

NHSC National Horizon
Scanning Centre

Canakinumab for cryopyrin associated periodic syndrome

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Canakinumab for cryopyrin associated periodic syndrome

Target group

Cryopyrin associated periodic syndromes (CAPS):

- Muckle-Wells Syndrome (MWS).
- Familial cold autoinflammatory syndrome (FCAS) also known as familial cold urticaria (FCU).
- Neonatal onset multisystem inflammatory disease (NOMID) also known as chronic infantile neurologic cutaneous articular syndrome (CINCA).

Background

CAPS is a family of three autoinflammatory syndromes MSW, FACS and NOMID. These syndromes have been linked to mutations in the gene (*CIAS-1*) encoding cryopyrin (NALP3), an immune system regulatory protein. Symptoms include varying severity of fever, fatigue, skin rashes, conjunctivitis, painful joints and muscles, and severe headaches associated with chronic meningitis. Skeletal and neurological abnormalities during growth and development are quite common, and include distortion of the face, knees, deafness and sometimes blindness. Features of the disease generally become evident shortly after birth, and those relating to acute inflammation persist in a fluctuating manner for the remainder of the patient's life. About 25% of patients develop systemic AA amyloidosis as a result of the chronic inflammation, typically in early adult life, resulting in renal failure, dialysis dependence and death within 5-10 years. Hearing loss during childhood is common.

Technology description

Canakinumab (ACZ885) is a fully human monoclonal antibody raised against IL-1 β which is involved in inflammation and tissue destruction. The mutations in cryopyrin are believed to cause over production of IL-1 β ¹. An adult dose is 150mg by subcutaneous injection (SC) every two months, a child's dose is 2mg/kg SC every two months.

Innovation and/or advantages

There is currently no licensed treatment for CAPS in Europe. It is anticipated that early and prolonged treatment with canakinumab will reduce or prevent long-term neurological, skeletal and amyloid sequelae.

Developer

Novartis Pharmaceuticals UK Ltd.

Availability, launch or marketing dates, and licensing plans:

Canakinumab has been given orphan drug status in the EU and is currently in phase III clinical trials.

Clinical need and burden of disease

Within the EU CAPS is estimated to affect 2,500 people². There are believed to be no more than 30 cases in the UK^a.

Existing comparators and treatments

There is no standard therapy for CAPS within the EU, treatments that have been used to date included:

^a Expert provided information.

- Currently severe flares are managed symptomatically with anti-inflammatory products.
- Recently riloncept was licensed for CAPS in the USA designated given orphan drug in the EU.
- Daily injections of anakinra (SC) have been reported to be effective in anecdotal case reports but has not been tested or evaluated for safety in controlled clinical trials.

Efficacy and safety

Trial	ACZ885; MWS, FCAS and NOMID; phase II.	NCT00465985: ACZ885 vs placebo; MWS; phase III ³ .	NCT00685373: ACZ885; CAPS; phase III ⁴ .
Sponsor	Novartis	Novartis	Novartis
Status	Published ^{5,6}	Ongoing	Ongoing
Location	EU (inc UK) and India.	EU (inc. UK), India, USA.	EU (inc UK), Turkey, USA.
Design	Open label, uncontrolled.	Randomised, double blind, placebo control.	Open label, single group.
Participants in trial	n=34: 4-75 years; molecular diagnosis and active disease . Stage 1: (4 patients) single dose 10mg/kg intravenous (IV), second single dose of 150mg SC. Stage 2: (30 patients) single dose 150mg SC on each relapse (children 4-16 yrs dose 2g/kg SC). If required rescue dose 5-10mg/kg IV.	n= 36; 4-75 years; molecular diagnosis and clinical symptoms resembling MWS. Part I: 8 wk open label active treatment Part II: 24 wk double blind, placebo-controlled. Part III: 8 wk open label, active treatment.	n=80; 4 years or older. An ACZ885 dose of 150mg (SC) every 8 wk.
Follow-up	Once phase II trial completed patients moved to either NCT00465985 or NCT00685373 phase III clinical trials.	48 wk.	6 months to 2 years depending upon timing of recruitment into study.
Primary outcome	Response and time of relapse.	Global assessment autoinflammatory disease activity, assessment of skin disease and inflammatory markers.	Adverse events including infections.
Secondary outcomes	Safety, tolerability and immunogenicity.	Overall response, disease progression with deafness, kidney function, neurological and ophthalmological symptoms.	Global assessment of autoinflammatory disease activity, assessment of skin disease and inflammation markers.
Key results	Improved clinical symptoms within 1 day and complete clinical remission after 7 days ⁵ . Median time to re-dosing was 92 days after first and 66 days after second treatment cycles ⁶ .	–	–
Expected	–	Completion expected	Completion expected

reporting date		October 2008.	June 2010.
Adverse effects	7 patients developed upper respiratory tract infections, 2 patients had elevated amylase and lipase, one patient experienced SAE ⁶ .	–	–

Estimated cost and cost impact

The cost of canakinumab has yet to be determined.

Potential or intended impact – speculative

Patients

- | | | |
|---|--|---|
| <input checked="" type="checkbox"/> Reduced morbidity | <input type="checkbox"/> Reduced mortality or increased survival | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers |
| <input type="checkbox"/> Quicker, earlier or more accurate diagnosis or identification of disease | <input type="checkbox"/> Other: | <input type="checkbox"/> None identified |

Services

- | | | |
|--|--|---|
| <input type="checkbox"/> Increased use | <input type="checkbox"/> Service reorganisation required | <input type="checkbox"/> Staff or training required |
| <input checked="" type="checkbox"/> Decreased use e.g. shorter length of stay, reduced referrals | <input type="checkbox"/> Other: | <input type="checkbox"/> None identified |

Costs

- | | | |
|--|--|---|
| <input type="checkbox"/> Increased unit cost compared to alternative | <input type="checkbox"/> Increased costs: more patients coming for treatment | <input type="checkbox"/> Increased costs: capital investment needed |
| <input checked="" type="checkbox"/> New costs: | <input checked="" type="checkbox"/> Savings: Potential if efficacy reduces other NHS costs | <input type="checkbox"/> Other: |

References

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