

# aHUS and Dialysis Insights

## 2016 aHUS Global Poll White Paper

People challenged with a rare disease or chronic illness know all too well that modifications are required in all areas of their lives, which additionally impact other people and their schedules. Modifications stretch far beyond time, appointments, relationships, and lifestyles to include a wide array of multiple societal and economic pressures.

To gain insight into the aHUS patient experience, the aHUS Alliance of patient organizations conducted a 2016 aHUS Global Poll open to all aHUS adult patients and caregivers of pediatric aHUS patients. Launched on world Rare Disease Day, 233 people from 23 nations responded during the polling period from 29 February through 15 April 2016. The survey premise for this patient and caregiver poll was to gather data that may provide better understanding and insight into aHUS diagnosis, treatment, and medical care.

Three questions specific to dialysis were part of the 2016 aHUS Global Poll to determine: whether dialysis was needed during the initial onset of aHUS activity (Question 15), the type or modality of dialysis utilized (Question 16), and what respondents consider to be the most significant issues facing aHUS patients on dialysis (Question 18). Currently the only approved drug to treat patients with aHUS is eculizumab (product of Alexion Pharmaceuticals), but it is not available at all in many countries, and drug access can be further limited by a country's healthcare or governmental regulations and policies. There are multiple studies which illustrate the ability of eculizumab to halt the uncontrolled complement activation that is a hallmark of aHUS activity.<sup>1</sup> The 2016 aHUS Global Poll results noted here include eculizumab within the context of discussion for aHUS patients to retain kidney function and thus avoid dialysis. As research and clinical trial data yield further developments within a rapidly changing landscape of potential therapies for rare diseases, the aHUS Alliance looks forward to providing additional information and insight on expanded therapeutic drug options for aHUS patients. (See note prior to citations.) Data from the 2016 aHUS Global Poll provides a deeper look into specific topics, offering greater understanding with views into the aHUS patient experience.<sup>2</sup>

### Question 15 – Need for Dialysis at Onset

Slightly more than two-thirds (68%) of aHUS patients needed dialysis at onset or required dialysis on a continuing basis, as represented by respondents in the 2016 aHUS Global Poll. In countries where eculizumab is available, 46% of respondents noted kidney function recovered, and dialysis was stopped. In nations outside the US & EU this 46% kidney recovery rate drops sharply, with only 30% of aHUS patients reported to regain kidney function (eGFR) and thus able to discontinue dialysis. Why?

A direct correlation of recovery of kidney function with eculizumab therapy for aHUS patients on dialysis has been reported in the literature. In a 2016 study of 41 adult aHUS patients<sup>3</sup>, 24 patients required baseline dialysis with five patients recovering kidney function before eculizumab therapy was initiated. Of the remaining 19 aHUS adult patients who were treated with eculizumab, 15 patients (79%) were able to discontinue dialysis and the study further reported quality-of-life measures significantly improved. In countries without access to eculizumab the aHUS patient outcomes differ sharply, with a more negative patient outcome in regard to dialysis needs. “Access to eculizumab for treatment of all aHUS patients worldwide plummets from 77% to only 37% of poll respondents in nations outside of the USA and Europe.”<sup>4</sup>

Many patient organizations and aHUS social media outlets around the world offer anecdotal reports that eculizumab is not available in their nation, or can be accessed only under limited conditions. The Alexion corporate site offers a ‘Select a Country’ tab heading, noting its operations in various nations. Listed are: (in North America) Canada, USA; (in Latin America) Argentina, Brazil, Colombia, Mexico; (in Europe, the Middle East, Africa) Alexion Europe, Belgium, Denmark, France, Germany, Ireland, Italy, Netherlands, Norway, Russia, Spain, Sweden, Switzerland, Turkey, United Kingdom; and (in Asian Pacific) Australia, China, India, and Japan. While that list indicates an Alexion corporate presence by geographic region, it should not be mistaken for an indication of eculizumab availability within those or other nations. Currently, eculizumab is not available as a therapy for any aHUS patient in India despite that country’s inclusion within the Alexion Asian Pacific group. Furthermore, drug access for aHUS patients can differ across a single nation, with some patients facing restrictions or limited access to eculizumab according to their regional healthcare policy and/or patient medical status.

Why aren’t all physicians able to prescribe eculizumab for their aHUS patients? According to 2016 aHUS Global Poll respondents, almost 4 in 10 aHUS patients note their physician reports that eculizumab is not available as a therapeutic drug option in their country. Cost is most often stated as the rationale for why healthcare and government policy blocks orphan drug use for small populations of rare disease patients. “Government interventions and regulations may opt to withhold a life-saving drug solely due to its high price and cost-effectiveness. Processes related to drug pricing, reimbursement, and thereby availability, vary between countries, thus having implications on patient care.”<sup>5</sup>

## 2016 aHUS Global Poll

### Q. 15 Did you (they) need dialysis during the initial illness?

2/3 of aHUS Patients worldwide (68%) needed Dialysis at Onset, or required Dialysis on a Continuing Basis



**In countries where eculizumab is available, 46% of respondents noted kidney function recovered, and dialysis was stopped.**  
**In countries without access to eculizumab, aHUS patient outcomes decline:**

**In nations outside the US & EU the 46% kidney recovery rate drops sharply, with only 30% of aHUS patients reported to regain kidney function (eGFR) and able to discontinue dialysis.**

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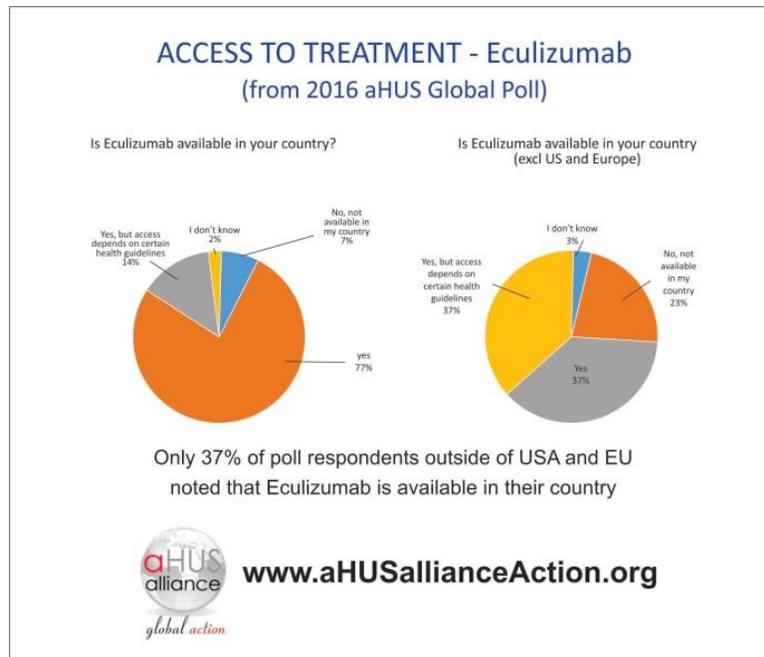
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## Graphic from the June 2016 RareConnect Webinar: aHUS Global Poll

<http://ow.ly/YMLA305r6zb>

### Access to Eculizumab

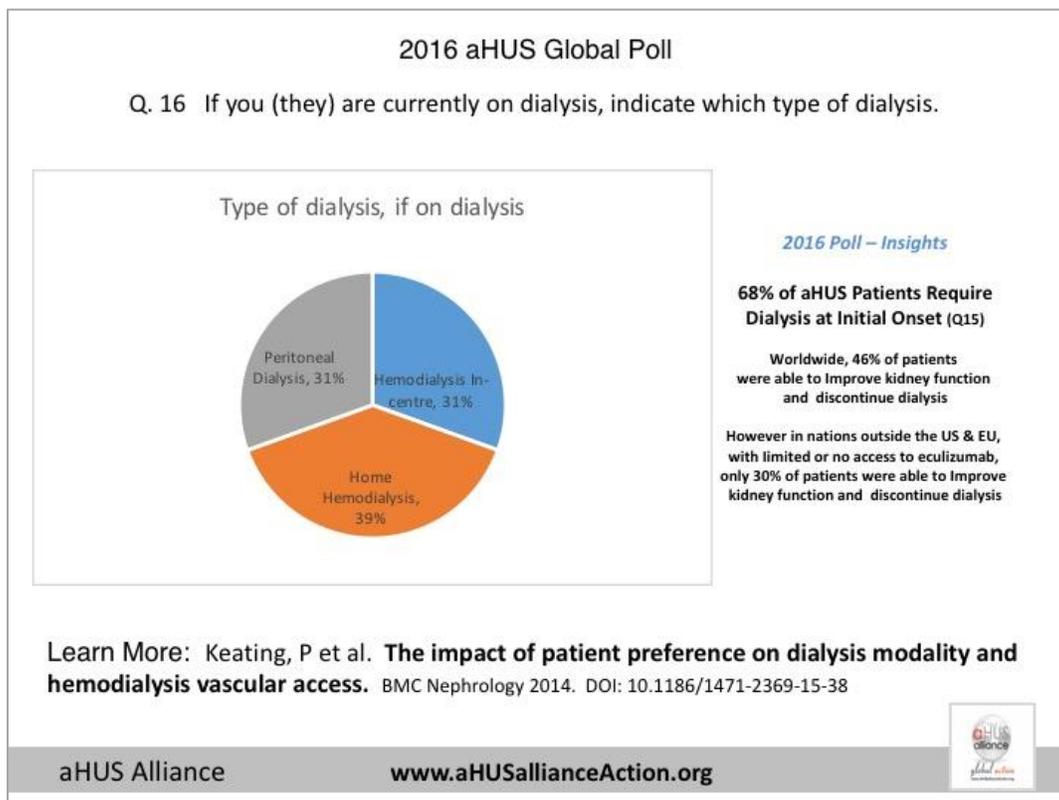


## Question 16 – aHUS Patients and Type of Dialysis

Whereas 68% of respondents noted that dialysis was needed at initial onset of aHUS activity (Q 15 from the 2016 aHUS Global Poll, N=233), poll question 16 examined type of dialysis modality preference for those aHUS patients needing dialysis. Adult aHUS patients and responses from caregivers of pediatric aHUS patients indicate just under half of aHUS patients (46%) need only temporary, stabilizing dialysis intervention at initial onset of aHUS episodes.

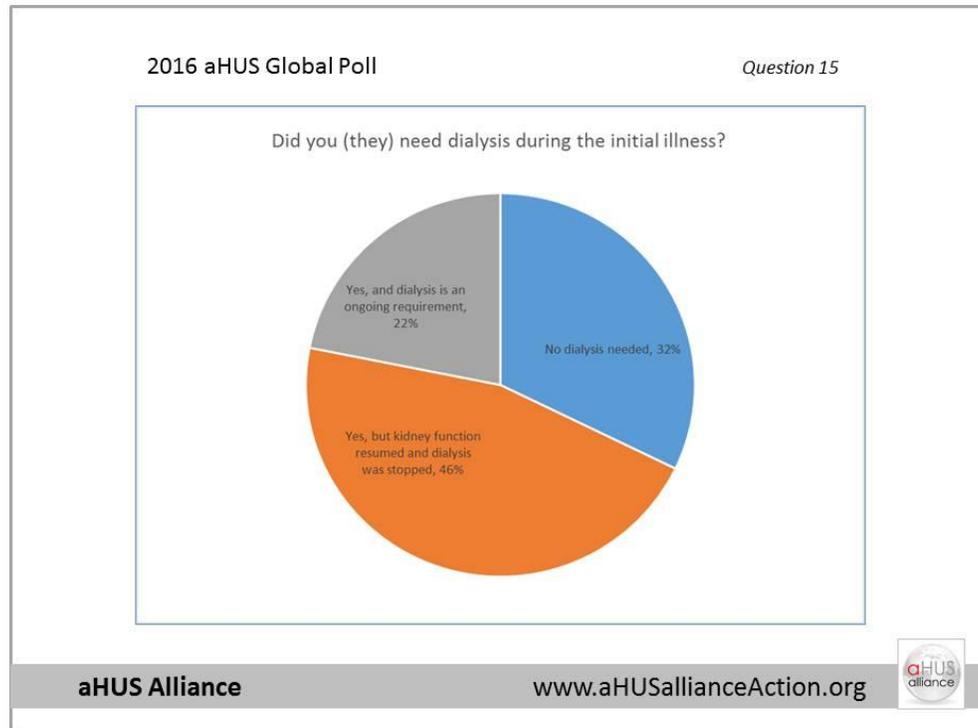
About 1 in 5 aHUS patients (22%) experienced severely reduced kidney function or kidney failure (late stage CKD or ESRD), with a permanent need for dialysis. Of the aHUS patients needing dialysis, about one-third of poll respondents (31%) utilize peritoneal dialysis and slightly more than two-thirds of patients preferring hemodialysis, with 39% of those choosing home hemodialysis.

“Compared to healthy people, patients with chronic kidney disease face many difficulties in participating in various fields of life, such as paid work, sports and social activities.”<sup>6</sup> Question 18 of the aHUS Alliance poll explored this aspect further, with respondents providing insight into life challenges for aHUS patients on dialysis.



**2016 aHUS Global Poll, 233 Respondents from 23 Nations**

**(Conducted 29 Feb through 15 April 2016)**



Question 18 – What are the most significant issues facing aHUS patients on dialysis?

Not surprisingly, the most prevalent concern of aHUS adult patients and caregivers of pediatric aHUS patients was the disruption dialysis treatment had upon their normal routines (about 46%, 107 of 233 respondents). Other responses were related to quality of life, medical concerns, and impact on work place or school issues.

About one-third of respondents faced issues related to the impact of dialysis on their family schedule or lifestyle (33%), with slightly more than one in four noting that dialysis negatively affects their work quality or school experience (28%). Dialysis co-morbidities and its impact on other organs were of concern to 28% of poll respondents, but that statistic would be amplified should consideration be given to other medical complications (such as infection in lines/fistulas – with 40 mentions, or fluid overload – with 54 mentions, or other related physical health problems).

Both dialysis and aHUS as a disease may impact body systems and organs other than the kidneys. “Most patients with chronic kidney disease (CKD) have other diseases that cause CKD or contribute to the risk of cardiovascular events or death. Managing these comorbidities is a challenge. Diabetes, hypertension, cardiovascular disease, and anemia are more common in CKD patients than in individuals who do not

have CKD, and the prevalence of these comorbidities increases as CKD progresses. Most patients (86%) with advanced CKD have at least 1 comorbidity.”<sup>7</sup>

Dialysis comorbidities and aHUS activity presenting with extra-renal involvement both may cause complex treatment concerns for aHUS patients and medical professionals. “Complement over activation in combination with defects in its regulation is described in an increasing number of TMA and if primary for the disease denominated as atypical hemolytic-uremic syndrome. Although TMA predominantly affects the renal microvasculature, extra-renal manifestations are observed in 20% of patients including involvement of the central nerve system, cardiovascular system, lungs, skin, skeletal muscle, and gastrointestinal tract.”<sup>8</sup>

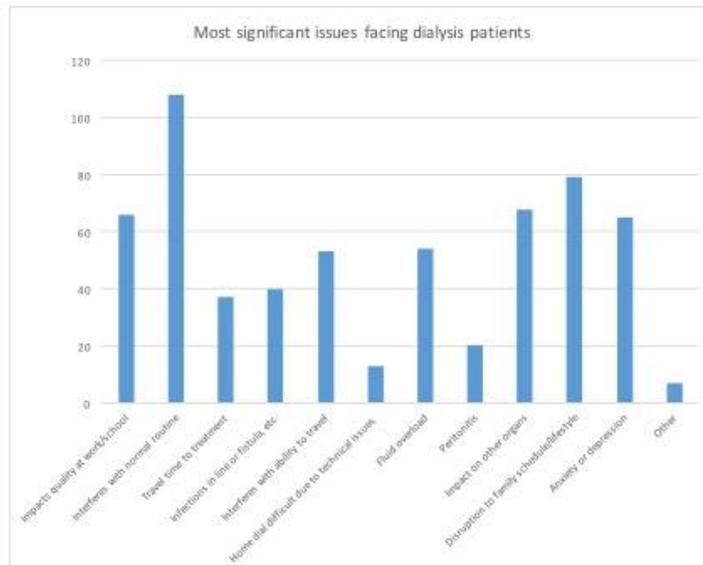
Mental health issues may be a concern for aHUS patients on dialysis, with about 1 in 4 patients represented in the 2016 aHUS Global Poll experiencing anxiety or depression (27%). “It should be noted that depression is the most common psychological complication of haemodialysis, which has a negative impact on the quality of patients’ life and their caregivers, affecting negatively their social, economic and psychological well-being. Depression includes high annual mortality, frequency of hospitalization, reduced compliance to medications and decreased quality of life.”<sup>6</sup>

Understandably health-related quality of life (HRQOL) focuses on patients but some components, especially for pediatric patients, cast ripples across many areas of patient life and therefore affect a wide number of people and relationships. “Today, the HRQOL concept addresses the effects of individual health (including the effects of both disease and its treatment) on physical, cognitive, and social functioning in day-to-day life. Patients with ESRD who are treated with dialysis experience many threats to HRQOL, both from the myriad symptoms of ESRD itself and from the physical and mental burden of dialysis treatment.”<sup>9</sup>

Multiple responses were allowed for Question 18 on the 2016 aHUS Global Poll, with the key concern being impact of dialysis upon the aHUS patient’s normal routine (noted by 108 respondents). Other top concerns of respondents were (in decreasing order, as mentioned by number of respondents): Disruption to the Family Schedule/Lifestyle (79), Impact on other Organs (68), Impacts Quality at Work/School (66), Anxiety or Depression (65), Fluid Overload (54), and Interferes with Ability to Travel (53). Other areas were mentioned, but garnered 40 or less responses by poll participants.

## 2016 aHUS Global Poll

Q. 18 Which do you consider to be the most significant issues facing dialysis patients?



### 2016 Poll – Insights

#### Top aHUS Dialysis Concerns

- 46% Interferes w/ Normal Routine
- 34% Disruption to Lifestyle/ Family Schedule
- 29% Impact on other Organs
- 28% Negative effect, Quality at Work/School
- 27% Anxiety or Depression

*Multiple responses were allowed.*  
(Percent of total poll responses.)

Learn More: Stavroula, G et al. **Concerns of patients on dialysis: A Research Study.** HEALTH SCIENCE JOURNAL , VOLUME 8 (2014),ISSUE 4 <http://ow.ly/sm2j301Ld5P>

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2016 aHUS Global Poll – Utilizing the Data regarding aHUS Patients on Dialysis

Quality of life measurement tools exist for patients with kidney disease (such as KDQOL) and some studies examine improvement of quality of life characteristics for transplant patients. Not surprisingly, ongoing dialysis creates multiple challenges for patients and quality of life measures improve dramatically for patients who have undergone kidney transplants. <sup>9, 10</sup>

When all aspects are considered, access to eculizumab and future drugs in development for aHUS makes the most cost-effective and long-term solution to maintaining kidney function in patients with this very rare disease. For those patients whose aHUS activity is so severe that kidney function is lost (End Stage Renal Disease) and dialysis is needed, kidney transplantation with supportive eculizumab therapeutic dosing is necessary to maintain the graft. “Renal transplantation remains the best treatment option for ESRD, providing recipients with an increased survival and quality of life, at lower costs than other renal replacement therapies.” <sup>10</sup>

Maintenance dialysis is an economic burden across all disease populations, for both patients and healthcare systems. “...the annual worldwide cost of maintenance ESRD therapy in the year 2001, excluding renal transplantation, will be between \$70 and \$75 billion US dollars. If current trends in ESRD

prevalence continue, as seems probable, the ESRD population will exceed 2 million patients by the year 2010. The care of this group represents a major societal commitment: the aggregate cost of treating ESRD during the coming decade will exceed \$1 trillion, a thought-provoking sum by any economic metric.”<sup>11</sup> More research is needed to provide updated information and a holistic view of the socio-economic impacts of dialysis.

When considering overall patient care costs, some look to the future of orphan drug development and to use of artificial kidneys. Perhaps biosimilars will yield lower orphan drug costs. “Although a range of regulatory definitions exist, a biosimilar drug generally is defined as a biological compound that is highly similar to the reference drug, with no clinically meaningful differences in safety, purity, and potency. In addition, biosimilars can be characterized by a value proposition centered on reducing healthcare costs while maintaining clinical efficacy and safety outcomes similar to the originator biologic. These objectives become particularly laudable for patient populations receiving biologic agents to treat chronic or life-threatening conditions.”<sup>12</sup> The aHUS community, both patients and medical professionals, currently have limited treatment options although scientific advancement does progress over time. Early discovery in the field of artificial kidneys offered limited potential. “No tissue-engineered kidney yet represents a credible alternative to extracorporeal dialysis; in fact, the most widely proclaimed bioartificial kidney is being pursued as more effective (and more expensive) treatment for acute dialysis, not as an implantable substitute for maintenance dialysis.”<sup>11</sup> Currently there are newer developments are of interest to aHUS patients on dialysis, such as a wearable artificial kidney (WAK) or implantable artificial kidney (IAK), though problems such as technical challenges are among the issues that remain unresolved.<sup>13</sup>

It’s clear from the 2016 aHUS Global Poll – patients and caregivers view access to eculizumab as an essential component to aHUS patient care, which echoes evidence-based findings across research and clinical trials. At present, aHUS patients receiving early treatment with eculizumab can maintain renal function and avoid dialysis, if physicians in that nation are able to prescribe this drug. For aHUS patients with ESRD, medical literature presents favorable outcomes when renal transplant with supportive eculizumab therapy is available to maintain the graft. By all metrics, aHUS patient outcomes improve when data-driven medicine centers patient care. The future of orphan drug development may bring lower cost but still effective aHUS therapeutics to market, but access now to eculizumab can either avoid the need for dialysis or can be part of a renal transplant plan for aHUS patients who have lost kidney function. Without weighing the full societal and broad economic impact of dialysis across all aspects, policy makers in some nations voice support for patient-centered and evidence-based medical care while still restricting patient healthcare options and drug access. While everyone looks forward to a brighter future, with lower healthcare costs and a better quality of life – for aHUS patients around the world, access to all current and developing treatment options is a future that needs to begin NOW.

*NOTE:* With medical advancements, new research will likely bring rapid change to the landscape of targeted therapies to treat aHUS patients. Updates, news and information related to aHUS can be viewed via national patient organization sites, and on aHUS Alliance outlets as an international networking hub for collaborative partnerships.

**Website:** [www.aHUSallianceAction.org](http://www.aHUSallianceAction.org)

Twitter: [@aHUSallianceAct](https://twitter.com/aHUSallianceAct) Facebook: [aHUS Alliance](https://www.facebook.com/aHUSAlliance) Email: [info@aHUSallianceaction.org](mailto:info@aHUSallianceaction.org)

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## **Learn More about Dialysis**

### **Dialysis Choices**

Written for Patients: Dialysis Options

This patient-friendly version that explains dialysis modalities (types), with recommendations for patients with end-stage renal disease (ESRD). Various options for renal replacement therapy (RRT) are outlined, with recommendations issued by the European Renal Best Practice (ERBP) Expert Group.

<http://ow.ly/YSWT301Mkqp>

### **Dialysis Modalities**

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