atypical Hemolytic Uremic Syndrome

aHUS CANADA

Supporting patients and families living with aHUS

Fact Sheet

About aHUS

- Atypical Hemolytic Uremic Syndrome (aHUS) is a very rare, chronic and life-threatening genetic condition
- Affecting between 60 to 90 patients in Canada, the incidence of aHUS is estimated to be 1 in 500,000 people per year in the United States[1]
- aHUS can occur at any age, and while the disease does affect children, almost one-half of people affected are adults.[2]
- aHUS is caused by chronic, uncontrolled activation of the complement system, a part of the body's natural immune system
- As a result, the immune system attacks the body's unhealthy and healthy cells, which can cause abnormal blood clotting and blood vessel damage[3,4]
- The presence of blood clots causes damage to organs, leading to heart attack, stroke, kidney failure and death[5]
- Within a year of diagnosis, over half of patients will need dialysis, will have irreversible kidney damage, or will not survive[6]
- The majority of patients progress to end-stage kidney failure within three years of diagnosis[5,7]
- Death rates amongst aHUS patients are as high as 25 per cent, and progression to end-stage kidney disease occurs in more than 50 per cent of patients[5,8]
- Kidneys are often transplanted in aHUS patients with permanent kidney failure, however, the disease recurs in 60 per cent of patients, and more than 90 per cent of patients experience failure of transplanted kidney[9]

Diagnosis

- Due to the rarity of aHUS, it can be difficult to diagnose, and many doctors have never encountered a case of it
- The causes of aHUS are not fully understood, but in 70 per cent of cases it is associated with an underlying genetic or acquired abnormality of the complement system[10]
- Doctors and their health care team must look at many factors when making a diagnosis – including clinical symptoms, lab findings, and results from more specialized tests such as gene analysis[11]
- During initial onset of aHUS, or during recurring episodes, tell-tale signs can be detected from lab findings relating to:[9]
    - platelet levels
    - hemoglobin and haptoglobin levels
    - creatinine levels
    - BUN (blood urea nitrogen) levels

Symptoms

- aHUS disease can be characterized by three key features:[12]
    - thrombocytopenia (low platelet count in the blood)
    - anemia (low red blood cell/platelet count in the blood)
    - kidney symptoms (starting as acute kidney failure but can progress to end-stage kidney disease)
- aHUS can be triggered by pregnancy, certain drugs, or an infectious event[1]
- There are a number of symptoms secondary to kidney failure, which include:[10]
    - nausea and vomiting
    - confusion
    - shortness of breath (dyspnea)
    - fatigue

- In aHUS, patients present with symptoms of diarrhea, fatigue, irritability, and lethargy to a point where hospitalization is needed[12]

Treatments – Then and Now

Plasma Therapy & Dialysis

- The prognosis for patients with aHUS is very poor,[13] with existing supportive therapies unproven and unreliable
- The management of aHUS has relied on plasma infusion and plasma exchange therapies with variable results[14]
- To date, there have been no well-controlled trials that show plasma exchange or plasma infusion to be safe or effective in aHUS[15]
- In studies where the majority of patients with aHUS were treated with plasma therapy, patient outcomes were reported as being poor[16]
- Despite plasma exchange or plasma infusion, 65 per cent of all aHUS patients die, require dialysis, or have permanent kidney damage within the first year after diagnosis[6]
- Dialysis cannot completely compensate for the loss of kidney function, and can lead to deadly infections and shortened life expectancy [17]
- Complications related to plasma exchange have been reported to occur in up to 55 per cent of plasma exchange sessions in children and in 15 per cent of sessions in adults[16]

Soliris

- Soliris (eculizumab) was recently approved by Health Canada as the first and only pharmaceutical treatment for aHUS[18]
- Soliris has shown greater efficacy than plasma therapy in the prevention and treatment of aHUS[16,19]
- The effectiveness of Soliris has revolutionized the management and outcomes of aHUS and has opened up the possibility of kidney transplantation in patients with aHUS[16]
- Soliris is on its way to becoming a new standard of care for aHUS, providing improved control of the disease over plasma exchange, with a good safety profile[16]
- Experts recommend the use of Soliris as first-line therapy in children with aHUS, and for adults with an unequivocal diagnosis of aHUS[16]
- Clinicians also advise that patients with native or transplanted kidneys whose aHUS recurs be treated with Soliris[16] and that treatment be initiated as early as possible for optimal recovery of kidney function[19]
- Switching from plasma therapy to Soliris has been shown to improve kidney function even in patients with long-lasting and stable chronic kidney disease[16]
- Evidence of plasma resistance or dependence should lead to a prompt switch to Soliris for optimal recovery of kidney function[16]
- In clinical trials, Soliris has been proven effective in preventing blood vessel damage and abnormal blood clotting[20, 21]
- In June 2013, an international study in the *New England Journal of Medicine* showed aHUS patients treated with Soliris were able to discontinue plasma infusion/exchange and dialysis therapies, and saw improved kidney function, reduced blood vessel damage and decreased risk of blood clots[22]
- Soliris has also been shown to significantly improve patients' health and quality of life[23]

Access to Treatment

- In Canada, Quebec is the only province to provide aHUS patients with public funding for Soliris through their exceptional access program, *Patient d'exception*
- In September 2013, National Health Service (NHS) England recommended that Soliris be funded for aHUS patients, following a positive reimbursement recommendation from the Clinical Priorities Advisory Group (CPAG). The funding decision is pending final ratification from the National Institute for Health and Care Excellence (NICE), anticipated in Spring 2014

- Soliris is approved and publicly funded in Canada for the treatment of another ultra-rare and life-threatening disorder called paroxysmal nocturnal hemoglobinuria (PNH)
- With so few patients living with this ultra-rare disease, the cost of funding Soliris represents a minute portion of public health spending

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