Atopic Dermatitis

Considerations for Clinical Trials

Presented by Symbio, LLC

Introduction

Atopic dermatitis (AD), often called eczema, is a common and often debilitating skin condition whose root cause remains unknown but is likely to be related to allergies and immune dysregulation. Atopic dermatitis manifests on the skin as an itchy and inflamed blotch of tiny red bumps. The disease is generally found in young children; 85% of all cases appear before the patient is five years of age. The condition affects 10 to 20 percent of all young children, but most will spontaneously remit before reaching late adolescence. Adults can suffer from AD as well, but in proportionally fewer numbers, with prevalence decreasing in adulthood to 1 to 3 percent (Kapur, Watson, and Carr 2018).[1]

No curative treatment exists for this condition and management usually consists of topical corticosteroids. In more severe cases, topical calcineurin inhibitors, biologics or immunosuppressants may be necessary. Unless remission occurs, AD is a chronic disease and needs to be suppressed through medication and vigorous hygiene practices. In almost all cases, areas of AD are overrun with Staphylococcus aureus bacteria. Frequent bathing and moisturization of affected areas help to shed infected skin and limit bacterial growth (Kapur, Watson, and Carr 2018).[1]

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AD is chronic, occurs regularly in young children and requires near-constant medication and care to suppress. Because sufferers are often so young, drug treatments must not only be effective, but safe for the bodily systems of kids and infants. While not life-threatening, AD is highly prevalent and can vastly reduce a patient's quality of life. AD's prevalence, lack of cure, and impact on life quality have driven continuous research and investment into novel therapies. Unless an extremely tolerable and efficacious treatment becomes available, this trend is likely to continue.

Clinical Research Challenges

Despite the present and real need for research, AD trials can be notoriously difficult to run. Rating the severity of a skin condition is inherently subjective and over sixty different scales have been utilized in clinical trials (Chopra and Silverberg 2018).[2] This lack of standardization in AD clinical trials can result in the use of poorly validated rating scales or the omission of potentially vital information. A study of AD trials conducted between 1994 and 2003 found only 27 percent used published severity scales and only 3 percent asked about the patients' quality of life (QOL) (Charman, Chambers, and Williams 2003).[3] Unclear rating scales lead to unclear results and make the evaluation of a treatment's efficacy difficult or impossible. Leaving out subjective patient data like QOL information restricts the trial's ability to evaluate patient well-being.

As can be seen in Symbio's data infographic on page 4, AD studies occur frequently and usually recruit large numbers of patients. These numbers have remained steady over time as there have been no novel therapies that have proven significantly better than the status quo.

Attempts have been made to proactively tackle AD as soon as it appears in infants and young children, as doing so may greatly reduce the risk of them developing food allergies and allergic sensitization in the future (Yamamoto-Hanada et al. 2018).[4] This proactive treatment, while useful for future life quality, requires that very young people be exposed to aggressive anti-inflammatory treatments. AD trials enrolling children and teenagers are likely to remain common in the future, as researchers attempt to develop therapies that can provide a safe early intervention for susceptible young people.

A particular difficulty of AD studies is that many patients are under five when their atopic dermatitis first begins to manifest. Studies involving young children are often more difficult to run, as the patients are too young to consent on their own and safety concerns are amplified. As the infographic on page 4 shows, most patients are adults and the youngest enrollable age in any of the listed studies was eight years old. Most study participants were of full adult age making up the much smaller percentage of those who do not remit in childhood. The majority of Symbio's subjects were also of lesser severity relative to the hodgepodge of rating scales used in AD studies. This is likely due to Symbio's inclination towards topical medications, which are generally used by those who present less severe cases.

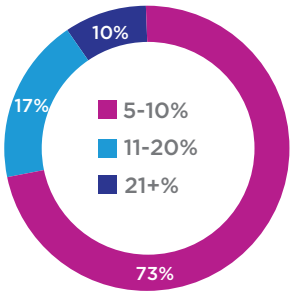
Another interesting trend in Symbio's data is the peak in study enrollment that occurs around late spring and early summer. As shown above, almost every study took about one year to complete. This makes it unlikely that the early summer skew is due to a bias in when the studies begin, as each study runs for almost every month of the year about once. Due to the allergic nature of AD, severity tends to peak in the spring and summer when seasonal allergies are at their worst.

All of the factors mentioned make AD trials very difficult to organize; there is no set way to evaluate patient health, there are several different classes of drug treatment, and often studies must go to great lengths to ensure the consent and well-being of underage subjects. When comparing a novel or generic AD drug to a placebo, it is also necessary to take into account local allergies, which differ greatly depending on the time of year and geographical region. These studies are conducted at clinical sites across the United States with unique environmental allergens emerging, peaking and declining at different times.

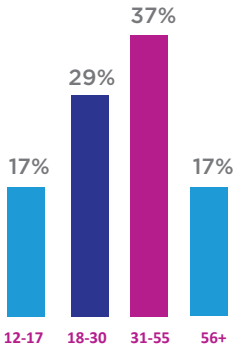
ATOPIC DERMATITIS

Studies: 7
Subjects: 3,674

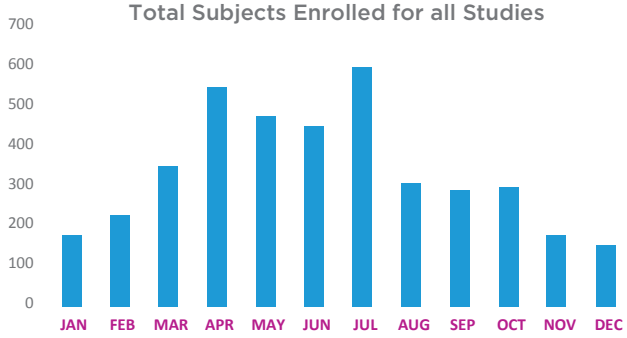
%BSA
From Studies 3 & 4



AGE



ENROLLMENT BY MONTH
Total Subjects Enrolled for all Studies



Studies Completed	Subjects Enrolled	Population	BSA	Sites	Enrollment	Average Enrollment Rate
Study 1 (A/B)	793 (438/355)	18 yrs+	10%+	42	12 months (8/4)	1.2 per site per month
Study 2 (A/B)	897 (483/414)	8 yrs+	10%+	51	13.5 months (9.5/4)	
Study 3	587	12 yrs+	5%+	50	13 months	
Study 4	582	12 yrs+	5%+	31	10.5 months	
Study 5	484	13 yrs+	N/A	50	11.5 months	
Study 6	122	18-65 yrs	5-20%	17	5 months	
Study 7	209	12 yrs+	4-24%	23	11 months	

SUCCESSFUL APPROACH

PLANNING
- ✓ Optimal Site Selection
- ✓ Establish Recruitment Plan

TRAINING
- ✓ Disease Diagnosis
- ✓ Primary Endpoint Assessments

EFFECTIVE PROJECT MANAGEMENT
- ✓ Track Study Progress Daily
- ✓ Early Trend Identification & Proactive Issue Resolution

Solutions

To help ensure patient safety and study efficacy, Symbio has made a habit of employing allergists as well as dermatologists for atopic dermatitis trials. By employing experts, Symbio can help discover regional discrepancies in data caused by allergies and minimize the impact they have on research data. Allergists commonly deal with atopic dermatitis and including them on the study staff allows them to lend their unique perspective on AD and aid in evaluating and protecting patients.

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AD research is affected by a vast number of factors, some more controllable than others. To ensure that potentially complicated studies like AD trials go off without a hitch, Symbio's talented project managers check in on each site daily, ensuring that the organization's high expectations for safety and enrollment speed are being met. For factors that are less controllable, Symbio's in-house data analytics department helps determine the safety and efficacy of trial medications by discovering and accounting for extraneous circumstances that may impact study data.

Managing difficult and often unwieldy AD trials requires an organization with a firm and experienced hand. Symbio began its history as a dermatology CRO, and has been performing AD trials for eighteen years, almost its entire lifetime as a business. Symbio's experienced staff can predict issues and pitfalls before they occur, mitigating potential sources of difficulty and error before they can cause harm. The company has a robust relationship with AD sites around the country, which form a reliable network for study enrollment and execution. This experience includes the regular enrollment of children and minors, putting Symbio in a prime position to help conduct research for an increasingly young cohort of patients.

Conclusion

In an exciting world of novel biologics and allergy treatments, AD continues to afflict children and teenagers in great numbers. Research is unlikely to dry up any time soon, supported by a lack of efficacious treatment options and a drive to protect youth from future medical complications. While clinical research in this area is often difficult and lacking in accepted convention, AD is an often-debilitating illness that desperately needs more research. Experienced CROs like Symbio help ensure that this vital work can proceed in the smoothest and safest way possible.

Symbio

Symbio, LLC has almost 20 years of experience performing atopic dermatitis trials and has accumulated large quantities of data on atopic dermatitis enrollment. This expertise allows us to organize studies that maximize enrollment speed by taking into account both the long- and short-term factors that affect atopic dermatitis enrollment.

Works Cited

1. Kapur, Sandeep, Wade Watson, and Stuart Carr. 2018. "Atopic Dermatitis." Allergy, Asthma, and Clinical Immunology: Official Journal of the Canadian Society of Allergy and Clinical Immunology 14 (Suppl 2): 52.

2. Chopra, Rishi, and Jonathan I. Silverberg. 2018. "Assessing the Severity of Atopic Dermatitis in Clinical Trials and Practice." Clinics in Dermatology 36 (5): 606–15.

3. Charman, Carolyn, Colette Chambers, and Hywel Williams. 2003. "Measuring Atopic Dermatitis Severity in Randomized Controlled Clinical Trials: What Exactly Are We Measuring?" The Journal of Investigative Dermatology 120 (6): 932–41.

4. Yamamoto-Hanada, Kiwako, Tohru Kobayashi, Hywel C. Williams, Masashi Mikami, Mayako Saito-Abe, Kumiko Morita, Osamu Natsume, et al. 2018. "Early Aggressive Intervention for Infantile Atopic Dermatitis to Prevent Development of Food Allergy: A Multicenter, Investigator-Blinded, Randomized, Parallel Group Controlled Trial (PACI Study)-Protocol for a Randomized Controlled Trial." Clinical and Translational Allergy 8 (November): 47.