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RHEUMATOLOGY TRIALS: STRATEGIES FOR SUCCESS IN THE AGE OF SMALL MOLECULES, BIOLOGICS, AND CELL AND GENE THERAPIES

Globally, autoimmune diseases affect up to 10% of people, and these conditions often lead to chronic tissue damage and organ dysfunction, and the burdens can include reduced quality of life, disability, and shortened lifespan. Rheumatologic diseases such as rheumatoid arthritis, systemic lupus erythematosus (SLE), Sjögren's syndrome, scleroderma, and inflammatory myopathies represent a significant share of these conditions.

Rheumatology clinical trials face distinct challenges, including complex study designs, competitive patient recruitment landscapes, and evolving regulatory requirements. These trials must also navigate the intricacies of advanced therapies such as cell and gene therapies (CGTs).

Reflecting on these complexities, Dr. Andrew Head, MD, Medical Director at Medpace, noted, "Many people are impacted by rheumatic diseases, there are relatively few approved treatments, and there's a large unmet need for more effective treatments."

In a recent webinar, Dr. Head and his colleagues at Medpace — Dr. Jeffrey Vassallo, PhD, Senior Director of Clinical Trial Management; Jackie Widmer, Director of Clinical Trial Management; and Miaesha Campbell, Executive Director of Patient Recruitment — shared insights and practical strategies to drive success in rheumatology trials.

Their discussion highlighted how cross-functional collaboration, proactive operational planning, and patient-centered engagement can help accelerate development and improve outcomes in these complex studies.

Read on to discover how these strategies are advancing rheumatology trials in the era of biologics, small molecules, and CGTs.

AUTOIMMUNE AND RHEUMATOLOGIC DISEASES: A GROWING BURDEN

Autoimmune and rheumatologic diseases affect millions of people worldwide, contributing to significant disability, reduced quality of life and, in many cases, increased mortality.

These conditions are often chronic, progressive, and challenging to manage, with a disproportionate impact on women and minority populations.

> ***"Autoimmune diseases are the second leading cause of chronic illness in the US. And as a category, they are the leading cause of morbidity in women."***
>
> — Dr. Andrew Head

The prevalence of these diseases continues to rise, driven by a combination of genetic, environmental, and diagnostic factors.

The economic burden is also substantial, with annual treatment costs for autoimmune diseases in the US estimated to exceed $100 billion.

Despite advancements in understanding disease mechanisms, many patients do not achieve sustained remission with current therapies. This underscores the urgent need for innovative treatments and precision medicine approaches that can better address the complexity and heterogeneity of these conditions.

UNMET NEEDS: THE LIMITATIONS OF TRADITIONAL THERAPIES

Despite decades of progress in the management of rheumatologic diseases, many patients still face substantial challenges in achieving sustained disease control.

Traditional treatments, such as conventional disease-modifying antirheumatic drugs (DMARDs), often act by broadly suppressing the immune system. While this can help reduce inflammation, it frequently leads to off-target effects, including an elevated risk of infections and other complications linked to generalized immunosuppression.

Many patients cycle through therapies in a frustrating trial-and-error process, enduring prolonged periods of uncontrolled disease and accumulating irreversible joint or organ damage.

Moreover, the response to these therapies is highly variable.

As Dr. Andrew Head noted, "For a couple of examples in rheumatology, patient surveys suggest about 75% of rheumatoid arthritis patients are not satisfied with treatments. In SLE, those in remission or low disease activity after starting on treatment, we see that a majority of these patients may not maintain the remission or low activity so there remains an unmet need for more effective and durable treatments."

THE PROMISE OF INNOVATIVE THERAPIES

Recent advances in scientific understanding and therapeutic development are transforming rheumatology trials, offering new hope for patients with autoimmune and rheumatologic diseases. The range of investigational therapies—spanning small molecules, biologics, and CGTs—reflects the effort to address long-standing unmet needs with targeted, durable treatments.

A recent analysis of active industry-sponsored trials as of May 2025 highlights this global effort, with over 400 trials recruiting for autoimmune indications across these therapeutic categories.

Small Molecules

Small molecules have long played a role in the management of autoimmune diseases, but next-generation agents are designed for greater precision. These drugs pass through cell membranes to disrupt intracellular pathways that produce inflammation.

Their key advantages include oral dosing convenience and reduced immunogenicity compared to larger molecules. However, they may be less targeted, with increased potential for drug-drug interactions.

As of May 2025, approximately 100 small-molecule trials for autoimmune diseases are actively recruiting.

Biologics

Biologics target extracellular components, such as cytokines and receptors, and have been in clinical use for over two decades in rheumatology. Ongoing innovations include novel combination antibody therapies and bispecific antibodies, which are designed to bind to two distinct antigens.

Biologics are highly targeted and generally have fewer drug-drug interactions, but challenges include parenteral administration (which may deter some patients), potential immunogenicity, storage, and stability requirements.

Today, approximately 160 biologic trials for intravenous (IV) or subcutaneous (SC) delivery in autoimmune indications are underway.

Cell and Gene Therapies (CGTs)

Building on advances from oncology treatment, CGTs modify patient or donor immune cells to correct abnormal immune responses in autoimmune diseases.

These therapies offer the exciting potential for prolonged, drug-free remission, as seen in oncology data. However, CGTs bring substantial complexity in manufacturing and administration, limited long-term safety data in autoimmune diseases, a smaller pool of eligible patients, patient hesitancy, and the need for more specialized sites which add further challenges.

Despite this, the field is advancing, with about 150 CGT trials for autoimmune diseases actively recruiting.

MATCHING THERAPIES TO PATIENT PROFILES AND ADVANCING PRECISION MEDICINE

Importantly, as Dr. Head emphasized in the webinar, these therapeutic approaches can each fit a different patient profile and disease severity:

- **Small-Molecule Trials:** These trials may suit patients with moderate disease activity who are on standard-of-care therapies (such as glucocorticoids) but still require additional control. These patients may prefer oral medications and may be reluctant to move to injectable therapies.
- **Biologic Trials:** Trials of biologic drugs often enroll patients with moderate to severe disease who have failed multiple standard treatments or biologics. These patients may already be familiar with injection or infusion therapies and are seeking more effective options without the burden of high-dose glucocorticoids.
- **CGT Trials:** CGT trials target patients with severe, refractory disease who have failed multiple standard and biologic therapies. These patients, often facing organ damage or reduced quality of life, may be motivated by the potential for a drug-free remission, provided they receive thorough education on the risks, requirements, and long-term follow-up involved.

From both the investigator's and patient's perspective, these categories can coexist within the same site, enabling the optimization of enrollment without direct competition.

For instance, investigators can leverage existing relationships, knowledge of patient clinical status, and site expertise to match the right patients with the most suitable trials, thereby advancing innovative therapies while addressing individual patient needs.

Beyond these modalities, biomarker discovery and precision medicine are driving the field forward. By identifying molecular signatures or immune pathways specific to each patient, researchers can improve stratification and treatment matching. This approach can also reduce unnecessary exposure to ineffective therapies and support more efficient trial designs.

Basket trials in which a therapy targets a shared mechanism across multiple autoimmune diseases are streamlining the development process, improving access, and accelerating the delivery of new treatments to patients.

Together, these innovations mark a shift in rheumatology trials, offering therapies that are more precise, durable, and tailored to each patient.

OPERATIONAL STRATEGIES FOR RHEUMATOLOGY TRIALS

Conducting rheumatology studies—especially those involving advanced therapies like CGTs—requires careful planning, strong cross-functional coordination, and proactive risk management.

These trials face unique complexities, from navigating diverse regulations and competitive recruitment landscapes to ensuring sites have the infrastructure and expertise for novel therapies.

As Ms. Widmer noted during the webinar, success depends on translating scientific innovation into operational excellence which safeguards data integrity, patient safety, and site readiness.

To address these challenges, she outlined four key operational pillars for designing and executing rheumatology trials **(Figure 1)**.

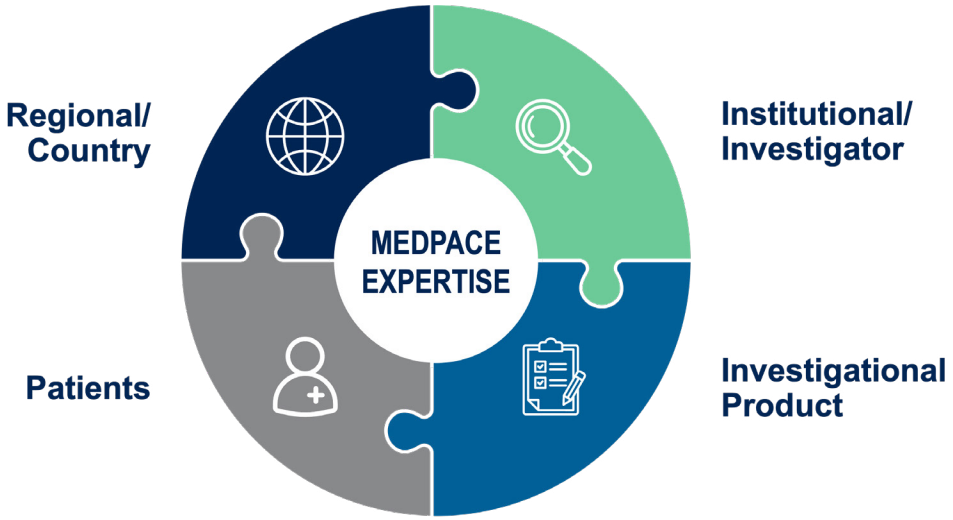

Figure 1. *Core operational pillars for planning and running effective rheumatology trials.*

Each pillar plays a vital role in building a robust operational framework to support the complex demands of modern rheumatology trials.

Regional and Country-Level Strategies

Successful rheumatology trials begin with a thoughtful regional and country-level strategy.

Selecting the right countries is critical—not only to ensure access to eligible patients, but also to support broader clinical development and commercialization goals.

Trial planners must evaluate where patient populations exist, what standard-of-care therapies are approved and reimbursed and how the competitive clinical landscape may affect recruitment.

> ***"Engaging with regulators early and obtaining scientific advice increases the likelihood of success."***
>
> — Ms. Jackie Widmer

Equally important is understanding the regulatory environment. Engaging early with regional regulators to seek scientific advice can improve trial design and support protocol quality.

Country-specific considerations—such as how to manage latent tuberculosis or kidney biopsy requirements in lupus trials—must be built into protocols from the outset.

For CGT studies, a focused one-country strategy during early phases is often recommended. This approach enables Sponsors to adapt protocols to dynamic regulatory environments and ensure the generation of robust data to support future global expansion. Planners must also account for regional differences in tissue testing standards and investigational product requirements to avoid operational bottlenecks.

Institutional and Investigator Feasibility

Institutional and investigator feasibility assessments are crucial for ensuring selected sites can meet both recruitment goals and deliver high-quality data.

Sites must have access to the appropriate patient population and sufficient operational and regulatory infrastructure to support complex trials—especially those involving CGTs. This includes experience with apheresis and infusion procedures, established collaboration between departments (such as rheumatology and hematology), and the ability to manage patient safety in real time.

Operational readiness also means understanding a site's internal review timelines, committee backlogs, and interdepartmental contract negotiation processes. Many sites underestimate these challenges, leading to delays in study start-up.

Clear communication, upfront planning, and education about investigational products can help mitigate these risks and support smooth trial execution.

In the case of CGTs, it is strongly recommended to work with sites that are accredited by FACT (Foundation for the Accreditation of Cellular Therapy) or JACIE (Joint Accreditation Committee of the International Society for Cellular Therapy). This ensures consistency in cell collection, processing, and administration and supports compliance with global standards for patient safety and protocol fidelity.

Investigational Product Logistics: Managing Complexity for CGT Success

As Dr. Vassallo highlighted, investigational product management—particularly for CGTs—requires detailed planning, robust supply chain coordination, and proactive risk mitigation.

CGTs are among the most complex to operationalize, demanding close attention to country-specific regulatory requirements, manufacturing timelines, and chain-of-custody controls.

> ***"We always recommend conducting dry runs at each investigational site with all stakeholders involved to pressure test the process and communication—and importantly to ensure the success of the trial."***
>
> — Dr. Jeffrey Vassallo

Sponsors must account for import/export procedures, Importer of Record obligations, and Qualified Person (QP) release based on the countries and manufacturing locations involved.

Large academic sites with FACT or JACIE accreditation typically have the necessary pharmacy capabilities and cell therapy labs to support CGT trials. However, if community-based sites are included, additional solutions—such as contract pharmacies—may be needed.

Product stability is another critical consideration. For autologous cell therapies, the leukapheresis product has limited stability and manufacturing can take up to six weeks. This may necessitate bridging therapy to manage disease activity during production. It is also essential to ensure that infusion materials match those validated during product development and are available at the site or supplied by the Sponsor or clinical research organization (CRO).

To safeguard quality and regulatory compliance, CGT trials require precise tracking of the chain of custody and identity through manual or electronic vein-to-vein systems. This includes coordination among cold chain vendors, manufacturers, sites, Sponsors, and CROs.

Patient Recruitment and Retention

As Ms. Campbell emphasized, successful rheumatology trials depend on strategies that not only recruit but also retain participants by placing the patient experience at the center of trial design and execution.

Medpace adopts a holistic approach that starts with understanding the patient persona—their health status, lifestyle, pain points, and motivations—and extends to building tailored engagement strategies that reduce burden and foster trust.

Recruitment efforts are most effective when they reach patients where they are. This includes outreach through site databases, primary care and specialist offices, advocacy networks, online support groups, and digital channels such as social media and search ads.

Equally important is providing patients with clear, accessible educational materials, maintaining personal communication, and offering practical support such as travel service to ease participation.

Once enrolled, patients benefit from transparent communication about their role in the study, personalized touchpoints throughout the trial, and thoughtful gestures—such as comfort care items—that help create a supportive environment.

This patient-centered philosophy extends across the entire trial journey.

As illustrated in **Figure 2**, Medpace's model combines education, consent tools, personalized participation support, and retention initiatives to ensure patients feel informed, valued, and empowered at every stage.

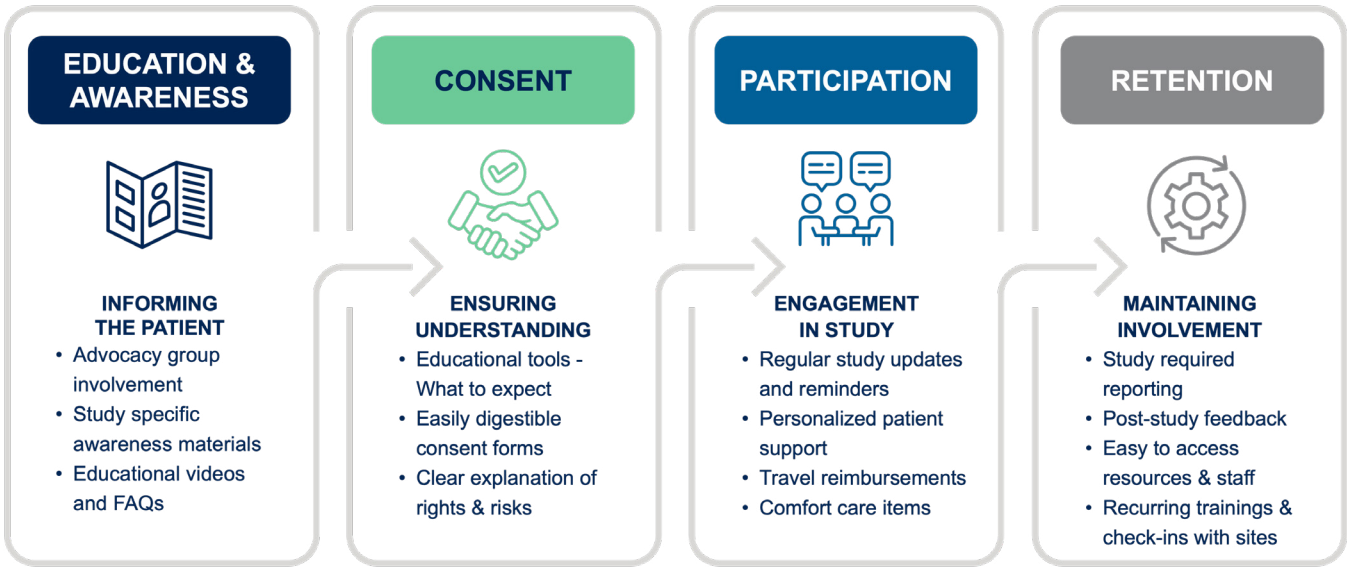

Figure 2. *Medpace's patient-centered approach for rheumatology trials: a comprehensive framework combining education, consent support, personalized participation tools, and retention strategies.*

This commitment to patient-centered engagement is further reinforced through comprehensive education programs and tailored support services.

Comprehensive Education and Support: Driving Engagement and Long-Term Retention

As highlighted in **Figure 3**, a truly patient-centered trial relies on a comprehensive education and support model that brings together the medical community, advocacy groups, and patient-focused tools to promote engagement and retention across the trial lifecycle.

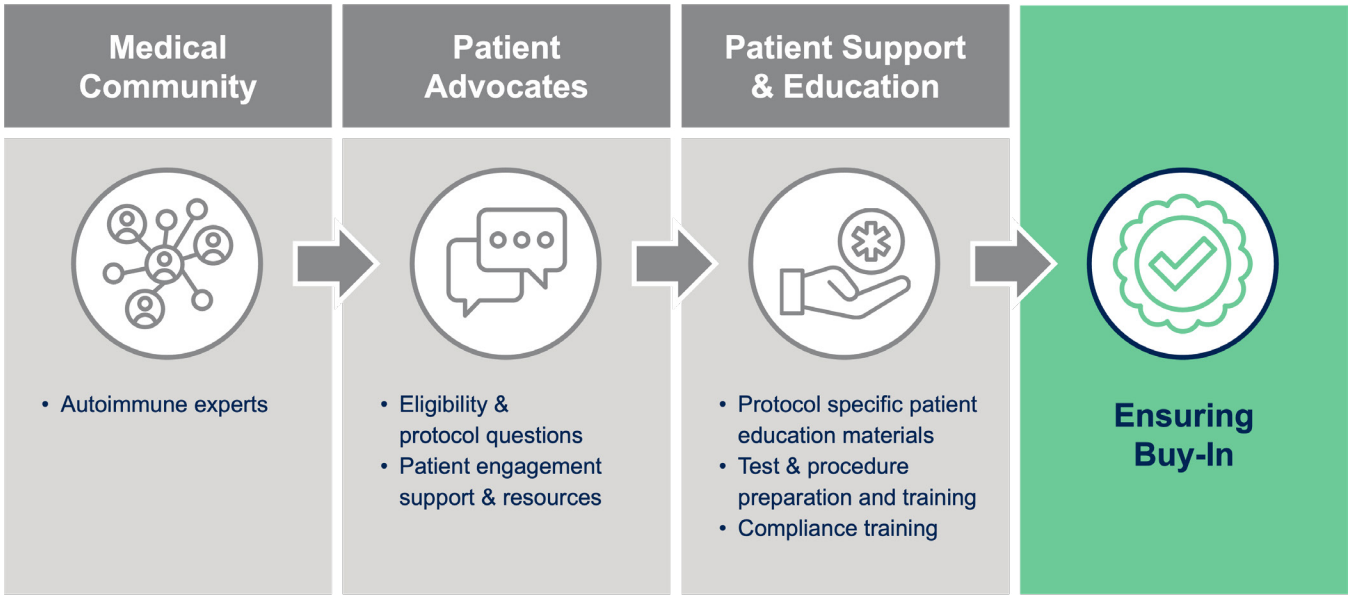

Figure 3. *Medpace's education and support model: an integrated approach combining autoimmune experts, advocacy, and patient engagement to enhance retention across the trial lifecycle.*

This integrated framework ensures that patients feel informed, valued, and supported at every stage—from initial awareness through long-term follow-up.

> ***"We really do want to make sure that [advocacy groups and patient representatives] have input, for instance, into the protocol, into the consent, into the study procedure, so that we can get their feedback. And once we get that feedback, we can better align on protocol requirements."***
>
> — Ms. Miaesha Campbell

During the webinar, Ms. Campbell emphasized that effective education begins with collaboration across key stakeholders. By involving autoimmune experts, referring physicians, and advocacy organizations early, Sponsors can build awareness, address eligibility and protocol questions, and gather feedback that helps refine study design and materials.

Advocacy groups, in particular play a critical role as trusted partners who can champion the study within their communities.

Tailored patient education materials, study-specific videos, compliance training, and procedure preparation tools further empower participants. These resources not only set expectations and reduce anxiety but also ensure that patients from diverse backgrounds understand how participation may positively impact their quality of life.

Complementing these efforts, Medpace's participant support services—ranging from travel coordination and reimbursements to the thoughtful provision of comfort items during long visits—help reduce logistical burdens and foster lasting trust.

Together, these strategies help ensure patients remain engaged and motivated throughout their participation in rheumatology trials.

LOOKING AHEAD: BRIDGING INNOVATION AND OPERATIONAL EXCELLENCE

As Dr. Head summarized, "As we look into the future rheumatology trials, we see there have been advancements in the understanding of the number of therapeutic targets and there are several therapeutic approaches that are being investigated."

This, combined with thoughtful trial design and execution, holds promise for addressing longstanding gaps in the treatment of rheumatologic diseases.

With the increasing complexity of rheumatology trials, collaboration among Sponsors, CROs, sites, regulators, and patients will be essential to ensure that innovative therapies reach those in need—efficiently, safely, and equitably.

To learn more, watch the on-demand webinar featuring rheumatology experts from Medpace.

WATCH NOW

This article was created in collaboration with the Xtalks editorial team.