**BUSTA 1**

**QUESITO:**

ELETTROFORESI

**OFFICE AUTOMATION**

Cosa si intende per "Office Automation"?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Biomarkers are required for decision making in drug development of disease-targeted therapies (DTTs). Biomarkers can be used to diagnose trial participants, identify subgroups within a diagnostic category to be included in a trial, demonstrate target engagement, assess disease course changes, enrich trial populations for assurance of decline, and monitor safety and adverse events. Biomarkers de-risk drug development programmes and change trials from 'shots in the dark' to 'shots on goal'. They may provide the basis for accelerated approval of treatments when the biomarker change is considered reasonably likely to predict clinical benefit.
Convergence of our understanding of the pathobiology of neurodegenerative disorders (NDDs), international collaborations, and advances in technology to measure low-concentration biomarkers that reflect central nervous system (CNS) events has enabled biological definitions of NDDs and accelerated discovery and deployment of biomarkers.

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**BUSTA 2**

**QUESITO:**

WESTERN BLOTTING

**OFFICE AUTOMATION**

Qual è l'obiettivo principale dell'automazione d'ufficio?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

These new biomarkers, when integrated into NDD drug development programmes, facilitate many aspects of the clinical trial process, allowing early assessment of treatment impact on brain pathology and expediting the ability to terminate programmes or progress them towards potential approval and availability to patients facing unrelenting cognitive or functional decline. Precision drug development advances when informative biomarkers are combined in programmes with a well-chosen target, acceptable pharmacokinetic parameters of the candidate therapy and rigorous dose determination. Identification of an appropriate trial population and excellent operational conduct of the trial complete the foundational aspects of drug development1,2,3.
The global burden of NDDs is enormous (Box 1). Alzheimer disease (AD) dementia currently affects 50 million individuals worldwide, a figure projected to increase to 150 million by 2050.

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**BUSTA 3**

**QUESITO:**

DOSAGGIO DELLE PROTEINE

**OFFICE AUTOMATION**

Quale tra questi NON è un software di Office Automation: Word, Excel, GIMP?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

When AD is combined with populations of individuals with Parkinson disease, dementia with Lewy bodies (DLB), amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), chronic traumatic encephalopathy (CTE), multiple system atrophy (MSA), Huntington disease (HD), limbic-predominant age-related transactive response DNA binding protein of 43 kDa (TDP43) encephalopathy (LATE), primary age-related tauopathy (PART) and limbic-predominant amnestic neurodegenerative syndrome (LANS)5, NDDs have a colossal personal, family, societal and economic impact6. Progress has been made in developing disease-targeted therapies (DTTs) for AD and ALS, but other NDDs have no approved therapies or have approved treatments limited to symptom relief (for example, Parkinson disease). Development of new treatments for these disorders is an urgent global unmet need. The introduction of biomarker-based decision making in drug development programmes will accelerate the emergence of much-needed new therapies for NDDs with transformative impact on the lives of patients.

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**BUSTA 4**

**QUESITO:**

TECNICHE DI IMMUNIOFLUORESCENZA

**OFFICE AUTOMATION**

Che differenza c'è tra software proprietario e software open source?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

A biomarker is a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes or responses to an exposure or intervention, including therapeutic interventions7. The context of use (CoU) of a biomarker defines its specific role in clinical trials. Use of biomarkers in NDD drug development is not a recipe that can be applied across all NDD trials — instead, biomarker choice will depend on unique aspects of the target and the drug. There is a constantly expanding repertoire of biomarkers that can be used in drug development and that have been detailed in excellent reviews8,9. However, enduring principles of the use of biomarkers as decision support tools in clinical trials and drug development can be formulated that apply widely to development programmes and emerging biomarker discoveries. Biomarkers have a major role in regulatory discussions where they buttress clinical observations and contribute importantly to the package in information provided for review.

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**BUSTA 5**

**QUESITO:**

TECNICHE DI PCR

**OFFICE AUTOMATION**

Qual è il ruolo del cloud nell'Office Automation?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

The CoU is a concise description of the specified role of the biomarker in a clinical trial. The Food and Drug Administration–National Institutes of Health (FDA–NIH) Biomarkers Working Group recognizes seven CoUs for biomarkers when used as DDTs (Table 1). The biomarker categories comprise susceptibility/risk, diagnostic, prognostic, predictive, pharmacodynamic response, monitoring and safety13. Risk, diagnostic and prognostic biomarkers pertain to the disease state; predictive, pharmacodynamic response, monitoring and safety biomarkers relate to the impact of the treatment on the disease or the individual (Fig. 1). Biomarkers may have more than one use in clinical trials. They may be taken through a qualification process that allows them to be used across trials or they may be used in individual clinical trials without having been fully qualified (Box 2). Determining the availability of biomarkers to answer the questions posed for the trial, understanding the developmental status and analytical validation of the biomarker, and establishing the specific part to be played by a biomarker in the trial (that is, the CoU) are crucial steps in integrating biomarkers into drug development and/or clinical trial programmes.

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**BUSTA 6**

**QUESITO:**

COLTURE DI CELLULE EUCARIOTE

**OFFICE AUTOMATION**

A cosa serve la funzione "Intestazione e piè di pagina"?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Nonclinical studies may provide preliminary information about translational biomarkers that are candidates for clinical trials (Box 3). Within a clinical development programme, biomarkers are deployed at all stages (Fig. 2 and Box 4).
Biomarkers provide crucial information about the readiness of a compound to be progressed from one phase to the next in the clinical development programme. If safety biomarkers do not suggest a safety risk, doses of agents assessed in phase I can be advanced to phase II. Drug therapies assessed in phase II that have safety plus biomarker evidence of target engagement can be advanced to phase III with greater confidence in the chance of technical success. Agents in phase III with biomarkers that reveal evidence of impact on key aspects of disease pathophysiology can be positioned as having demonstrated an effect on the underlying disease, enhancing the chance of observing a durable clinical effect on disease course. Failure to demonstrate the expected biomarker outcomes at each phase of drug development should raise cautions about advancing the agent.

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**BUSTA 7**

**QUESITO:**

COLTURE DI CELLULE PROCARIOTE

**OFFICE AUTOMATION**

Quale software è usato per fare calcoli e grafici?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Interrogation of industry pipelines shows that candidate therapies are more likely to successfully transition from one phase to the next if there is supporting biomarker evidence of efficacy14,15,16. In some therapeutic areas (that is, oncology, diabetes), progression to approval is linked to the use of biomarkers17. The relationship of developmental success to effective use of biomarkers is evident in the programmes leading to approvals for multiple sclerosis, AD and ALS. Susceptibility or risk biomarkers indicate the potential to develop a disease or condition. Genetic and non-genetic risk factors have been identified for NDDs. Other diseases, such as diabetes and obesity, are risk factors for NDDs, including AD and Parkinson disease, and could be used for trial selection of specific agents18. Carriers of causative mutations who do not yet have biomarker evidence of the disease are at high risk for the development of an NDD and are candidates for prevention trials. Autosomal dominant AD, HD, ALS-causing superoxide dismutase 1 (SOD1) mutation, FTD/ALS-C9orf72, FTD-GRN and FTD-MAPT, as well as certain monogenic forms of Parkinson disease are examples of populations that may be discovered before the occurrence of biomarker changes and could be candidates for participation in prevention trials1.

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**BUSTA 8**

**QUESITO:**

TECNICHE MICROSCOPICHE

**OFFICE AUTOMATION**

Cosa rappresenta una "cella" in Excel?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

GBA1 encodes glucosylceramidase β1 (also known as glucocerebrosidase), an enzyme necessary for glucosylceramide metabolism in lysosomes. Researchers made the initial link of the gene to Parkinson disease after discovering increased risk for Parkinson disease among people with Gaucher disease, a lysosomal storage disorder associated with mutations in the same gene29. Like LRRK2, GBA1 variation may explain greater percentages of Parkinson disease in some populations. For example, a recent study revealed a novel variant in GBA1 to be common in people of African descent30. Variations in LRRK2 or GBA1 are not fully penetrant; manifestations are age dependent and are likely influenced by other genetic and environmental factors. Drugs that target the pathology associated with LRRK2 and GBA1 mutations are in development24,31,32. If successful in people with manifest symptoms, these treatments may ultimately benefit carriers of these mutations in preventing future symptom onset.

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**BUSTA 9**

**QUESITO:**

TECNICHE DI CENTRIFUGAZIONE

**OFFICE AUTOMATION**

Cosa significa la cella "B5"?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Identification of causative mutations of FTD has led to corresponding identification of preclinical mutation carriers at risk of progression to manifest disease33.
Data from ever-larger genome-wide association and whole-genome sequencing studies and the use of polygenic risk scores in combination with other disease risk indicators may offer value for identification of individuals with preclinical NDDs who would benefit from early intervention33,34,35,36
Diagnostic biomarkers help to select patients for trial enrolment. Participants chosen solely on the basis of clinical criteria may lack the pathology of interest, are more likely to progress at different rates from those with defined pathologies and may respond differently to candidate interventions owing to uncharacterized biology37. When diagnostic biomarkers are available, sponsors should use them in DTT trials to ensure that the target biology of the disease state is present.

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**BUSTA 10**

**QUESITO:**

TECNICHE DI IBRIDAZIONE PER DNA E RNA

**OFFICE AUTOMATION**

Che formula somma i valori da A1 a A10?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Several NDDs do not currently have diagnostic biomarkers (for example, FTD, Parkinson disease, DLB, PSP, CBD, MSA), and trial eligibility depends on an appropriate phenotype with supporting but not definitive biomarker evidence (for example, atrophy patterns on MRI or evidence of neuronal dysfunction or degeneration with single photon emission computed tomography (SPECT) or fluorodeoxyglucose (FDG)-positron emission tomography (PET)). Diagnostic biomarkers are well developed for AD (Table 2 and Fig. 3); amyloid PET is commonly used to establish a diagnosis of AD in trials of both amyloid-β (Aβ)-directed and non-Aβ-directed therapies38,39,40. Amyloid PET scans can be read visually as positive or negative, semi-quantified with standardized uptake value ratios (SUVRs) or measured quantitatively on a centiloid (CL) scale. The latter was established to enable interpretation across different amyloid PET ligands. Visually, a negative scan shows increased signal restricted to white matter with no involvement of cortical regions.

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**BUSTA 11**

**QUESITO:**

PCR QUANTITATIVA

**OFFICE AUTOMATION**

A cosa serve un software di presentazione?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

In a visually positive scan, cortical grey matter binding is equal to or greater than binding in the white matter with loss of grey-to-white matter contrast41. A positive visual read corresponds to values greater than 24–25 CL42,43. In trial applications, a positive visual read may suffice for diagnosis of AD. Use of CL measurements is essential when determination of the magnitude of amyloid reduction is a biomarker outcome for the trial.
PET ligands for the assessment of tau pathology are available (Table 2 and Fig. 3). A positive visual read on tau PET corresponds to an SUVR of 1.1–1.4 depending on the PET tracer used. A positive visual read on tau PET does not always correspond to increased SUVR, as a significant fraction of participants have focal uptake that is not captured by standard quantification methods. Approaches such as the CenTauR method using data from five tau PET cohorts and a joint propagation statistical model for data harmonization or the Uni-Tau approach are being advanced to improve interpretation across tau PET ligands

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**BUSTA 12**

**QUESITO:**

ELISA

**OFFICE AUTOMATION**

Quale software Microsoft gestisce email e calendario?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

A positive tau PET scan is strongly associated with a positive Aβ PET scan45, suggesting that tau PET may serve as an alternative to Aβ PET, particularly when identification of tau pathology at baseline is a key aspect of the clinical trial (Fig. 3b).
There is one tau PET ligand approved by the FDA and the EMA — [18F]flortaucipir. This agent has demonstrated accuracy in the detection of combined three-repeat and four-repeat isoforms of tau occurring in AD but does not bind to forms of tau found in other types of tauopathy46.
The Aβ protein is generated from amyloid precursor protein as monomeric peptides that aggregate into progressively more complex entities — dimers, trimers, oligomers, protofibrils, fibrils and plaques47.
Amyloid PET is a measure of plaque amyloid; CSF and plasma assays measure the lower-molecular-weight species of Aβ, for example, monomers, dimers, low-molecular-weight oligomers. Positive amyloid PET and abnormal Aβ42 to Aβ40 ratio or Aβ42 to phospho-tau (p-tau)181 ratio in CSF support a diagnosis of AD.

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**BUSTA 13**

**QUESITO:**

TECNICHE CROMATOGRAFICHE

**OFFICE AUTOMATION**

Che cosa significa CC in un'email?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Plasma p-tau217 or p-tau217 to non-phosphorylated tau (np-tau) or the p-tau217 to Aβ42/Aβ40 ratio are highly correlated with amyloid PET positivity and may become an acceptable diagnostic biomarker for trial and clinical application48,49,50,51,52,53,54. Plasma measurements have equivalent performance to CSF Aβ42 in predicting Aβ positivity on amyloid PET50,55. In many circumstances, p-tau217 measurement will be sufficient to support a diagnosis of AD. When used together, the plasma p-tau217 to np-tau ratio, plasma Aβ42 to Aβ40 ratio, age and APOE genotype slightly improved the accuracy, sensitivity and specificity for prediction of PET amyloid positivity.

Several plasma p-tau isoforms including p-tau181, p-tau205, p-tau217 and p-tau231, as well as microtubule binding domain region tau243 (MTBR-tau243) are increased in AD compared with other dementias5 Several plasma p-tau isoforms including p-tau181, p-tau205, p-tau217 and p-tau231, as well as microtubule binding domain region tau243 (MTBR-tau243) are increased in AD compared with other dementias.

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**BUSTA 14**

**QUESITO:**
TECNICHE SPETTROSCOPICHE

**OFFICE AUTOMATION**

A cosa serve il campo BCC?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

For example, p-tau231, p-tau217 and p-tau181 all change early in disease, around the same time as amyloid pathology, whereas p-tau205 and MTBR-tau243 change later in disease closer to the time when tau tangle pathology is detectable by PET58,59,60,61,62,63. MTBR-tau243 correlates most consistently with abundance of mature intracellular tau aggregation (neurofibrillary tangles) as shown on tau PET64. In the revised Alzheimer's Association consensus AT(N) diagnostic framework for AD, Aβ (PET, CSF) or p-tau measurements (CSF, plasma) are core biomarkers sufficient to establish the presence of AD pathology65. Several AD drug development programmes have identified participants by their mutation carrier status, including the Dominantly Inherited Alzheimer's Disease Trials Unit (DIAN-TU) studies of gantenerumab and solanezumab and ongoing trials of lecanemab and E2814 (refs. 66,67,68). Members of a large Columbian AD kindred with an inherited presenilin 1 mutation participated in clinical trials of an anti-amyloid monoclonal antibody, crenezumab.

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**BUSTA 15**

**QUESITO:**

DETERMINAZIONE DELL'ATTIVITA' ENZIMATICA

**OFFICE AUTOMATION**

Che differenza c'è tra file e cartella?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Mutation status can be used to identify presymptomatic AD, and it provides risk and prognostic information as mutation carriers progress to develop symptomatic AD in the absence of protective mutations or premature death. Current clinical diagnosis of Parkinson disease requires the presence of bradykinesia in combination with rest tremor or rigidity71. However, misdiagnosis occurs in about 20% of cases72. Two neuropathological hallmarks offer ultimate confirmation of Parkinson disease: degeneration of dopaminergic neurons in the substantia nigra pars compacta and the presence of intraneuronal α-synuclein pathology73. Although not a direct measure of nigral neurodegeneration, reduced striatal uptake of [123I]FP-CIT ([123I]ioflupane) measured with SPECT is useful to visualize striatal presynaptic dopamine transporters and is approved as an adjunct to clinical evaluation in people with suspected parkinsonian disorders, as well as DLB. Dopamine transporter imaging has been used as a diagnostic inclusion criterion in clinical trials of Parkinson disease, including recent trials of α-synuclein-directed immunotherapy.

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**BUSTA 16**

**QUESITO:**

TECNICHE DI SEQUENZIAMENTO GENICO

**OFFICE AUTOMATION**

Qual è il vantaggio di usare OneDrive?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

It can limit inclusion of people who are symptomatic without evidence of dopamine degeneration (SWEDD), a group that comprises approximately 15% of cases when using clinical criteria alone81,82. PET with [18F]fluorodopa is approved to support Parkinson disease diagnosis, although direct comparison between the two suggests that [123I]FP-CIT may offer greater sensitivity for detection of dopamine system abnormalities. Total α-synuclein protein in CSF is significantly reduced in people with Parkinson disease but substantial overlap with healthy control levels prevents its use as a diagnostic biomarker84,85. There is progress in validating the α-synuclein seed amplification assay (SAA)86,87,88 to confirm the presence of α-synuclein pathology in CSF and other tissues and biofluids, supporting this assay as a diagnostic or enrichment biomarker89. Integration of SAA into Parkinson disease clinical trials is still exploratory90 but is aligned with efforts to establish a more biological definition of Parkinson disease91,92. Studies are currently addressing digital quantification of the SAA and application to serum, which could expand its use..

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**BUSTA 17**

**QUESITO:**

VETTORI DI ESPREEIONE

**OFFICE AUTOMATION**

Cosa si intende per backup?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

CSF dopamine decarboxylase was shown in proteomic studies to be elevated in both idiopathic and genetic forms of Parkinson disease as well as in DLB and may complement other approaches to Parkinson disease. Dopamine decarboxylase concentrations in plasma are less informative.

Significant effort has sought to image α-synuclein by PET scanning of the brain96,97. Although recent success in detecting α-synuclein pathology in people with Parkinson disease and MSA, a related synucleinopathy, suggests that such a tracer may be possible, more work is needed to optimize these approaches before they can be integrated into clinical trials. For Parkinson disease, mutations in LRRK2 and GBA1 have been used as selection criteria in trials of LRRK2 kinase inhibitors and GBA1-directed therapies24,26,27,100. In this context, the mutation can provide diagnostic confirmation of specific genetic forms of Parkinson disease and support testing of more mechanistically precise therapies. In FTD, diagnostic biomarkers are less developed than in AD. FTD is variably associated with TDP43, tau or, rarely, fused-in sarcoma (FUS) proteinopathies; disease-specific biomarkers are needed.

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**BUSTA 18**

**QUESITO:**
UTILIZZO DEGLI ANTICORPI IN LABORATORIO

**OFFICE AUTOMATION**

Qual è lo scopo di un antivirus?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Thus far, there are no validated biomarkers that can positively demonstrate the presence of characteristic underlying pathologies in vivo and distinguish among aetiological subtypes102. Measurements of total p-tau proteins and their fragments in biological fluids have not yielded consensual biomarker profiles to effectively distinguish between FTD-tau and FTD-TDP43, and the tau ligands used in PET have failed to establish diagnostic utility103,104,105. Recent studies of extracellular vesicles bearing TDP43 or 3R/4R tau suggest that plasma measurements of these proteins are feasible and may become available for diagnosis106. The detection of misfolded TDP43 by SAA (or RT-QuiC)107,108 and the analysis of STMN2, HDGLF2, UNC13A cryptic exons or peptides in biofluids resulting from TDP43 loss of function hold promise for the diagnosis of TDP43 proteinopathies107,109. Cryptic exons are DNA splicing variants erroneously included in mature mRNA owing to the protein binding function of TDP43. There are no approved neuroimaging tracers for TDP43 protein.

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**BUSTA 19**

**QUESITO:**
ALLESTIMENTO DI UN PREPARATO ISTOLOGICO

**OFFICE AUTOMATION**

Che cos'è un firewall?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**
FTD may be caused by loss-of-function granulin precursor mutations (FTD-GRN) or by C9orf72 repeat expansion (FTD/ALS-C9orf72) and, less frequently, by MAPT and other genetic causes33. Serum and CSF progranulin levels are decreased in FTD-GRN mutation carriers with levels remaining relatively stable from the presymptomatic to the clinical stage, providing a robust diagnostic marker110,111. A diagnostic approach to identify patients with FTD involves determining which patients have low plasma progranulin levels followed by confirmation of the progranulin mutation110. Similarly, in individuals with a clinical syndrome of FTD, the diagnosis of FTD-GRN, FTD/ALS-C9orf72, FTD-MAPT and of other genetic forms of FTD can be confirmed by genetic testing, allowing construction of trial populations of genetically defined forms of FTD. Genetically determined trial populations are more homogeneous, as all the genetic forms (including GRN and C9orf72) are associated with a TDP43 proteinopathy, with the exception of mutations in the MAPT gene, which cause a tau proteinopathy.

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**BUSTA 20**

**QUESITO:**
APPLICAZIONE DI GENI REPORT

**OFFICE AUTOMATION**

Cos'è il phishing?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**
In the phase III VALOR trial of tofersen for the treatment of SOD1-related ALS, participants were required to have weakness attributable to ALS and a confirmed SOD1 mutation112. This trial led to the accelerated approval of tofersen for the SOD1-related genetic form of ALS, demonstrating the value of identifying subpopulations with mutations amenable to biologically informed therapeutic manipulation. HD is caused by a CAG repeat expansion in the Huntingtin gene. Genetic testing can be used to validate the diagnosis and distinguish HD from other choreiform disorders. Genetically proven participants can then be involved in clinical trials.
A key application of prognostic biomarkers is to enrich trial populations. Biomarkers that identify those most likely to decline in the time frame of a trial ('fast progressors') that can ensure placebo decline and improve the probability of demonstrating a drug–placebo difference with an effective therapy. Smaller sample sizes, shorter duration and less capital may be required to establish a treatment effect in enriched populations.

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**BUSTA 21**

**QUESITO:**
TECNICHE DI SEPARAZIONE CELLULARE

**OFFICE AUTOMATION**

Che cos'è un malware?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

In AD, p-tau181 and p-tau217 predict cognitive decline at 1 year and correlate with Aβ PET and tau PET positivity114,115. p-tau217 demonstrated Aβ-correlated changes over 4–6 years in both preclinical and symptomatic disease phases; the changes correlated with clinical decline and brain atrophy116. Tau PET is strongly associated with subsequent cognitive decline in Aβ-positive individuals117. Biomarkers of AD co-pathology such as glial fibrillary acidic protein (GFAP) and the α-synuclein SAA have been associated with more rapid decline in AD.

Prognostic biomarkers have a major role in AD prevention trials. These studies involve agents for secondary prevention (for example, cognitively normal individuals with biomarker evidence indicating the presence of the disease) or primary prevention (for example, cognitively normal individuals without biomarker evidence of the disease but who are known to be at high risk of its occurrence). In the A4 secondary prevention trial, patient selection was by amyloid PET.

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**BUSTA 22**

**QUESITO:**
PURIFICAZIONE DI ACIDI NUCLEICI

**OFFICE AUTOMATION**

Cosa fa la funzione =MEDIA(A1:A5)?

**LETTURA E TRADUZIONE DEL BRANO IN LINGUA INGLESE**

Trial observations showed that high levels of brain amyloid, positive tau PET and high levels of plasma p-tau217 all had prognostic value, indicating which participants were most likely to exhibit cognitive decline or to progress to symptomatic AD120. In the absence of symptoms, slowing of decline by use of a DTT requires demonstration of an impact on a biomarker or following the disease until symptoms occur to determine whether symptom onset is delayed with treatment. Alternatively, slowing of cognitive decline may be demonstrated on very sensitive cognitive assessments such as the Preclinical Alzheimer Cognitive Composite (PACC), PACC-5 or Alzheimer Prevention Initiative Composite Cognitive Test score. For Parkinson disease, dopamine imaging can offer prognostic insight into whether an individual may be more likely to exhibit certain clinical features or disease complications (for example, tremor, levodopa-induced dyskinesias, certain non-motor features) although this may be useful only when assessed at earlier disease stages. Mutations and variation in GBA1 are associated with greater likelihood of motor and cognitive decline.

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