CASE STUDY

Unlocking CNS insights: Continuous CSF sampling in first-in-human Alzheimer's trials

A KEY QUESTION

How can specialized early-phase capabilities unlock CNS insights that conventional sampling cannot?

KEYWORDS Clinical Trials, Early Phase Development, CNS Biomarkers, CSF Sampling, Alzheimer's Disease

Introduction

This case study highlights how Fortrea enabled continuous cerebrospinal fluid (CSF) sampling in a first-in-human (FIH) Alzheimer's study—an approach that allowed the sponsor to capture dynamic CNS biomarker movement and significantly enhance decision-making.

Challenges

- **CNS signal needed early:** The sponsor required early biomarker readouts—Aβ, tau and PK/PD—in CSF, to assess CNS penetration and mechanism alignment
- **Invasive procedure risk:** Lumbar puncture is a specialist, invasive procedure requiring meticulous attention to safety, discomfort minimization and controlled execution
- **Operational complexity:** The protocol required continuous CSF sampling via an indwelling lumbar catheter, enabling extended collection windows (up to ~30 hours)
- **Phase I feasibility:** The sponsor needed tight integration within an early-phase clinical environment without dependency on external hospital infrastructure

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Actions

1 In-house procedural delivery

Fortrea deployed skilled clinical medics within its FIH clinics to conduct lumbar punctures, helping to maintain:

- Standardized technique
- Controlled post-tap monitoring
- Strong focus on participant comfort and tolerability

2 Enabling continuous CSF sampling

Fortrea operationalized workflows for both:

- Indwelling catheter–based continuous CSF collection (for extended time-course biomarker analysis)
- Single timepoint taps (as needed by the protocol)

3 Co-designing a fit-for-purpose sampling schema

Fortrea teamed up with the sponsor to design a sampling schedule aligned to:

- Mechanism of action
- Biomarker kinetics
- CNS PK/PD time-course

4 Integrated early-phase operations

CSF collection, processing and chain-of-custody were embedded in existing Phase I operations, reducing handoffs and minimizing risk of sample variability.

Results

- **Decision-grade data:** Continuous CSF sampling provided time-course insights impossible with single-point collection—enhancing understanding of CNS biomarker movement and exposure
- **Reduced variability:** Dynamic sampling decreased between-timepoint noise, strengthening PK/PD modeling inputs
- **Positive participant experience:** In-house medics, consistent technique and comfort-focused protocols delivered strong tolerability despite the invasive nature of the procedure
- **Streamlined execution:** Delivering continuous CSF sampling within Fortrea's own CRU infrastructure simplified operations and maintained early-phase efficiency

Lessons learned

- **Align early on CSF strategy:** Continuous vs. single-point sampling should be decided up front and embedded into protocol design, staffing and model expectations
- **In-house personnel are essential:** Skilled medics and standardized tools reduce risk around safety, timing and sample integrity
- **Participant-centric design pays off:** Proactive comfort measures and clear participant communication improve acceptance and compliance
- **Continuous CSF sampling is one of our key early-phase capabilities:** Extended CSF collection can unlock CNS insights that meaningfully accelerate Phase I evidence generation

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