Patient 5. ADAS COG, and MRI scan. Prescribed Aricept, but taken off drug due to nausea, and is then signed up for a clinical trial of varenicline.

**Medical Conditions**

Hypertension

Acute Coronary Syndrome

Alzheimer’s Disease

Gastro-Oesophageal Reflux DIsease

**Medications**

Carvedilol 6.25mg bid

Atorvastatin 20mg od

Clopidogrel 75mg od

Donepezil Discontinued

Omeprazole 20mg od

**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

CLOPIDOGREL – inhibitor

CARVEDILOL - major



2C9

CARVEDILOL - major

CLOPIDOGREL - inhibior



2C19

OMEPRAZOLE – major strong

CLOPIDOGREL (See notes below)



2D6

CARVEDILOL – unclassified substrate

DONEPEZIL substrate



3A4 -

ATORVASTATIN major substrate

DONEPEZIL substrate



**CYP2C19 poor metabolizer status** is associated with diminished response to **Clopidogrel**. The optimal dose regimen for poor metabolizers has yet to be determined. (Dosage and Administration-Pharmacogenetics) Based on Literature data, patients with genetically reduced CYP2C19 function have lower systemic exposure to the active metabolite of clopidogrel and diminished antiplatelet responses and generally exhibit higher cardiovascular event rates following myocardial infraction than do patients with normal CYP2C19 function. (Precautions-Pharmacogenetics) CYP2C19 is involved in the formation of both the active metabolite and the 2-oxo-clopidrogrel intermediate metabolite. Clopidrogrel active metabolite pharmacokinetic and antiplatelet effects as measured by ex vivo platelet aggregation assays, differ according to CYP2C19 genotypes. The prevalence of CYP2C19 alleles that result in intermediate and poor CYP2C19 metabolism differs according to race/ethinicity. (Clinical Pharmacology-Pharmacogenetics) (From FDA)

**Adverse Drug Reaction**

**Donepezil – Nausea**

**Drug Trial Information**

List of Studies Ongoing

**“A Phase 2 Multicenter, Double-Blind, Placebo-Controlled, Crossover Trial of Varenicline Tartrate (CP-526,555) in Patients With Mild to Moderate Alzheimer's Disease”**

1. Assess the efficacy of varenicline, relative to placebo, on a performance based measure of cognition in patients with mild to moderate Alzheimer's disease

2. Evaluate the effects of varenicline on clinically relevant measures including attention and executive function, behavior, and clinician rated global change.

3. Evaluate the safety and tolerability of varenicline, relative to placebo, in patients with mild to moderate Alzheimer's disease

4. Evaluate the pharmacokinetics of varenicline in patients with mild to moderate Alzheimer's disease.

Study Type: Interventional

Study Design: Treatment, Randomized, Double Blind (Subject, Caregiver, Investigator), Crossover Assignment, Safety/Efficacy Study

Study Primary Completion Date: January 2010

**Intervention(s) in this Clinical Trial**

* Drug: Varenicline
	+ 0.5 mg once daily for 1 week followed by 0.5 mg twice daily for 1 week followed by 1 mg twice daily for 4 weeks
* Drug: Placebo
	+ Placebo once daily for 1 week followed by placebo twice daily for 5 weeks.

**Arms, Groups and Cohorts in this Clinical Trial**

* Experimental: Varenicline
* Placebo Comparator: Placebo

**Outcome Measures for this Clinical Trial**

**Primary Measures**

* Alzheimer's Disease Assessment Scale-Cognitive Subscale 75 (ADAS-Cog 75) at week 6
	+ Time Frame: 6 weeks
	Safety Issue?: No

**Secondary Measures**

* Alzheimer's Disease Assessment Scale-Cognitive Subscale 75 (ADAS-Cog 75) at week 3
	+ Time Frame: 3 weeks
	Safety Issue?: No
* Alzheimer's Disease Assessment Scale-Cognitive Subscale 70 (ADAS-Cog 70)
	+ Time Frame: 3 and 6 weeks
	Safety Issue?: No
* Clinical Global Impression - Improvement
	+ Time Frame: 6 Weeks
	Safety Issue?: No
* Neuropsychiatric Inventory
	+ Time Frame: 3 and 6 weeks
	Safety Issue?: Yes
* Computerized Test Battery for Cognition
	+ Time Frame: 1, 3 and 6 weeks
	Safety Issue?: No
* Adverse events, vital signs (blood pressure, pulse rate, respiration), body weight, electrocardiogram, physical exam, laboratory tests
	+ Time Frame: 1, 3 and 6 weeks
	Safety Issue?: Yes

Inclusion Criteria:

* Males or females, age 55-85
* Diagnosis of probable Alzheimer's disease, consistent with criteria from both: 1)
* National Institute of Neurological and Communicable Disease and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) and 2)
* Diagnostic and Statistical Manual of Mental Disorders (DSM IV)
* Mini-mental status exam score of 14-26 inclusive
* Rosen-Modified Hachinski Ischemia Score of < or = 4

Exclusion Criteria:

* Diagnosis or history of other dementia or neurodegenerative disorders
* Diagnosis or history of clinically significant cerebrovascular or cardiovascular disease
* Subjects with pulmonary disease or evidence of clinically significant pulmonary symptoms

Gender Eligibility for this Clinical Trial: Both

Minimum Age for this Clinical Trial: 55 Years

Maximum Age for this Clinical Trial: 85 Years

Are Healthy Volunteers Accepted for this Clinical Trial?: No

**Clinical Trial Sponsor Information**

Lead Sponsor: Pfizer

**Overall Clinical Trial Officials and Contacts**

Pfizer CT.gov Call Center Study Director Pfizer

Overall Contact: Pfizer CT.gov Call Center 1-800-718-1021

**Additional Information**

Information obtained from ClinicalTrials.gov on November 05, 2009

Link to the current ClinicalTrials.gov record. http://clinicaltrials.gov/show/NCT00744978

Study ID Number: A3051101

ClinicalTrials.gov Identifier: NCT00744978

Health Authority: Korea: Food and Drug Administration

[To obtain contact information for a study center near you, click here.](https://trialinfoemail.pfizer.com/pages/landing.aspx?StudyID=A3051101&StudyName=Evaluation%20of%20the%20Efficacy%20of%20Varenicline%20on%20Cognition%2C%20Safety%2C%20Tolerability%20and%20Pharmacokinetics%20in%20Subjects%20with%20Mild-to-Moderate%20Alzhei)

**Clinical Trials Authorship and Review**

Clinical Trials content is provided directly by the U.S. National Institutes of Health via ClinicalTrials.gov and is not reviewed separately by ClinicalTrialsFeeds.org. Every page of specific clinical trials information contains a unique identifier which can be used to find further details directly from the National Institutes of Health.

**General Literature to Support Trial**

**Varenicline Is a Partial Agonist at 42 and a Full Agonist at 7 Neuronal Nicotinic Receptors**

**Karla B. Mihalak, F. Ivy Carroll, and Charles W. Luetje**

Department of Molecular and Cellular Pharmacology, University of Miami Miller School of Medicine, Miami, Florida (K.B.M., C.W.L.); and Organic and Medicinal Chemistry, Research Triangle Institute, Research Triangle Park, North Carolina (F.I.C.)

**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 |  137 |
| [Potassium](http://july.fixedreference.org/en/20040724/wikipedia/Potassium) (K) | 3.5 - 5.0 mmol/L | 4 |
| [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 | 104 |
| [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 | 80 |
| [Albumin](http://july.fixedreference.org/en/20040724/wikipedia/Albumin) | 30 - 50 g/L | 39 |
| Total [Bilirubin](http://july.fixedreference.org/en/20040724/wikipedia/Bilirubin) | 2 - 14 μmol/L | 13 |
| Direct Bilirubin | 0 - 4 μmol/L | 2 |
| [Alanine transaminase](http://july.fixedreference.org/en/20040724/wikipedia/Alanine_transaminase) (ALT) | 8 - 40 U/L | 51 |
| Alkaline phosphatase (ALP) | 40 - 130 U/L | 122 |
| Gamma glutamyl transferase | < 50 U/L | 134 |

**Other enzymes and proteins**

|  |  |  |
| --- | --- | --- |
| [Creatine kinase](http://july.fixedreference.org/en/20040724/wikipedia/Creatine_kinase) (CK) | 22 - 198 U/L | 77 |
| Aspartate transaminase (AST) | 8 - 35 U/L | 36 |
| [Lactate dehydrogenase](http://july.fixedreference.org/en/20040724/wikipedia/Lactate_dehydrogenase) (LDH) | 85 - 285 U/L | 222 |
| [Amylase](http://july.fixedreference.org/en/20040724/wikipedia/Amylase) | 25 - 125 U/L | 90 |
| [C-reactive protein](http://july.fixedreference.org/en/20040724/wikipedia/C-reactive_protein) (CRP) | <8 mg/L | 7 |

**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 | 2.9 |
| Total [cholesterol](http://july.fixedreference.org/en/20040724/wikipedia/Cholesterol) | 3.0 - 5.5 mmol/L | 5.5 |
| [HDL cholesterol](http://july.fixedreference.org/en/20040724/wikipedia/High_density_lipoprotein) (male) | 0.7 - 1.9 mmol/L | 1.5 |
| (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 | 4 |

**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 |   |

**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 | 21 |
| Free [triiodothyronine](http://july.fixedreference.org/en/20040724/wikipedia/Thyroid_hormone) (FT3) | 2.5 - 5.3 pmol/L | 5 |
| [Adrenocorticotropic hormone](http://july.fixedreference.org/en/20040724/wikipedia/Adrenocorticotropic_hormone) (ACTH) | 1.3 - 15 pmol/L | 4 |
| [Cortisol](http://july.fixedreference.org/en/20040724/wikipedia/Cortisol) (0830 h) | 250 - 850 nmol/L | 502 |
| 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 | 131 |
| (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 | 92 |
| Mean cell haemoglobin (MCH) | 26 - 34 pg | 34 |
| Red cell count (male) | 4.5 - 6.5 x1012/L | 5 |
| (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) |  | 12 |

**White blood cells**

|  |  |  |
| --- | --- | --- |
| Total white blood cells | 4.0 - 11.0 x109/L | 10 |
| 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 | 9 |
| [INR](http://july.fixedreference.org/en/20040724/wikipedia/International_normalized_ratio) | 0.8 - 1.2 | 1.0 |
| 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 |