TFS HealthScience
Clinical Research Excellence

Onychomycosis Rescue

Case study

General information

TFS was selected to rescue a phase 3 onychomycosis study from another CRO that was unable to meet the recruitment expectations of the client. TFS provided full CRO services for this study, which was a multi-centre, randomized, two-armed, parallel group and evaluator-blinded study of efficacy and safety of a topical treatment for mild to moderate distal subungual onychomycosis.

Results

Patients

3500 patients were screened to obtain 450 randomised patients

Study specific

Countries

50 sites across Europe (Germany, Poland and the UK) were selected

Challenges

- **Site transfer to TFS** was slower than anticipated due to protracted contractual negotiations
- Recruitment was halted during the transfer of sites from the previous CRO to TFS
- **Vendor contracts** needed to be renegotiated rather than just transferred to TFS
- **The protocol** was of a very challenging design that had been developed without Key Opinion Leader (KOL) input. This significantly affected the delivery of the study. In order for each patient to be enrolled in the study **three separate criteria** had to be met:
  - **Visual diagnosis conducted via a vendor:** a photograph of the nail was taken, sent to a blinded assessor KOL, who assessed suitability for inclusion on a pass/fail basis
  - **Laboratory diagnosis:** a sample of the nail was sent to a central mycology laboratory to test for fungal growth
  - **Microscopy:** to confirm presence of fungus
- Considering all three factors needed to be positive before a patient could be enrolled, there was a very **high screen failure rate**, 3500 patients screened to enroll only 450 patients. This affected the morale at sites and was a key factor in sites deciding not to continue with the study, as their contracts did not include payments for screening

13% enrolled patients (450 from 3500)

- The success of the study was also reliant on the **efficacy evaluations included in the protocol**. However, the fungal growth evaluations selected for this study by the client are inherently inaccurate, and are associated with a 30% false negative rate

30% false negative rate

- **Patient recruitment** was very challenging, despite this indication being very common, since it is an indication/condition often disregarded or overlooked by patients. Sites generally do not have databases of patients with this condition to draw on, and enrollment relies on taking appropriate steps to advertise the study and its benefits, and to engage patients. The client had engaged a recruitment vendor to assist with recruitment activities, and they focussed on leveraging social media to locate patients. Not one patient was enrolled as a result of the €200,000 investment in social media campaigns on Facebook, Google and other social media outlets

€200,000

investment in social media campaigns

Solutions and lessons learned

Transition

- In order to speed up the transition from the incumbent CRO to TFS client involvement is vital to facilitating the handover
- Leveraging relationships between the client and the sites significantly improves the transition process for the sites, as it improves motivation and provides continuity during the transition process
- When taking on established studies, it is important not to underestimate the amount of time required for the contracting processes with both sites and vendors. This needs to be factored into the study timelines agreed with the client, to ensure that expectations are realistic for this stage of the process
- TFS arranged for additional contracting support during the transition of the rescue studies, to minimise the length of time between award of project and the start of TFS' work with the sites, to avoid halted recruitment

Protocol design

TFS reviewed the protocol and reasons for the high screen failure rate, and recommended a simple protocol amendment which meant that based on mycology results the investigator was able to determine eligibility. This considerably improved the screen failure rate, and enrollment rate

TFS recommends that for similar studies a medic from our Dermatology Centre of Excellence is involved in the protocol development, since this team is expert in dermatology protocol design, the multiple diagnostic tools available, and the appropriate tools for use in validating efficacy and avoiding false negatives

Site motivation

- TFS encouraged the client to visit and engage with the sites. This additional visibility was well received by the sites, it enhanced site motivation and improved the sites' experience with the client and study
- The majority of site contracts did not include sufficient payment for screening activities, mainly payment for participation in the study once a patient had been enrolled. Sites were required to conduct extensive advertising and recruitment activities to gain interest from potential patients, and time spent for these activities were not reimbursed by the client. This significantly affected morale and motivation and led to sites deciding to withdraw from the study. One site contract did include payment for these activities, and that site performed very well, maintained its motivation

throughout the study, and the quality of the data was very good. For this type of study TFS highly recommends that clients recompense sites for the considerable work done prior to enrolling patients, as this will improve site experience, motivation and participation

Recruitment strategies

- Site motivation visits were conducted by TFS, during which recruitment strategies were discussed and agreed, and TFS supported the site during the development of appropriate solutions
- TFS worked with each site on an individual basis to develop appropriate recruitment strategies that were site and patient specific. Understanding the site and the regional differences and preferences was the most important feature in reaching the patient population. In general the best recruitment advantage was obtained from local radio and newspaper advertisements. The largest proportion of patients were female, mainly due to aesthetics and wearing of sandals
- Motivational bonus strategies were implemented within TFS, with a minimal cash bonus being awarded to CRAs that helped sites achieve recruitment. This had minimal impact on the CRA motivation and recruitment overall and is unlikely to benefit future studies

Client advantages

TFS has a very strong background in dermatology, and by working with the client at the protocol development stage TFS can provide protocol optimisation to avoid the issues encountered with this particular protocol. By working closely with this client and using the knowledge provided by our Dermatology Centre of Excellence team TFS was able to significantly reduce the screen failure rate by including a protocol amendment. This improved the enrollment rate and also improved site morale

Taking into account TFS experience the client was able to build strong relationships with the sites which benefitted the client in this study and will be invaluable for future studies

Why choose TFS for Dermatology studies

Track record of delivering more than 200 dermatology trials within the past five years — accelerated submission and recruitment processes due to very extensive dermatology experience and dermatology study teams

Network of global KOLs combined with a global network of 3500 Dermatology investigative sites with access to hundreds of thousands of patients

Advisory board meetings to define product development strategies

Dermatology specialized full operations team including project managers, physicians, start-up teams, CRAs, data managers and medical monitoring by certified dermatologists in pivotal trials

In-house Investigator site with full oversight of all important ongoing trials in dermatology

About TFS

TFS HealthScience is a global Contract Research Organization (CRO) that supports biotechnology and pharmaceutical companies throughout their entire clinical development journey. In **partnership** with customers, we build **solution-driven teams** working for a healthier future. Bringing together nearly 700 professionals, TFS delivers **tailored clinical research services** in more than 40 countries and supports customers with **comprehensive solutions** through three strong business models: Clinical Development Services (CDS), which provides full-service support at all stages of the clinical development process, Strategic Resourcing Solutions (SRS), which offers expert insourcing and targeted recruitment services, and Functional Services (FSP), to provide customers with strategic workforce management solutions.

Detailed information about TFS, and its business offerings can be obtained through **www.tfscro.com.**