REAL-WORLD EXPERIENCE OF SUBCUTANEOUS BERINERT® 2000/3000 (C1-INH): PERSPECTIVES FROM DR ANNA SALA-CUNILL

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KEY PATIENT INFORMATION

Name: Catherine

Current age: 72 years

Sex: Female

Past medical history (other than HAE): Dyslipidaemia due to use of androgens

Year of first recorded HAE symptoms: 1967, at age 18 years

Triggers: Stress, trauma

Symptoms: Presented with severe and frequent angioedema attacks, most frequently in the abdomen, face, periphery, genitals and larynx

Family history:

- Catherine is unaware if her mother, father or other ancestral family members had the disease
- She has two daughters and one son. Two of her children have HAE. Catherine was diagnosed with HAE Type I when her son was diagnosed. These diagnoses prompted the investigation of all of the family members for HAE

Age at diagnosis: 62 years

Diagnosis: HAE Type I

PATIENT PRESENTATION

Reason for presentation: Catherine has been receiving long-term prophylactic treatment with danazol and experienced safety concerns (dyslipidaemia) and poor efficacy

2010

PATIENT PRESENTATION AND DIAGNOSIS

Date of diagnosis: 2010 (a delay of ~43 years)
Number of attacks per month: 3-4 (36 attacks per year)
Number of hospital admissions per year: 0 or 1
Laboratory testing:

- C1-INH protein level 0.049 mg/ml (reference range: 0.18-0.32 mg/ml[1])
- C1-INH function 30% (reference range: 70-130% of normal plasma[1])
- Complement C4 level 0.07 mg/ml (reference range: 0.16-0.38 mg/ml[1])
- Complement C1q level 0.225 mg/ml (reference range: 0.1-0.25 mg/ml)

Diagnosis: HAE Type I

TREATMENT 1

Date: January 2010
Patient presentation: Catherine was experiencing 3 attacks per month
Treatment: Stanozolol for long-term prophylaxis (2 mg every 8 hours)
Treatment outcome: After 3 months, Catherine's disease was more controlled (1 attack every 3-4 months treated on demand with plasma derived C1-INH [IV]) and her dose of stanozolol was decreased to 2 mg every 48 hours
Adverse events: None

2016

TREATMENT 2

Date: March 2016
Patient presentation: Spain ran out of stock of stanozolol and Catherine did not want to receive prophylaxis with C1-INH (IV), due to fear and a perceived difficulty of intravenous self-administration. Catherine chose to continue with oral androgens and initiated danazol; she was fully informed of the possible adverse events
Treatment: Danazol for long-term prophylaxis (50 mg every 24 hours)
Treatment outcome: Catherine's disease was controlled. She experienced 1 attack every 3 months.
Adverse events: Dyslipidaemia (February 2019)
Adverse event management: Danazol was decreased to 50 mg every 48 hours. Catherine's disease was less well controlled, and the dyslipidaemia did not improve

2020

TREATMENT 3

Date: June 2020
Patient presentation: Catherine's disease activity was less well controlled (2 attacks per month) since the decrease of the danazol dose (50 mg every 48 hours)
Considerations for treatment:

- Lack of disease control
- Dyslipidaemia due to androgen therapy
- Catherine is unable to self-administer plasma-derived C1-INH (IV)
- Catherine has poor venous access

Treatment: Berinert® 2000/5000 for long-term prophylaxis (SC; 4000 IU, twice a week)
Treatment outcome: Catherine's disease was well controlled; she was attack-free for the first 3 months and only experienced 1 mild peripheral attack during the past 6 months, without any adverse events. Catherine's dyslipidaemia and quality of life have also improved
Adverse events: None

Rationale for prescribing Berinert® 2000/3000 (SC):

- Berinert® 2000/3000 for subcutaneous injection is indicated for prevention of recurrent HAE attacks in adolescent and adult patients with C1-esterase inhibitor deficiency. The recommended dose of Berinert® 2000/3000 is 60 IU/kg body weight twice weekly (every 3-4 days)[2]
- Catherine had poor venous access and was unable to self-administer plasma-derived C1-INH (IV). She also experienced a lack of disease control and dyslipidaemia due to androgen therapy
- Catherine was prescribed Berinert® 2000/3000 as data from the COMPACT*† clinical programme has shown that Berinert® 2000/3000:
  - Reduces attack rates by a median of 95% versus placebo[3]
  - Reduces attack severity versus placebo; 9% of patients treated with 60 IU/kg Berinert® experienced severe attacks versus 69% of placebo patients[3]
  - Produces long-term‡, statistically significant§ differences in QoL measures, including EQ-5D Health State Value and Visual Analog Scale, anxiety and depression (HADS), WPAI-assessed presenteeism, work productivity loss and activity impairment, and TSQM-assessed treatment effectiveness and overall satisfaction[4]
  - Adverse events (most commonly mild and transient local site reactions) occurred in similar proportions of patients who received Berinert® or placebo[3]
- Moreover, the WAO/EAACI guidelines recommend C1-INH as the first-line treatment for long-term prophylaxis[5]

Biggest challenge experienced by the patient during treatment:

- Understanding their disease
- Understanding that specific, highly efficacious treatments for HAE are available that allow disease control without adverse events

Advice for the patient:

- Thoroughly explain how HAE affects your day-to-day life and any preferences you have regarding treatment
- Develop a trusting relationship with your HAE specialist to allow for co-decision making to select the most suitable therapy

Biggest challenge experienced by the clinician during treatment:

- Effectively conveying that androgens, although oral, may not be the most effective way to treat HAE and more efficacious alternatives are available

Advice for the clinician:

- Each patient is different and therefore treatment has to be individualised according to the patient's lifestyle and preferences

KEY LEARNING:

- Trust, built on an understanding of the fears and preferences of your patient, is vital to:
  - Confidently discuss treatment options
  - Ensure good adherence and consequently efficacy

*COMPACT was an international, prospective, multicentre, randomised, double-blind, placebo-controlled Phase 3 study. Patients ≥12 years of age with symptomatic type I or II HAE (N=90) were randomly assigned to twice-weekly treatment with Berinert® 40 IU/kg or 60 IU/kg. Patients initiated 16 weeks of active treatment or placebo and crossed over for the subsequent 16 weeks. Primary efficacy endpoint: number of attacks (investigator reported). Secondary efficacy endpoints: response rate (percentage of patients who had a ≥50% reduction in number of attacks vs placebo), number of times rescue medication was used[3]. †COMPACT-OLE was an open-label extension of the COMPACT study, including 126 type I or type II HAE patients who had completed the Phase 3 study (n=64) or who were treatment naive (n=62) and who were randomised 1:1 to receive 40 IU/kg or 60 IU/kg Berinert® (SC) twice weekly. Primary endpoints: person-time incidence rates of related serious AEs. AEs leading to premature discontinuation, AEs of special interest (thromboembolic events and anaphylaxis), HAE attacks resulting in hospitalisation, injection-site reactions graded severe by the investigator, and the development of neutralising anti-C1-INH antibodies. Secondary endpoints: additional safety parameters, percentage of patients with a time-normalised attack frequency of less than 1 attack per 4-week period, percentage of responders.[2] ‡Point estimates with confidence intervals that excluded zero were considered statistically significant and interpreted to be indicative of a relevant treatment difference between Berinert® 2000/3000 and placebo.[4]

This patient case presentation is inspired by a real patient. To protect the patient's identity, their name and photograph have been changed.

ABBREVIATIONS

AE, adverse event; C1-INH, C1-esterase inhibitor; EAACI, European Academy of Allergy and Clinical Immunology; EQ-5D, EuroQol-5 Dimension; HADS, Hospital Anxiety and Depression Scale; HAE, hereditary angioedema; IV, intravenous; QoL, quality of life; SC, subcutaneous; TSQM, Treatment Satisfaction Questionnaire for Medication; WAO, World Allergy Organization; WPAI, Work Productivity and Activity Impairment Questionnaire.

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REAL-WORLD EXPERIENCE OF SUBCUTANEOUS BERINERT® 2000/3000 (C1-INH): PERSPECTIVES FROM DR MARIA PEDROSA

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Consultant Allergist

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KEY PATIENT INFORMATION

Name: Meghan

Current age: 14 years

Sex: Female

Past medical history (other than HAE): Pollinosis

Triggers: Infections, trauma, and psychological stress

Symptoms:

- Meghan experienced moderate-to-severe abdominal attacks, many peripheral attacks, and some attacks with upper respiratory involvement
- Her attacks typically lasted 3 days but some attacks, mainly peripheral, have lasted up to 5 days
- Most of the abdominal attacks, some of the peripheral attacks, and those attacks involving the respiratory tract have led to emergency room visits and, in a few cases, admission for an observation period

Family history: Father, uncle, and grandfather have been diagnosed with HAE Type I

Age at diagnosis: 7 months

Diagnosis: HAE Type I

PATIENT PRESENTATION

Reason for presentation:

- Meghan was not able to participate in school activities in the same way as her peers
- She felt unable to perform at the expected academic level
- She was anxious about the unpredictability of the disease
- Her parents were worried about letting her participate in the same activities as her brother (e.g. short trips with school and spending holiday periods alone with her grandparents)

2007

DIAGNOSIS

Date of diagnosis: 19 March 2007

Symptoms: At the age of diagnosis, Meghan was asymptomatic

Laboratory testing:

- C1-INH protein level: 6.17 mg/dL (reference range: 16–33 mg/dL)
- C1-INH function: 26.84% (reference range: 70–130% of normal plasma)
- Complement C4 level: 4.13 mg/dL (reference range: 14–60 mg/dL)

Diagnosis: HAE Type I

2013

TREATMENT 1

Date: 2013

Patient presentation: Meghan had been asymptomatic until age 7 when she started to experience abdominal attacks

Number of attacks per year: 8

Number if hospital admissions per year: 1–2

Treatment: Berinert® 500 IU for acute attacks (IV; 20 IU/kg)

Treatment outcome: Meghan's attacks resolved within a few hours when treatment was administered early. When treatment was delayed, her attacks lasted 24–36 hours

Adverse events: None

2014

TREATMENT 2

Date: November 2014

Patient presentation: Meghan's attacks had become more frequent (12 attacks in the previous year)

Treatment: Tranexamic acid for long-term prophylaxis (oral; 40 mg/kg; divided in three doses)

Treatment outcome: Tranexamic acid did not improve Meghan's symptoms

Adverse events: None

2015

TREATMENT 3

Date: March 2015

Patient presentation: Meghan's attack rate had increased to 3 or 4 attacks per month

Treatment: Berinert® 500 IU for acute attacks (self-administered IV; 20 IU/kg)

Treatment outcome: As treatment was self-administered at the earliest sign of an attack, attacks resolved within 1–3 hours after infusion

Adverse events: None

2015

TREATMENT 4

Date: June 2015

Patient presentation: Meghan had experienced 9 attacks in the previous 3 months. She had missed many school days, felt anxious and reported a poor QoL

Treatment: C1-INH for long-term prophylaxis (IV; 500 IU, twice weekly)

Treatment outcome: Meghan's symptoms improved and she was asymptomatic for 6 months; after which, the treatment was suspended to determine if the patient's period of increased disease activity had resolved. She was treated with on-demand therapy until June 2019

Adverse events: None

2019

TREATMENT 5

Date: June 2019

Patient presentation: Meghan had experienced 2 attacks per month in the previous 3 months. She continued to miss school days, experience anxiety and still reported a poor QoL

Treatment: Berinert® 2000/3000 for long-term prophylaxis (SC; 60 IU/kg, twice weekly)

Treatment outcome: Meghan's symptoms improved, and she was asymptomatic for 6 months; after which, the treatment was suspended to determine if the patient's period of increased disease activity had resolved and she was treated with on-demand therapy

Adverse events: Mild injection-site pain resolved without treatment after a few minutes

Rationale for prescribing Berinert® 2000/3000 (SC):

- Berinert® 2000/3000 for SC injection is indicated for the prevention of recurrent HAE attacks in adolescent and adult patients with C1-INH deficiency. The recommended dose of Berinert® 2000/3000 is 60 IU/kg body weight twice weekly (every 3–4 days)[2]
- Meghan had reported an increased frequency of attacks (2 attacks per month)
- The unpredictability of painful attacks limited her social life and academic potential, as well as impacting her mental health
- Data from the COMPACT*† clinical program has shown that Berinert® 2000/3000:
  - Reduces attack rates by a median of 95% vs placebo[3]
  - Reduces attack severity vs placebo; 9% of patients treated with Berinert® 60 IU/kg experienced severe attacks vs 69% of placebo patients[3]
  - Produces long-term,‡ statistically significant§ differences in QoL measures, including: EQ-5D Health State Value and Visual Analog Scale, anxiety and depression (HADS), WPAI-assessed presenteeism, work productivity loss and activity impairment, and TSQM-assessed treatment effectiveness and overall satisfaction[4]
  - Adverse events (most commonly mild and transient local injection-site reactions) were similar in patients who received Berinert® and placebo[3]
- Moreover, the WAO/EAACI guidelines recommend C1-INH as the first-line treatment for long-term prophylaxis[5]

Biggest challenge experienced by the patient during treatment:

- Learning how to self-administer C1-INH (IV)

Advice for the patient:

- Be confident in your ability to learn how to self-administer your treatment
- Do not hesitate to communicate to your clinician the impact HAE has on your daily life
- Do not let the disease control your life but do everything you can to control the disease

Biggest challenge experienced by the clinician during treatment:

- Educating an adolescent patient on how to self-administer a non-oral treatment

Advice for the clinician:

- Consider injected therapies for routine prophylaxis in adolescents, as any perceived treatment burden is outweighed by the potential reduction in anxiety caused by the unpredictability of attacks
- Encourage your adolescent patients to self-administer their prophylactic therapies
- Monitor your patient's disease activity regularly and adjust treatment regimens, as appropriate

KEY LEARNING:

- Adolescent patients can learn to self-administer non-oral therapies
- Self-administration of long-term prophylactic treatments can improve a patient's QoL by increasing their autonomy and decreasing anxiety

*COMPACT was an international, prospective, multicenter, randomized, double-blind, placebo-controlled Phase 3 study. Patients aged ≥12 years with symptomatic Type I or II HAE (N=90) were randomly assigned to twice-weekly treatment with Berinert® 40 IU/kg or 60 IU/kg. Patients initiated 16 weeks of active treatment or placebo and crossed over for the subsequent 16 weeks. Primary efficacy endpoint: number of attacks (investigator reported). Secondary efficacy endpoints: response rate (percentage of patients who had a ≥50% reduction in number of attacks vs placebo) and number of times rescue medication was used[3]; †COMPACT-OLE was an open-label extension of the COMPACT study, including 126 Type I or II HAE patients who had completed the Phase 3 study (n=64) or who were randomised 1:1 to receive Berinert® (SC) 40 IU/kg or 60 IU/kg twice weekly. Primary endpoints: person-time incidence rates of related serious AEs, AEs leading to premature discontinuation, AEs of special interest (thromboembolic events and anaphylaxis), HAE attacks resulting in hospitalisation, injection site reactions graded severe by the investigator, and the development of neutralising anti-C1-INH antibodies. Secondary endpoints: additional safety parameters, percentage of patients with a time-normalised attack frequency of less than 1 attack per 4-week period, percentage of responders[4]; ‡Point estimates with confidence intervals that excluded zero were considered statistically significant and interpreted to be indicative of a relevant treatment difference between Berinert® 2000/5000 and placebo.[4]

This patient case presentation is inspired by a real patient. To protect the patient's identity, their name and photograph have been changed.

ABBREVIATIONS

AE, adverse event; C1-INH, C1-esterase inhibitor; C4, complement component 4; EAACI, European Academy of Allergy and Clinical Immunology; EQ-5D, EuroQol-5 Dimension; HADS, Hospital Anxiety and Depression Scale; HAE, hereditary angioedema; HAE-C1-INH, hereditary angioedema with deficient C1-esterase inhibitor; IV, intravenous; OLE, open-label extension; QoL, quality of life; SC subcutaneous; TSQM, Treatment Satisfaction Questionnaire for Medication; WAO, World Allergy Organization; WPAI, Work Productivity and Activity Impairment Questionnaire.

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REAL-WORLD EXPERIENCE OF SUBCUTANEOUS BERINERT® 2000/3000 (C1-INH): PERSPECTIVES FROM DR THOMAS BUTTGEREIT

Thomas Buttgereit, MD

Dermatologist

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KEY PATIENT INFORMATION

Name: Beth

Current age: 36 years

Sex: Female

Past medical history (other than HAE):

- Hypertension: In 2018, Beth was prescribed ACE inhibitors for her hypertension, which worsened her HAE disease activity. The ACE inhibitor was later changed to a calcium antagonist
- Poor dental status: Dental/surgical procedures are known to induce attacks and require the use of pre-procedural prophylactic treatments[1]

Triggers: Stress at school (1995-2003), dental surgery (i.e. July 2017)

Symptoms: Lip swelling, abdominal pain and erythema marginatum (typical clinical presentation)

Family history:

- Unknown: Parents died in a car accident. Beth was raised by her grandparents. Grandmother reports that Beth's mother had sporadic swelling during her adolescence without diagnosis

Age at diagnosis: 15 years

Diagnosis: HAE Type I

PATIENT PRESENTATION

Reason for presentation: Blood pressure medications (such as ACE inhibitors) taken since 2018 have impacted Beth's HAE disease activity

1995

TREATMENT 1

Date: 1995

Patient presentation: Cyrated erythema and swelling of the lip. Note: *At this time, Beth's HAE was undiagnosed*

Treatment: Antihistamines (4 mg dimetindene) and systemic corticosteroids (100 mg prednisolone)

Treatment outcome: No response, persistence of lip swelling for 4 hours. Note: *The lack of response is not surprising as bradykinin-mediated angioedema does not respond to antihistamines. Lack of response to antihistamines can help differential diagnosis*

Adverse events: None

2000

DIAGNOSIS

Date of diagnosis: July 2000

Number of attacks per year: 8

Number of hospital admissions per year: 2-3

Laboratory testing:

- C1-INH protein level 0.05 mg/ml (reference range: 0.18-0.32 mg/ml[2])
- C1-INH function 40% (reference range: 70-130% of normal plasma[3])
- Complement C4 level 0.09 mg/ml (reference range: 0.16-0.38 mg/ml[2])

Diagnosis: HAE Type I

TREATMENT 2

Date: 2000

Treatment: Berinert® 500/1500 for acute attacks (IV; 20 IU/kg, usually once or twice a month)

Treatment outcome: Acute attacks controlled with on-demand treatment

Adverse events: None

COMMON ATTACK FACED BY BETH

Date: 2009

Patient presentation: Abdominal attack with severe pain and erythema marginatum

Treatment: Berinert® 500/1500 (IV; 20 IU/kg)

Treatment outcome: Regression of abdominal pain

Adverse events: None

Frequency at which patient faced this type of attack: 7-14 times a year

2009

2017

TREATMENT 3

Background: In July 2017, Beth experienced an attack in her lip after dental surgery

Date: October 2017

Patient presentation: Dental surgery required due to cavities

Treatment: Berinert® 500/1500 for pre-procedural prophylaxis (IV; 1000 IU, <6 hours prior to dental surgery)

Treatment outcome: Successful prevention of post-procedural attacks. Beth was advised to administer pre-procedural prophylaxis ahead of any future surgeries

Adverse events: None

2020

TREATMENT 4

Date: December 2020

Patient presentation: Beth has been treating acute attacks with on-demand Berinert (IV), but reports increased frequency of attacks (5 attacks per month), poor disease control (AECT=6) and impaired QoL (AE-QoL=83)

General health, wellbeing and lifestyle before starting treatment:

- Beth is a young, open-minded, well-educated, busy woman with an active life style and several hobbies (hiking, mountain biking, etc.)
- The unpredictability of painful abdominal attacks severely limited her social life
- Beth wishes to start a family

Considerations for treatment:

- Increased frequency of attacks
- Tendency to develop frequent tooth infections

Treatment: Berinert® 2000/3000 for long-term prophylaxis (SC; 3000 IU, every 3-4 days)

Treatment outcome:

- Absence of attacks
- Increased QoL (AE-QoL=26) and disease control (AECT=15)

Adverse events: None

Rationale for prescribing Berinert® 2000/3000 (SC):

- Berinert® 2000/3000 for subcutaneous injection is indicated for prevention of recurrent HAE attacks in adolescent and adult patients with C1-esterase inhibitor deficiency. The recommended dose of Berinert® 2000/3000 is 60 IU/kg body weight twice weekly (every 3-4 days)[3]
- Beth reported an increased frequency of attacks (5 attacks per month), poor disease control (AECT=6) and impaired QoL (AE-QoL=83)
- The unpredictability of painful abdominal attacks severely limited her social life and she was prone to developing tooth infections
- Beth also wishes to start a family
- Beth was prescribed Berinert® 2000/3000 as data from the COMPACT[4] clinical programme has shown that Berinert® 2000/3000:
  - Reduces attack rates by a median of 95% versus placebo[4]
  - Reduces attack severity versus placebo; 9% of patients treated with 60 IU/kg Berinert® experienced severe attacks versus 69% of placebo patients[4]
  - Produces long-term[5], statistically significant[4] differences in QoL measures, including EQ-5D Health State Value and Visual Analog Scale, anxiety and depression (HADS), WPAI-assessed presenteeism, work productivity loss and activity impairment, and TSQM-assessed treatment effectiveness and overall satisfaction[6]
  - Adverse events (most commonly mild and transient local site reactions) occurred in similar proportions of patients who received Berinert® or placebo[4]
- Moreover, the WAO/EAACI guidelines recommend C1-INH as the first-line treatment for long-term prophylaxis[1]

Biggest challenge experienced by the patient during treatment:

- Understanding the need for short- and long-term prophylactic treatment
- Experiencing an increased frequency of attacks (5 attacks per month), poor disease control (AECT=6) and impaired QoL (AE-QoL=83) before initiating Berinert® (SC)
- Learning to identify and treat an attack as early as possible

Advice for the patient:

- New therapeutic options in HAE allow patients to live a near-normal life as well as reduce the burden of the disease and its treatment
- Stay in touch with your physician to learn about the latest therapeutic options

Biggest challenge experienced by the clinician during treatment:

- Sharing decision making on the need for long-term prophylaxis
- Obtaining the exact medical and treatment history to identify trigger factors

Advice for the clinician:

- Avoid using ACE inhibitors/ARBs in patients with HAE because these drugs can worsen disease activity
- Consider disease-related QoL, disease control and disease activity in your treatment decision making
- Be aware that some patients experience prodromal signs (e.g. erythema marginatum); erythema marginatum should not be mistaken for urticaria
- Consider prescribing short-term prophylaxis before procedures that may induce attacks (e.g. dental surgery)

KEY LEARNING:

- A detailed history of secondary diagnoses and medications is important when treating HAE
- Consideration of disease-related QoL, disease control and attack frequency is critical to evaluate the need for long-term prophylaxis

[4]COMPACT was an international, prospective, multicentre, randomised, double-blind, placebo-controlled Phase 3 study. Patients ≥12 years of age with symptomatic type I or II HAE (N=90) were randomly assigned to twice-weekly treatment with Berinert® 40 IU/kg or 60 IU/kg. Patients initiated 16 weeks of active treatment or placebo and crossed over for the subsequent 16 weeks. Primary efficacy endpoint: number of attacks (investigator reported). Secondary efficacy endpoints: response rate (percentage of patients who had a ≥50% reduction in number of attacks vs placebo) and number of times rescue medication was used[1]. [5]COMPACT OLE was an open-label extension of the COMPACT study, including 126 type I or type II HAE patients who had completed the Phase 3 study (n=64) or who were treatment naive (n=62) and who were randomised 1:1 to receive 40 IU/kg or 60 IU/kg Berinert® (SC) twice weekly. Primary endpoints: person-time incidence rates of related AEs. AEs leading to premature discontinuation, AEs of special interest (thromboembolic events and anaphylaxis), HAE attacks resulting in hospitalisation, injection-site reactions graded severe by the investigator, and the development of neutralising anti-C1-INH antibodies. Secondary endpoints: additional safety parameters, percentage of patients with a time-normalised attack frequency of less than 1 attack per 4-week period, percentage of responders.[6] Point estimates with confidence intervals that excluded zero were considered statistically significant and interpreted to be indicative of a relevant treatment difference between Berinert® 2000/3000 and placebo.[4]

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ABBREVIATIONS

ACE, angiotensin-converting enzyme; AE, adverse event; AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; ARB, angiotensin II receptor blocker; C1-INH, C1-esterase inhibitor; EAACI, European Academy of Allergy and Clinical Immunology; EQ-5D, EuroQol 5 Dimension; HADS, Hospital Anxiety and Depression Scale; HAE, hereditary angioedema; IV, intravenous; OLE, open-label extension; QoL, quality of life; SC, subcutaneous; TSQM, Treatment Satisfaction Questionnaire for Medication; WAO, World Allergy Organization; WPAI, Work Productivity and Activity Impairment Questionnaire.

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