

CRST – Excellence in proving your concept



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Clinical Research Services Turku CRST – partnering with Turku PET Centre

- ✓ University-based CRO that conducts clinical, preclinical and bioanalytical studies for the pharmaceutical industry and for other customers
- ✓ Experienced in demanding phase 0-2 clinical trials and proof-of-concept studies
- ✓ Employing Positron Emission Tomography (PET) to assess efficacy and pharmacokinetics

CRST

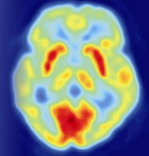
Scientific and regulatory consultancy
Medical writing, regulatory submissions
Subject recruitment
Investigators, study nurses and clinical wards with 24/7 safety monitoring
In-house bioanalytical laboratory for analysis of PK and biomarker samples
Clinical study monitoring
Project management

Turku PET Centre

State-of-the-art PET imaging facilities
MRI, CT and ultrasound imaging
PET radiochemistry expertise with cyclotrons and GMP radiopharmaceutical laboratories
Extensive track record in pharma trials from preclinical to clinical

www.pet.fi

Focus on PET and CNS disorders



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Valuable information for the advancement of CNS drug development programs

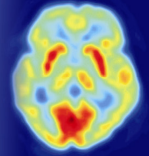
Unique benefits

- Detection of early signs of efficacy
- Confirmation of mode-of-action
- Dose guidance for Phase II/III studies
- Improved patient selection and stratification
- Monitoring of the time extent and course of drug binding

Useful applications

- Visualization and quantitation of CNS disease-specific biological targets and events
- Receptor/transporter occupancy after single or multiple doses of a test drug
- A broad range of disease and target-specific tracers in Turku PET Centre

Focus on PET and CNS disorders



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Applications for the clinical testing of Alzheimer's disease drugs

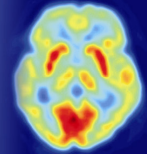
Several PET tracers are available for visualization and quantitation of

- beta-amyloid deposits
- glial inflammation markers in the brain
- cholinergic neurotransmission

Imaging approaches for treatments with other primary mechanisms of action

- Imaging of brain glucose consumption is possible with ^{18}F -FDG
- Changes in many neurotransmitter and receptor systems may be investigated with the broad range of PET tracers available in Turku

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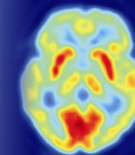


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Commonly used tracers for neurotransmitter receptors, transporters and enzymes

Target system	Tracer	Mechanism and target
Opioid system	¹¹ C-Carfentanil	μ-opioid receptor agonist
Neurokinin system	¹⁸ F-SPA-RQ	Neurokinin 1 (NK ₁) receptor antagonist
Monoamine oxidase B (MAO-B)	¹¹ C-Deprenyl	MAO-B ligand
GABAergic system	¹¹ C-Flumazenil	GABA _A -receptor antagonist
Cholinergic system	¹¹ C-Nicotine	Nicotinic receptor agonist
	¹¹ C-MP4A	Acetylcholinesterase (AChE) analog (for AChE activity studies)
	¹¹ C-MP4B	Butyrylcholinesterase (BChE) analog (for BChE activity studies)
Serotonergic system	¹¹ C-MADAM	Serotonin transporter (SERT) ligand
	¹¹ C-WAY100635	5-HT _{1A} receptor antagonist
Adenosine system	¹¹ C-TMSX	Adenosine A _{2A} receptor antagonist
Dopaminergic system	¹⁸ F-DOPA	Dopamine precursor (dopamine synthesis and storage)
	¹¹ C-Raclopride	D ₂ /D ₃ receptor antagonist (for striatal receptors)
	¹¹ C-FLB457	D ₂ /D ₃ receptor antagonist (for extrastriatal/cortical receptors)
	¹¹ C-SCH22390	D ₁ /D ₅ receptor antagonist (striatal and extrastriatal receptors)
	¹¹ C-PE2I	Dopamine transporter (DAT) ligand

Focus on PET and CNS disorders



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Success stories of the utilization of PET imaging in CNS drug development

- Occupancy study of antidepressant target in the brain of healthy volunteers – provided important guidance for dose level selection in Phase II trials and helped to reach a no-go decision before Phase III
Bergström M et al., Biol Psychiatry 2004, 55:1007-12
Link to MEDLINE: <http://www.ncbi.nlm.nih.gov/pubmed/15121485>
- Occupancy study of therapeutic target in the brain of Alzheimer's patients and healthy control subjects – provided important information for Phase II dose selection
Hirvonen J et al., Clin Pharmacol Ther 2009, 85:506-12
Link to MEDLINE: <http://www.ncbi.nlm.nih.gov/pubmed/19129751>
- Amyloid imaging study to assess efficacy of anti-amyloid therapy in Alzheimer's disease – suggested that the treatment has anti-amyloid efficacy and that ^{11}C -PiB PET imaging is useful in assessing the effects of potential anti-amyloid treatments in Alzheimer's disease
Rinne JO et al., Lancet Neurol 2010, 9:363-72
Link to MEDLINE: <http://www.ncbi.nlm.nih.gov/pubmed/20189881>