

How to assess the outcome of therapy – what outcomes are most relevant?

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Why is this topic important?

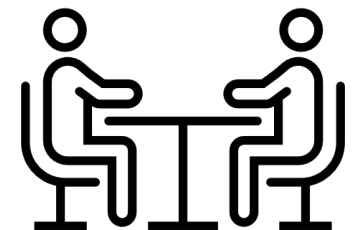
C1-INH biomarker for diagnosis of HAE

Currently there are no reliable biomarkers for:

- Disease activity
- Severity
- Attack probability
- Treatment outcome
- ...

We have no biomarkers. But we need information for treatment decisions and treatment monitoring.

But we are in touch with the people we care for. **Let's ask them!**



Why is this topic important?

PROM patient-related outcome

Disease activity

mild

moderate

severe

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PROM patient-related outcome

Disease activity

mild

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severe

Disease activity is more than number and severity of attacks

Duration, impact on physis, on daily activities, on appearance and self-rating

Why is this topic important?

PROM patient-related outcome

AAS

Disease activity

mild

moderate

severe

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Duration, impact on physis, on daily activities, on appearance and self-rating

Why is this topic important?

PROM patient-related outcome

Quality of life (QoL)

- QoL is much more than “How are you?”
- QoL can be general, organ-specific, disease-specific, symptom-specific
- QoL is a multi-faceted measure (e.g. functioning, mood, fears/shame, food, ...)

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AE-QoL

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PROM patient-related outcome

Disease control

Items/domains

AE signs and symptoms

Impact of AE

Effectiveness of therapy

General concept

AE control

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graph LR; A[AE signs and symptoms] --- B[Impact of AE]; B --- C[Effectiveness of therapy]; C --- D[AE control];
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Why is this topic important?

PROM patient-related outcome

Disease control

AECT

Items/domains

AE signs and symptoms

Impact of AE

Effectiveness of therapy

General concept

AE control

Well-controlled

Not well-controlled

What does the science say?

[EFFICACY, PHARMACOKINETICS, PHARMACODYNAMICS, AND SAFETY OF INTRAVENOUS C1 INHIBITOR FOR LONG-TERM PROPHYLAXIS AND TREATMENT OF BREAKTHROUGH ATTACKS IN JAPANESE SUBJECTS WITH HEREDITARY ANGIOEDEMA: A PHASE 3 OPEN-LABEL STUDY].

Fukunaga A, Morita E, Miyagi T, Eto K, Shimizu A, Kagami S, Yamamoto H, Vardi M, Tang Y, Wang Y, Hide M.

Alerugi. 2020;69(3):192-203. doi: 10.15036/arerugi.69.192.

PMID: 32435020 Clinical Trial. Japanese.

Clinically meaningful mean change from baseline in the angioedema-quality of life (AE-QoL) total score was shown during treatment with C1-INH. Pharmacokinetic data showed markedly higher and enduring post-baseline plasma levels of C1-INH functional activity and C1-I ...

Evaluation of avoralstat, an oral kallikrein inhibitor, in a Phase 3 hereditary angioedema prophylaxis trial: The OPuS-2 study.

Riedl MA, Aygören-Pürsün E, Baker J, Farkas H, Anderson J, Bernstein JA, Bouillet L, Busse P, Manning M, Magerl M, Gompels M, Huissoon AP, Longhurst H, Lumry W, Ritchie B, Shapiro R, Soteres D, Banerji A, Cancian M, Johnston DT, Craig TJ, Launay D, Li HH, Liebhaber M, Nickel T, Offenberger J, Rae W, Schrijvers R, Triggiani M, Wedner HJ, Dobo S, Compropt M, Clemons D, Fang L, Collis P, Sheridan WP, Maurer M.

Allergy. 2018 Sep;73(9):1871-1880. doi: 10.1111/all.13466. Epub 2018 Jun 17.

PMID: 29688579 Free PMC article. Clinical Trial.

The LS mean duration of all confirmed attacks was 25.4, 29.4, and 31.4 hours for the avoralstat 500 mg, avoralstat 300 mg, and placebo groups, respectively. Using the Angioedema Quality of Life Questionnaire (AE-QoL), improved QoL was observed for the avorals ...

Omalizumab rapidly improves angioedema-related quality of life in adult patients with chronic spontaneous urticaria: X-ACT study data.

Staubach P, Metz M, Chapman-Rothe N, Sieder C, Bräutigam M, Maurer M, Weller K.

Allergy. 2018 Mar;73(3):576-584. doi: 10.1111/all.13339. Epub 2017 Dec 11.

PMID: 29058822 Free PMC article. Clinical Trial.

RESULTS: Ninety-one patients were randomized and 68 (omalizumab, n = 35; placebo, n = 33) completed the 28-week treatment period. At baseline, the mean (SD) total Angioedema QoL (AE-QoL): 56.2 [18.7] and 59.9 [19.2]) and Dermatology Life Quality Index (DLQI): 1 ...

H1-antihistamine-refractory chronic spontaneous urticaria: it's worse than we thought - first results of the multicenter real-life AWARE study.

Maurer M, Staubach P, Raap U, Richter-Huhn G, Bauer A, Ruëff F, Jakob T, Yazdi AS, Mahler V, Wagner N, Lippert U, Hillen U, Schwinn A, Pawlak M, Behnke N, Chaouche K, Chapman-Rothe N.

Clin Exp Allergy. 2017 May;47(5):684-692. doi: 10.1111/cea.12900. Epub 2017 Mar 2.

PMID: 28160338 Clinical Trial.



Validated PROMs are routine in clinical studies



Validated PROMs are used in daily practice



Validated PROMs are recommended by guidelines

My experiences

PROMs are helpful

Retrospective PROMs (*ad hoc* evaluation) are especially helpful

Supports with treatment decisions and monitoring treatment

Support to compare outcomes (real life and clinical studies)

Caveat: Too many, too much, too often may annoy patients