Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

IBC-Ab002

Evidence Summary

PD-1/PD-L1 inhibition has improved cognitive function and disease pathology in models of Alzheimer's, though benefits may depend on many factors. IBC-Ab002 has not been tested in humans yet.

Neuroprotective Benefit: PD-L1 inhibition has ameliorated cognitive impairment and disease pathology in AD mice. But other groups have failed to reproduce these findings. Benefits may depend on stage of disease and additional sensitizing factors.

Aging and related health concerns: No studies have tested IBC-Ab002 for age-related diseases. However, several anti-PD-L1 and anti-PD-1 antibodies are approved for the treatment of cancer.

Safety: A phase I study of IBC-Ab002 is planned in Alzheimer's patients where safety and tolerability will be assessed. Single-agent anti-PD-L1 therapies in cancer patients have toxicities similar to placebo, though rarely, serious inflammatory toxicities occur.

Availability: not available; under clinical development	**Dose**: Dose has not been established for humans. In a PK study in Cynomolgus monkeys, a dose of 13 mg/kg, i.v. was used.	**Chemical formula:** not publicly documented **MW**: not publicly documented
Half life: not publicly documented	**BBB**: N/A; aimed at modulating the peripheral immune system	
Clinical trials: No clinical trials have been completed. A first-in-human phase I study of IBC-Ab002 is expected to start in the first half of 2022.	**Observational studies**: not available	

What is it? IBC-Ab002 is an antibody against human programmed death-ligand 1 (PD-L1), an inhibitory immune checkpoint. Immune checkpoints regulate immune activation and maintain immune homeostasis while preventing autoimmunity. PD-L1 is expressed by several cell types, including myeloid cells, epithelial cells, and regulatory T cells, and is a ligand for programmed cell death protein 1 (PD-1), which is expressed in a variety of activated effector memory immune cells (e.g., CD4+ T cells). PD-L1 binding to PD-1 downregulates memory T cell responses, including proliferation and cytokine production (Gotsman et al., 2007; Carter et al., 2002). Immune checkpoint inhibitors, including inhibitors of PD-1 and PD-L1, have been studied most extensively for the treatment of different types of cancers where immune tolerance occurs.

IBC-Ab002 is under clinical development by ImmunoBrain Checkpoint Inc, a biopharmaceutical company developing novel immune therapies for neurodegenerative diseases. Blockade of the PD-1/PD-L1 inhibitory immune pathway increases interferon-γ (IFN-γ) in the choroid plexus, enabling mobilization of peripheral macrophages into the brain to enhance removal of neurotoxic proteins and resolving local inflammation (Baruch et al., 2016). Studies suggest that the blood-cerebrospinal-fluid barrier comprised of the choroid plexus epithelial cells can serve as a physiological gateway that allows selective immune cell access upon brain injury or pathology, but that this gateway is impaired with aging and in Alzheimer's disease in animal models (Baruch et al., 2014; Schwartz et al., 2019). ImmunoBrain Checkpoint plans to start IBC-Ab002's first-in-human phase I clinical study in early 2022 (R01AG071810-01; Alz.org/partthecloud).

Neuroprotective Benefit: PD-L1 inhibition has ameliorated cognitive impairment and disease pathology in AD mice. But other groups have failed to reproduce these findings. Benefits may depend on stage of disease and additional sensitizing factors.

Types of evidence:

- 2 observational studies examining PD-1 and/or PD-L1 expression in Alzheimer's patients
- 1 review paper on the inverse relationship between Alzheimer's and cancer
- 1 poster describing the pharmacokinetic profile of IBC-Ab002
- Several laboratory studies assessing PD-1 or PD-L1 inhibition

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:
There is no data from humans with IBC-Ab002.

In a review paper describing the inverse relationship between Alzheimer's disease and cancer, authors cite literature suggesting that patients with a history of cancer in the past have a lower risk of developing Alzheimer's disease, and vice versa (Rogers et al., 2020). The authors argue that the immune checkpoint targets may be good candidates that underlie this inverse relationship. In other words, people who have survived cancer may have a proinflammatory immune system with diminished immune tolerance, which could aid in the prevention/clearance of Alzheimer's pathology in the brain. Because all studies are observational in nature, the cause versus effect cannot be teased apart.

Human research to suggest benefits to patients with dementia:
NIH and the Alzheimer's Association are supporting a first-in-human phase 1 study to evaluate the safety, tolerability, and pharmacokinetics of IBC-Ab002 in 40 individuals with early Alzheimer's disease (R01AG071810-01; Alz.org/partthecloud). The phase I study is a randomized, double-blind, placebo-controlled study of multiple intravenous doses. The single-ascending dose study will be carried out first, followed by the multiple-ascending dose study, with a 12-week interval between administrations. The team will perform brain scans and analyze blood and cerebrospinal fluid samples to study biomarkers and brain inflammation. This project is scheduled to commence in the first half of 2022 and is scheduled to be completed in August 2024 (GlobeNewsWire).

In a biomarker study of 35 Alzheimer's patients, 30 people with mild cognitive impairment, and 30 healthy controls, the PD-1/PD-L1 pathway was assessed. At basal conditions, expressions of PD-1 and PD-L1 on immune cells were reduced in patients with mild cognitive impairment or Alzheimer's disease,

compared to healthy age-matched controls (Saresella et al., 2012). Specifically, the number of PD-1-expressing CD4+ T cells (helper T cells), the density of PD-L1 on CD14+ antigen presenting cells, IL-10 production, and the number of PD-L1-expressing/IL-10-producing CD14+ antigen presenting cells were significantly reduced in patients with Alzheimer's or mild cognitive impairment compared to healthy controls. The interaction between PD-1 and PD-L1 results in IL-10 production and the apoptosis of antigen-specific cells. Patients with mild cognitive impairment or Alzheimer's disease had diminished numbers of Aβ-specific CD4+ T cells that undergo apoptosis, and upon *in vitro* stimulation with Aβ peptides, these cells proliferated more (higher fraction of Aβ-specific Ki67+ CD4+ T lymphocytes in Alzheimer's and mild cognitive impairment patients). Together, these results show that in Alzheimer's disease, fewer Aβ-specific CD4+ T cells bind scarcer quantities of PD-L1 on the surface of CD14+ antigen presenting cells, leading to a reduced Aβ-induced production of IL-10, an increased proliferation of Aβ-stimulated T lymphocytes, and a reduced susceptibility of these T lymphocytes to undergo apoptosis. These findings suggest that the PD-L1/PD-1 pathway is impaired or downregulated in people with mild cognitive impairment and Alzheimer's disease.

In the cerebral spinal fluid of Alzheimer's patients, PD-L1 is increased by more than two-fold compared to control subjects (Kummer et al., 2021). In postmortem brain tissue, PD-L1 expression was detected in astrocytes near amyloid plaques in Alzheimer's patients, but PD-L1 was not expressed in astrocytes in control subjects. In Alzheimer's patients, PD-1 is increased and colocalized with microglia near amyloid plaques.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:
A 2020 AAIC poster by ImmunoBrain Checkpoint Inc. reported data testing anti-PD-L1 antibodies in 3 mouse models of Alzheimer's disease, as well as pharmacokinetic profiles in mice and monkeys (Baruch et al., 2020, AAIC poster). IBC-Ab002, the clinical candidate for Alzheimer's patients, cross-reacted with monkey and human PD-L1. In cells (CHO cells) expressing human PD-L1, IBC-Ab002 neutralized PD-1 binding to PD-L1 with an IC50 of 3.2 x 10^{-10}M. IBC-Ab002 has a modification on the Fc region (point mutations), and it showed comparable *ex vivo* potency compared to the Fc-non-modified antibody, while the pharmacokinetic profile was altered such that there was a significantly faster clearance in monkeys (13 mg/kg, i.v.) compared to the non-modified antibody, IBC-Ab001.

In 3 models of Alzheimer's disease (6-month old 5xFAD mice, 8-9-month old K257T/P301S double mutant "DM-hTAU" mice, and 8-9-month old PS19 mice), anti-PD-L1 antibodies were tested for therapeutic benefits, using Fc-modified and Fc-non-modified versions (Baruch et al., 2020, AAIC poster). These antibodies had human IgG1 backbone and high binding affinity to mouse PD-L1. A single injection

of the Fc-modified anti-PD-L1 antibody (1.5 mg/mouse) improved cognitive function measured 1 month after treatment to the same extent as the Fc-non-modified anti-PD-L1 antibody. The radial arm water maze task was used for the 5xFAD mice to assess spatial learning and memory. The T-maze task was used for the 2 tauopathy mice to assess short-term memory.

In a mouse model of tauopathy (DM-hTAU mice), a single treatment with the Fc-modified anti-PD-L1 (0.1 mg, 0.5 mg, 1.5 mg/mouse) showed a dose-dependent effect on cognitive performance measured with T-maze 4 weeks after treatment, which was accompanied by reduced tau pathology (Baruch et al., 2020, AAIC poster).

In the same tauopathy mice, repeated anti-PD-L1 antibody treatment every 6 weeks for 3 times (1.5 mg/injection, i.p.) showed long-lasting cognitive improvement measured using the T-maze task for at least 5 months after treatment initiation and persisted for at least 8 weeks after the final injection (Baruch et al., 2020, AAIC poster).

The foundation for the above clinical development efforts by ImmunoBrain Checkpoint originated in a series of high-profile publications by the laboratory of Michal Schwartz, PhD, at the Weizmann Institute of Science; she is the co-founder and chief scientific officer of ImmunoBrain Checkpoint.

In a mouse model of Alzheimer's disease (5xFAD mice, 10 months of age) with advanced cerebral pathology, two injections with anti-PD-1 (250 µg, i.p.; rat isotype; clone RPM1-14; BIOXCELL), 3 days apart, led to clearance of Aβ from the cerebral cortex and hippocampus and improvement in cognitive performance, measured by the radial arm water maze task (Baruch et al., 2016). Anti-PD-1 treatment also significantly increased IFN-γ-dependent systemic immune response at the choroid plexus, a selective gateway for leukocyte trafficking into the brain. They next examined whether the immune checkpoint inhibition using the anti-PD-1 antibody results in recruitment of monocyte-derived macrophages into the brain. In 5xFAD mice that were treated with the anti-PD-1 antibody, higher frequencies of infiltrating myeloid cells (CD45highCD11b+ cells) were seen compared to mice receiving control IgG treatment. These infiltrating myeloid cells expressed a distinct mRNA profile consistent with their phenotype, including high expression of lymphocyte antigen 6c and chemokine receptor CCR2, which is associated with myeloid cell neuroprotection in Alzheimer's disease. These cells also expressed scavenger receptor A (SRA1), which is an Aβ-binding scavenger receptor associated with Aβ-plaque clearance (El Khoury et al., 1996).

In the same 5xFAD mice, 2 sessions of anti-PD-1 antibody treatment, with a one-month interval between sessions, resulted in improved cognitive performance 2 months after the first session relative to the control IgG-treated or untreated 5xFAD control mice; the anti-PD-1-treated mice reached performance levels comparable to those of wild-type mice (Baruch et al., 2016). Mice that received a single session of anti-PD-1 antibody that were examined 2 months after the treatment showed only a marginal improvement in memory compared to IgG-treated mice, suggesting that repeated treatment sessions are needed to maintain the effects on cognitive function. In these same mice, clearance of Aβ plaque pathology was more pronounced after 2 sessions of anti-PD-1 treatment compared to 1 session. Astrogliosis (measured by GFAP staining) was reduced in the hippocampus of 5xFAD mice treated with either 1 or 2 sessions of anti-PD-1 antibody compared to the IgG-treated controls.

In a different mouse model of Alzheimer's, the APP/PS1 mice, which develops Aβ pathology at a more advanced age than 5xFAD mice, anti-PD-1 antibody treatment at 8 or 15 months of age significantly reduced Aβ plaque load in the hippocampus 1 month after treatment (Baruch et al., 2016). The authors pointed out that the immune checkpoint blockade is not meant to target a single disease pathology, but rather to strengthen the ability of the immune system to clear numerous pathologies.

In a follow-up study by the same group, anti-PD-L1 antibodies were compared with the anti-PD-1 antibodies and similar efficacy in disease modification was observed in 3 mouse models of Alzheimer's/tauopathy (5xFAD mice, K257T/P301S mice, DM-hTAU mice)(Rosenzweig et al., 2019). In 5xFAD mice, a single i.p. dose of anti-PD-L1 antibody resulted in improved radial arm water maze performance at the two higher doses (0.5 and 1.5 mg, but not at 0.1 mg) compared to the control IgG treatment, and the magnitude of improvement was comparable to that of anti-PD-1 treatment. Anti-PD-L1 treatment (as well as anti-PD-1 antibody) also significantly decreased Aβ pathology and increased expression of synaptophysin and IL-10 in the hippocampi of mice.

In 5.5-month-old 5xFAD mice, prior to anti-PD-L1 treatment, there were significant cognitive deficits, but 1 month after anti-PD-L1 treatment (single injection of 1.5 mg, i.p.), robust improvement in radial arm water maze performance was observed that was not seen in the control IgG-treated mice (Rosenzweig et al., 2019).

In 8-month-old mice that express two mutations of the human tau (K257T/P301S DM-hTAU mice), anti-PD-L1 antibody (0.5 mg) or anti-PD-1 antibody (0.5 mg) treatment resulted in improved performance on the T-maze test 1 month later compared to the control IgG-treated mice (Rosenzweig et al., 2019). Both anti-PD-L1 and anti-PD-1 antibody treatments resulted in reduced expression of pro-inflammatory

cytokines, TNF-α, IL-6, IL-12p40, and IL-1β, in the brain. In DM-hTAU mice, anti-PD-L1 treatment resulted in a significant reduction in IL-1β protein levels in the hippocampus, and a significant reduction in tau aggregation in cortical and hippocampal regions, when compared with IgG control-treated mice. When an additional anti-PD-L1 antibody, a human anti-PD-L1 clone that cross-reacts with mouse PD-L1 ligand, was tested in DM-hTAU mice, a similar improvement in cognitive performance was observed.

The infiltrating monocyte-derived macrophages were heterogeneous but expressed unique scavenger molecules that could possibly mediate disease modification, including macrophage scavenger receptor 1 (Msr1, aka, SRA1, SCARA1, or CD204), a phagocytic receptor required for the engulfment of misfolded proteins, and insulin-like growth factor-1 (igf1) anti-inflammatory macrophage markers, lyve1 and stab-1, and scavenger receptors, Siglec1 and Mrc1 (Rosenzweig et al., 2019).

Controversies: Despite the compelling data presented by the laboratory of Michal Schwartz, PhD, at the Weizmann Institute of Science, numerous efforts to replicate these findings have not been successful.

In studies of various Alzheimer's mouse models performed across 3 pharmaceutical companies (Sanofi, Janssen, and Eli Lilly), the efficacy of anti-PD-1 antibodies was examined to determine whether the effect on Aβ pathology is specific to PD-1 target engagement (Latta-Mahieu et al., 2018). This question arose because in the previous work (Baruch et al., 2016), a rat monoclonal antibody was used in mouse models, raising the possibility that the observed effects were not necessarily due to PD-1 inhibition, but attributed to the xenogeneicity. For anti-PD-1, the same isotype used by Baruch et al., 2016 (RPM1-14 rat IgG2a from BioXcell), as well as 2 mouse chimeric variants (RPM1-14 chimeric mouse Fc IgG1, RPM1-14 chimeric mouse Fc IgG2a) were tested (Latta-Mahieu et al., 2018).

In ThyAPP/PS1M146L mice (Sanofi), anti-PD-1 treatment (RPM1-14 chimeric mouse Fc IgG1) induced a systemic IFN-γ-associated peripheral immune response, demonstrating target engagement (Latta-Mahieu et al., 2018). However, in these mice treated with anti-PD-1, only a trend for an increase of IFN-γ expression in the choroid plexus was seen and this did not result in monocyte-derived macrophage infiltration into the brain. When ThyAPP/PS1M146L mice were treated with anti-PD-1 for 2 months, with 2 treatment sessions 1 month apart, amyloid pathology (number or total area of deposits) was not reduced.

Eleven-month-old ThyAPPL/PS1A246E amyloid mice (Janssen) with amyloid pathology were treated for 2 months with the same anti-PD-1 antibody used by Baruch et al., 2016 and amyloid load increased after treatment, with no significant differences observed between anti-PD-1-treated mice versus the control

IgG2a-treated mice (Latta-Mahieu et al., 2018). Another experiment using the same anti-PD-1 regimen but conducted in 21-month-old APP/PS1 mice showed similar results.

In 18-month-old PD-APP mice (Eli Lilly), anti-PD1 antibody (chimeric version of the same RPM1–14 antibody with a mouse Fc domain IgG2a) treatment for 3 sessions (1 month between each session) did not result in significant differences in Aβ burden in the cortex and hippocampus compared to the control IgG2a-treated mice (Latta-Mahieu et al., 2018).

Authors from the 3 pharmaceutical companies emphasized that the *in vivo* efficacy studies were carried out with high statistical power (n=9-25 mice per group) with analysis conducted blind to experimental groups (Latta-Mahieu et al., 2018). The authors suggest that the inhibition of PD-1 checkpoint signaling by itself is not sufficient to reduce amyloid pathology and that additional factors might have contributed to previous findings by the laboratory of Michal Schwartz, PhD. These factors may include differences in intestinal microbiota that impact inflammatory processes (Harach et al., 2017), the stage of pathology when intervention was initiated, or additional sensitizing factors.

In an independent study by a different group, the same anti-PD-1 antibody used by Baruch et al., 2016 (10 mg/kg, i.p., rat IgG2a isotype, clone RPM1-14, BioXcell) but at a weekly dosing schedule for 12 weeks in female JNPL3 tauopathy mice (10-11 months of age) modestly increased locomotor activity compared to the control IgG-treated mice, but no improvements were seen in cognitive function or tau pathology (Lin et al., 2020). Cognitive function was measured by object recognition test, spontaneous alternation task, novel location task, the Barnes maze task, and fear conditioning test. Anti-PD-1-treated group and the IgG control group showed no statistically significant differences in these cognitive measures. Total tau, insoluble tau, soluble tau, and phospho-tau levels were assessed in whole-brain homogenates and Western blots. Levels were comparable between the anti-PD-1-treated group and the IgG control group. A commentary by Baruch and Yoles (2020) argued that there were conceptual and technical differences in the study design of Lin and colleagues compared to their line of work. They argued that the 10-11-month-old JNPL3 mice were at a much more advanced stage of disease with a severe motor deficit, and the weekly treatment of anti-PD-1 was not ideal, as temporary intermittent blocking of immune checkpoint can only be achieved by treatments that are more spaced out, such as monthly or 6-week-interval treatment (Baruch et al., 2016).

In a mouse model of Alzheimer's disease (APP/PS1 mice), deletion of microglial PD-1 increased inflammation and Aβ deposition, while reducing microglial Aβ uptake, suggesting that PD-1 is important for Aβ uptake and that a complete loss of PD-1 signaling by using a PD-1 knockout model worsens

progression of plaque pathology and cognitive function (Kummer et al., 2021). The authors argued that the effects demonstrated by the Schwartz group with anti-PD1 in mouse models of Alzheimer's (Baruch et al., 2016) could be due to the inhibition of astrocyte-to-microglia PD-L1/PD-1 signaling, thereby rescuing the innate immune response in the brain, instead of, or in addition to, the actions of monocyte-derived macrophages entering the brain (Kummer et al., 2021).

Studies in models of Alzheimer's disease suggest that the beneficial effect of inhibiting the immune checkpoint may depend on disease stage (reviewed in Rogers et al., 2020). Depletion of regulatory T cells using an anti-CD25 antibody during the early phase of disease pathology (4-5 weeks of age in APP/PS1 mice or 4 weeks of age in 3xTg-AD mice) worsened cognitive function and amyloid load (Dansokho et al., 2016; Baek et al. 2016). But depleting or inhibiting regulatory T cells at a later stage of disease (10-month-old 5xFAD mice) mitigated Alzheimer's pathology and reversed cognitive decline (Baruch et al., 2015). Immune checkpoint inhibition using anti-PD-1 antibody was efficacious also at the later stage of disease (10-month-old 5xFAD mice)(Baruch et al., 2016). These studies suggest that some level of immune tolerance (by regulatory T cells) might be beneficial at the early stages of Alzheimer's pathology where excessive inflammation may be prevented. At the later stages of disease, inhibition of immune checkpoint could allow passage of immune cells to the brain to help eliminate disease pathology.

APOE4 interactions: Unknown.

Aging and related health concerns: No studies have tested IBC-Ab002 for age-related diseases. However, several anti-PD-L1 and anti-PD-1 antibodies are approved for the treatment of cancer.

Types of evidence:

- 0 clinical trials
- 0 laboratory studies

No studies have tested the efficacy of IBC-Ab002 for age-related peripheral diseases, as it is designed for the treatment of Alzheimer's disease and other dementias.

Blockade of the PD-1/PD-L1 pathway is considered a major advance in the treatment of cancer. There are several anti-PD-1 and anti-PD-L1 therapies approved by the FDA for the treatment of 11 types of cancer: nivolumab, pembrolizumab, avelumab, durvalumab, and atezolizumab (Rogers et al., 2020).

These therapies are particularly favorable in cancers induced by carcinogens or viral infections (e.g., Hodgkin's lymphoma, Merkel cell carcinoma of the skin, microsatellite instability-high cancers, and desmoplastic melanoma), with response rates around 50-90%.

Safety: A phase I study of IBC-Ab002 is planned in Alzheimer's patients where safety and tolerability will be assessed. Single-agent anti-PD-L1 therapies in cancer patients have toxicities similar to placebo, though rarely, serious inflammatory toxicities occur.

Types of evidence:

- 0 clinical trials
- Several review papers on immune checkpoint inhibitors in cancer treatment
- Several laboratory studies

For IBC-Ab002, no studies in humans have been completed to date. In the first half of 2022, a first-in-human phase 1 is scheduled to be initiated to evaluate the safety, tolerability, and pharmacokinetics of IBC-Ab002 in early Alzheimer's disease patients (R01AG071810-01; GlobeNewsWire).

Several PD-L1 inhibitors (and PD-1 inhibitors) are approved for the treatment of various cancers. PD-L1 inhibitors can have severe and fatal immune-mediated effects. In cancer patients, immune-mediated pneumonitis, interstitial lung disease, hepatitis, colitis, endocrinopathies (e.g. thyroid dysfunction, adrenal insufficiency, diabetes mellitus, etc.), nephritis, dermatitis, and others (myocarditis, pericarditis, vasculitis, meningitis, encephalitis, etc.) have been reported for Atezolizumab (Drugs.com). The majority of patients receiving single-agent anti-PD-1 or anti-PD-L1 therapy have toxicities similar to placebo, with very few patients discontinuing therapy due to toxicities (under 5%)(Ribas and Wolchok, 2018). The most common treatment-related adverse events are fatigue, diarrhea, rash, and pruritis. However, in a smaller percentage of patients, toxicities are more serious, where the immune system infiltrates a hormone-producing gland that leads to endocrinopathies, such as thyroid disorders, hypophysiitis, adrenal gland disorders, and type I diabetes. Although rare (~1%), inflammatory toxicities of other organs have been reported, including encephalopathy, meningitis, pneumonitis, myocarditis, hepatitis, nephritis, esophagitis, colitis, and others, which can be life-threatening.

IBC-Ab002 has a modification on the Fc region, and while showing comparable potency compared to the Fc-non-modified antibody (IBC-Ab001), it had significantly faster clearance in monkeys (13 mg/kg, i.v.)(Baruch et al., 2020, AAIC poster). The authors of the poster noted that the faster clearance profile

of IBC-Ab002 is preferable in Alzheimer's disease to achieve temporary immune checkpoint inhibition, while more chronic exposure and inhibition are sought for cancer immunotherapy.

PD-1 or PD-L1 inhibition has been shown to rapidly induce diabetes in a mouse model of type I diabetes (female nonobese diabetic mice) (Ansari et al., 2003). In 9-week-old female nonobese diabetic mice that were prediabetic, a single injection of Fc-modified anti-PD-L1 (1.5 mg/mouse, i.p.) resulted in only 10% of the mice developing diabetes after 17 days, compared to 90% of the mice receiving the Fc-non-modified anti-PD-L1 (Baruch et al., 2020, AAIC poster). Thus, the Fc-modified anti-PD-L1 showed a better safety profile compared to the non-modified anti-PD-L1 in terms of autoimmune diabetes in susceptible mice.

Drug interactions: Drug interactions with IBC-Ab002 have not been documented.

Sources and dosing: IBC-Ab002 is under clinical development by ImmunoBrain Checkpoint Inc. Doses have not been established for humans. In a pharmacokinetic study in Cynomolgus monkeys, a dose of 13 mg/kg, i.v. was used. In a planned phase 1 study of IBC-Ab002, dosing will have 12-week intervals (R01AG071810-01).

Research underway: NIH is currently funding a first-in-human phase 1 study to evaluate the safety, tolerability, and pharmacokinetics of IBC-Ab002 in early Alzheimer's disease patients (R01AG071810-01). The study is also funded in part by a grant from the Alzheimer's Association under the 2020 Part the Cloud + Bill Gates Partnership Grant Program. The phase I study is a randomized, double-blind, placebo-controlled study of multiple intravenous doses. The single-ascending dose study will be carried out first, followed by the multiple-ascending dose study, with a 12-week interval between administrations. This project started in September 2021 and is scheduled to end in August 2024.

Search terms:
Pubmed, Google: IBC-Ab002, PD-L1

Websites visited for IBC-Ab002:

- Clinicaltrials.gov (0)
- NIH RePORTER
- DrugAge (0)
- Geroprotectors (0)
- Drugs.com (0)

- WebMD.com (0)
- PubChem (0)
- DrugBank.ca (0)
- Cafepharma (0)
- Pharmapro.com (0)

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