For many years we have not had a clear understanding of the underlying mechanism of immune mediated inflammatory diseases (IMID). Because of significant and continuing research and ongoing clinical trials on the pathology and genetic links involving IMIDs, we have now discovered that the underpinning of all of these diseases is inflammation involving the immune system. These discoveries have led us to a more comprehensive understanding of immune mediated mechanisms.

Immune mediated inflammatory diseases encompass a wide range of immune-inflammatory disorders. They include rheumatology, multiple sclerosis, dermatology (which has an inflammatory backyard), psoriasis, autoimmune conditions, inflammatory bowel diseases, COPD, fibrosis and asthma to mention just a few. Immunosuppression within transplantation and other minor therapies and pathologies, like some ultra rare diseases, also can be included.

Trial Challenges for Immune Mediated Inflammatory Diseases

There are some unique challenges CROs confront when conducting IMID clinical trials.

Research naïve locations. Because of the complexity and regulatory issues surrounding the conducting of clinical trials on immune mediated inflammatory diseases, there has been a move to set up clinical trial sites in more non-traditional countries. While these countries can present real opportunities in the relative treatment of native patients, they typically tend to be more research naïve. This can pose problems both in research methodologies and having adequate staff development, expertise and training. More control and monitoring by experts are needed at these sites. In addition, research staff needs to be fully conversant with all rating scales being utilized, and the kinds of pathology and drugs being managed, in the clinical trial. Without these strict guidelines, patients can't be monitored in an efficient way.

For instance, in a rheumatology study, each investigator will use a subset of joints to assess joint function, whereas in a clinical trial, investigators will use a specific and prescribed set of joints with each patient. In trials for IMIDs, clinical practices sometimes diverge from the clinical trials in primary rating scores. This can result in overlaying sets of assessments that provide investigators with contradictory results that need to be resolved at the time.

Standardized protocols. Sometimes protocols are not applicable in the real world because investigators were not following what was happening during the trial. So attention needs to be paid in adopting protocols that will allow investigators to follow true disease processes going on in the real world.

Lack of full drug utilization. A further challenge in conducting IMID clinical trials is the evidence we are seeing of some investigators, particularly in Eastern European countries, seeming to jump from traditional treatments directly to the next group of research agents without allowing patients to exhaust all their treatment options. On one level this is understandable. With the advent of so many new drug therapies, treatment options are more plentiful. But these drugs can have slightly different mechanisms, which can be difficult to translate into clinical efficacy or safety.

Additional Obstacles in Locating and Registering Patients

The registration of the correct kinds and numbers of patients for each clinical trial also pose problems for CROs, especially for immune mediated inflammatory diseases. It can be difficult for these sites to reach the number of patients needed for any given trial. In fact, finding sufficient numbers of patients who are motivated to take part in clinical trials is one of the biggest challenges we face in IMID research.

Within this research space there are some very complex and demanding sets of clinical studies. It takes a significant amount of commitment, not just on behalf of the doctors and study staff, but also on patients to conduct these trials properly. The number of assessments at a particular visit can be fairly onerous. Additionally, there is data and medication compliance that must be tracked.

So we ask a lot of patients who participate in clinical trials, particularly the impact it can have on their work and family lives. Given this set of factors, participants in IMID trials tend to be semi or fully retired. They go from trial to trial because they have time and are looking to refine their therapy.

Additionally, because of the level of research and development within IMID, and the need for a significant commitment to the trials, the supply of patients and resources can be quickly exhausted. As medication costs have risen, and healthcare systems in the west catch up, CROs are moving clinical trials increasingly eastward. While the move to non-traditional countries does present us with unique opportunities in studying native patients, there also are patients further down the treatment pathway that we may not necessarily be able to provide for in these countries.

Perhaps most significant of all, investigators conducting a clinical trial in the past gave a drug regime until the patient failed. Investigators made three or four attempts to find a suitable treatment for a patient. If they failed after these attempts, it was assumed that the treatment failed. As we have moved eastward, patients are going from traditional agents to modifying agents, and investigators are going from first failure directly into a research study, which is good for clinical trials, but not necessarily for the patient.

A New Revolution in Biologics

Despite some of these challenges in IMID trials, a new series of biologic therapies have revolutionized treatment of immune mediated inflammatory diseases. In addition to new drug combinations, there has been a progressive move toward more convenience and better forms of dosing, in terms of self- administration. Auto injectors are moving from infusion to subcutaneous injection, which allows patients more accuracy, but they are expensive.

However, the people who are developing these biologic drugs were surprised by some of the regulatory requirements that were put in place. They thought they would be able to slim down clinical drug programs, which looked at similarity. But the scope and intensity of these clinical drug programs are as complicated and sophisticated as the innovative product itself.

Until now, using a new biologic meant showing the drug was somewhat better within a certain efficacy; it had to be better than placebo. Now drug developers have to show that the clinical benefit is better than current therapies and present biologics. And they have to demonstrate that the safety of the drug is more improved. All of this is difficult, so we are raising the bar for new biologics.

The Need for Qualified Investigators and CROs

Because there is great interest in the field of IMID research, interest in the area is not going to die down. With the continued importance of the area, there will be ongoing research advances. More innovative agents will be tested and more biosimilars and additional formulations of existing treatments will be discovered.

These factors are driving a population of investigators who have traditionally participated in immune mediated inflammatory disease trials, and their level of activity has increased in terms of additional sites and countries that have research interests.

All of this underscores the importance of engaging not just today's, but tomorrow's and the day after's, investigators. It's the up-and-coming investigators, and the ones with the authoritative names in the future, which we need to work with to ensure that we have the bandwidth for future drug development.

Most companies who want to bring the next wave of biologic agents through just don't have enough qualified investigators on the ground, so these organizations are totally reliant on CROs to deliver their projects. As we know, CROs are absolutely integral to the IMID clinical trial process. Regulatory start-up processes, clinical management and project management are required for a broad range of countries where many mainstream pharmaceutical companies are conducting trials. And CROs have the familiarity and expertise to deliver on the ground.

The challenge for many smaller organizations is that they don't have the footprint, let alone the expertise in particular therapeutic areas, to run complex IMID studies. They can certainly work with freelancers and other agencies, but when it comes to getting the consistency of evaluation, minimizing placebo care and improving rating scales, CROs with a larger footprint and in-depth expertise and experience are needed.

Larger CROs also offer experience in the exposure of different drugs and patient populations, as well as advancing more insight to investigators. Because larger CROs are working with sites around the world on an ongoing basis, they provide valuable feedback on how best to improve the design of studies, as well as underscoring emerging trends. That regular feedback results in better feedback to study investigators and participants, which leads to better clinical trial outcomes.

Given all these elements, it's important that CROs continue to work with clinicians and research naïve sites to become more research savvy. And we need to help investigators fully utilize traditional treatments to their full capacity in order to dissuade them from approaching treatment in a shotgun manner. We also need to target patient populations and offer treatment in a holistic and measurable methodology that will further positive outcomes for both the patient and the trial.