

#### INITIAL SCANS USING [ $^{18}$ F]ACI-12589, A NOVEL PET-TRACER FOR $\alpha$ -SYNUCLEIN

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### Disclosures

- Ruben Smith report no disclosures
- Francesca Capotosti, Tanja Touilloux, Valerie Hliva, Jerome Molette, Yannis Dimitrakopoulos, Andrea Pfeifer, Marie Kosco-Vilbois and Johannes Streffer are fulltime employees of AC Immune SA.
- Martin Schain is a full-time employee of Antaros Medical
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#### ACI-12589: a potential a-syn<sup>1</sup> PET<sup>2</sup> tracer

[3H]ACI-12589 specific binding on brain tissue from different a-synucleinopathy cases





- ACI-12589 displays a clear autoradiography signal which correlates with the presence of pathological a-syn
- Binding affinities are measured in the range of 8-30 nM with Bmax/Kd ratios of ~ 5-10

(1) alpha-synuclein ; (2) Positron emission tomography; (3) Parkinson's disease with G51D SNCA mutation; (4) Multiple system atrophy; (5) Immunohistochemistry



### Participant characteristics

25 participants with α-synuclein related disorders scanned

Dynamic 0-90 min scans with arterial blood sampling

	Control	PD	MSA	DLB
n	8	7	8	2
Sex (M/F)	5/3	6/1	3/5	2/0
Age (± SD)	63±11	67±7	62±8	81±1
Inj Dose (MBq)	314±39	311±60	297±15	289±1
UMSARS I + II	N/A	N/A	50±24	N/A
UPDRS-III	N/A	65±16	N/A	N/A

### Kinetic modelling – Plasma input and metabolism

• [<sup>18</sup>F]ACI-12589 shows a favorable metabolic stability with 60-80% of the parent compound remaining 90 min post injection.



# Kinetic modelling –Time Activity Curves



Cerebell\_ped = Cerebellar peduncles; MSA = Multiple system atrophy; SUV = Standardized Uptake Value Ratio; TAC – Time activity curve

### Kinetic modelling – Logan / MA1 analysis

- Logan graphical analysis and Ichise multilinear analysis (MA1) performs well.
- High agreement of  $V_T$  values between these methods



Logan plot and MA1 both provide good fits for the kinetic [<sup>18</sup>F]ACI-12589 data

### Kinetic modelling - reference regions

- No difference in cerebellar grey matter or occipital cortex  $V_T$ s between diagnostic groups
- High correlation between data derived using cerebellar grey matter and occipital cortex reference regions



Both cerebellar cortex and occipital cortex suitable reference regions

#### Kinetic modelling - SUVR

• Strong correlations between SUVR values and Logan ref  $BP_{ND}s$  (and MA1  $BP_{ND}s$ ). Data more noisy in the 30-50 min interval





### Cerebellar white matter [<sup>18</sup>F]ACI-12589 retention



BPnd = Binding Potential, non-displaceable; Ctrl = Control; DLB = Dementia with Lewy Bodies; MA1 = Ichise multilinear analysis; MSA-C = Multiple system atrophy – cerebellar phenotype; MSA-P = Multiple system atrophy – parkinsonian phenotype; PD = Parkinson's Disease; SUVR = Standardized Uptake Value Ratio



### Globus pallidus [18F]ACI-12589 retention



High retention in globus pallidus in MSA-P patients but also in one control.

BPnd = Binding Potential, non-displaceable; Ctrl = Control; DLB = Dementia with Lewy Bodies; MA1 = Ichise multilinear analysis; MSA-C = Multiple system atrophy – cerebellar phenotype; MSA-P = Multiple system atrophy – parkinsonian phenotype; PD = Parkinson's Disease; SUVR = Standardized Uptake Value Ratio

# Pre/post Selegiline



MA1 = Ichise multilinear analysis; SUVR = Standardized Uptake Value Ratio; VT = Total volume of distribution

### Conclusions

- [<sup>18</sup>F]ACI-12589 shows a rapid brain uptake and fast signal equilibrium.
- SUVR can be used with occipital or cerebellar grey reference region.
- No relevant binding to MAO-B in cerebellar white matter
- Strong binding in expected regions in MSA
- Completely separates MSA from other synucleinopathies and controls
- [<sup>18</sup>F]ACI12589 is a promising radiotracer for supporting a diagnosis of MSA and  $\alpha$ -synuclein drug target engagement
- Further studies needed in Parkinson's Disease

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