VACSYN STUDY: A BIOMARKER-BASED PHASE 2 CLINICAL TRIAL TO EVALUATE ACI-7104.056, A NOVEL ACTIVE IMMUNOTHERAPY FOR PARKINSON'S DISEASE

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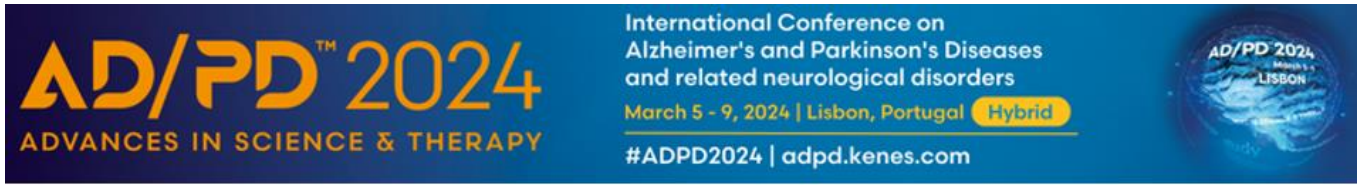

AC Immune

Disclaimer

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Disclosures

Dymitr Kostrica is an employee of AC Immune entitled to stock options.

Parkinson’s disease

Pathological deposition of alpha-synuclein

Most common neurodegenerative movement disorder
Affects ~1% of the population over 65 years

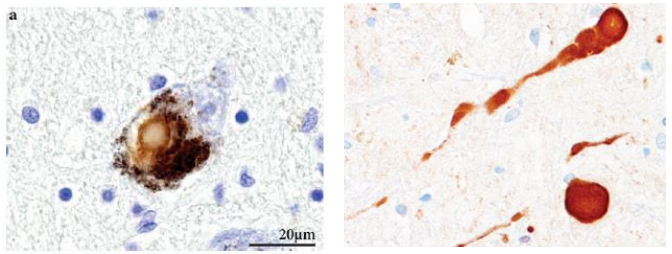
Etiology
5-10% genetic, 90-95% idiopathic, unknown cause

Cardinal motor symptoms
Tremor, rigidity, bradykinesia

Common non-motor symptoms
Sleep disorder, depression, cognitive impairment

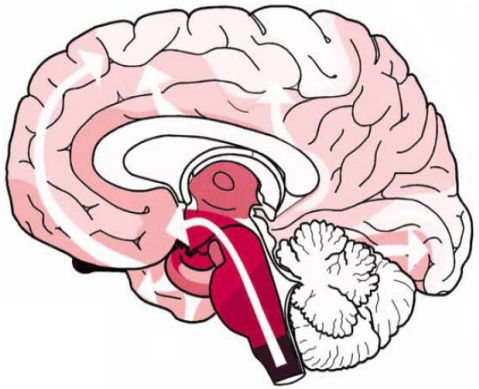
Pathological hallmarks
Neuron loss, alpha-synuclein aggregates – Lewy bodies

Main component of Lewy bodies: Alpha-synuclein



Halliday et al. 2011

Progression of pathology



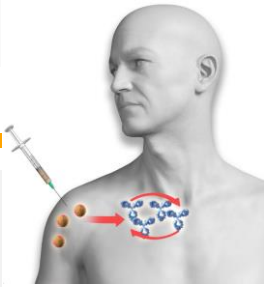
Braak et al. 2003

Active immunotherapy: clear advantages for long-term use

Provides opportunity to prevent AND treat neurodegenerative diseases globally

ACTIVE Immune Therapy

- Long-lasting specific immunity for pathological target, consistent, boostable, durable
- Limited annual dosing (once or twice) after priming year
- Safety profile well suited to long-term use
- Cost-effective (attractive healthcare economics across global populations)
- Improved access (ease of administration, simple logistics)

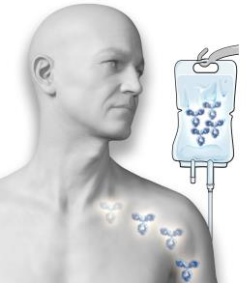


Active immunotherapy

Vaccines stimulate the patient's immune system to produce antibodies

Passive immunotherapy

Externally generated monoclonal antibodies require administration every two to four weeks

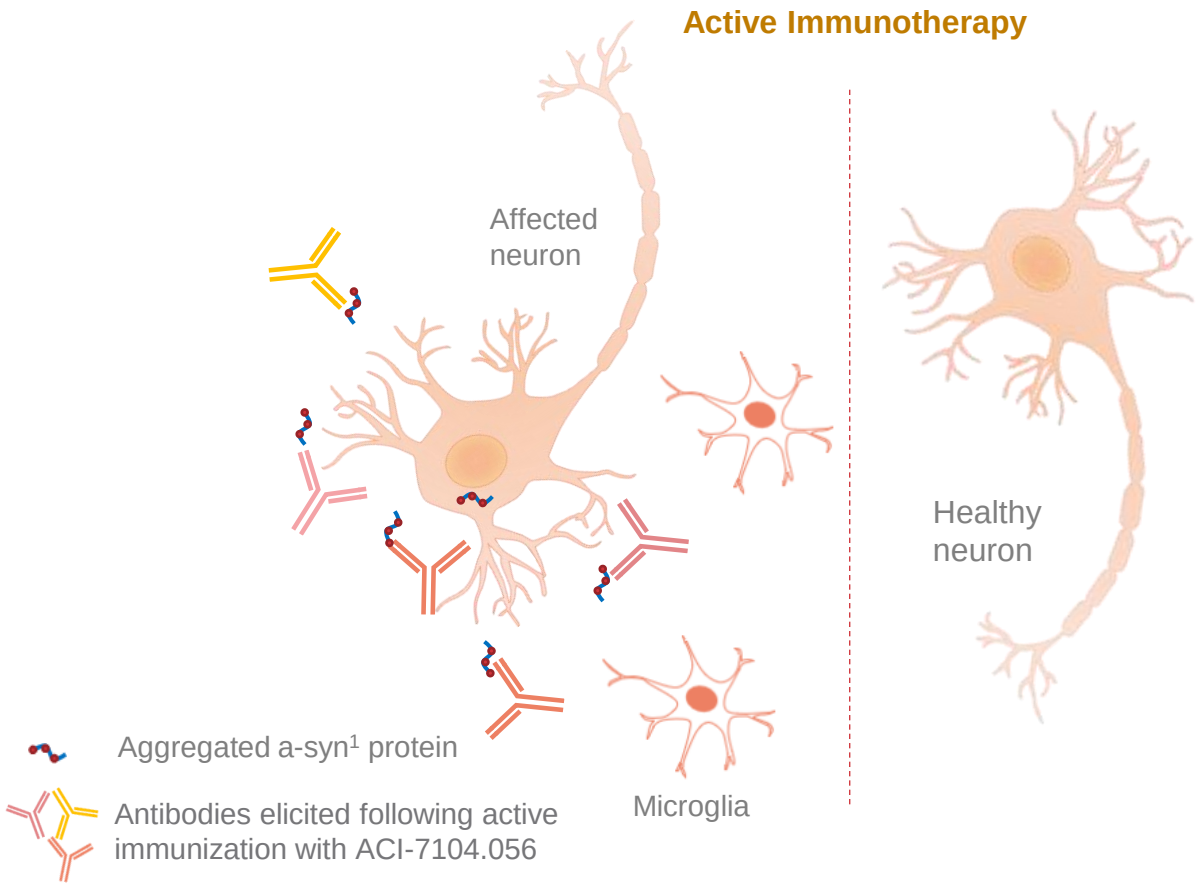


- Active immunotherapy is potentially the only option for global prevention of NDDs[1]

(1) Neurodegenerative diseases

Inhibiting of α-syn propagation to other neurons

ACI-7104.056 potential first disease – modifying active immunotherapy



ACI-7104.056

- Induces a strong IgG response against α-syn[1] aggregates observed after two immunizations and maintained at a high level until NHP[2] study end.
- Active immunization elicits antibodies that bind α-syn[1] aggregates with high specificity and bind to the pathological α-syn[1] present in brain tissue from patients
- Antibodies reduced the number of intracellular α-syn aggregates in a primary neuronal seeding assay demonstrating efficient blockage of α-syn[1] propagation

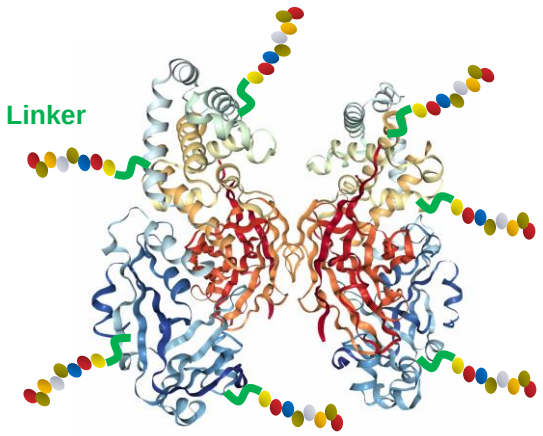
Please visit for more details poster P0996 / #1513 presented by Guenther Staffler

(1) alpha-synuclein; (2) Non-Human Primate

Immunological potential of ACI-7104 vaccine

Optimized peptide-conjugate vaccine formulation

Antigenic Peptide (B-cell peptide)



CRM197 carrier (delivers T cell help)

Generates target-specific antibody response

Safely engages target-unrelated T-cells to enhance & maintain response

Preclinical & Clinical Performance[1]

Immunogenicity	✓
Target specificity	✓
Selective for aggregated α-syn	✓
Sustainability of response	✓
Boosting	✓
Class switching IgM to IgG	✓
Evidence of memory B cells	✓
Preclude activation of T cells specific for α-syn	✓

- ACI-7104 is an optimized vaccine formulation and a successor of PD01A vaccine
- Robust immunogenicity and strong safety demonstrated in preclinical models and humans
- Evidence for lasting immune response supporting a disease prevention approach

(1) Volc et al., Lancet Neurol. 2020;

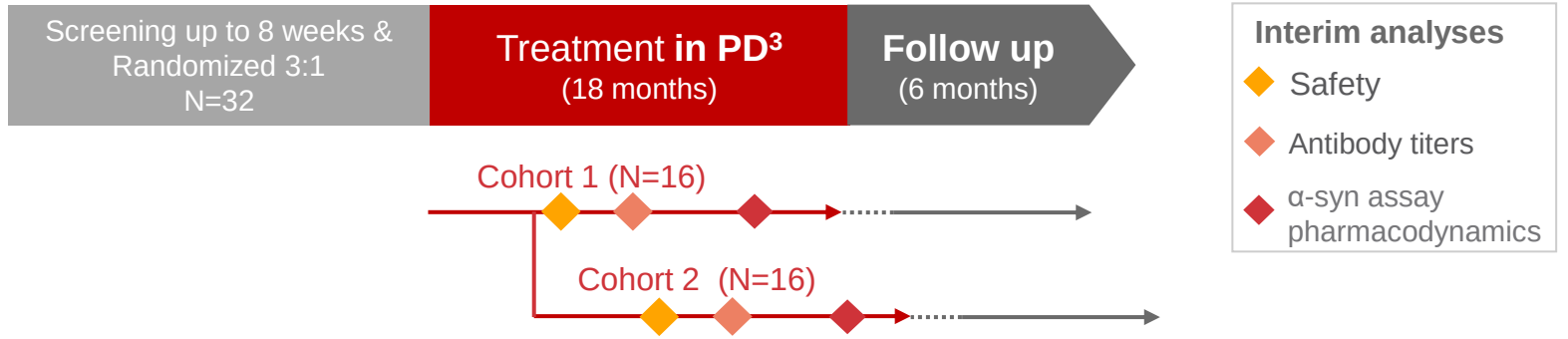
Please visit for more details poster P0996 / #1513 presented by Guenther Staffler

VacSYn: an adaptive biomarker-based Phase 2 study of ACI-7104 in early PD[1]

Placebo-controlled Phase 2 Study Overview (NCT06015841)

Part 1: Safety & PD[2]

- Key immunogenicity measures
- Measures of pathological α-syn[4] (a-syn oligomers and aggregates)



Part 2: Clinical PoC[5]

- Motor and Non-Motor Functioning (UPDRS[6] based)
- Degeneration of dopaminergic terminals (DaT SPECT[7] imaging)
- Advanced MRI (including ASL[8] and DTI[9])
- Digital biomarkers of motor and non-motor function
- Functional and patient reported outcomes

All participants from Part 1 will contribute to final analysis

(1) Parkinson's disease; (2) Pharmacodynamics; (3) Participants must have idiopathic PD and be stable on up to 300 mg of L-Dopa treatment and dopaminergic deficit determined by Dopamine Transporter Single Photon Emission Computed Tomography; (4) alpha-synuclein; (5) Proof-of-concept; (6) Unified Parkinson's disease rating scale; (7) Dopamine Transporter Single Photon Emission Computed Tomography; (8) Arterial spin labeling; (9) Diffusion tensor imaging

VacSYn study design

double blind placebo-controlled Phase 2 study overview (NCT06015841)

Key Inclusion Criteria

- Aged ≥40 to ≤75 years
- Diagnosis of clinically established early PD (confirmed by DaT-SPECT)
- ≤ 2 years from time of onset motor symptoms
- H&Y Stage I to II
- Monotherapy treatment with L-Dopa at 300 mg per day or treatment naïve

Key Exclusion Criteria

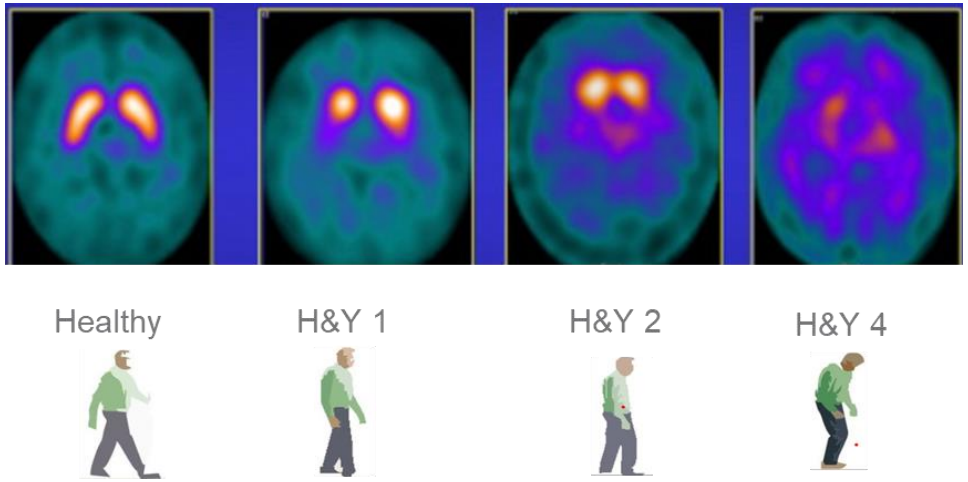
- carriers of certain familial PD gene mutations
- Parkinsonian syndrome other than idiopathic PD
- Significant CNS disease

- Enrolment status: 26 patient from sites in Spain (14), Germany (2) and UK (10)

Baseline characteristics of VacSYn trial

Variable	Unit	Total
Total number of patients	n	26
Age (years) (mean (std)	mean (std)	62.2 (7.34)
Sex		
Male	n (%)	16 (61.5%)
Female	n (%)	10 (38.5%)
Hoehn and Yahr stage		
Stage I	n (%)	8 (30.7%)
Stage II	n (%)	18 (69.23%)
MDS-UPDRS scores		
Part 1: Non-motor experiences of daily living	mean (std)	4.00 (2.859)
Part 2: Non-motor experiences of daily living	mean (std)	4.52 (3.084)
Part 3: Motor examination	mean (std)	23.00 (10.253)
PD Treatment		
treatment-naïve	n (%)	9 (34.62%)
on L-Dopa 300mg/day	n (%)	17 (65.38%)
Dat-SCAN type:		
Type 1	n (%)	9 (34.62%)
Type 2	n (%)	9 (34.62%)
Type 3	n (%)	8 (30.77%)

Dat-SCAN type vs Hoehn and Yahr stage



Adapted from A .Antonini, *et al.* 2004

For more details, please attend:

presentation by ***Nuno Mendonça*** *on* ***March 6th, 2024***

State-of-the-art of treatment and diagnosis of alpha-synuclein pathologies symposium

Blinded Treatment-Emergent Adverse Events (TEAE) Summary[1]

1. **No deaths**
2. **No other Serious TEAEs**
3. **No TEAEs Leading to Discontinuation from the Study**
4. **Most common TEAEs were Injection Site Reactions (e.g. redness, itching)**
5. **All TEAEs mild or moderate in severity**

Up to the present date, no significant risks, either known or anticipated, were associated with ACI-7104.056

(1) cut-off date 1 March 2024

Conclusions

- Phase 2 study in early PD subjects is based on an innovative two-part trial design
- The approach is designed for early de-risking and simultaneously to allow for fast acceleration and enables a rapid entry into a pivotal clinical phase.
- Targeting early PD population
- Good safety and tolerability profile with no safety concerns identified thus far
- Finishing randomization to Part 1 scheduled for March 2024

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