

Case Study:

FROM COMPLEXITY TO CONSISTENCY: CENTRAL IMAGING IN DESMOID TUMOR CLINICAL DEVELOPMENT

BACKGROUND

A Phase III study in adult patients with progressing Desmoid Tumors/Aggressive Fibromatosis (DT/AF)

100+
PATIENTS

50+
SITES

7
COUNTRIES

CHALLENGES & SOLUTIONS

PRIMARY, SECONDARY, AND EXPLORATORY ENDPOINTS BASED ON CENTRAL IMAGING ASSESSMENTS

- **Challenge:** Study success was dependent on the data from the central imaging assessments, so there were high expectations for the MCL team due to increased responsibilities in terms of the amount of activities completed and expedited timelines. Due to the priority of the study, there was close oversight from both Sponsor and Medpace management to ensure data availability, quality, and integrity at each time point.
- **Solution:** Appropriate resources were allocated to the study team, and a customized process workflow was put in place. Sponsor had direct access to study reports and metrics, weekly study calls, and open communication.

UNPREDICTABLE CLINICAL COURSE AND HIGHLY COMPLEX MORPHOLOGY OF DT/AF

- **Challenge:** Because of their fluctuating tissue composition, lesion appearance on magnetic resonance imaging (MRI) or computed tomography (CT) scans can be amorphous, variable, and change over time. This heterogeneity makes it difficult for radiologists to accurately trace tumor boundaries or gauge treatment success using standard dimensional criteria like Response Evaluation Criteria in Solid Tumors (RECIST).
- **Solution:** Appropriate and consistent imaging protocol, experienced radiologist serving as central reviewers, 2+1 paradigm (2 primary reviewers and 1 adjudicator), and variability analysis on primary endpoint were conducted. Beyond RECIST 1.1, secondary and exploratory endpoints, tumor volume, and T2 hyperintensity were also measured as well as advanced imaging biomarkers.

TUMOR LESIONS FOR CENTRAL REVIEW DETERMINED BY SITE AT BASELINE

- **Challenge:** To ensure inclusion criterion was met, the target lesions followed during the trial (up to 5) were selected by the local radiologist, and not by the central reviewer. This modification differs from RECIST 1.1 criteria which relies on central readers to select target lesions for assessment. To ensure the site target lesion selection information was unequivocally transferred, and the central reviewer could correctly identify the lesions, MCL put a process in place to collect annotated images from sites with target lesions clearly identified. These annotated images were stored in the image management database with other imaging records.
- **Solution:** Information about the location of target tumor(s) on screening imaging and related screenshots was shared by the site with MCL and Central Reviewers to allow for proper assessment.

CENTRAL RADIOLOGICAL ASSESSMENT DETERMINING STUDY CONTINUATION

- **Challenge:** The central reviewer was blinded to clinical context of participant and could only make a radiological assessment based on images, so the output could differ from that of an on-site radiologist with broader view and visibility to treatment efficacy (other than radiological ones) on patient status. Central review determined study endpoints, but local review and investigators determined patient treatment. This led to occasional discordance between site and central image assessments during the course of the trial.
- **Solution:** Progression report was sent to site according to the central assessment of each scan and mediation service was put in place to have an in-house radiologist to review discordant cases with the site radiologists when requested (later, Task Order amendment to include clinical progression).

RESULTS



Primary, secondary, and exploratory imaging related endpoints met



Database lock successfully completed on time and final data transfer timelines met



1400+ scans QCed, 2500+ central reads for primary endpoints, 500+ central reads for secondary/exploratory endpoints, 25+ data transfers



FDA approval

MCL-0018-1026

MAKING THE COMPLEX
SEAMLESS

