Table 4: Evidence and Mechanism of Drugs for Alzheimer's Disease, predicted by Transductive Model

Model	Drug Candidates	Evidence for AD	Drug Mechanism
KG-Predict (baseline)	Levocarnitine	No clinical trial for levocarnitine itself, but clinical trial NCT02955706 for its derivative Acetyl-L-carnitine (L-carnitine is a synonym for levocarnitine)	Prevent and treat a lack of carnitine in patients with kidney disease on dialysis. A carrier of long chain fatty acids to mitochondria for energy.
	Epicriptine	No reference, but with indication in Alzheimer's disease on Drug Central website and its analog dihydroergocristine is proved to delay progression of Alzheimer's disease: refer to drugbank website and the paper: The FDA-approved natural product dihydroergocristine reduces the production of the Alzheimer's disease amyloid-? peptides.	Nootropic to treat signs and symptoms of an idiopathic decline in mental capacity. mainly due to the agonistic activity on dopamine receptor
	Tacrine	Tacrine: first drug approved for Alzheimer's disease	Treat AD. A powerful acetylcholinesterase inhibitor (AChE)
	Donepezil	NCT02787746(completed), NCT04661280(recruiting)	Treat AD. Inhibiting the acetylcholinesterase enzyme
	Galantamine	NCT01054976	Manage mild to moderate dementia associated with Alzheimer's Disease. An acetylcholinesterase inhibitor.
Non-augmented	Levocarnitine	No clinical trial for levocarnitine itself, but clinical trial NCT02955706 for its derivative Acetyl-L-carnitine (L-carnitine is a synonym for levocarnitine)	Prevent and treat a lack of carnitine in patients with kidney disease on dialysis. A carrier of long chain fatty acids to mitochondria for energy.
	Donepezil	NCT02787746(completed), NCT04661280(recruiting)	Treat AD. Inhibiting the acetylcholinesterase enzyme
	Tacrine	Tacrine: first drug approved for Alzheimer's disease	Treat AD. A powerful acetylcholinesterase inhibitor (AChE)
	Epicriptine	No reference, but with indication in Alzheimer's disease on Drug Central website and its analog dihydroergocristine is proved to delay progression of Alzheimer's disease: refer to drugbank website and the paper: The FDA-approved natural product dihydroergocristine reduces the production of the Alzheimer's disease amyloid-? peptides.	Nootropic to treat signs and symptoms of an idiopathic decline in mental capacity. mainly due to the agonistic activity on dopamine receptor
	Galantamine	NCT01054976	Manage mild to moderate dementia associated with Alzheimer's Disease. An acetylcholinesterase inhibitor.
Augmented (Propagation)	naltrexone	Reference: Naltrexone and Alzheimer's disease; Effect of naltrexone on senile dementia of the Alzheimer type. (but show no significant improvement)	Treat alcohol dependence and block the effects of exogenously administered opioids. It is a pure opiate antagonist and has little or no agonist activity.
	Lasofoxifene	Selective estrogen receptor modulators as brain therapeutic agents (further study are needed)	Prevent and treat osteoporosis and vaginal atrophy. It is a naphthalene derivative and exhibits both significant estrogenic and antiestrogenic activity both in vitro and in vivo, targeting any tissues that possess ERs.
	Olanzapine	NCT00015548(completed, olanzapine is used in combination with other two drugs)	Manage schizophrenia, bipolar 1 disorder, and agitation associated with these disorders. It has antagonism of multiple neuronal receptors including the dopamine receptor D1, D2, D3 and D4 in the brain, the serotonin receptors 5HT2A, 5HT2C, 5HT3 and 5HT6, the alpha-1 adrenergic receptor, the histamine receptor H1 and multiple muscarinic receptors.
	Donepezil	NCT02787746(completed), NCT04661280(recruiting)	Treat AD. Inhibiting the acetylcholinesterase enzyme
	Ziprasidone	Reference: Use of atypical antipsychotic drugs in patients with dementia; Therapeutic effect of small dose of ziprasidone combined donepezil hydrochloride on Alzheimer's disease and its effect no glucose and lipid metabolism in patients	Manage schizophrenia, bipolar mania, and agitation in patients with schizophrenia. It is a dopamine and 5HT2A receptor antagonist with a unique receptor binding profile.

Table 5: Evidence and Mechanism of Drugs for Alzheimer's Disease, predicted by Semi-Inductive Model

Model	Drug Candidates	Evidence for AD	Drug Mechanism
Non-augmented	Aducanumab	NCT04241068 (active, not recruiting), NCT02477800(terminated with results)	Treat AD. It is a human immunoglobulin gamma 1 (IgG1) monoclonal antibody which selectively targets and binds aggregated soluble oligomers and insoluble fibril conformations of A? plaques.
	Ipidacrine	Also named Neiromidin or Neuromidin(translated from Russian). Reference: Neuromidin in mixed vascular and Alzheimer's dementia	Treat memory disorders of different originsa. A reversible acetylcholinesterase inhibitor
	Dexamethasone	Reference: Intrathecal corticosteroids might slow Alzheimer's disease progression (It is just case report and hypothesis, needs further validation)	Treat inflammatory conditions such as bronchial asthma, endocrine and rheumatic disorders. It is glucocorticoid which binds to glucocorticoid receptor, inhibiting pro-inflammatory signals, and promoting anti-inflammatory signals
	Bortezomib	No reference. Perhaps worsen Alzheimer disease since Bortezomib is a proteasome inhibitor and proteasome activity is already inhibited in Alzheimer patients (Synaptic proteasome is inhibited in Alzheimer's disease models and associates with memory impairment in mice)	An antineoplastic agent (cancer medicine). It binds the catalytic site of the 26S proteasome with high affinity and specificity. Proteasome inhibition may prevent degradation of pro-apoptotic factors, thereby triggering programmed cell death in neoplastic cells.
	Sodium stibogluconate	No reference	Treat leishmaniasis. Mechanism is not understood. It has been postulated that the reduction in ATP and GTP synthesis contributes to decreased macromolecular synthesis such as DNA, RNA, protein etc.
Augmented (Common Neighbors)	Ipidacrine	Also named Neiromidin or Neuromidin(translated from Russian). Reference: Neuromidin in mixed vascular and Alzheimer's dementia	Treat memory disorders of different originsa. A reversible acetylcholinesterase inhibitor
	Aducanumab	NCT04241068 (active, not recruiting), NCT02477800(terminated with results)	Treat AD. It is a human immunoglobulin gamma 1 (IgG1) monoclonal antibody which selectively targets and binds aggregated soluble oligomers and insoluble fibril conformations of A? plaques.
	Nanaomycin D	No reference	An enantiomer of the antibiotic kalafungin, is a natural product found in Streptomyces and Streptomyces rosa.
	Nelfinavir	Contradictory reference. Nelfinavir is a protease inhibitor, which has potential roles in Alzheimer's disease (Refer to: Potential roles of protease inhibitors in Alzheimer's disease), but this paper (The effect of HIV protease inhibitors on amyloid-? peptide degradation and synthesis in human cells and Alzheimer's disease animal model) indicates that HIV portease inhibitors increase risk for Alzheimer disease.	Antiviral drugs in the treatment of HIV. It is a potent HIV-1 protease inhibitor
	Acetyl Dithranol	No reference	It is in the experimental group. Cell cycle inhibitors,Lipid peroxidation inhibitors.

Table 6: Evidence and Mechanism of Drugs for Alzheimer's Disease, predicted by Non-augmented Zero-shot Transductive and Semi-Inductive Models

Drug Candidates	Evidence for AD	Drug Mechanism
Non-augmented 0-shot Transductive		
Tacrine	First drug approved for Alzheimer's disease	treat AD. A powerful acetylcholinesterase inhibitor (AChE)
Levocarnitine	No clinical trial for levocarnitine itself, but clinical trial NCT02955706 for its derivative Acetyl-L-carnitine (L-carnitine is a synonym for levocarnitine)	prevent and treat a lack of carnitine in patients with kidney disease on dialysis. A carrier of long chain fatty acids to mitochondria for energy.
Donepezil	NCT02787746(completed), NCT04661280(recruiting)	treat AD. Inhibiting the acetylcholinesterase enzyme
Ipidacrine	Also named Neiromidin or Neuromidin(translated from Russian). Reference: Neuromidin in mixed vascular and Alzheimer's dementia	treat memory disorders of different originsa. A reversible acetylcholinesterase inhibitor
Epicriptine	No reference, but with indication in Alzheimer's disease on Drug Central website and its analog dihydroergocristine is proved to delay progression of Alzheimer's disease: refer to drugbank website and the paper: The FDA-approved natural product dihydroergocristine reduces the production of the Alzheimer's disease amyloid-β peptides.	nootropic to treat signs and symptoms of an idiopathic decline in mental capacity. mainly due to the agonistic activity on dopamine receptor
Non-augmented 0-shot Semi-Inductive		
Aducanumab	NCT04241068 (active, not recruiting), NCT02477800(terminated with results)	treat AD. It is a human immunoglobulin gamma 1 (IgG1) monoclonal antibody which selectively targets and binds aggregated soluble oligomers and insoluble fibril conformations of Aβ plaques.
Ipidacrine	Also named Neiromidin or Neuromidin(translated from Russian). Reference: Neuromidin in mixed vascular and Alzheimer's dementia	treat memory disorders of different originsa. A reversible acetylcholinesterase inhibitor
Maxacalcitol	Reference: Active form of vitamin D analogue mitigates neurodegenerative changes in Alzheimer's disease in rats by targeting Keap1/Nrf2 and MAPK-38p/ERK signaling pathways (but in animal model)	treat the secondary hyperparathyroidism of hemodialysis (HD) patients. A vitamine D derivative. It suppresses synthesis and secretion of parathyroid hormone, and decreases a concentration of parathyroid hormone in blood.
Diosmin	Reference: Diosmin reduces cerebral A? levels, tau hyperphosphorylation, neuroinflammation, and cognitive impairment in the 3xTg-AD mice (but in animal model)	a dietary supplement used to aid treatment of hemorrhoids and venous diseases. The mechanism of action of Diosmin is undefined.
Pegademase	No reference	treat adenosine deaminase deficiency. It is a modified form of bovine adenosine deaminase

Table 7: Evidence and Mechanism of Drugs for Alzheimer's Disease, predicted by Augmented Models in Transductive Setting

Drug Candidates	Evidence for AD	Drug Mechanism
Katz		
Levocarnitine	(mentioned earlier)	(mentioned earlier)
Epicriptine	(mentioned earlier)	(mentioned earlier)
Tacrine	First drug approved for Alzheimer's disease	treat AD. A powerful acetylcholinesterase inhibitor (AChE)
Donepezil	NCT02787746(completed), NCT04661280(recruiting)	treat AD. Inhibiting the acetylcholinesterase enzyme
Galantamine	NCT01054976	manage mild to moderate dementia associated with Alzheimer's Disease. An acetylcholinesterase inhibitor.
Common Neighbors		
Lasofoxifene	Selective estrogen receptor modulators as brain therapeutic agents (further study are needed)	prevent and treat osteoporosis and vaginal atrophy. It is a naphthalene derivative and exhibits both significant estrogenic and antiestrogenic activity both in vitro and in vivo, targeting any tissues that possess ERs.
Olanzapine	NCT00015548(completed, olanzapine is used in combination with other two drugs)	manage schizophrenia, bipolar 1 disorder, and agitation associated with these disorders. It has antagonism of multiple neuronal receptors including the dopamine receptor D1, D2, D3 and D4 in the brain, the serotonin receptors 5HT2A, 5HT2C, 5HT3 and 5HT6, the alpha-1 adrenergic receptor, the histamine receptor H1 and multiple muscarinic receptors.
naltrexone	Reference: Naltrexone and Alzheimer's disease; Effect of naltrexone on senile dementia of the Alzheimer type. (but show no significant improvement)	treat alcohol dependence and block the effects of exogenously administered opioids. It is a pure opiate antagonist and has little or no agonist activity.
Rivastigmine	NCT01585272(completed), NCT02989402(completed)	treat mild to moderate dementia in Alzheimer's and Parkinson's. It is a (acetyl)cholinesterase inhibitor
Ziprasidone	Reference: Use of atypical antipsychotic drugs in patients with dementia; Therapeutic effect of small dose of ziprasidone combined donepezil hydrochloride on Alzheimer's disease and its effect no glucose and lipid metabolism in patients	manage schizophrenia, bipolar mania, and agitation in patients with schizophrenia. It is a dopamine and 5HT2A receptor antagonist with a unique receptor binding profile.
Louvain		
naltrexone	(mentioned earlier)	(mentioned earlier)
Lasofoxifene	(mentioned earlier)	(mentioned earlier)
Olanzapine	(mentioned earlier)	(mentioned earlier)
(S)-Fluoxetine	Reference: Fluoxetine ameliorates Alzheimer's disease progression and prevents the exacerbation of cardiovascular dysfunction of socially isolated depressed rats through activation of Nrf2/HO-1 and hindering TLR4/NLRP3 inflammasome signaling pathway (but it is in animal model)	Treat major depressive disorder, bulimia, OCD, premenstrual dysphoric disorder, panic disorder, and bipolar I. It is a serotonin reuptake inhibitor
Clomipramine	Reference: A double-blind placebo-controlled study of clomipramine in depressed patients with Alzheimer's disease. (But it treats depression, not alzheimer's disease directly)	Treat disorder with obsessive-compulsive component such as depression, schizophrenia, and Tourette's disorder. It works by inhibit the re-uptake of the neurotransmitters norepinephrine and serotonin by nerve cells and it also affect the receptor sensitivity.
K-Core		
Galantamine	(mentioned earlier)	(mentioned earlier)
Lasofoxifene	(mentioned earlier)	(mentioned earlier)
Olanzapine	(mentioned earlier)	(mentioned earlier)
Bromocriptine	NCT04413344(completed)	treat galactorrhea due to hyperprolactinemia and other prolactin-related conditions, as well as in early Parkinsonian Syndrome. It is a dopamine D2 receptor
Amantadine	Reference: Amantadine and the end-stage dementia of Alzheimer's type (only several cases, needs further validation)	treat dyskinesia in Parkinson's patients receiving levodopa, as well as extrapyramidal side effects of medications. Mechanism is not fully understand. It has been shown to cause an increase in dopamine release in the animal brain, and does not possess anticholinergic activity.

Table 8: Evidence and Mechanism of Drugs for Alzheimer's Disease, predicted by Augmented Models in Semi-Inductive Setting

Drug Candidates	Evidence for AD	Drug Mechanism
Katz		
Aducanumab	NCT04241068 (active, not recruiting), NCT02477800(terminated with results)	treat AD. It is a human immunoglobulin gamma 1 (IgG1) monoclonal antibody which selectively targets and binds aggregated soluble oligomers and insoluble fibril conformations of Aβ plaques.
Ipidacrine	Also named Neiromidin or Neuromidin(translated from Russian). Reference: Neuromidin in mixed vascular and Alzheimer's dementia	treat memory disorders of different originsa. A reversible acetylcholinesterase inhibitor
Nanaomycin D	No reference	an enantiomer of the antibiotic kalafungin, is a natural product found in Streptomyces and Streptomyces rosa
TMC-310911	The reference is contradictory. TMC-310911 is a protease inhibitor potentially beneficial for Alzheimer's disease. However, the paper "The effect of HIV protease inhibitors on amyloid-β peptide degradation and synthesis in human cells and Alzheimer's disease animal model" suggests that HIV protease inhibitors might increase Alzheimer's disease risk.	an antiviral drug as a treatment for HIV/AIDS. It is a Novel Human Immunodeficiency Virus Type 1 Protease Inhibitor.
Hepatitis B immune globulin	No reference	prevent the development of hepatitis B. It is a human immunoglobulin made from blood and contains antibodies to hepatitis B
Louvain		
Ipidacrine	(mentioned earlier)	(mentioned earlier)
Aducanumab	(mentioned earlier)	(mentioned earlier)
CMLVAX100	No reference	reduce residual disease in some patients with chronic myeloid leukemia. It is a vaccine targeting the BCR-ABL-derived p210 fusion protein
Hepatitis B immune globulin	(mentioned earlier)	(mentioned earlier)
Nanaomycin D	(mentioned earlier)	(mentioned earlier)
K-Core		
Ipidacrine	(mentioned earlier)	(mentioned earlier)
Aducanumab	(mentioned earlier)	(mentioned earlier)
TMC-310911	(mentioned earlier)	(mentioned earlier)
Hepatitis B immune globulin	(mentioned earlier)	(mentioned earlier)
Nanaomycin D	(mentioned earlier)	(mentioned earlier)
Propagation		
Aducanumab	(mentioned earlier)	(mentioned earlier)
Ipidacrine	(mentioned earlier)	(mentioned earlier)
Bortezomib	No reference. Perhaps worsen Alzheimer disease since Bortezomib is a proteasome inhibitor and proteasome activity is already inhibited in Alzheimer patients (Synaptic proteasome is inhibited in Alzheimer's disease models and associates with memory impairment in mice)	an antineoplastic agent (cancer medicine). It binds the catalytic site of the 26S proteasome with high affinity and specificity. Proteasome inhibition may prevent degradation of pro-apoptotic factors, thereby triggering programmed cell death in neoplastic cells.
Dexamethasone	Reference: Intrathecal corticosteroids might slow Alzheimer's disease progression (It is just case report and hypothesis, needs further validation)	treat inflammatory conditions such as bronchial asthma, endocrine and rheumatic disorders. It is glucocorticoid which binds to glucocorticoid receptor, inhibiting pro-inflammatory signals, and promoting anti-inflammatory signals
Dexmedetomidine	NCT06052254 (not yet recruiting)	used for sedation during various procedures. Dexmedetomidine is a specific and selective alpha-2 adrenoceptor agonist. By binding to the presynaptic alpha-2 adrenoceptors, it inhibits the release if norepinephrine, therefore, terminate the propagation of pain signals.