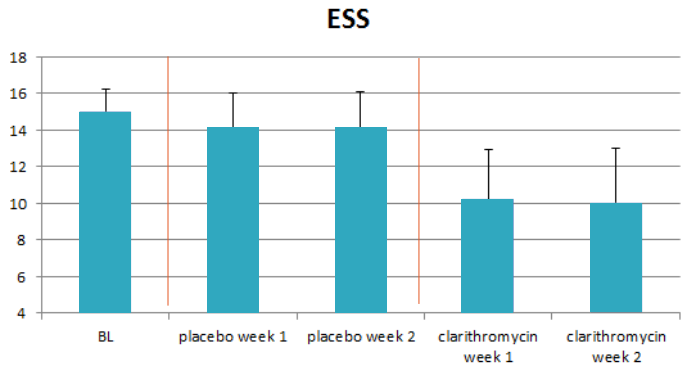
Primary outcome measure: median reaction time (psychomotor vigilance task)



P = NS

Trotti LM, Annals Neurology, 2015

Secondary outcome measures:
Epworth Sleepiness Scale



P < 0.005

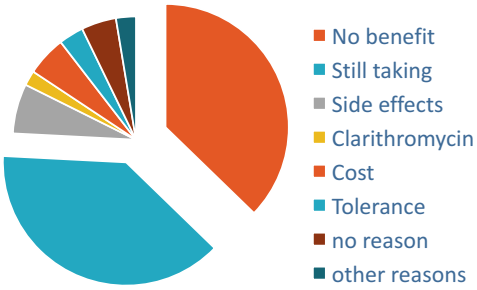
CL < PL = B

Trotti LM, Annals Neurology, 2015

Compounded flumazenil

hypersomnia foundation.org

Clinical experience with flumazenil (n = 153)



Benefit reported by 63%

Ongoing treatment in 39%

ESS change (n = 40):

- baseline 15.0 +/- 4.7
- flumazenil 10.3 +/- 5.1
- $p < 0.0001$

Trotti LM, JCSM, 2016

Levothyroxine and IH (with long sleep time)

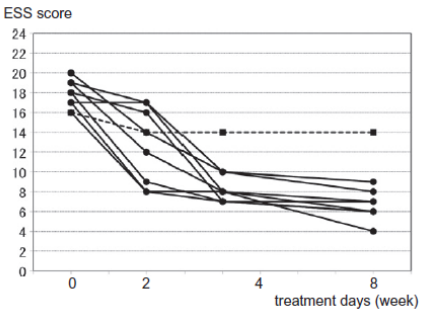
Case series

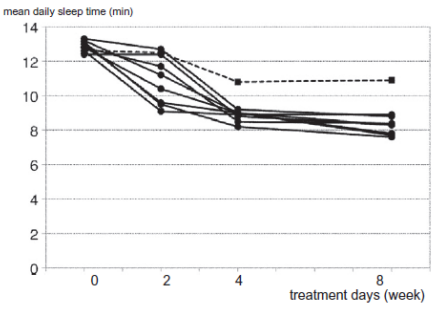
9 patients with IH + LST

NORMAL thyroid function

- TSH average 1.71
  - range 0.66-3.42

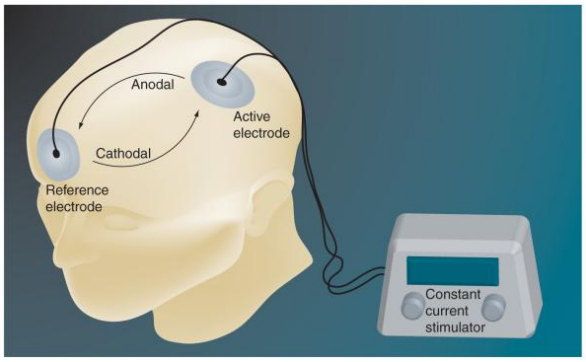
Levothyroxine 25 mcg





Shinno H, Sleep Med, 2011

Transcranial direct current stimulation in untreated patients with IH



- 8 previously untreated IH patients
- 3 stimulations per week x 4 weeks, performed between 8 and 11 am
- 5.75 point decrease in ESS, 7/8 reporting improvement in sleepiness, and improvements in reaction times on attention test

Galbiati A, Archives italiennes de biologie, 2016;
Schlaug G, Expert Rev Med Devices, 2008

Thank you!