Case Study

Sjögren Syndrome

A single-centre study with salivary gland biopsies and complex biomarkers in 27 Sjögren patients enrolled within 10 months in CRO's Phase I Unit in Berlin

Introduction

In 2012, a major sponsor approached us with a Phase IIa, single dose, double-blind, placebo-controlled, parallel group study designed to assess the PD, PK and safety and tolerability of a monoclonal antibody in patients with primary Sjögren syndrome. We immediately recognized this as an ideal opportunity to utilise and showcase our single-centre approach and the benefits of harnessing our centres of excellence environment.

Challenges

This particular study required the enrolment of n=27 pSS patients meeting the revised European US consensus criteria. The patients required a EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) ≥6, residual salivary flow and seropositivity for either anti-SSA ± anti-SSB antibodies, or ANA ≥1:160 with rheumatoid factor. Conventional industry thinking would have likely assumed this study required a multi-centre set-up, with perhaps up to 15 sites needed to cope with recruitment as the perceived rate-limiting step. The study was also challenging from an operational perspective, with requirements that included complex clinical assessments and biomarker sampling. For example, primary and secondary clinical outcomes included EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI), EULAR Sjögren's Syndrome Patient Response Index (ESSPRI), Multidimensional Fatigue Index (MFI) and stimulated as well as non-stimulated salivary flow, ocular staining with lissamine green and high resolution contrast ultrasound parotid gland imaging with elastography. In short, this study demanded a combination of clinical expertise, operational excellence and very effective recruitment for us to conduct it successfully in a single-centre environment.

Solution

In terms of clinical expertise, we could build on long established experience in the field of autoimmune diseases. We involved Prof. Dr. Thomas Dörner, a renowned KOL from the Charité Division of Rheumatology and Clinical Immunology, to provide consultancy on study design, inclusion and exclusion criteria as well as endpoint review. He also acted as PI for the study and he supported our own clinical team with the required labial salivary gland biopsies. Biopsy analysis was performed at a specialist site for pathology and neuropathology in Berlin. For high resolution ultrasounds and ophthalmologic assessments, we worked closely with experts from the Charité radiology and ophthalmology departments. ß2-microglobulin analysis in serum and saliva – among other lab assessments – were performed by Dr. Robert Sabat, Charité expert for molecular immunopathology. All these experts and specialist partners were subcontracted by CRO and integrated seamlessly into the trial conduct. All the sponsor had to do was sign one contract with CRO and stay in touch with our assigned project manager as the single point of contact for the entire study.

In terms of recruitment, we used an innovative approach to meet study enrolment targets. First of all, it is important to note that referrals do not work as well as many people like to think - at least not to the extent needed to facilitate recruitment of a study in n=27 Sjögren patients using a single-centre approach. We primarily relied on our tried and tested direct-to-patient marketing approach. Firstly, we placed online advertisements to reach out to patients in the wider Berlin area. We also employed a logistically challenging "German-wide" marketing approach to recruit patients from other parts of the country – bringing them backwards and forwards to participate in the study in our Berlin unit. →

Charité Research Organisation GmbH
Charitéplatz 1 | 10117 Berlin

Telefon +49 30 450 539 211
Telefax +49 30 450 539 900

enquiries@charite-research.org
www.charité-research.org

Case Study

Sjögren Syndrome

Study Population

Sjögren's Disease

Area
Autoimmune diseases

Approach
n=27 patients in a single-centre setting

Challenges
- ✓ Complex biomarkers
- ✓ Labial salivary gland biopsies
- ✓ HR ultrasound parotid gland imaging

Enrolment Rates
2-3 patients per month

Recruitment Strategy
Direct-to-patient marketing and existing database

Duration of Participation
- ✓ 4 weeks SCR
- ✓ 24 weeks treatment + FUP
- ✓ Long-term FUP

Interviewed	Informed	Screened	Enrolled
101	80	55	27

Completion 27

Results

The study was successfully recruited using the single-centre approach, with enrolment rates of n=2-3 patients per month. This approach was essential to allow the complex clinical assessments and biomarkers to be meaningfully integrated into the trial. This ensured the most consistent treatment and assessment of all the patients, resulting in high data integrity. This in turn allowed the sponsor to take a more informed decision regarding next steps in the development process. Last but not least, running the study single-centre – instead of opening multiple sites – had huge benefits in terms of cost-effectiveness, data quality and timelines – in particular regarding study start-up.

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