Study Protocol 1.0

Title: Fibroblast Activation Protein-Targeted PET/CT Imaging for Quantifying Glandular Inflammation in Primary Sjögren's Syndrome: A Prospective Cohort Study

NCT Number: Not available for now

Document Date: July 1, 2025

1. Background

Primary Sjögren's syndrome (pSS) is an autoimmune disorder characterized by lymphocytic infiltration and dysfunction of exocrine glands. Current diagnostic tools (serology, histopathology, conventional imaging) lack sensitivity for early inflammation detection. Fibroblast activation protein (FAP) on inflammation-associated fibroblasts is a promising biomarker. Preliminary evidence suggests \[^{68}Ga\]Ga-FAPI-04 PET/CT may quantify fibroblast-driven inflammation in pSS.

2. Objectives

- Primary: Evaluate salivary gland \[^{68}Ga\]Ga-FAPI-04 uptake in pSS versus controls.
- Secondary:
  - Correlate FAPI uptake with clinical indices (ESSDAI/ESSPRI), serological markers (IgG/RF/ESR), and SGUS scores.
  - Assess FAP expression via immunohistochemistry (IHC) in labial salivary glands.
  - Monitor treatment response via longitudinal FAPI-PET.

3. Study Design

- Type: Prospective cohort study.
- Duration: October 2023–March 2025.
- Setting: Peking Union Medical College Hospital (PUMCH).

4. Participants

- Inclusion Criteria (pSS):
  - Age 18–80 years.
  - Meets 2016 ACR-EULAR pSS criteria.
- Exclusion Criteria:
  - Secondary Sjögren's syndrome.
  - Pregnancy/lactation.
- Controls: Age-/sex-matched; no sicca symptoms/autoantibodies.
- Sample Size: 70 participants (35 pSS, 35 controls).

5. Interventions/Methods

- Clinical Assessment:

  - ESSDAI/ESSPRI, serology (ANA/RF/anti-SSA/SSB/IgG/ESR), SGUS (4-grade scoring).

- PET/CT Protocol:

  - Tracer: \[^{68}Ga\]Ga-FAPI-04 (1.85–2.22 MBq/kg).

  - Imaging: Whole-body PET/CT 40–60 min post-injection.

  - Analysis: SUVmax, SUVmean, T/B ratio (MIM software).

- IHC: FAP staining (H-score) in labial salivary gland biopsies (subset).

- Follow-up: Repeat PET/CT post-treatment (5–15 months).

6. Statistical Analysis

- Primary Comparison: FAPI uptake (SUVmax/T/B) in pSS vs. controls (independent t-test/Mann-Whitney U).

- Correlations: Spearman’s rank (FAPI vs. clinical/serological/SGUS scores).

- Diagnostic Performance: ROC analysis (AUC for parotid/lacrimal glands).

- Software: SPSS v26.0, GraphPad Prism v9.0.

7. Ethics

- Approved by PUMCH IRB (No. ZS-2531).

- Written informed consent obtained.

Statistical Analysis Plan (SAP) 1.0

Title: Statistical Analysis Plan for FAPI-PET in Primary Sjögren's Syndrome

NCT Number: Not available for now

Document Date: July 1, 2025

1. Primary Analysis

- Objective: Compare FAPI uptake (SUVmax, T/B ratio) in pSS vs. controls.
- Method:
  - Independent t-test (normal data) or Mann-Whitney U (non-normal).
  - Outcome: $p < 0.05$ (two-tailed).

2. Secondary Analyses

- Correlations:
  - Spearman's rank coefficient (r) between:
    - Parotid SUVmax vs. ESSDAI/ESSPRI/IgG/RF/SGUS.
    - Lacrimal SUVmax vs. age/complement levels.
  - Threshold: $r > 0.3$ (medium effect), $p < 0.05$.
- Subgroup Comparisons (pSS only):
  - Extra-glandular involvement: Lacrimal/parotid SUVmax (Mann-Whitney U).
  - Parotid enlargement: SUVmax (t-test).
- ROC Analysis:
  - AUC for parotid/lacrimal glands (diagnostic accuracy for pSS).

3. Longitudinal Analysis (Follow-up)

- Method: Paired t-test/Wilcoxon signed-rank for:
  - ΔSUVmax/ΔT/B vs. ΔESSDAI/ΔESSPRI post-treatment.
- Subgroups: GC-treated vs. non-GC-treated.

4. IHC Correlation

- Spearman's r: H-score vs. SUVmax/SUVmean.

5. Software & Reporting

- Tools: SPSS v26.0 (descriptive/inferential), GraphPad Prism v9.0 (graphs).
- Data Presentation: Mean ± SD (continuous), frequencies (categorical).

Informed Consent Form (ICF) 1.0

Title: Informed Consent Form for FAPI-PET Study in Sjögren's Syndrome

NCT Number: Not available for now

Document Date: July 1, 2025

1. Study Purpose

We invite you to participate in a research study evaluating a new PET/CT scan (\[^{68}Ga\]Ga-FAPI-04) to measure gland inflammation in Primary Sjögren's syndrome (pSS).

2. Procedures

- Clinical Assessments: Questionnaires (ESSDAI/ESSPRI), blood tests (ANA/RF/IgG), salivary gland ultrasound.
- PET/CT Scan: Injection of a radioactive tracer (\[^{68}Ga\]Ga-FAPI-04) followed by a 60-min scan.
- Optional Biopsy: Labial salivary gland biopsy (if clinically indicated).
- Follow-up: Repeat PET/CT after 5–15 months (if receiving treatment).

3. Risks/Benefits

- Risks:
  - Radiation exposure (PET/CT; equivalent to 3 years of natural background radiation).
  - Discomfort during blood draw/biopsy.
- Benefits:
  - No direct therapeutic benefit.
  - May improve future pSS diagnosis/monitoring.

4. Confidentiality

Your data will be anonymized (assigned a study ID). Records stored securely at PUMCH; only the research team accesses identifiable information.

5. Voluntary Participation

You may withdraw anytime without affecting your clinical care. Refusal incurs no penalty.

6. Contact Information

- Principal Investigator: [Name/Contact]

- Ethics Committee: PUMCH IRB (+86-10-6915xxxx).

Consent Statement

I confirm I have read this form, understand the study, and voluntarily agree to participate.

Participant Signature: _____ Date: _____

Investigator Signature: _____ Date: _____