A holistic approach to managing female patients with HAE who wish to become pregnant

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Disclosures

- This talk is sponsored by CSL Behring
- Slides may contain off-label content

HAE disease course during puberty

- Women with HAE tend to have more frequent and more severe attacks compared with men[1]
- Individuals with HAE-C1INH generally become symptomatic during adolescence or childhood[1–4]
  - Around **50%** of patients manifest symptoms of swelling by the age of 10 years
  - Approximately **50%** of all female patients develop their first attack before the age of 12, and **90%** by the time they are 23 years old
  - The frequency and severity of attacks often increase after puberty, particularly in females
  - Up to **62%** of women with HAE report their disease worsened during puberty
- For undiagnosed female patients with HAE, the increased severity at puberty – triggered by menstruation and ovulation – may result in a longer diagnostic delay[1]
- It is important to raise awareness of the dynamic nature of HAE during adolescence and physicians should proactively assess the psychological impact of the disease at all stages, and continually reassess the treatment plan

HAE, hereditary angioedema; HAE-C1INH, HAE with C1-esterase inhibitor deficiency.

1. Hsu FI, *et al. Allergy Asthma Clin Immunol* 2022;18(1):64; 2. Maurer M, *et al. Allergy* 2022;77(7):1961–1990; 3. Farkas H, *et al. Allergy* 2017;72(2):300–313; 4. Bouillet L, *et al. Am J Obstet Gynecol* 2008;199(5)484.e1–4.

What should be considered prior to contraception?

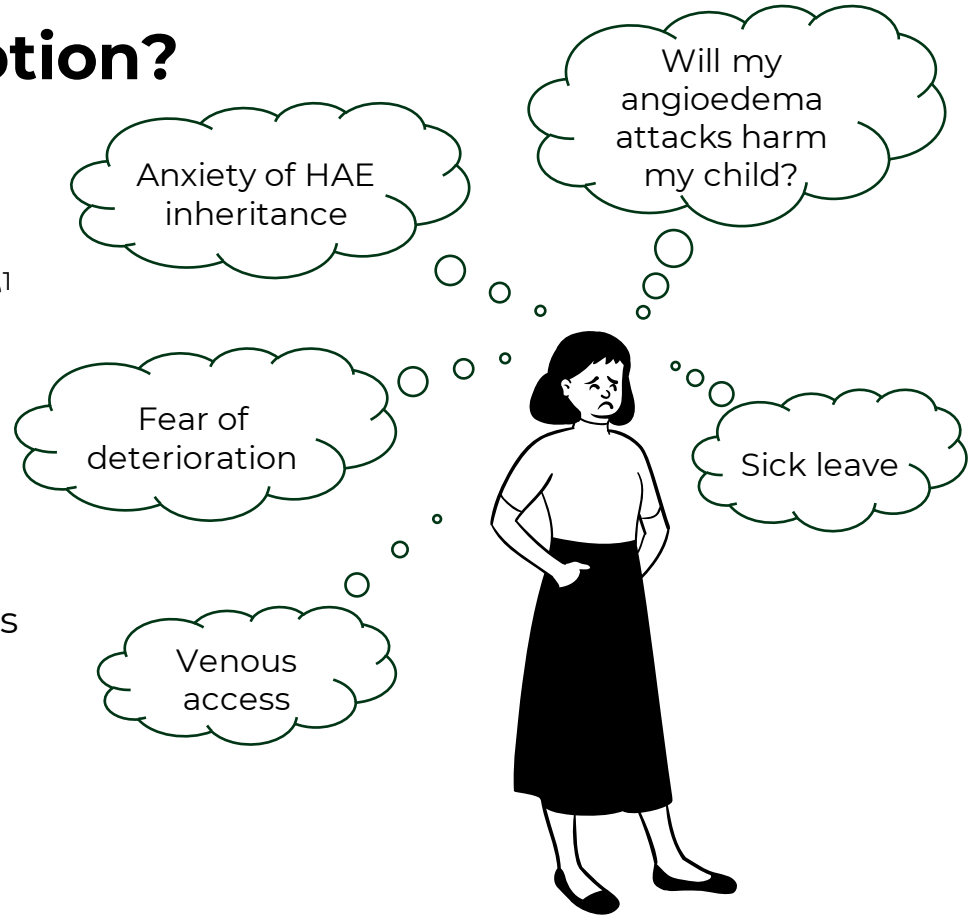
- Oestrogen-containing contraceptives can increase FXII, prekallikrein, kallikrein and HMWK levels and therefore increase bradykinin-mediated vasodilation, and may also decrease C1INH levels[1]
- Aggravation of HAE (more frequent and more severe attacks) occurs in **60–80%** of women with HAE-C1INH who use oestrogen-containing contraceptives[1]
- Barrier methods, IUDs and progesterone-only contraception may be used as alternatives to oestrogen-containing contraceptives[1]
- Treatment options for HAE must be considered carefully for both disease control and family planning decisions
- It is important to consider the effects of oestrogen-containing contraceptives in patients with HAE and interactions with HAE medications (e.g. some HAE treatments may increase concentrations of oral contraceptives metabolised by CYP3A4)[1,2]

C1INH, C1-esterase inhibitor; FXII, factor XII; HAE, hereditary angioedema; HAE-C1INH, HAE with C1INH; HMWK, high molecular weight kininogen; IUD, intrauterine device.

1. Hsu FI, *et al. Allergy Asthma Clin Immunol* 2022;18(1):64; 2. Orladeyo. Summary of Product Characteristics. Updated February 2023.

What should be considered prior to conception?

- Female patients with HAE should be informed that anatomical, physiological, and hormonal changes during pregnancy may influence the manifestations and affect the course and treatment of their disease[1]
- Disease management decisions for women of childbearing age may be more complex and require additional considerations[1,2]
  - Treatment options during the conception period and during pregnancy and lactation become more limited
  - Data on the safety and effects of on-demand and prophylactic treatment during pregnancy are limited – C1INH is recommended as first-line therapy
  - Emotional distress may increase angioedema attacks
  - In case of infertility and IVF treatment, stimulation of ovulation may induce angioedema attacks
- Pregnant patients with HAE require vigilant care and meticulous monitoring by an HAE expert[1]



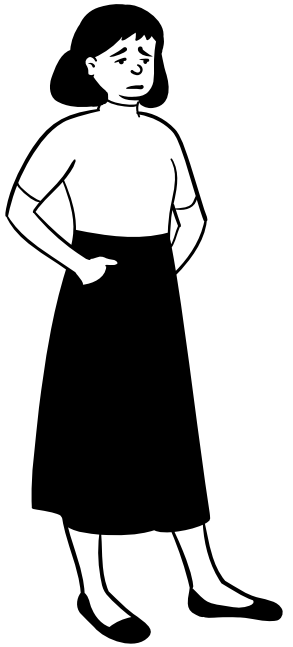
HAE, hereditary angioedema; C1INH, C1-esterase inhibitor; IVF, in vitro fertilisation.

1. Maurer M, *et al. Allergy* 2022;77(7):1961–1990; 2. Hsu FI, *et al. Allergy Asthma Clin Immunol* 2022;18(1):64.

Patient case

Personal history

- Female, 33 years old
- **Anxiety**
- No known drug allergy
- Smoker (10 cigarettes per day)
- Allergic bronchial asthma with sensitisation to pollens and house dust mites
- HAE type I



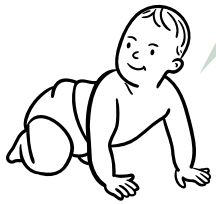
Family history

- **Mother:** HAE type I
- **Maternal grandmother:** fatal laryngeal oedema without any previous diagnosis

HAE, hereditary angiodema.

Diagnosis

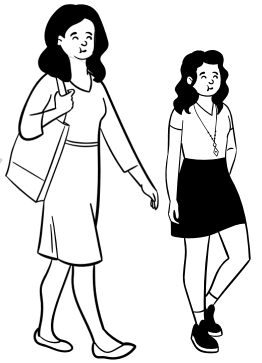
Peripheral edema, perimenstrual abdominal pain



Born in **1990**

Onset of symptoms in **2004** (14 years old)

Diagnosis: **HAE type I** in 2004



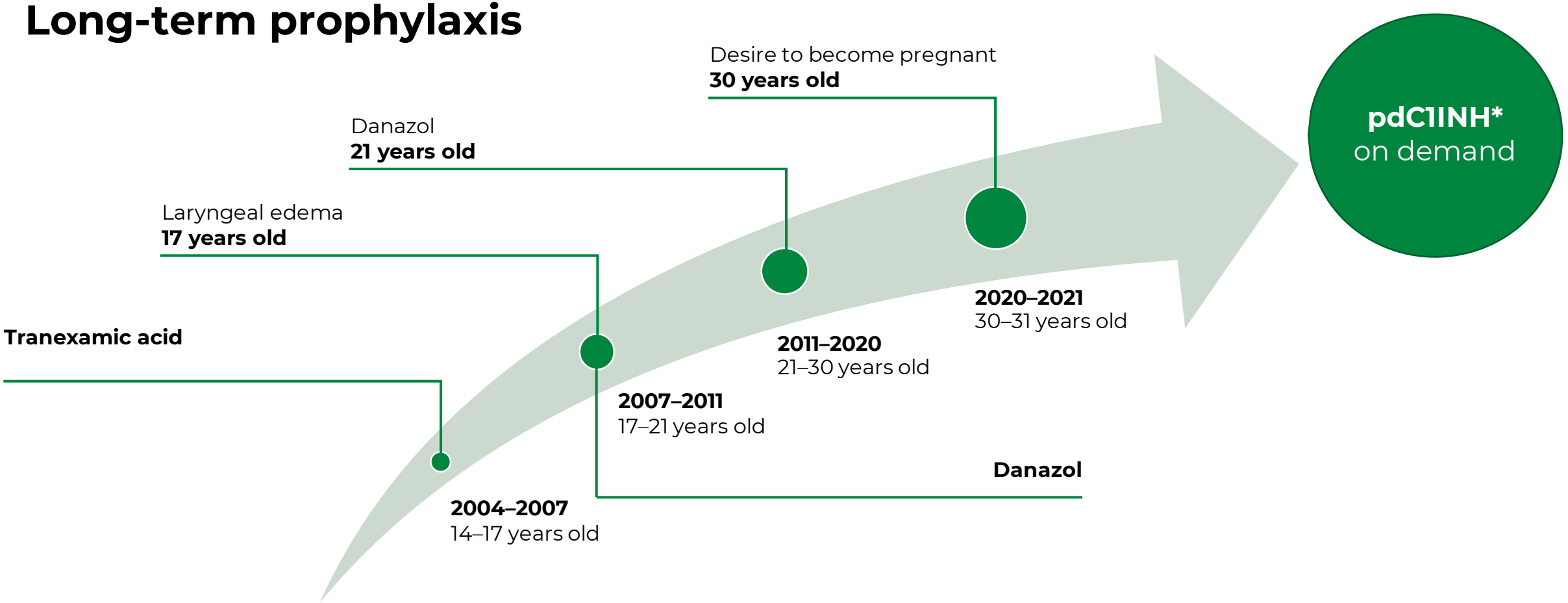
Diagnosed in 2004

Fatal laryngeal oedema, never diagnosed

Laboratory tests		Genetic study
C1INH	**2.88 mg/dL** (22–34)	SERPING1
fC1INH	**20.1%** (70–130)	Cr11_Exon4
C4	**5.38 mg/dL** (10–40)	c.(550+1_686-1)del

C1INH, C1-esterase inhibitor; fC1INH, functional C1INH; C4, complement component 4; HAE, hereditary angiodema.

Long-term prophylaxis

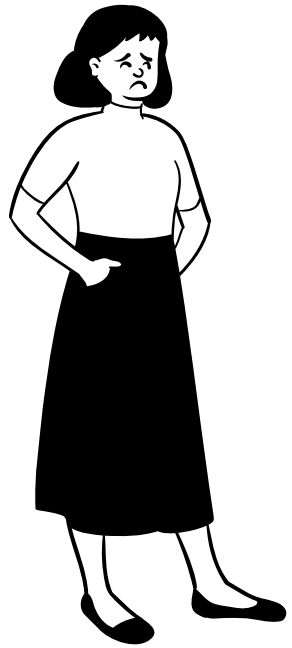


*According to the Summary of Product Characteristics for plasma-derived C1INH products, there is limited data that indicate no increased risk from the use of plasma-derived C1INH in pregnant woman. Plasma-derived C1INH should be given to pregnant women only if clearly indicated.
AE, adverse event; IU, international unit; pdC1INH, plasma derived C1 esterase inhibitor.

Poor HAE control exacerbates preexisting anxiety and depression

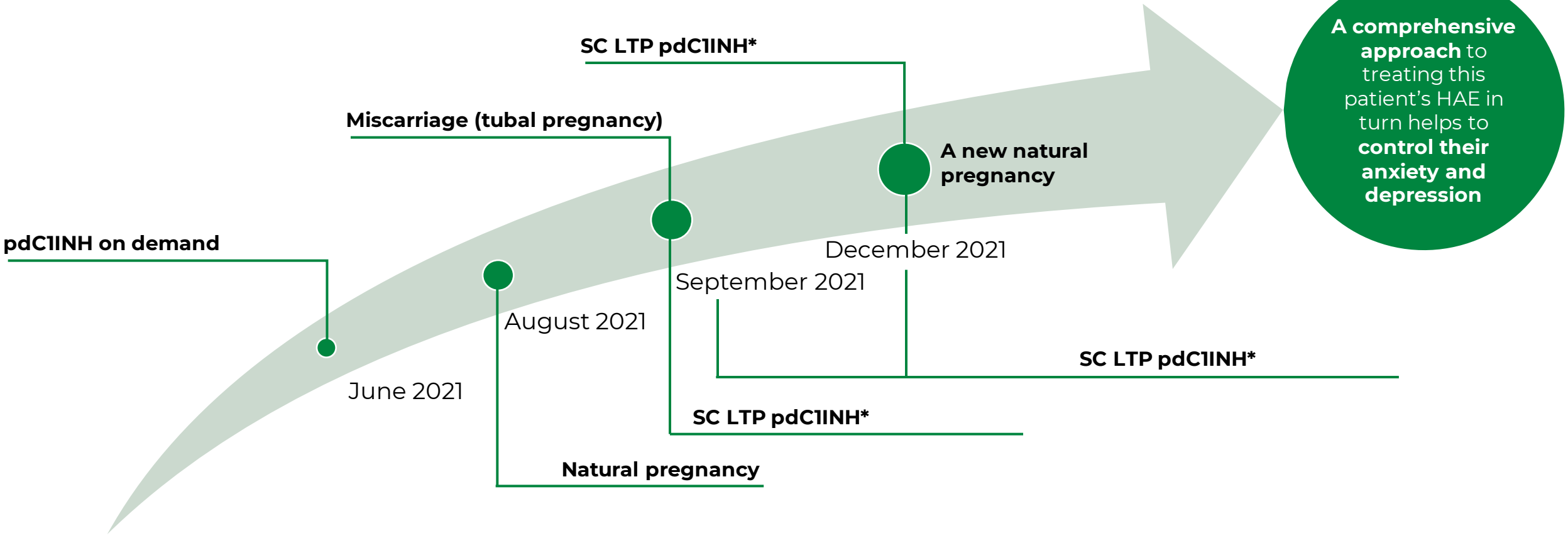
2017–2021

- **High anxiety** and **depressive thoughts** made worse by the patient's poor disease control despite treatment with danazol and on-demand therapy
- Further complicated by unstable employment, frequent changes of place of work and residence
- As a first step, treatment with citalopram and lormetazepam was initiated and a psychological assessment was conducted



HAE, hereditary angioedema.

Holistic HAE control – journey to pregnancy



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HAE, hereditary angioedema; LTP, long-term prophylaxis; pdC1INH, plasma-derived C1 esterase inhibitor; SC, subcutaneous.

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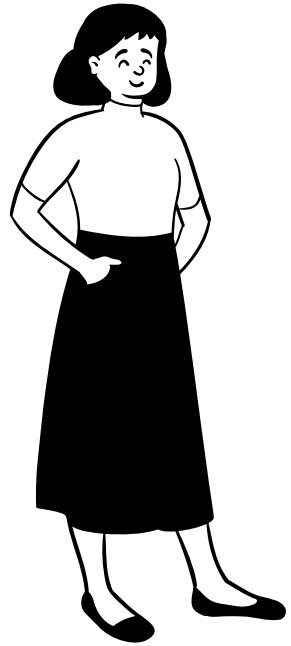
Enabling holistic consultation during preconception

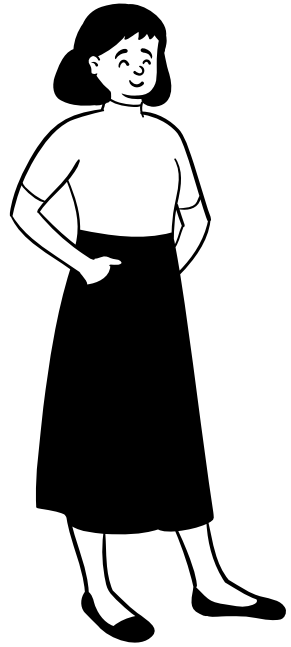
- Due to the continuous change of workplace and residence, the patient had the option of online and telephone consultation with the HAE unit
- LTP was discussed at every contact point, and the patient was trained in self-administration of her medication
- A flexible dosing schedule was designed to adapt to her needs
- Psychological assessment was conducted and maintained



HAE, hereditary angioedema; LTP, long-term prophylaxis.

Outcome of treatment plan

- **Once LTP with pdC1INH* SC was established**, the patient had a successful pregnancy in December 2021
- **Her symptoms were considered mild**, and she suffered fewer attacks with no life-threatening events in the preconception period and during pregnancy
- **Better quality of life was achieved** as measured by patient-reported outcome questionaries
- **Minimal adverse reactions**, with only local injection-site reactions reported
- Safe and easy home administration



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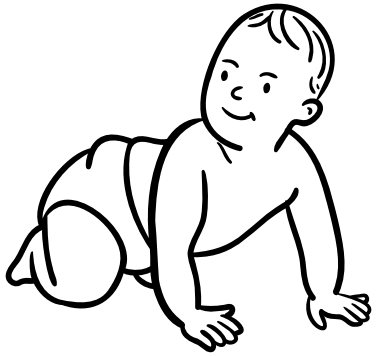
Take-home messages

- Female patients with HAE who desire to become pregnant **should be comprehensively treated**
- If **psychological support** and therapy is needed, these should be **considered and provided** to the patient
- LTP should be **adapted to the patient's needs** and wishes and should be considered at every visit
- Quality of life may be measured using **patient-reported outcome** questionaries
- Close follow-up and **easy access to HAE specialists** should be provided during the preconception journey

HAE, hereditary angioedema; LTP, long-term prophylaxis.

A holistic treatment plan was followed during this patient's preconception phase, which encompassed psychological support as well as effective management of her HAE, and she delivered a healthy baby boy in August 2022



HAE, hereditary angioedema.

Thank you for your attention!

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