Patient 3. Diagnosed solely on the score of ADAS COG. Prescribed Aricept.

Arthritis

Back Pain –Non Specific

Constipation

Gastro-Esophogeal Reflux Disease

Drugs

Codeine 30-60mg QID

Celecoxib 200mg BID

Docusate Sodium 200mg BID

Lactulose 15mls BID

Omeprazole 40mg od

New Medication :

Donepezil 10mg od

**Pharmacogenetic Data**

**CYP2C9 Variants PM and EM genotypes and drug exposure**; “Patients who are known or suspected to be P450 2C9 poor metabolizers based on a previous history should be administered celecoxib with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.”

**5.9 Ultra-rapid Metabolizers of Codeine**Some individuals may be ultra-rapid metabolizers due to a specific CYP2D6\*2x2 genotype. These individuals convert codeine into its active metabolite, morphine, more rapidly and completely than other people. This rapid conversion results in higher than expected serum morphine levels. Even at labeled dosage regimens, individuals who are ultra-rapid metabolizers may experience overdose symptoms such as extreme sleepiness, confusion, or shallow breathing.
The prevalence of this CYP2D6 phenotype varies widely and has been estimated at 0.5 to 1% in Chinese and Japanese, 0.5% to 1% in Hispanics, 1 to 10% in Caucasians, 3% in African Americans, and 16 to 28% in North Africans, Ethiopians, and Arabs. Data are not available for other ethnic groups. (Precautions 5)

When physicians prescribe codeine-containing drugs, they should choose the lowest effective dose for the shortest period of time and inform their patients about these risks and the signs of morphine overdose. [see Use in Specific Populations (8)] There is no relevant effect of genetic variation in CYP2B6, CYP2C9, CYP2C19, or CYP3A5 on the pharmacokinetics of prasugrel’s active metabolite or its inhibition of platelet aggregation. (12 Clinical Pharmacology 12.5 Pharmacogenomics) Whereas the pharmacokinetics of prasugrel’s active metabolite are not known to be affected by genetic variations in CYP2B6, CYP2C9, CYP2C19, or CYP3A5, the pharmacokinetics of clopidogrel’s active metabolite are affected by CYP2C19 genotype, and approximately 30% of Caucasians are reduced-metabolizers. (14 Clinical Studies)

**Drug Interactions and Metabolism**

**Cytochrome P 450 Subtype**

**Subtype indicated describes the specific isoenzymes of the P450 System responsible for the metabolism of the specific drugs patient has in their profile – this data can be found in Facts and Comparisons, Micromedex, The Drug Information Handbook, and is available to prescribers – It will likely be most accurate from these sources, which are at a fee.**

**(graphs indicate data we need to figure out how to obtain from genetic profiling and Pharm GKB and provide to the prescriber!)**

1A2



2C8



2C9

CELECOXIB – unclassified



2C19

OMEPRAZOLE – major strong



2D6

CODEINE Major

DONEPEZIL substrate



3A4 -

CODEINE -Minor

DONEPEZIL substrate



Avoid Alcohol

St, Johns wart may decrease levels of codeine

Avoid St Johns wart, kava kava, gotu kola

Genetic/Biomarker associations : In no specific Order of Importance

|  |  |
| --- | --- |
| NEUROLOGY 2009;73:761-767© 2009 [American Academy of Neurology](http://www.neurology.org/misc/terms.shtml) **Effect of a *CYP2D6* polymorphism in the efficacy of donepezil in patients with Alzheimer disease****Alberto Pilotto, MD, M. Franceschi, MD, G. D’Onofrio, PsyD, A. Bizzarro, MD, F. Mangialasche, MD, L. Cascavilla, MD, F. Paris, MD, M. G. Matera, BiolD, Andrea Pilotto, MD, A. Daniele, MD, P. Mecocci, MD, C. Masullo, MD, B. Dallapiccola, MD and D. Seripa, BiolD****Conclusions:** The single nucleotide polymorphism rs1080985 inthe *CYP2D6* gene may influence the clinical efficacy of donepezilin patients with mild to moderate Alzheimer disease (AD). Theanalysis of *CYP2D6* genotypes may be useful in identifying subgroupsof patients with AD who have different clinical responses todonepezil.Psychiatry (Edgmont). 5(2): 51–56. Published online 2008 February.  | PMCID: PMC2731690 |

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Biomarkers for the Identification and Treatment of Dementia

Steven D. Targum, MD

The currently available cholinesterase-inhibitor drug therapies are based on the “cholinergic hypothesis” and suggest that AD is due to reduced biosynthesis of the neurotransmitter acetylcholine. In clinical practice, the acetylcholinsterase-inhibitors (AchE-I) only treat symptoms of the disease and have neither halted nor reversed it. Although these drugs provide some initial benefit, they do not affect the underlying molecular basis of AD and are therefore not neuroprotective. Instead, contemporary research has focused on whether or how to interfere with the toxic effects of the aggregated abnormal proteins, β-amyloid and tau. Essentially, there is no clinical value-added for measuring biomarkers during treatment with cholinesterase-inhibitors.

**Neuro-Imaging**

Am J Psychiatry 162:676-682, April 2005
© 2005 [American Psychiatric Association](http://ajp.psychiatryonline.org/misc/terms.shtml)

## Does Donepezil Treatment Slow the Progression of Hippocampal Atrophy in Patients With Alzheimer’s Disease?

**Mamoru Hashimoto, M.D., Ph.D., Hiroaki Kazui, M.D., Ph.D., Keiji Matsumoto, M.D., Yoko Nakano, M.D., Ph.D., Minoru Yasuda, M.D., Ph.D., and Etsuro Mori, M.D., Ph.D.**

**CONCLUSIONS:**Donepezil treatment slows the progression of hippocampal atrophy,suggesting a neuroprotective effect of donepezil in Alzheimer’sdisease.

**This Fake Patient’s Values are in the Far Right Column**

**Electrolytes and Metabolytess**

|  |  |  |
| --- | --- | --- |
| **Test** | **Range** | **Comments** |
| [Sodium](http://july.fixedreference.org/en/20040724/wikipedia/Sodium) (Na) | 130 - 145 mmol/L |  130 |
| [Potassium](http://july.fixedreference.org/en/20040724/wikipedia/Potassium) (K) | 3.5 - 5.0 mmol/L | 3.9 |
| [Urea](http://july.fixedreference.org/en/20040724/wikipedia/Urea) | 2.6 - 6.8 mmol/L | 5 |
| [Creatinine](http://july.fixedreference.org/en/20040724/wikipedia/Creatinine) | 50 - 110 μmol/L | 100 |
| [Glucose](http://july.fixedreference.org/en/20040724/wikipedia/Glucose) (fasting) | 4.2 - 6.1 mmol/L | 5 |

**Liver function tests**

|  |  |  |
| --- | --- | --- |
| Total Protein | 60 - 80 g/L | 70 |
| [Albumin](http://july.fixedreference.org/en/20040724/wikipedia/Albumin) | 30 - 50 g/L | 45 |
| Total [Bilirubin](http://july.fixedreference.org/en/20040724/wikipedia/Bilirubin) | 2 - 14 μmol/L | 11 |
| Direct Bilirubin | 0 - 4 μmol/L | 4 |
| [Alanine transaminase](http://july.fixedreference.org/en/20040724/wikipedia/Alanine_transaminase) (ALT) | 8 - 40 U/L | 50 |
| Alkaline phosphatase (ALP) | 40 - 130 U/L | 120 |
| Gamma glutamyl transferase | < 50 U/L | 100 |

**Other enzymes and proteins**

|  |  |  |
| --- | --- | --- |
| [Creatine kinase](http://july.fixedreference.org/en/20040724/wikipedia/Creatine_kinase) (CK) | 22 - 198 U/L | 84 |
| Aspartate transaminase (AST) | 8 - 35 U/L | 32 |
| [Lactate dehydrogenase](http://july.fixedreference.org/en/20040724/wikipedia/Lactate_dehydrogenase) (LDH) | 85 - 285 U/L | 201 |
| [Amylase](http://july.fixedreference.org/en/20040724/wikipedia/Amylase) | 25 - 125 U/L | 80 |
| [C-reactive protein](http://july.fixedreference.org/en/20040724/wikipedia/C-reactive_protein) (CRP) | <8 mg/L | 4 |

**Other ions and trace metals**

|  |  |  |
| --- | --- | --- |
| Ionised [calcium](http://july.fixedreference.org/en/20040724/wikipedia/Calcium) (Ca) | 1.15 - 1.29 mmol/L |  1.01   |
| Total calcium (Ca) | 2.05 - 2.55 mmol/L | 2.09 |
| [Copper](http://july.fixedreference.org/en/20040724/wikipedia/Copper) (Cu) | 11 - 26 μmol/L |  |
| [Zinc](http://july.fixedreference.org/en/20040724/wikipedia/Zinc) (Zn) | 10 - 17 μmol/L |  |

**Lipids**

|  |  |  |
| --- | --- | --- |
| [Triglycerides](http://july.fixedreference.org/en/20040724/wikipedia/Triglyceride) | 0.4 - 2.0 mmol/L | 2.2 |
| Total [cholesterol](http://july.fixedreference.org/en/20040724/wikipedia/Cholesterol) | 3.0 - 5.5 mmol/L | 6 |
| [HDL cholesterol](http://july.fixedreference.org/en/20040724/wikipedia/High_density_lipoprotein) (male) | 0.7 - 1.9 mmol/L | 1 |
| (female) | 0.9 - 2.4 mmol/L |  |
| [LDL cholesterol](http://july.fixedreference.org/en/20040724/wikipedia/Low_density_lipoprotein) | 2.4 - 4.0 mmol/l | 5 |

**Tumour markers**

|  |  |  |
| --- | --- | --- |
| [Alpha-fetoprotein](http://july.fixedreference.org/en/20040724/wikipedia/Alpha-fetoprotein) (AFP) | 1-15 kIU/L |  |
| CA-125 | <65 kU/L |  |
| [Prostate specific antigen](http://july.fixedreference.org/en/20040724/wikipedia/Prostate_specific_antigen) (total PSA) | <2.0 μg/L | 3  |

**Hormones**

|  |  |  |
| --- | --- | --- |
| [Thyroid stimulating hormone](http://july.fixedreference.org/en/20040724/wikipedia/Thyroid-stimulating_hormone) (TSH) | 0.5 - 4.7 mIU/L | 4 |
| Free [thyroxine](http://july.fixedreference.org/en/20040724/wikipedia/Thyroid_hormone) (FT4) | 9.0 - 24 pmol/L | 20 |
| Free [triiodothyronine](http://july.fixedreference.org/en/20040724/wikipedia/Thyroid_hormone) (FT3) | 2.5 - 5.3 pmol/L | 3 |
| [Adrenocorticotropic hormone](http://july.fixedreference.org/en/20040724/wikipedia/Adrenocorticotropic_hormone) (ACTH) | 1.3 - 15 pmol/L | 6 |
| [Cortisol](http://july.fixedreference.org/en/20040724/wikipedia/Cortisol) (0830 h) | 250 - 850 nmol/L | 401 |
| Cortisol (1630 h) | 110 - 390 nmol/L |  |
| [Prolactin](http://july.fixedreference.org/en/20040724/wikipedia/Prolactin) (male) | <450 mIU/L |  |
| (female) | <580 mIU/L |  |
| [Testosterone](http://july.fixedreference.org/en/20040724/wikipedia/Testosterone) (male) | 8 - 38 nmol/L |  |
| (male prepuberty) | 0.1 - 0.5 nmol/L |  |
| (female) | 0.3 - 2.5 nmol/L |  |

**Haematology**

**Red blood cells**

|  |  |  |
| --- | --- | --- |
| [Haemoglobin](http://july.fixedreference.org/en/20040724/wikipedia/Hemoglobin) (Hb) (male) | 130 - 180 g/L | 140 |
| (female) | 115 - 160 g/L | Sex difference negligible until adulthood. |
| [Haematocrit](http://july.fixedreference.org/en/20040724/wikipedia/Hematocrit) (Hct) (male) | 0.38 - 0.52 |  |
| (female) | 0.35 - 0.47 |  |
| Mean cell volume (MCV) | 80 - 98 fL | 89 |
| Mean cell haemoglobin (MCH) | 26 - 34 pg | 31 |
| Red cell count (male) | 4.5 - 6.5 x1012/L | 6 |
| (female) | 3.8 - 5.8 x1012/L |  |
| Reticulocytes | 10 - 100 x109/L | 20 |
| [Erythrocyte](http://july.fixedreference.org/en/20040724/wikipedia/Erythrocyte_sedimentation_rate)[sedimentation rate](http://july.fixedreference.org/en/20040724/wikipedia/Erythrocyte_sedimentation_rate) (ESR) |  | 11 |

**White blood cells**

|  |  |  |
| --- | --- | --- |
| Total white blood cells | 4.0 - 11.0 x109/L | 5 |
| Neutrophil granulocytes | 2.0 - 7.5 x109/L | 7 |
| [Lymphocytes](http://july.fixedreference.org/en/20040724/wikipedia/Lymphocyte) | 1.0 - 4.0 x109/L | 2 |
| Monocytes | 0.0 - 0.8 x109/L | 0.4 |
| Eosinophil granulocytes | 0.0 - 0.5 x109/L | 0.4 |
| Basophil granulocytes | 0.0 - 0.2 x109/L | 0.1 |

**Coagulation**

|  |  |  |
| --- | --- | --- |
| [Prothrombin time](http://july.fixedreference.org/en/20040724/wikipedia/International_normalized_ratio) (PT) | 7 - 10 s | 11 |
| [INR](http://july.fixedreference.org/en/20040724/wikipedia/International_normalized_ratio) | 0.8 - 1.2 | 1 |
| Activated partial thromboplastin time (APTT) | 29 - 41 s |  |
| Thrombin clotting time (TCT) | 11 - 18 s |  |
| [Fibrinogen](http://july.fixedreference.org/en/20040724/wikipedia/Fibrin) | 1.8 - 4.0 g/L | 3 |
| [Bleeding time](http://july.fixedreference.org/en/20040724/wikipedia/Bleeding_time) | 2 - 8 minutes | 6 |

**Immunology**

|  |  |  |
| --- | --- | --- |
| Antinuclear antibodies (ANA) |  | Not Indicated |
| Extractable nuclear antigen (ENA) |  | Not Indicated |