

Implementing Patient-Centric Strategies in a Natural History Trial: A Case Study

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Learning Objectives

Attendees will be able to:

- Summarize patient-centric strategies to be integrated into the protocol
- Describe how different patient-centric strategies can be operationalized
- Explain global factors to consider when implementing different patient-centric strategies
- Implement tools allowing the study to focus on the needs and interests of the study participants

Orphan Drug Development

- Pro: POC can be established in a small number of patients
- Cons:
 - Patient populations are very small
 - Accurate diagnosis is challenging
 - Choice of endpoint, exploratory endpoints

Clinical Trials in Nephrology

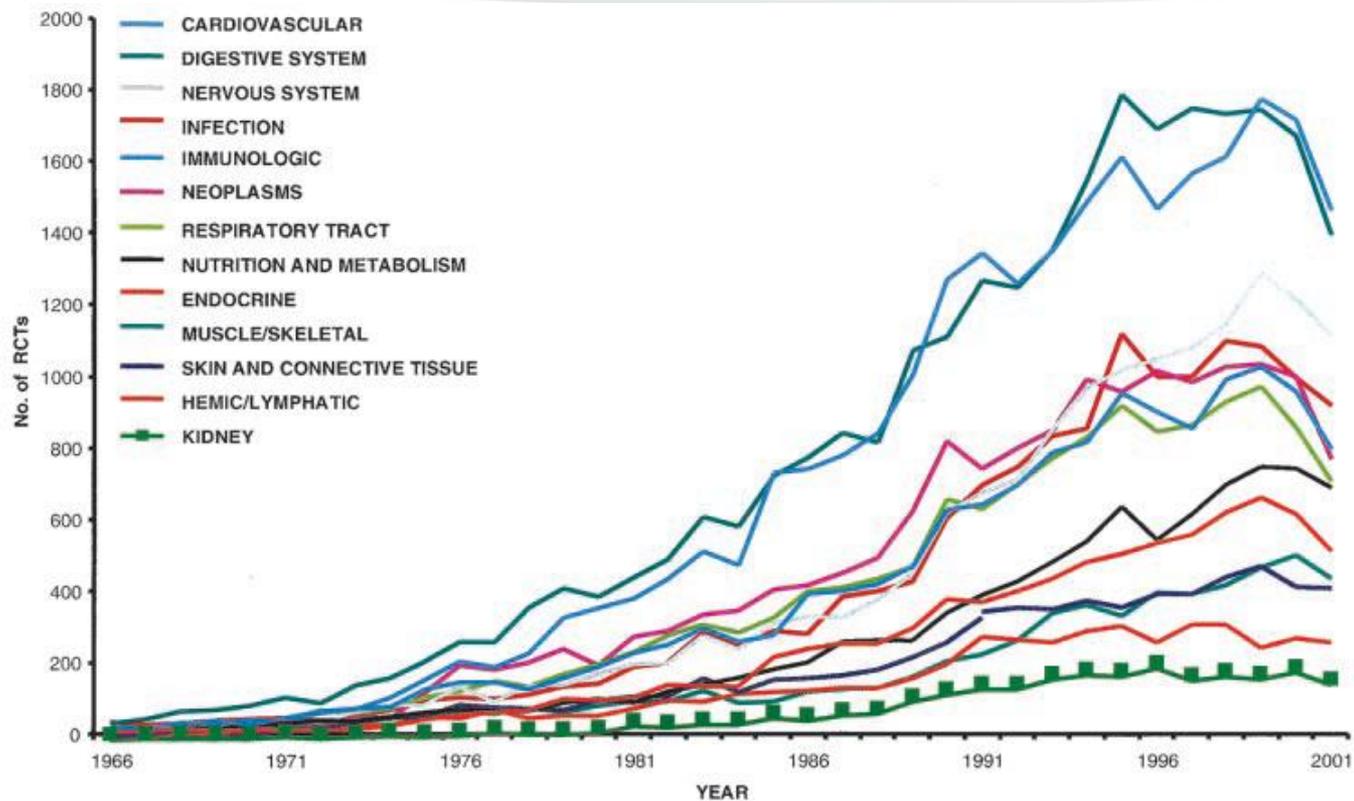


Figure 1. Number of randomized controlled trials (RCT) published in nephrology and 12 other specialties of internal medicine from 1966 to 2002.

Background: Alport Syndrome

- Disease overview:
 - *Genetic disorder* - mutations in certain types of collagen
 - *Orphan disease* (~20-30k patients in the US)

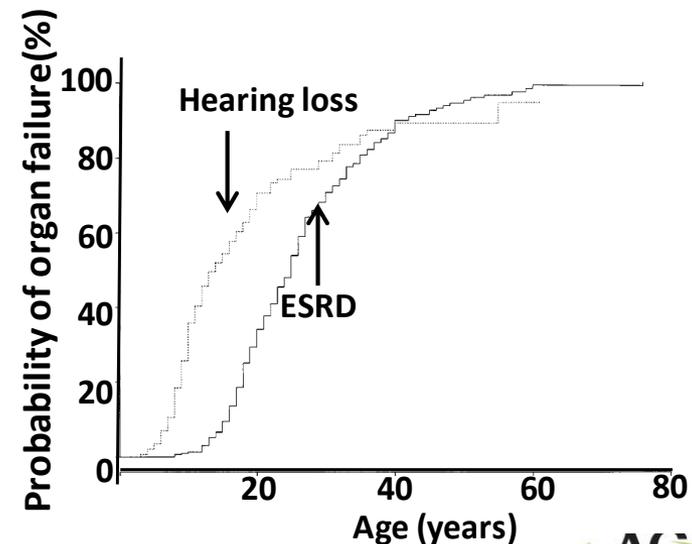
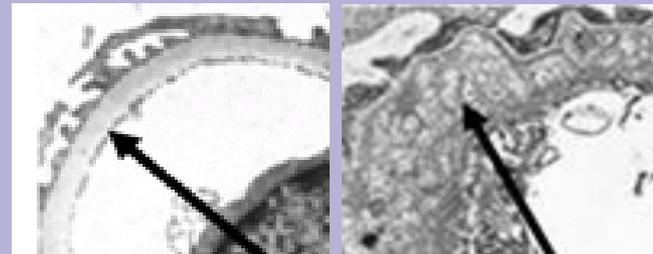
High unmet medical need:

- Progressive loss of kidney function, hearing & ocular abnormalities
- ~80% patients reach end stage renal disease (ESRD) before age 35

Glomerular basement membrane

Normal

Alport



(Jais, JP, et al (2000) J Am Soc Nephrol 11: 649)

Natural History Study

- Follows a group of people over time who have a specific medical condition or disease.
- Often submitted to the regulatory agencies as a baseline for the disease course for untreated patients

Natural History Study

- Rate of decline of established biomarkers (GFR) have not been clearly documented over time
- A study with sequential sampling of urine and blood of Alport syndrome patients will allow an assessment of the rate of decline in GFR and other renal biomarkers
- This study may also identify other surrogate markers or renal function decline that correlate to time to end-stage renal disease

The Advice I was Given (How to make the study Patient-Centric)

- Make sure the protocol is patient-friendly
- Use a home nursing service
- Establish a patient reimbursement program
- Engage a travel service

- Other considerations
- Patient Advocacy

Patient-Centric Study Design

Focus on the study design from the patient perspective

Patient-Centric Strategies: 24 Urine Collection Transportation



Protocol: Natural History Study Design

■ Design:

- Non-treatment, global, multicenter
- To observe disease progression, standard of care and investigate biomarkers in Alport Syndrome Patients

■ Patients:

- Patients with Alport Syndrome with GFR between 30-75 mL/min (inclusive)
- Male and Female ≥ 16 years of age
- Up to 120 subjects enrolled in the study at 15 global investigative sites
- Site locations: US, Canada, Germany, France, UK and Australia

■ Duration:

- Visits every 12 weeks (clinic and home health visits) for up to 120 weeks



Protocol: Natural History Study Entry Criteria

Inclusion:

- Able to understand and comply with study requirements and provide written informed consent; pediatric subjects must provide assent;
- Age ≥ 16 years
- Confirmed diagnosis of Alport syndrome (clinical, histopathologic, and/or genetic diagnosis of Alport syndrome)
- Measured GFR 30-75 ml/min by iohexol method, within 30 days of enrollment.

Exclusion:

- Use of investigational drug within 30 days, or 5 half-lives of enrollment, whichever is longer
- Ongoing chronic hemodialysis therapy, and/or renal transplant recipient



Patient-Centric Protocol

- Patient Visit Schedule:
 - SOC for nephrologists treating Alport syndrome patients is one visit every 12 months
 - Cut back on the visit schedule - was every 6 weeks, but reduced to every 12 weeks
- Provided protocol to patient advocacy groups for review
 - Question of confidentiality
 - Requested input regarding visit schedule, 24 hour urine, genotyping, home nursing and measured GFR
 - Advocates also provided input on sites

Patient-Centric Strategies: Home Nursing

Challenge: Visit schedule required blood and urine collection every 12 weeks

- Easy Answer: Engage home nursing service allowing for patients to have study assessments conducted at home or work at their convenience therefore reducing travel burden and additional clinic visits.

Patient-Centric Strategies: Home Nursing

Unexpected Challenges: Hospital did not want to use external home nursing service, wanted to use their own

- Provided documentation of the GCP training, study-specific training and study-specific equipment required to perform the home visits (centrifuge, lab kits, dry ice, etc.)

Patient-Centric Strategies: Home Nursing

Unexpected Challenges: PI discomfort with responsibility for home health nurse who is not part of their staff

- Unexpected Challenges: PI protective of their patient, discomfort with sending a stranger to their patient's home
- The home health nurses were added to the site's delegation of authority log.
 - Provide CVs to the PI
 - Provide training materials and training records to PI for review
 - Make arrangements for a phone or in-person interview

Patient-Centric Strategies: Home Nursing

Unexpected Challenges: PI and site staff concerned about AE Reporting for home visits

- Provided PI and site staff overview of AE reporting plan at the Investigator Meeting and SIV training
- Recommend including the Project Manager from the home nursing service

Patient-Centric Strategies: Home Nursing

Unexpected Challenges: Timely turnaround of source documents for home visits

- Delay of originals is due to a QC step performed by the home nursing service Project Manager. Copies of source docs were provided to sites in advance of the originals for timely data entry.

Patient-Centric Strategies: Home Nursing

Unexpected Challenges: Procedures that nurses are allowed to perform are not equivalent in all countries

- Example: Nurses in Germany are not allowed to perform “Physical Exams” however they may perform a “Body System Assessment” so the Protocol and CRF were revised to reflect that requirement

Patient-Centric Strategies: Home Nursing

Unexpected Challenges: Nurses are not allowed to transport dry ice in some countries

- Arranged for courier to arrive with dry ice, and revised the lab manual to have a “wet ice” procedure for sample processing

Patient-Centric Strategies: Home Nursing

Unexpected Challenges: Home visits take more time than patients expect

- Have the Study Coordinator include this as part of the discussion during the Informed Consent process to manage the expectations

Patient-Centric Strategies: Home Nursing

Unexpected Challenges: Global study and home nursing not available in all countries

- Important to address during the site selection process
 - Could get more sites to cover the country
 - Or, ensure there is enough of a patient pool a short distance from the site

Patient-Centric Strategies: Home Nursing

Unexpected Challenge: Investigators have expressed concerns about ordering home health visits for patients that live in a different state than the Investigator's medical license covers.

- In these cases a relationship between the patient's primary care physician and study Investigator can be established so that the PCP can sign-off on the Physician Order Form.

Patient-Centric Strategies: Patient Reimbursement Program

Challenge: Patients will have to incur out of pocket costs when traveling to the site

- Easy Answer: Use a service to provide reimbursement and pay patient stipends through an ATM card

Patient-Centric Strategies: Patient Reimbursement Program

Challenge: Countries don't allow patient information to be transferred to the company providing reimbursement

- France: Banks froze all of our patient reimbursement accounts because of dummy data. Still an ongoing issue. Looking at a company that has gotten CNIL approval for their process.

Patient-Centric Strategies: Patient Reimbursement Program

Challenge: Culture does not use ATM or credit cards routinely

- Australia: Direct deposit
- Germany: Site reimburses patients directly
- Spain: Does not allow for patient stipends

Patient-Centric Strategies: Patient Reimbursement Program

Challenge: Banks charge fees for use of the ATM card

- Approved fees to be entered as a manual payment on the card

Patient-Centric Strategies: Patient Reimbursement Program

Challenge: Patients do take advantage

- Provide a clear travel policy that the patients review with the study coordinator and sign
- Be sure to include allowances for the caregiver and multi-day visits in the travel policy

Patient-Centric Strategies: Travel Service

Expected Challenge: Patients will incur large costs for hotel and airline travel for this study

- Easy Answer: Engage a travel service that will arrange and pay for these services, so the patient is not burdened

Patient-Centric Strategies: Travel Service

Unexpected Challenges: IRB HIPAA concerns about providing patient information to travel agent (and home health agency and reimbursement service too)

- Ensure the ICF clearly states what information will be provided to the travel agent
- Be ready to provide documentation of the vendor's privacy policy, including the Safe Harbor certification

Other Items to Consider

- Niche CROs provide important insights
- Site Selection
 - ID KOLs was easy but generally less experienced in clinical trials
 - Mostly academic centers
 - Long startup times
 - Negotiated referrals from sites that were not selected

Other Items to Consider



- 13 active sites total for study
- 6 countries: US, Canada, UK, Germany, France, Australia

Other Items to Consider

- Esoteric biomarkers required validation work
- Protocol waivers are frequent
- Patient Management:
 - Provide infrastructure for patient travel across borders
 - Provide infrastructure for patient transfer to another site

Patient Advocacy Groups as partners

- Study Design – make sure the results are meaningful to the patient
- Education about confidentiality, GCP and IRB approvals
- Provide IRB approved content for Facebook, Twitter and Pinterest
- Output:
 - Newsletters
 - E-mail blasts
 - Surveys

■ How are patients finding the website?

- Advocacy Groups
- Facebook Page
- Google Click Ads
- ASTOR Website
- Web Search
- Social Media
- Institution Websites



The screenshot shows the ATHENA website homepage. The header features the ATHENA logo (a stylized starburst) and the tagline "MAPPING THE COURSE OF ALPORT SYNDROME". Navigation links include "What is Alport syndrome?", "Study Site Locator", "Understanding Clinical Studies", "Clinical Studies FAQs", and "Resources & Links". The main content area is titled "About the ATHENA Study: Mapping the Course of Alport syndrome" and includes a photograph of a doctor, a woman, and a young boy looking at a tablet. The text provides information about the study's purpose and eligibility criteria.

ATHENA
MAPPING THE COURSE OF ALPORT SYNDROME

What is Alport syndrome? Study Site Locator Understanding Clinical Studies Clinical Studies FAQs Resources & Links

About the ATHENA Study: Mapping the Course of Alport syndrome

- Do you have Alport syndrome?
- Do you know someone who does?

Now is your chance - do your part to map the course of Alport syndrome. Contact a location near you to learn about the ATHENA study if you:

- Are 16 years of age or older, and
- Have been diagnosed with Alport syndrome

You are not qualified for this study if you:

- Have received a kidney transplant
- Are currently on dialysis

Information obtained from this study is critical in designing future clinical trials in patients with Alport syndrome.

The ATHENA study is designed to learn more about the changes in the kidneys in patients with Alport syndrome.

Find a Study Site Near You

Select a Country or State

Search Reset

Share this website

Advocates get the word out about new sites

ALPORT SYNDROME Alport Syndrome Foundation of USA added 2 new photos.
May 11 at 7:30am · 🌐

It's possible YOU can help Alport Syndrome research!
ATHENA has announced two new study sites within the United States: Texas and Georgia. This observational study on Alport Syndrome also has locations in Vancouver, Toronto and across Europe. Visit AlportStudy.com to learn about qualifications and find a site closest to you. All accepted patients receive free genotyping!
***If you're unsure or uneasy about participating in a study, read about Kristen's ATHENA experience and h... [See More](#)



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Sponsorship of Patient Meetings

We heard you when you asked for more face-to-face interaction with other families. We answered by creating the Alport Family Meetings!



Mark your calendars and plan to attend the event closest to you!

- May 21-22, 2016- Los Angeles - **Registration is now open!**
- July 30-31, 2016 - St. Louis - Registration coming soon!
- Fall 2016 - East Coast location TBA

These informational and action-packed meetings will include breakouts from top doctors in the field of Alport Syndrome research and care, opportunities to socialize with other families, and programs for parents/adults and teen/young adults (13 to 21 years), as well as childcare for school-age children (5 to 12 years).

Register today for the Los Angeles Alport Family Meeting!

Be sure to reserve lodging before April 29 to guarantee the special ASF rate.

Thank you to our National Visionary Sponsor:



Advocates go to Washington

18 shares

Write a comment...

ALPORT SYNDROME **Alport Syndrome Foundation of USA**
March 2 · 🌐

ASF President Sharon Lagas had a very productive day on Capitol Hill advocating for rare disease awareness!
Thank you for your tireless efforts, Sharon! ❤️



Like Comment Share

👍❤️ 88 Chronological



Collaborate with Patient Registries

If you are unable to view this e-mail, [click here](#).



Greetings from the Directors!

Thank you for being a part of ASTOR, the central registry for patients with Alport syndrome. The primary objective of establishing and sustaining this registry is to enable clinical natural history studies and therapeutic trials to be conducted in patients with Alport syndrome. In addition, the registry seeks to provide updates about relevant research and provide the most up-to-date information about Alport syndrome treatments to patients, physicians, and other health care professionals. Please encourage anyone you know with an Alport syndrome diagnosis to contact us and enroll in this important registry!



Clifford E. Kashtan, MD
Executive Director
Division Director and
Professor of Pediatrics
Division of Pediatric
Nephrology



Michelle Rheault, MD
Assistant Director
Assistant Professor of
Pediatrics
University of Minnesota
Masonic Children's Hospital

ASTOR NEWS



The University of Minnesota continues to participate in the ATHENA study. We have enrolled 17 participants at our site, have classified 3 people as screen fails and expect to screen several more potential subjects. Several participants identified through the ASTOR database have been enrolled at other study sites. This study will continue into 2016 and 2017.



For me, it's personal



And it's a Team effort



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References

- Rare Diseases: Common Issues in Drug Development, Guidance for Industry
<http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm458485.pdf>