# Table S1 *Blood/plasma/serum*

**Associations between putative blood, plasma and serum biomarkers and clinical measures of disease severity, in longitudinal studies included in the systemic review of biomarkers for disease progression in Alzheimer’s disease**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | |  |  | **Association of change in substance measured with change in:** | | | | |
| **Substance measured** | **Reference**  **(first author, year)** | **n at baseline** | **Number of sampling intervals** | **Time between first and last samples (years)** | **MMSE** | **Modified ADAS-cog** | **CERAD battery** | **CIBIC+** | **DAD** |
| Platelet amyloid beta precursor protein (AβPP) isoform ratio | Baskin, 20001 | 10 | 2 | 3.0 | R = 0.69(\*) |  |  |  |  |
| Borroni, 20012 | 20 | 2 | 0.1 | NSA |  |  |  |  |
| Liu, 20073 | 66 | 2 | 1.0 | R = 0.316◘ |  |  |  |  |
| Neopterin | Blasko, 20074 | 43 | 2 | 1.5 | Rs = -0.401\*\*† |  | Rs = -0.353\* |  |  |
| C-reactive protein (CRP) | Blasko, 20074 | 43 | 2 | 1.5 | NSA† |  | NSA |  |  |
| Tumour necrosis factor-alpha (TNF-α) | Alvarez, 20095 | 207 | 3 | 0.5 |  | NSA |  | NSA | NSA |
| Insulin-like growth factor-1  (IFG-1) | Alvarez, 20095 | 207 | 3 | 0.5 |  | NSA |  | NSA | NSA |
| Alvarez, 20095 | ? ‡ | 3 | 0.5 |  |  |  | R = -0.158◘ | R = 0.191\* |
| Alvarez, 20095 | ? § | 3 | 0.5 |  |  |  | R = -0.205◘ | R = 0.223\* |
| Homeostasis model assessment (HOMA)• | Isik, 20096 | 40 | 4 | 1.5 | NSA |  |  |  |  |
| Modified HOMA• | Isik, 20096 | 40 | 4 | 1.5 | NSA |  |  |  |  |
| Afternoon cortisol test (ACT) | Weiner, 19977 | 9 | 3 | 3.0 |  | POS\* |  |  |  |
| 12:00 hours plasma cortisol concentration | Weiner, 19977 | 9 | 3 | 3.0 |  | POS\* |  |  |  |

**Key**

† Multiple regression analysis considering the influence of changes of neopterin and CRP on the CERAD battery (controlled for age, gender, ApoE4 presence and the time interval between both measurements) was also performed, in addition to the basic correlation analyses detailed in the table above. The change in z-scores relating to each of the subsections of the CERAD battery and the total sum of all seven CERAD z-scores were considered as dependent variables. The regression with variable MMSE, constructive praxis immediate recall and sum of all CERAD subscores were significantly associated with an increase of neopterin (P=0.009-0.036) and also with a decrease in CRP (P=0.008-0.037). The paper fails to state what the outcome of the regression was when the total CERAD battery score was the dependent variable.

‡ Exact number of patients included not clear, but does state examined a subgroup with late-onset Alzheimer’s disease.

§ Exact number of patients included not clear, but does state examined a subgroup of female patients with late-onset Alzheimer’s disease.

• The homeostasis model assessment (HOMA) is an estimate of steady state beta cell function and insulin sensitivity based on serum glucose and plasma insulin measurements.

Superscript numbers correspond to the list of references

**Correlations**

Pearson’s correlation coefficient R

Spearman’s correlation coefficient Rs

NSA No significant association No symbol: P not significant, but actual value not stated

POS Significant positive association ◘ P ≥ 0.05

NEG Significant negative association (\*) P significant, but actual value not stated

SIG Significant association direction not stated \* P < 0.05

\*\* P < 0.01

\*\*\* P < 0.001

**Clinical Rating Scales**

CERAD battery Consortium to Establish a Registry for Alzheimer’s Disease battery total score8

CIBIC+ Clinician Interview-Based Impression of Change with Caregiver Input (ADCS version)9

DAD Disability assessment for Dementia10

MMSE Mini-Mental State Examination11

Modified ADAS-cog Modified Alzheimer’s Disease Assessment Scale – cognitive subpart12 (modified as word recognition test omitted)

**References**

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