



HAE Australasia

hope • advocacy • education

Australasian Patient Organisation for Hereditary Angioedema

Patient and Carer Webinar

HAE Basics, Treatment and Clinical Trials

Prof CH Katelaris

Campbelltown Hospital and Western Sydney University

Acknowledgement of Country

Acknowledgement of Country

We would like to begin by acknowledging the Traditional Owners of the land on which we meet today. We would also like to pay respects to Elders past and present.

HAE Basics, New & Current
Treatments, Clinical Trials
Prof. Connie Katelaris



Hereditary Angioedema

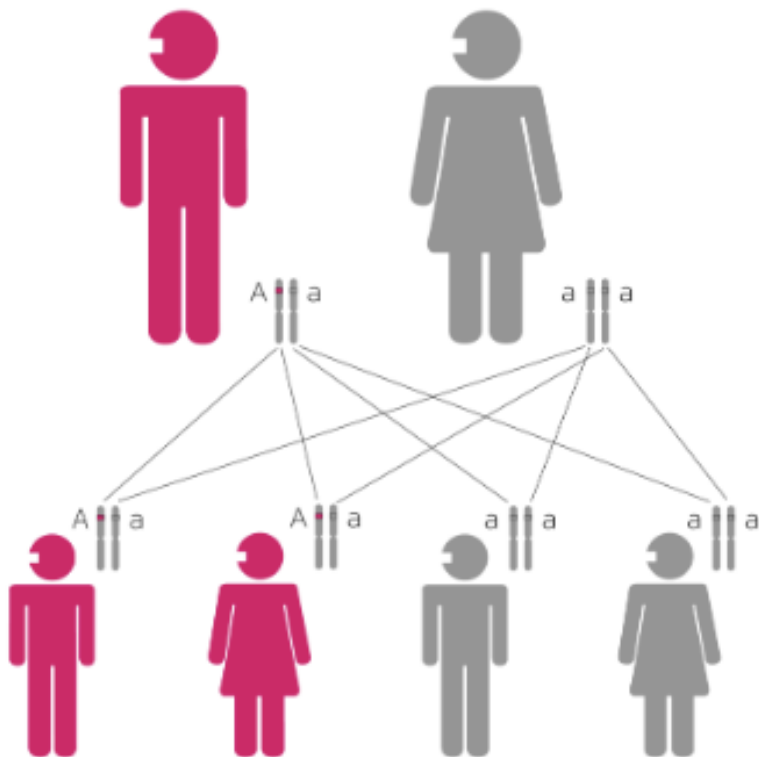
Rare, inherited condition -1:50,000 population

Caused by a deficiency in C1 inhibitor protein

Random angioedema or swelling attacks that can affect many parts of body and can be fatal



HAE Inheritance



What does autosomal dominant inheritance mean?

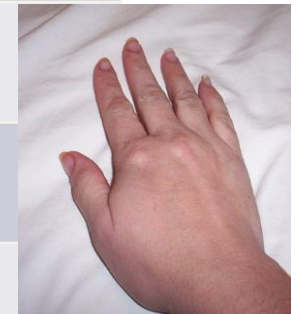
- Autosomal means that the altered gene is located on one of the 22 pairs of non-sex chromosomes (autosomes) and can be inherited from either the mother or the father. This type of inheritance is not limited to a specific gender and can affect both males and females
- It is usually seen in every generation of a family, with affected individuals typically having an affected parent. Each child of an affected parent has a 50% chance of inheriting the mutated gene and developing the autosomal dominant disease
- Spontaneous mutations occur -25% have a spontaneous mutation

Areas involved in HAE attacks

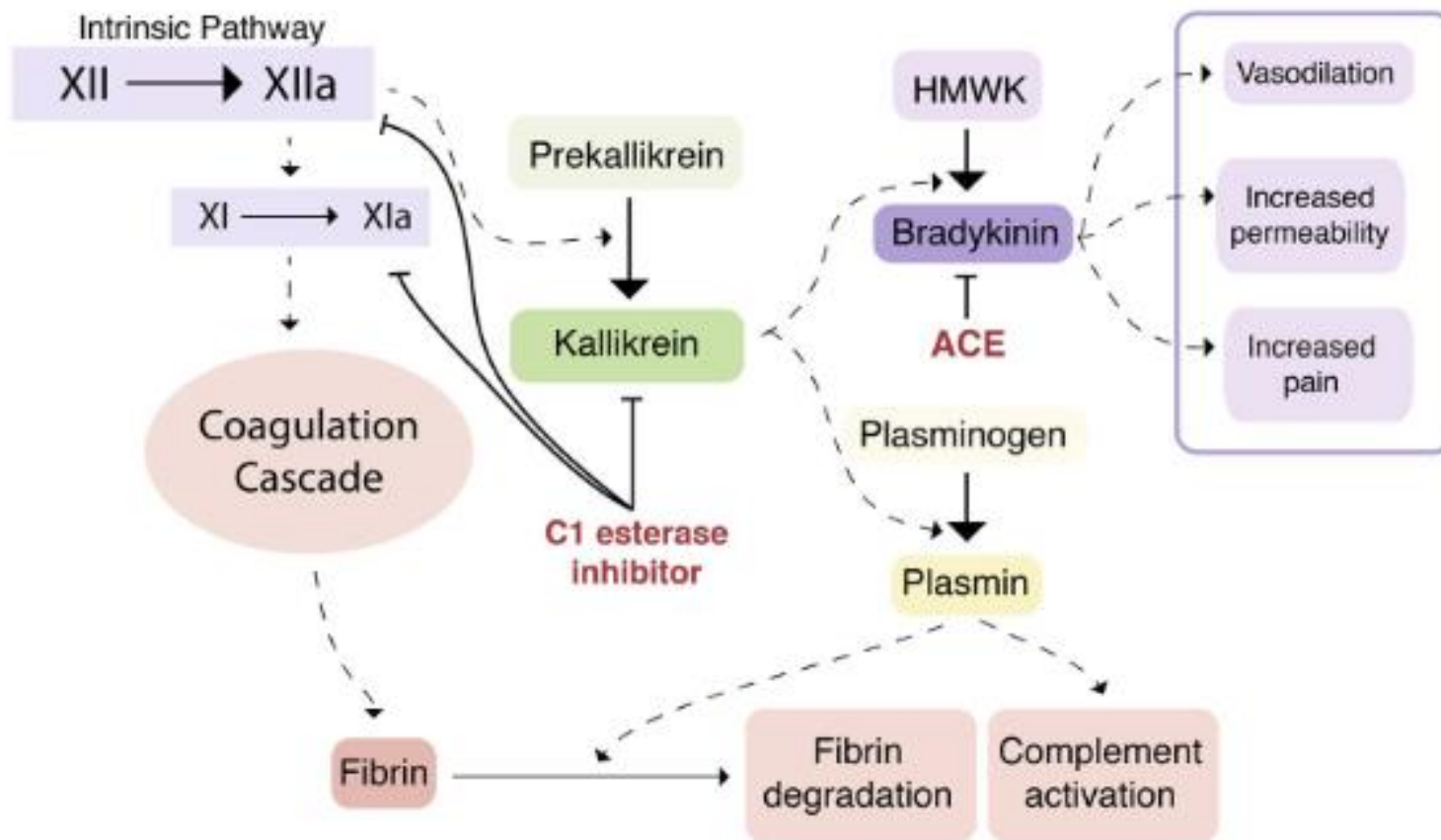
Swelling can occur in any part of the body and often involves multiple sites

In a study by Bork et al in 2006:

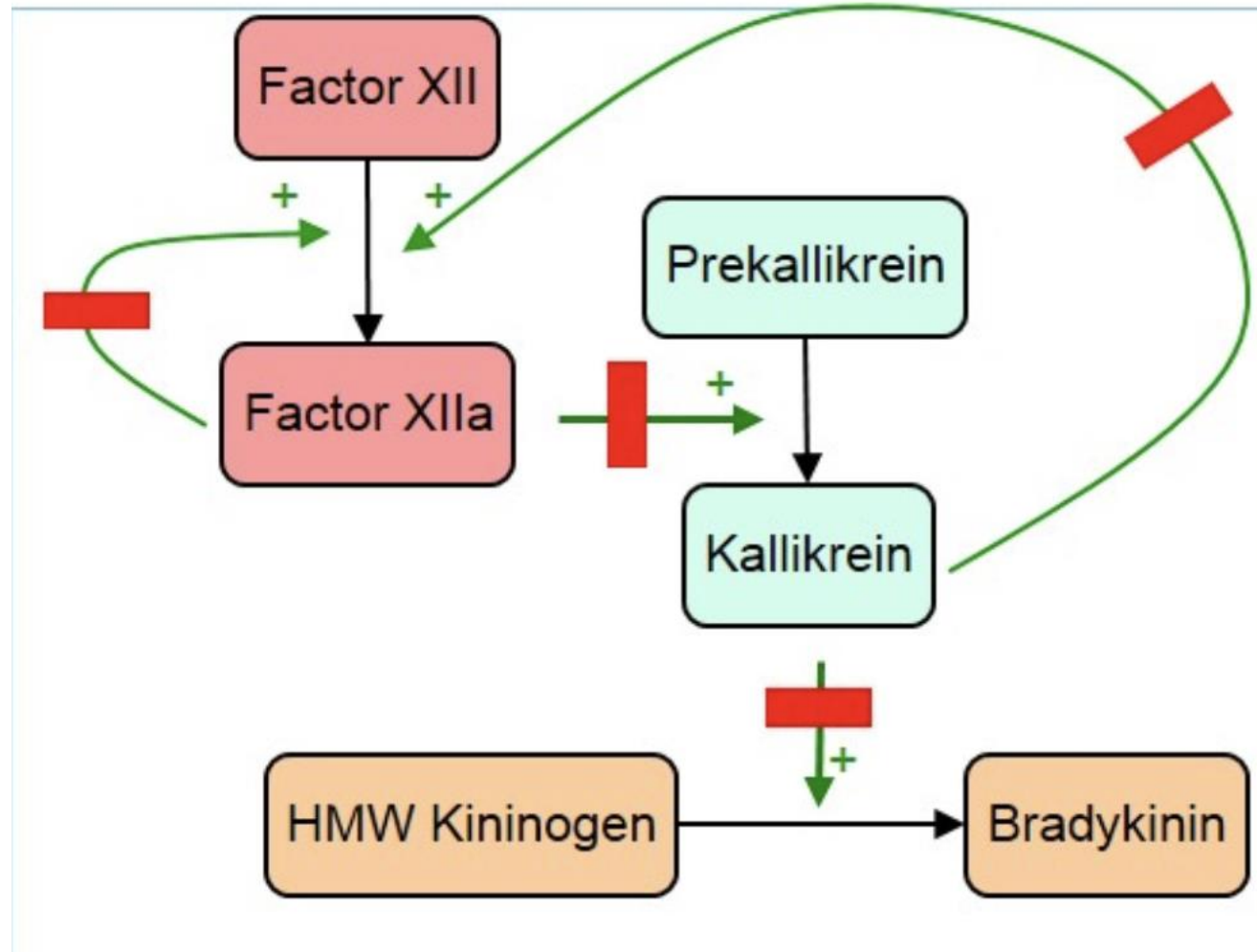
Site	Incidence
Extremity	97.5%
Abdomen	93%
Face	79%
Genital	65%
Laryngeal	52%

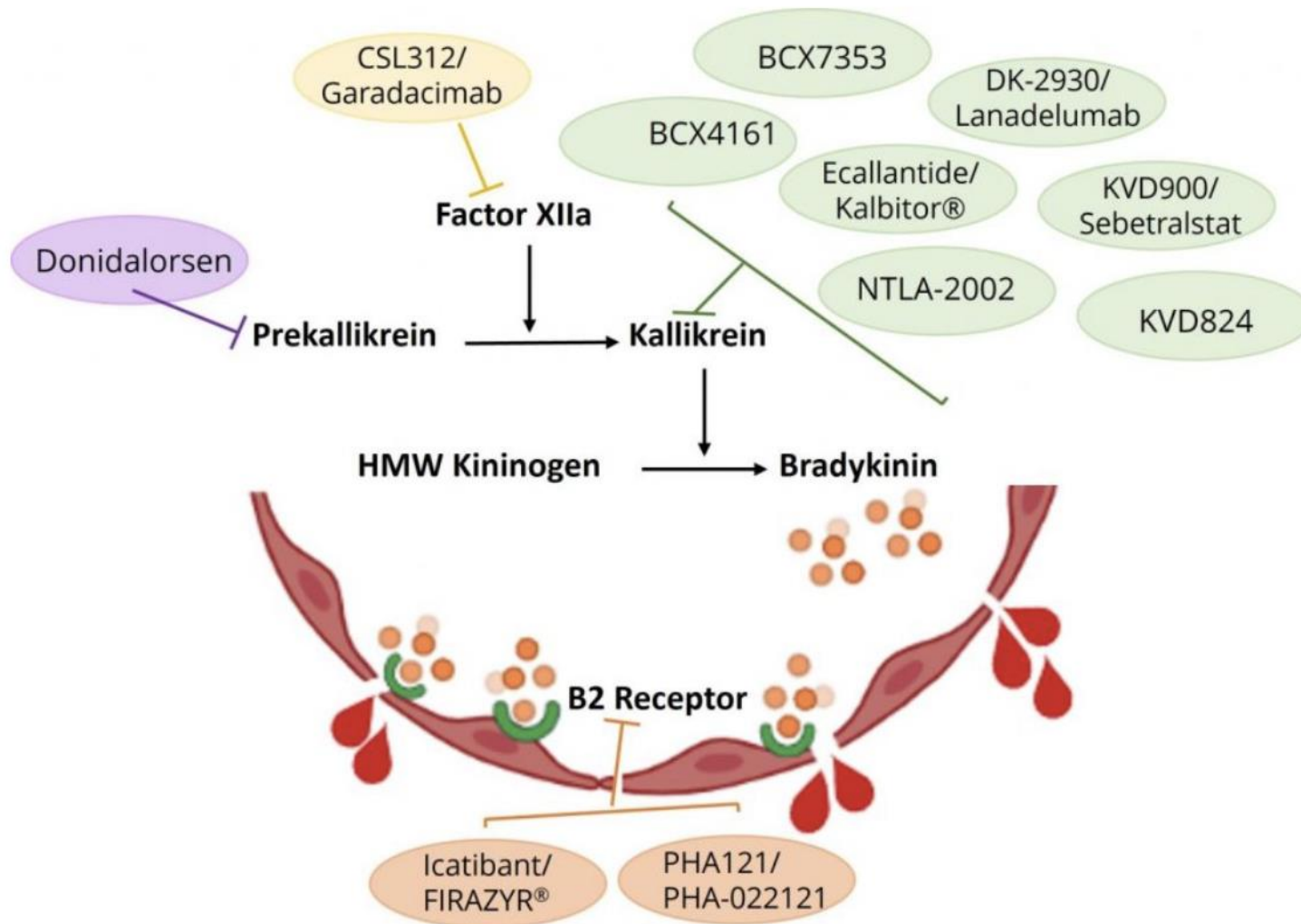


Kallikrein-Bradykinin Pathway



C1 inhibitor blocks pathway at multiple sites





Consensus statements on treatment goals

The ultimate goals for HAE treatment are to...

95%

..achieve complete disease control

100%

...normalise patients' lives

Three levels of treatment are necessary

On demand
treatment
(Acute)

To promptly stop an acute
attack

Short term
prophylaxis

To prevent an attack when
subjected to a known risk
(eg.surgery, dental
procedure)

Longterm
prophylaxis

To decrease frequency and
severity of recurrent attacks
Must have acute treatment
always available

Individualise treatment to to deliver optimal care for the patient and restore quality of life; review regularly

Management-acute attacks



C1 INH concentrate (Berinert IV) as intravenous preparation



Icatibant –subcutaneous injection -2 doses on hand at all times

Short-term prophylaxis



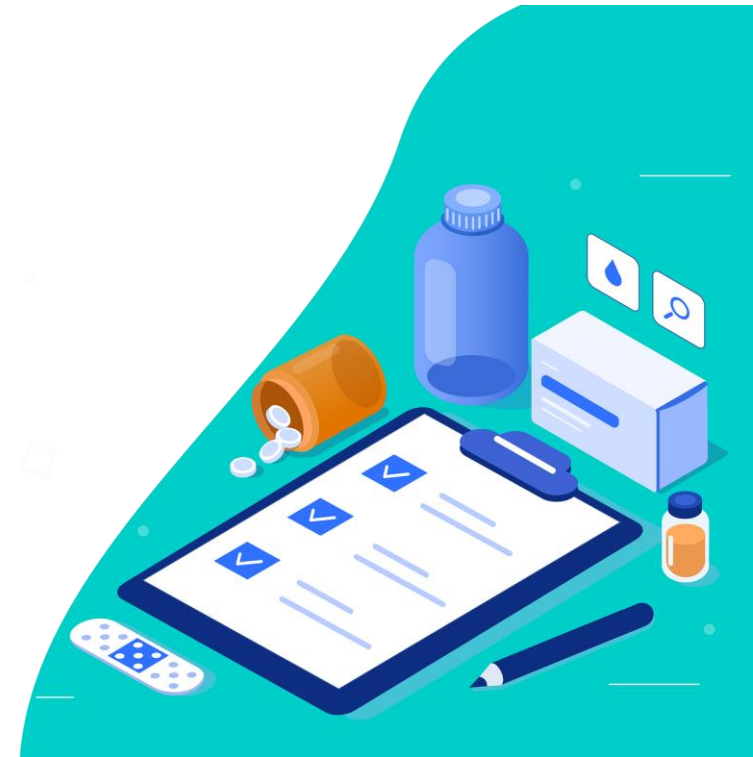
BERINERT IV GIVEN 30-60
MINS BEFORE PROCEDURE




HAVE MORE TREATMENT
ON HAND

Long-term prophylaxis in Australia

- Berinert SC – need 8 attacks in a month to qualify!
- Lanadelumab - 12 attacks over 6 months
- Old treatments – Danazol; tranexamic acid



Identifying Appropriate Patients for LTP

- 
- Patients should be evaluated for LTP at every visit
 - Disease burden caused by frequency, severity, and location of attacks, and response to on-demand therapy and availability of urgent care should be considered
 - This is a shared decision, and patient preferences should be taken into consideration

Development of HAE Impact Tool

<https://scriptixptyltd.snapforms.com.au/form/hae-impact-consent-form>

HAE management

General

- Avoid oral contraceptive pill, ACE inhibitor medication
- Premedicate before procedures requiring radiocontrast media or streptokinase as they may decrease C₁ INH levels
- Treat infections promptly
- Genetic counselling and screening
- Reassurance; address issues such as ongoing stress
- Written management plan


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www.allergy.org.au

MANAGEMENT PLAN FOR Hereditary Angioedema (HAE)

Patient details

Name: _____

Date of birth: _____

Photo: 

Family/emergency contact name: _____

Work Ph: _____

Mobile Ph: _____

Plan prepared by: _____

Doctor: _____

Signed: _____

Date: _____

Contact Ph: _____

Additional information: _____

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ACUTE HAE ATTACKS

Peripheral swelling

- If appropriate administer medication as described below.

Abdominal pain

- Administer medication as described below.
- Seek urgent hospital treatment if symptoms worsen or last longer than 24 hours.

ADDITIONAL HOSPITAL TREATMENT:

- Opiate analgesia.
- IV fluid rehydration.
- Give dose of C1-INH (Berinert®) IV if inadequate response after 1 hour.
- Consider other causes of abdominal pain if no response to specific treatment.

Airway swelling (tongue or throat swelling, difficulty breathing, talking, swallowing).

Phone ambulance - 000 (AU) or 111 (NZ)

- Seek urgent hospital treatment.
- Administer medication as described below.

ADDITIONAL HOSPITAL TREATMENT:

- Prepare for emergency intubation or cricothyrotomy.
- Give dose of C1-INH (Berinert®) IV if inadequate response after 1 hour.

MEDICATION DOSES FOR ACUTE TREATMENT

Medication	Adults and Children >50Kg	Children
Icatibant ^{1,2}	30mg/3ml syringe subcutaneous (SC)	12 - 25Kg 10mg (1ml) 26 - 40Kg 15 mg(1.5ml) 41 - 50Kg 20mg (2ml) subcutaneous (SC)
C1-INH (Berinert®)	20 U/Kg IV	20 U/Kg IV

SHORT TERM PROPHYLAXIS

For invasive medical, dental procedures, intubation or oropharyngeal instrumentation:

- Administer C1-INH (Berinert®) IV 20 U/Kg, 1-6 hours before procedure
- Have further doses of acute treatment (Icatibant or Berinert®) available.

LONG TERM PROPHYLAXIS

Medication and dose: Not applicable

C1-INH (Berinert®) IV: _____

C1-INH (Berinert®) SC: _____

Lanadelumab (Takhzyro®): _____

Danazol: _____

Tranexamic acid: _____

NOTES:

1. Adrenaline, antihistamines and corticosteroids are not effective for HAE attacks.
2. Use patient's own supply either at home or at hospital.
3. This information is specific for HAE treatments that are registered for use in Australia and New Zealand.
4. Please refer patient for immunology review after hospital presentation.

Clinical trials in HAE

PROF CONNIE KATELARIS
CAMPBELLTOWN HOSPITAL





New treatment studies in HAE

- Paediatric garadacimab – recruiting now
- Deucricitibant – about to start
- Gene editing study – later this year

Garadacimab in children

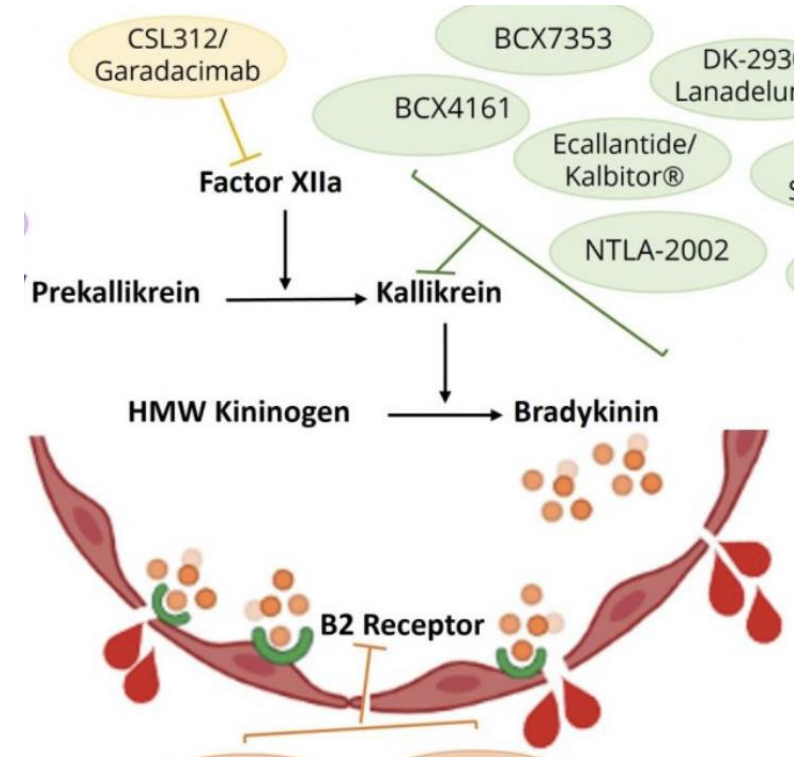
Background

- Frequent HAE attacks are uncommon in childhood BUT have a huge impact:
 - Child can feel different
 - Illness behaviour
 - Feel limited in doing sports and other activities
 - Early school loss
 - Psychological impact can be very large
- Current prophylactic treatment for children limited
 - Tranexamic acid – very poorly effective
 - Berinert SC – twice weekly infusions



Garadacimab

- Monoclonal antibody directed against factor 12a



Garadacimab (CSL Behring)

Phase 3 studies completed – 200mg once/month 12 yrs and older

6-month treatment period

Mean number of attacks per month garadacimab group (0.27, 95% CI 0.05 to 0.49) than in the placebo group (2.01, 1.44 to 2.57; $p < 0.0001$) -a percentage difference of **-87%** (95% CI -96 to -58; $p < 0.0001$).

The median number of attacks per month was 0 for garadacimab and 1.35 for placebo

Longterm open label study – out to >2 yrs-no significant side effects and very effective

Paediatric study

- Open label study
- 2-11 yrs
- Confirmed HAE by blood tests
- Documented at least 2 attacks in last 6 months
- Off any other form of prophylaxis for 2 weeks before starting trial
- Study lasts 15 months
- Will have study visits-about 8 in total-some may be at home
- All travel expenses for these are reimbursed
- Children 2-5 yrs-1 injection every 2 months
- Older child-1 every month
- Detailed information available



Deucricitibant study-Background

- Icatibant has been very effective for managing acute HAE attacks
- Works best when used EARLY!
- Many people delay use:
 - Dislike pain of injection
 - Carrying the needle is inconvenient, embarrassing
 - Worries about travelling with syringes
- To have an oral form of treatment will be much more convenient!!



Deucricitibant study (Phavaris)



- “oral form of icatibant”
- Very rapidly absorbed capsule formulation
- 12-75yrs with HAE
- Can be on stable prophylaxis as long as still having occasional attacks
- Study consists of having 2 attacks-one will be treated at first with placebo and one will have study drug in random order-rescue medication available to use if not responding to treatment
- Early studies have not shown any significant side effects

Gene-editing study (Intellia)

- Early phase 1 and 2 studies have been very successful!
- Now commencing Phase 3 study in near future
- Double blind, placebo-controlled cross over
- 2 infusions in total-one will be placebo and one will be the active treatment-all study participants will have a dose of active treatment by study end!
- Regular hospital visits/phone calls
- Need to keep diary
- No significant side effects reported in early studies



Interested or want more information?



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Questions