Lessons Learnt from conducting clinical trials in childhood-onset SLE

Academic Perspective

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Disclosures

Consultancies/honoraria (<$10,000): AbbVie, AlfaSigma, Amgen, Astra Zeneca Biogen, Boehringer, Bristol-Myers Squibb, Celgene, Eli Lilly, EMD Serono, GlaxoSmithKline, F. Hoffmann-La Roche, Johnson & Johnson, Merck, Novartis, Pfizer and UCB. The Cincinnati Children's Hospital, where HBR works as a full-time public employee, has received contributions (>$10,000 each) from the following industries in the past 3 years: Bristol-Myers Squibb, F. Hoffmann-La Roche, Janssen, Novartis, and Pfizer. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment to third parties.

Overview

Screening & Enrollment	• Patient identification/recruitment • Eligibility Criteria • The issue of placebo
During the Study	• Potentially flaring patient & central laboratories • Socioeconomic barriers • PRO collection
After the study	• Access to Study Medications

Delays in start & completion of pediatric studies – Example of IV Belimumab Study (NCT01649765)

- EMA:
  - 2009 – PIP initial submission
  - Randomized withdrawal study, n=134, staggered enrollment; 5+ yrs @ enrollment
  - **Oct 2011: change to DB parallel design, n=100 (updated stats)**
- FDA:
  - iPSP is not typically made publicly available
  - **March 2011 – adult SLE indication - Pediatric Study Start: July 25, 2012**
  - 2014: GSK extension request to 3/2018 of due to enrollment problems
  - 2016: GSK requests reduction of subjects to 70
  - 6/2018: CSR submitted – priority review requested by GSK and granted by FDA
  - **4/26/2019 - FDA approval in children**

Study Registration Dates	
First Submitted	2012-07-23
First Submitted that Met QC Criteria	2012-07-23
First Posted (Estimated)	2012-07-25

Results Reporting Dates	
Results First Submitted	2018-07-23
Results First Submitted that Met QC Criteria	2018-07-23
Results First Posted	2018-08-15

Study Details | NCT01649765 | Pediatric Lupus Trial of Belimumab Plus Background Standard Therapy | ClinicalTrials.gov
https://www.fda.gov/media/127912/download

Delayed Study Start Makes Recruitment More Difficult

- **Pre-FDA approval use in cSLE patients 5-17years of age:**
  - IV belimumab: 191 patients from 33 HCO
  - SC belimumab: 343 patients from 43 HCO
  - IV anifrolumab: 104 patients from 33 HCO

TrinetX DB review (5/29/26)
HCO Health Care Organizations

June 2026

Pharmacy Updates

Summarize

Yung, Elaine

Reply | Reply All | Forward

To Angeles-Han, Sheila; Grom, Alexei; Matt, Michael; OConnor, Shannon; Ogbu, Ekemini; Rodriguez-Smith, Jackeline; Schulert, Grant; Vater, McKenzie (She/Her/Hers); **+23 others**

Tue 6/2/2026 3:59 PM

for existing + new patients now and rejecting Xeljanz Rxs, temporary workaround is to do Xeljanz DAW Rx

- For patients with OH Medicaid on Xeljanz, will be routing providers new Xeljanz Rxs to fill DAW [no new PAs needed]

Saphnelo (anifrolumab-fnia)

- Pen formulation now available
- 120mg once weekly SUBQ

- **Uplizna (inebilizumab) and Blincyto (blinatumomab)**
  - Both anti-CD19
  - IV and SUBQ med, respectively
  - Phase 2 study (adults, not at CCHMC) ongoing for refractory SLE

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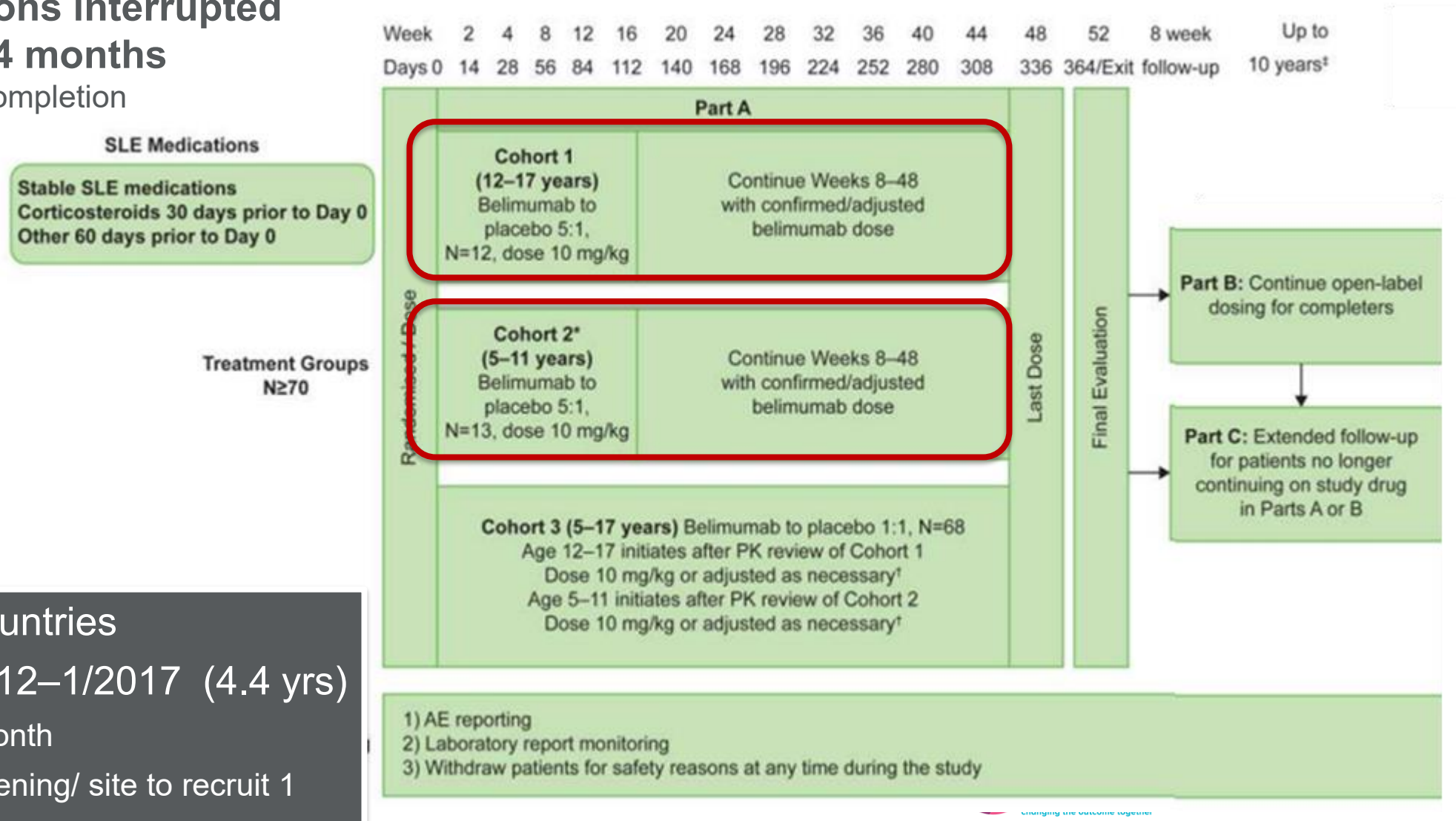
Intravenous Belimumab PLUTO Study (NCT01649765)

Brunner HI, et al. Ann Rheum Dis 2020;**79**:1340–1348

Cohort 1 pk-evaluations interrupted enrollment of about 4 months

Delays overall study completion



- 29 centers, 10 countries
- Enrollment : 9/2012–1/2017 (4.4 yrs)
  - 1.77 patients / month
  - 16 month of screening/ site to recruit 1 patient

Recruitment Delays from Study Design

- **Interruption of enrollment of about 3-4 months for pk-evaluation**
  - Delays overall study completion
  - Study personnel need to be reassigned – paid by visit
- **Even later start of Cohort 2 (5-11 yrs at baseline)**
  - Delayed overall study completion
  - All 13 patients were enrolled ex-U.S.

Sanchez-Rodriguez A et al.: Ac & R. 2025 Apr;77(4):451-459; Wong Pediatr Nephrol. 2026 Dec;41(1):89-100. doi ; Hiraki Arthritis Rheum. 2012 Aug;64(8):2669-76. doi: 10.1002/art.34472

Adolescent-only Studies or Inclusion of Adolescent into Studies focused on Adults

Pediatric Drug Development Under PREA/BPCA: Scientific Considerations

Draft 2023; Early FDA engagement (latest 60 days after EOP2 meeting)), iPSP early....

Voclosporin in Adolescents With Lupus Nephritis

Last updated: October 19, 2023 Sponsor: Aurinia Pharmaceuticals Inc. Overall Status: Active - Recruiting

Phase	Condition	Treatment	Clinical Study ID
3	Lupus Nephritis Kidney Disease Nephritis	Voclosporin Placebo Oral Capsule	NCT05288855 AUR-VCS-2020-03

Ages 12-17

All Genders

DISCONTINUED

Recruiting

Phase 3 Study to Evaluate Two Regimens of Ianalumab on Top of Standard-of-care Therapy in Patients With Systemic Lupus Erythematosus (SIRIUS-SLE 1) (SIRIUS-SLE 1)

ClinicalTrials.gov ID NCT05639114

Sponsor Novartis Pharmaceuticals

Information provided by Novartis (Novartis Pharmaceuticals) (Responsible Party)

Last Update Posted 2025-05-13

12+ years

SEEMINGLY ONLY ADULT SITES

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Placebo Exposure (continuation of SOC) Limits Interest in Study Participation

- **Rationale of placebo in the setting of limited sample size is unclear**
  - Safety ? Efficacy ?
- **Favorable randomization scheme does not help with recruitment**
  - Takes a lot of enthusiasm of family to participate in such a study
  - Young children are considered even more vulnerable
- **Risk of receiving placebo despite active cSLE makes also providers hesitant to consider their patient for the trial**
  - Moderately active cSLE (undertreated) can result in damage, especially if present for a longer time

Highly Restrictive Eligibility Criteria

Intravenous Belimumab PLUTO Study (NCT01649765)

Inclusion Criteria

- 5 years to 17 years of age at enrollment
- SLE according to the American College of Rheumatology (ACR) classification criteria.
- Have active SLE disease at screening and baseline: SLEDAI score ≥ 6 – initially 8
- Positive anti-nuclear antibody (ANA) or ds-DNA test results – 2 times incl day 0
- On a stable SLE treatment regimen at a fixed dose for a period of at least 30 days prior to Day 0.- MAX 0.5 mg/kg/day
- Females of childbearing age are willing to use appropriate contraception

Exclusion Criteria

- Treatment with any B cell targeted therapy (for example, rituximab) or an investigational biological agent in the past year.
- Within 90 days of day 0: TNFi, IVIG , plasmapheresis
- Within 60 days of day 0:
  - Prednisone or equivalent (>1.5mg/kg/day),
  - IV cyclophosphamide
  - New immunosuppressive agent
  - New anti-malarial agent
  - IV/IM antibiotics/hospitalization for acute/chronic infections
- Have severe lupus kidney disease
- Have active neuropsychiatric disease
- Have an IgA deficiency

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Highly Restrictive Eligibility Criteria

- **Long wash-out periods before even allowing screening in the setting of active cSLE are a challenge**
- **Flares during the wash-out period are real**
  - Disease control often requires prohibited medications (such as IV steroids) to prevent major disease exacerbations
- **Many wash-out periods with active cSLE can only be addressed when enrolling newly diagnosed patients**
  - Obstacles:
    - Minimum disease duration
    - Minimum time on SOC treatment

Protocol available at clinicaltrials.gov

Example: IV anifrolumab study (NCT05835310)

3.2.2 Exclusion criteria related to concomitant medications

(b) Where prednisone is not the single standard of care medication (ie, the subject is concurrently receiving at least one medication listed in inclusion criterion 7(c)):

(i) Any addition of a new oral prednisone therapy (or equivalent) any time from 2 weeks prior to signing of the informed consent form through Day 1, OR any change in/ discontinuation of current oral prednisone dose (or equivalent) anytime within the 2 weeks prior to randomisation (see Appendix V for examples of prednisone equivalency)

(ii) Any addition of a new dose of any of the following anytime in the 12 weeks prior to signing of the informed consent through Day 1, or change in/ discontinuation of current dose anytime in the 8 weeks prior to signing of the informed consent through Day 1: azathioprine; any antimalarial (eg, chloroquine, hydroxychloroquine, quinacrine); mycophenolate mofetil/mycophenolic acid; oral, SC, or intramuscular methotrexate; mizoribine

Open-label SC Belimumab Study in cSLE (NCT04179032)

- Open-label but eligibility criteria similar to IV study
- **Roll-over from IV study not allowed - rationale??**
- Few young & non-white patients

Recruitment periods: 2.1 years
11 sites

Table 1. Patient baseline characteristics (ITT population)*

	All patients (N = 25)
Female, n (%)	21 (84.0)
Age, mean (SD), y	14.0 (2.1)
Age range, min–max, y	10–17
Ethnicity, n (%)	
Hispanic or Latino	11 (44.0)
Not Hispanic or Latino	14 (56.0)
Race, n (%)	
American Indian or Alaska Native	3 (12.0)
Asian	4 (16.0)
Black or African American	1 (4.0)
Multiracial	1 (4.0)
Native Hawaiian or other Pacific Islander	0
White	16 (64.0)

Brunner HI et a. . Arthritis Care Res (Hoboken). 2026 Jun;78(6):761-770.

Study Start (Actual)
2019-11-28

Primary Completion (Actual)
2023-01-16

Study Completion (Estimated)
2027-04-26

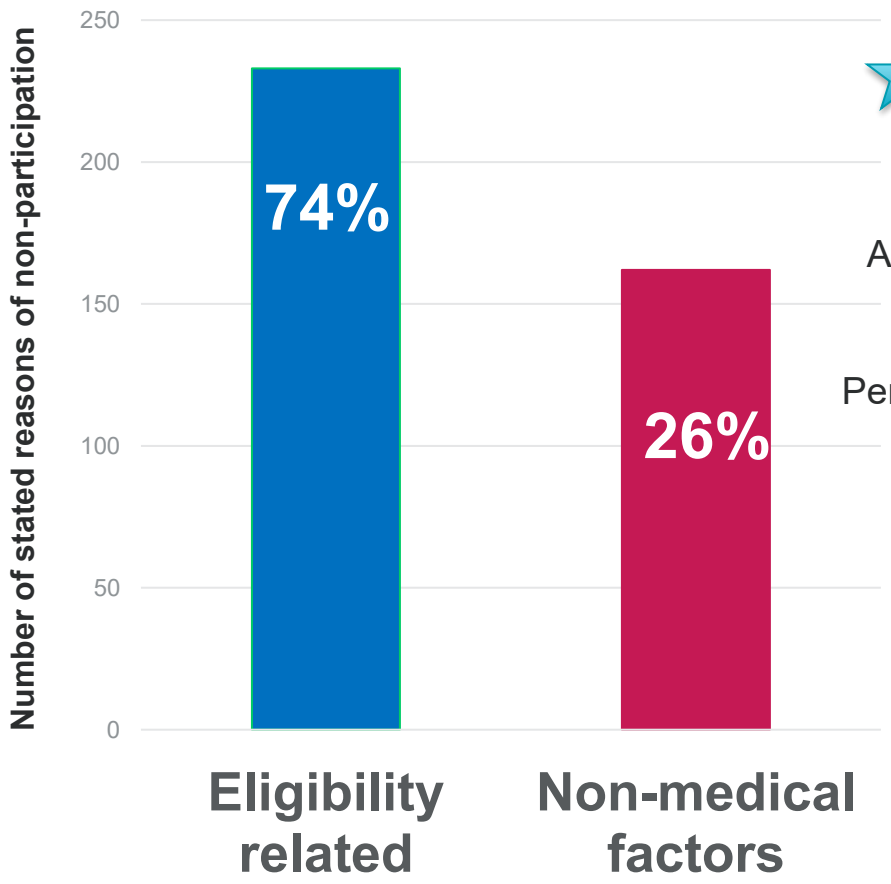
Enrollment (Actual)
25

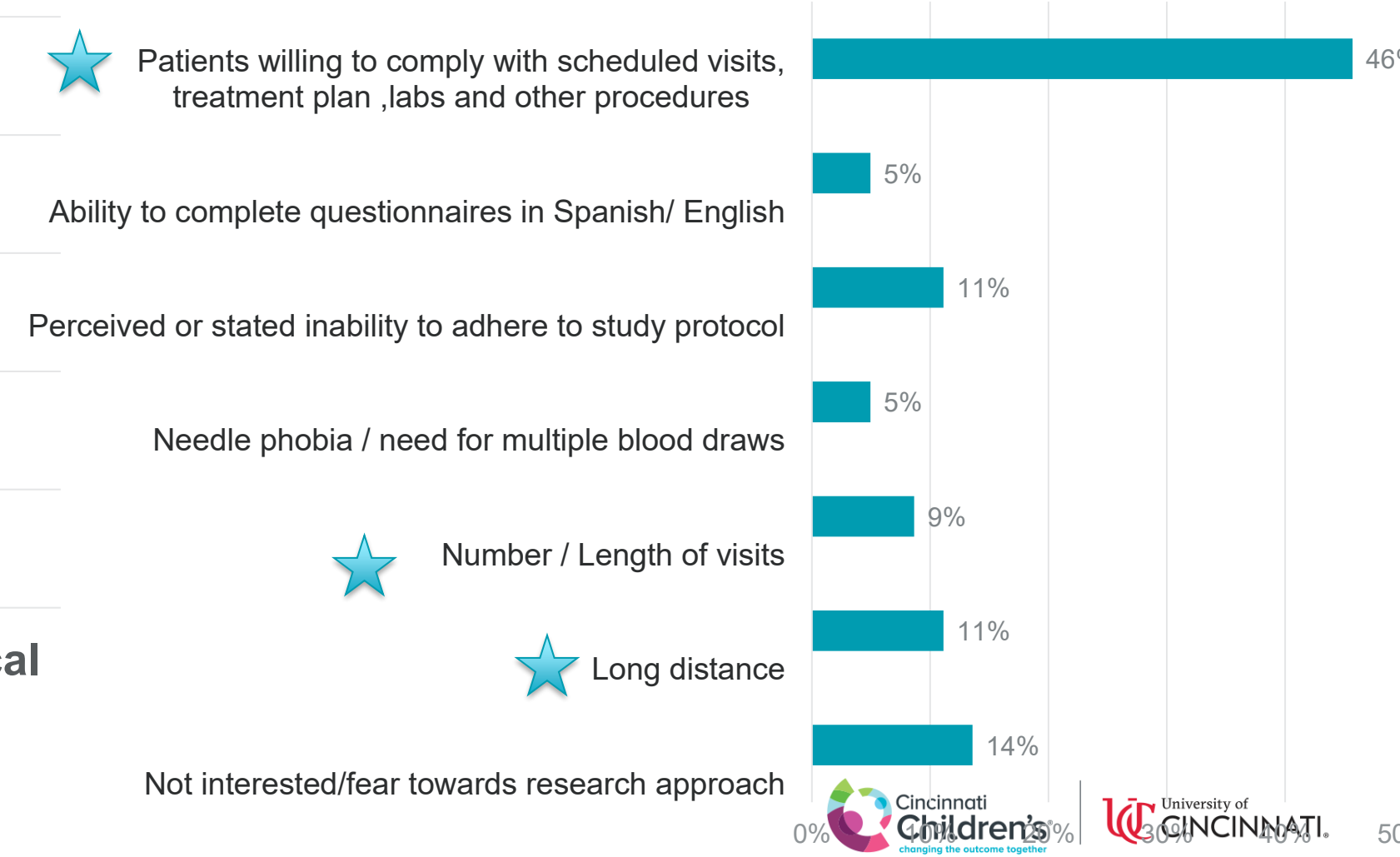
Study Type
Interventional

Phase
Phase 2

Socioeconomic barriers are substantial

Example PLUMM Trial in pediatric LN (NCT05538208) – active comparator !





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Loss of income	Multiple jobs	Missing school	Language barriers
Long travel to site	Severely impacted by disease – fatigue, pain	Burden of regular multi-provider clinical care	Childcare / activities of other kids

Site coordinator/PI to help arrange usual multidisciplinary care, flights, hotels, manage reimbursement delays, coordinate visits with other providers.

< 400 Pediatric rheumatologists in the U.S. Country
10 states without any provider

The Issue of the Central Laboratory

Screening visit → Shipping of blood **(after incubation)** to Central Lab → Results take 5-7 days to return → Redraw ? 7-10 days → Baseline visit

1+ weeks delay in receiving results - delay baseline visit

Duplicate “shadow labs” for safe clinical care ?

Redraw blood - extra travel / more delay in starting the study medication

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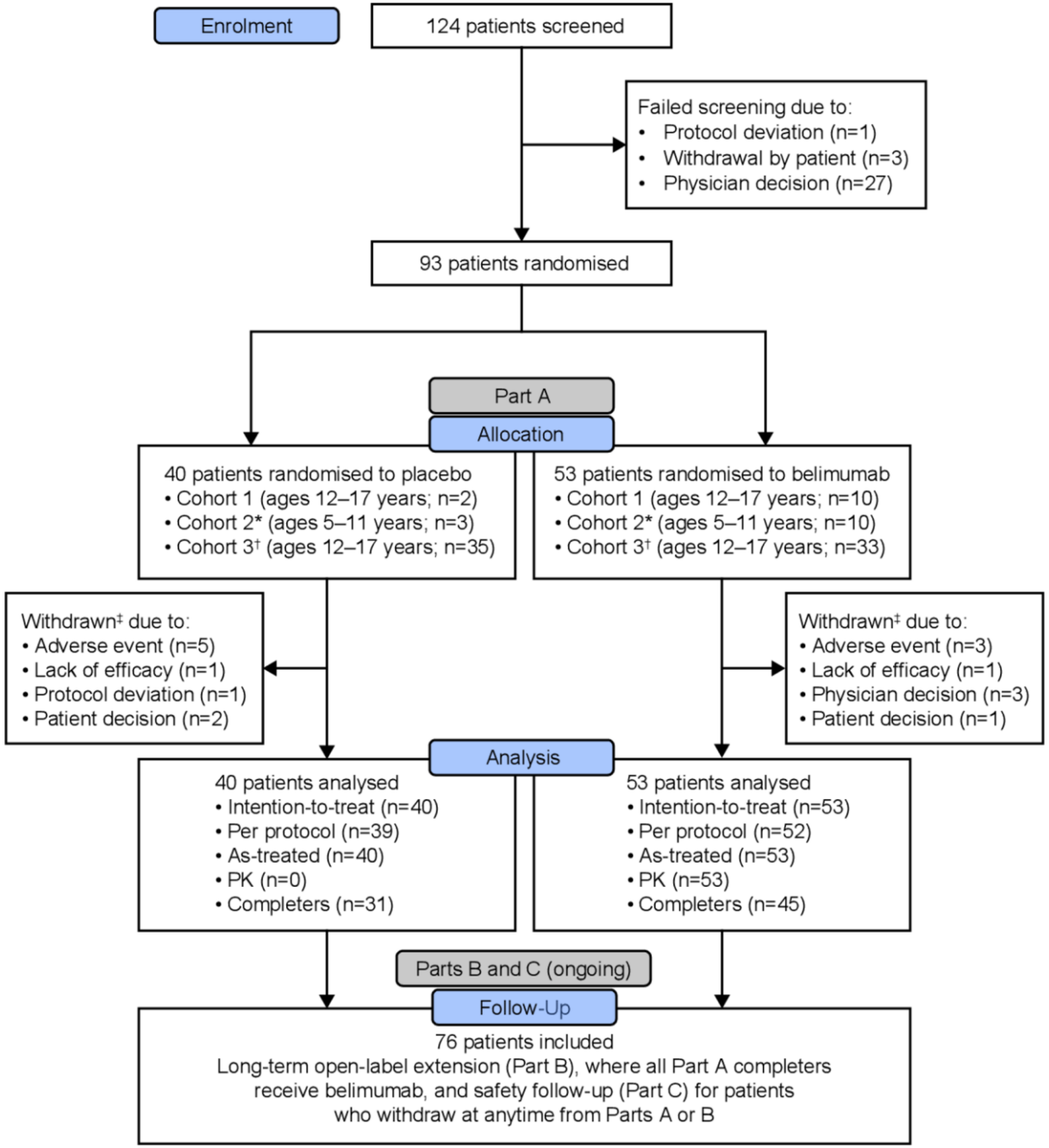
Medication Access after the Study

- **Uncertain access to study medication after completing the study**
  - FDA approval and addition to pharmacy lists is often delayed
  - Insurance may not cover medication
  - LTE studies offer easy way to collect more safety data
- **Individual INDs are not a sustainable strategy for investigative sites**

Key Messages

- **Delay in starting cSLE studies make recruitment more difficult**
  - Off-label use is a problem
- **Duplication of eligibility criteria and designs for adult studies limit enrollment into cSLE studies**
  - Multiorgan disease
  - Wash-out and minimum disease duration
- **Placebo exposure is a major problem – irrespective of randomization scheme**
- **Central Laboratory use adds to study burden and complexity**
  - Frequent need for re-draws, limitations to schedule study visits, delays in receiving results
- **The entire family participates in the clinical trial**
  - School, income loss of parent, childcare, long commutes to investigative sites
  - More difficult in lower resourced families



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