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# Highlights AEDV

## In 77TH AAD Congress

## 1-5 March 2019

★ Washington ★

Scientific Initiative of:

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NOVARTIS

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# Immune mediated dermatosis: urticaria & hidradenitis

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Scientific Initiative of:

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# HIGHLIGHTS IN CHRONIC URTICARIA: NEW EMERGING THERAPIES: LIGELIZUMAB

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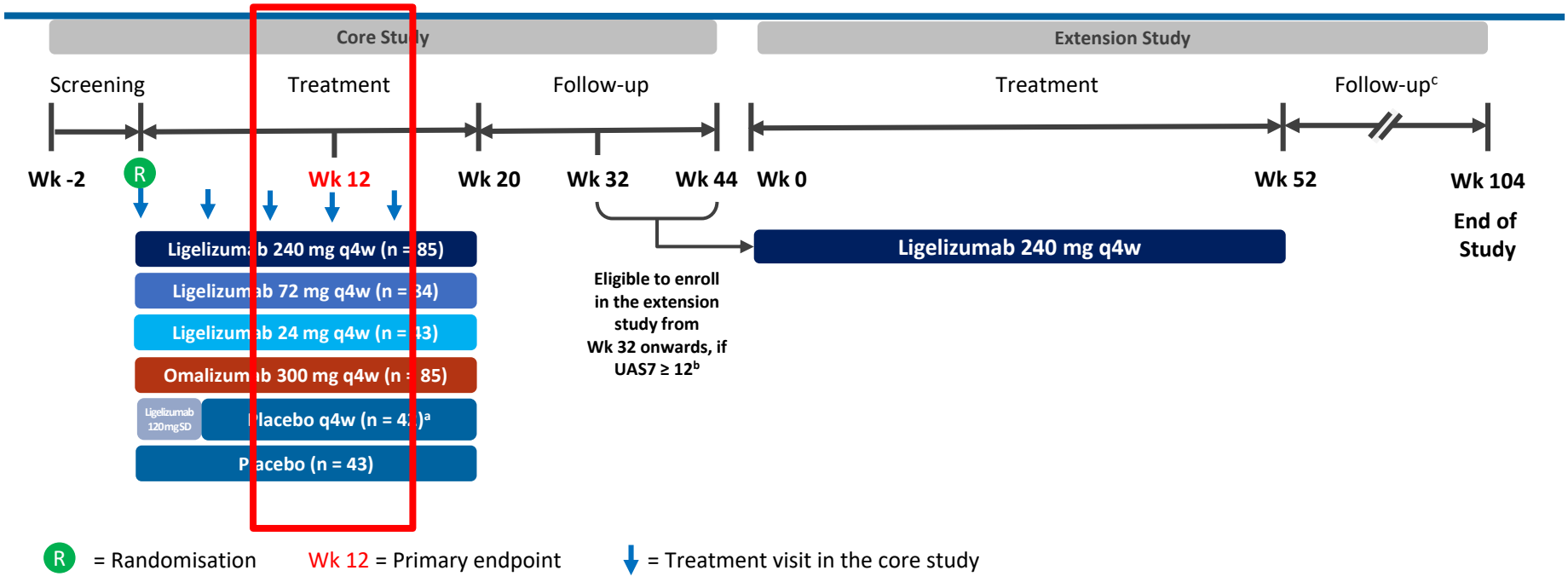
## Ligelizumab* achieves sustained symptom control up to 1 year in the majority of patients with chronic spontaneous urticaria

*Results of the 1-year extension study of the Phase 2b trial*

*QGE031, fully humanized IgG1 monoclonal antibody directed against human IgE that binds with greater affinity than omalizumab (Xolair).



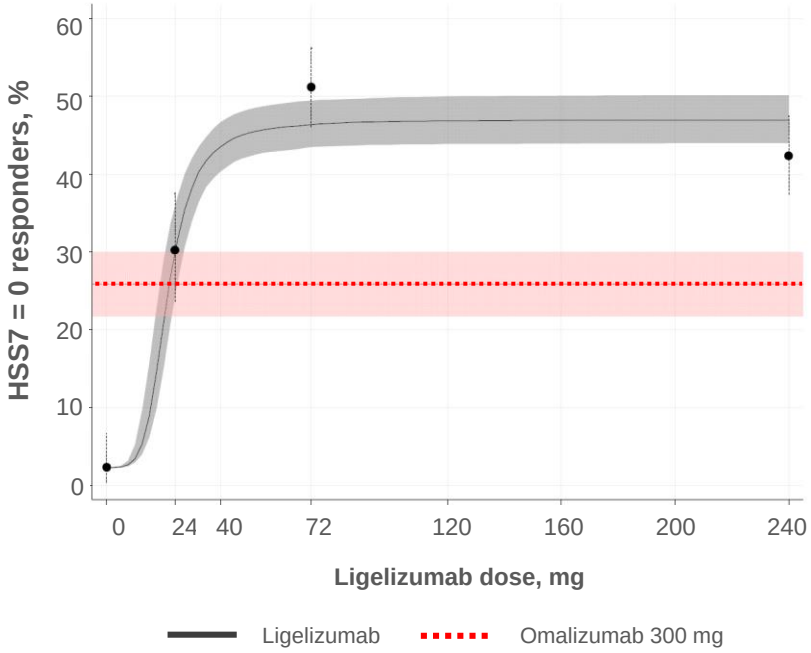

*q4w, every 4 weeks; sc, subcutaneous; SD, single dose; Wk, week*

*[a]The 120 mg single-dose (SD) arm was chosen to characterise the pharmacokinetics/pharmacodynamics. Data from this arm assesses the duration of the response and correlates this with the concentration of drug in the serum at the time when symptoms reappear. [b]Patients who remained in the follow-up period for at least 12 weeks and had active disease (UAS7 ≥ 12), could enter the extension study from Week 32 onwards. [c]Following the 52-week open label period, patients entered a 52-week treatment free follow up period to assess durability of treatment effect, including potential for disease modification*

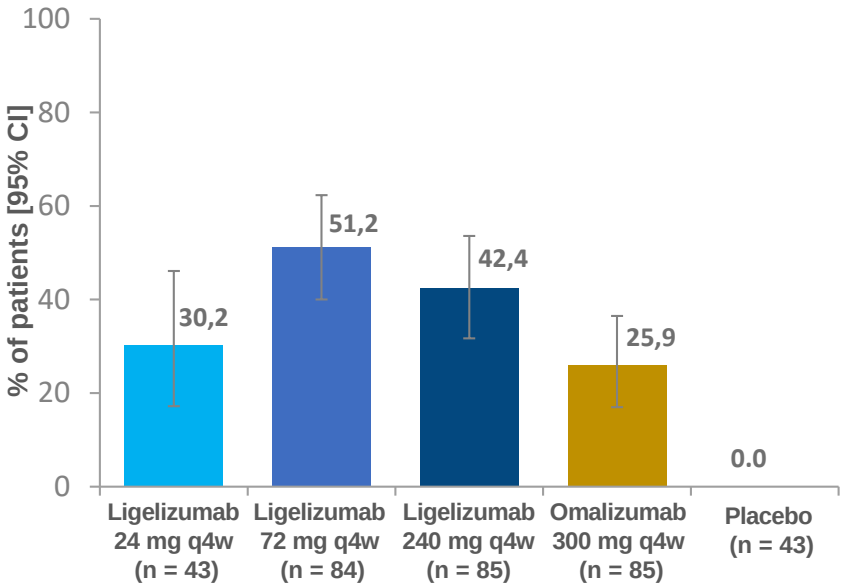
# LIGELIZUMAB EXHIBITED A CLEAR DOSE-RESPONSE IN THE ACHIEVEMENT OF COMPLETE HIVES RESPONSE AT WEEK 12[a] DURING THE CORE STUDY



**Dose-response curve based on HSS7=0 response at Week 12[b]**




**Proportion of patients achieving HSS7=0 at Week 12**

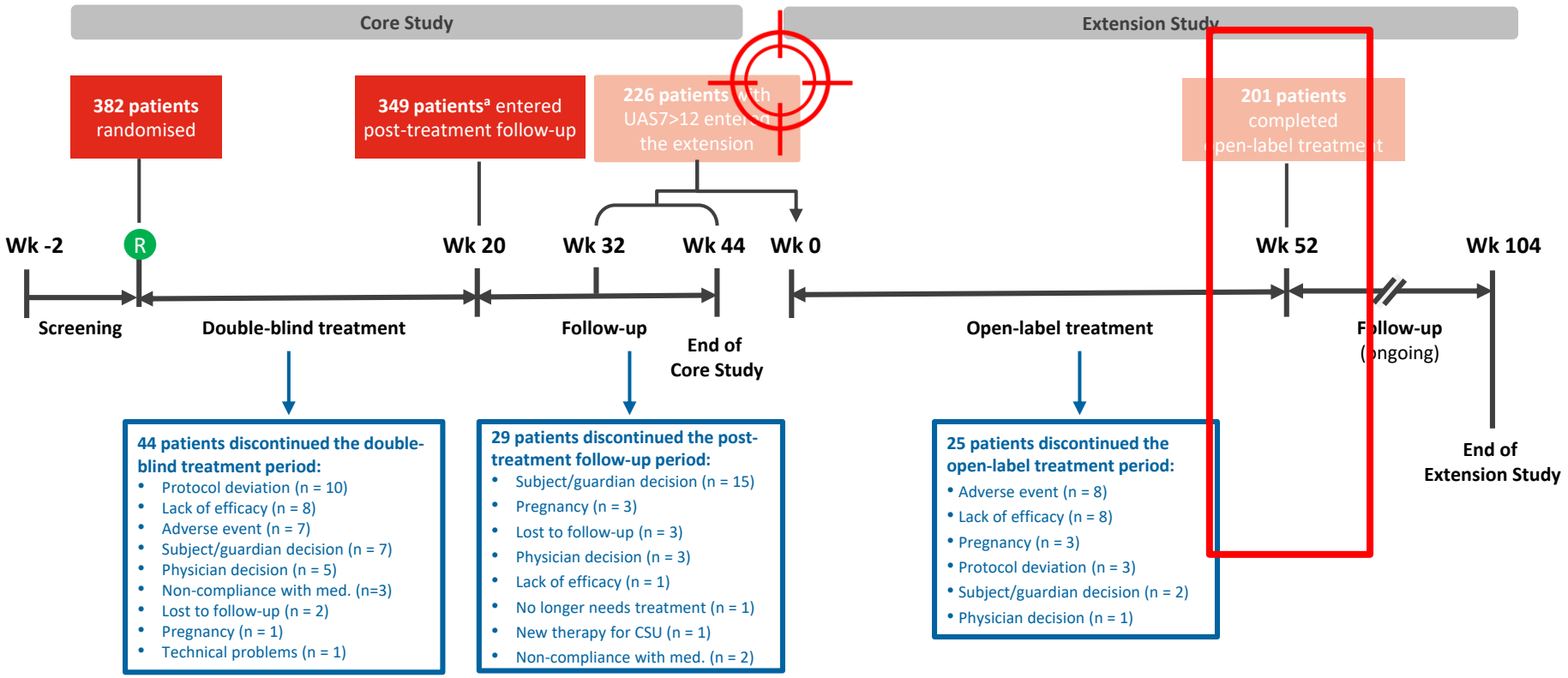



*HSS7, 7-day hives severity score*

*[a]The proportion of patients achieving HSS7=0 Week12 was the primary endpoint of the core study; [b]The dose-response curve shows the median, 20 and 80 percentile, from 1000 bootstrap samples. Dots with error bars represent point estimates and asymptotic 60% confidence interval for each dose in observed data.*

# PATIENT DISPOSITION DURING THE CORE PHASE 2B TRIAL AND THE OPEN-LABEL, SINGLE-ARM EXTENSION STUDY

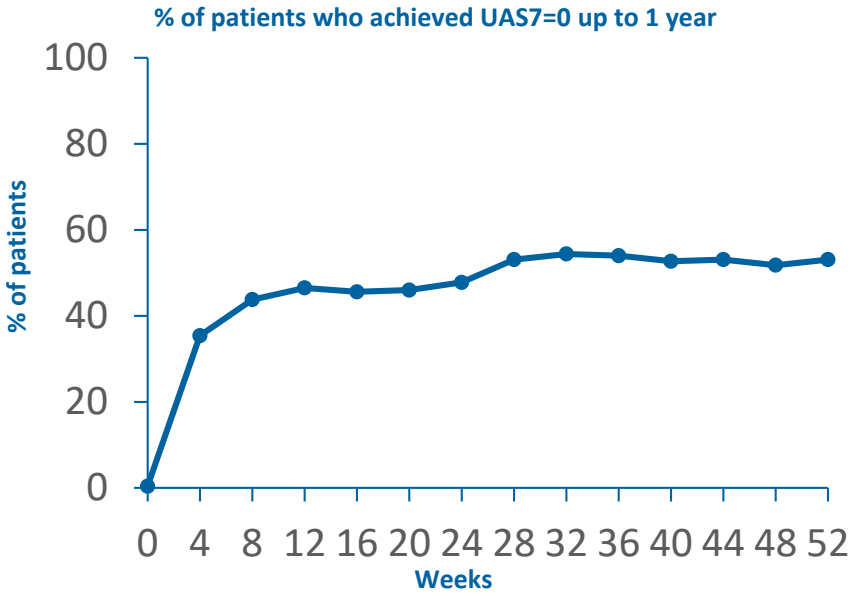


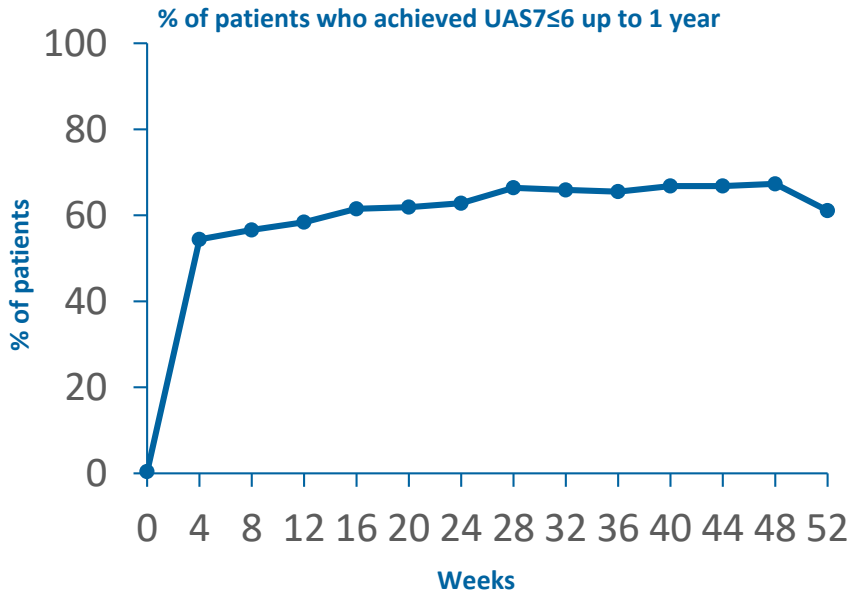



*aPatients who discontinued treatment during the double-blind period were encouraged to remain in the study for the safety analysis and enter the post-treatment follow-up*

# A HIGH RATE OF SUSTAINED AND COMPLETE SYMPTOM CONTROL WAS ACHIEVED WITH LIGELIZUMAB 240 MG Q4W UP TO 1 YEAR






- Complete responses were sustained and over 50% of patients achieved UAS7=0 at the end of Week 52
- Over 50% of patients were well-controlled (UAS7≤6) at Week 4 after one dose of ligelizumab 240 mg

CSU, chronic spontaneous urticaria; q4w, every 4 weeks; UAS7, 7-day urticaria activity score

**High rates of complete (UAS7=0) and well-controlled (UAS7≤6) responses sustained up to 1 year**

# COMPARABLE RATES OF ADVERSE EVENTS RATES WERE REPORTED DURING THE PHASE 2B CORE AND 1-YEAR EXTENSION STUDIES



**CURRENTLY ONGOING:**

Two Phase 3 trials examining the efficacy and safety of ligelizumab 72 and 120 mg q4w treatment up to 1 year in patients with CSU inadequately controlled with $H_1$-antihistamines at approved doses

| | Phase 2b Core Study | | | | | | | Extension |
|---|---|---|---|---|---|---|---|---|
| Category | Ligelizumab q4w | | | Omalizumab 300 mg q4w (N= 85) | Placebo (N = 43) | Ligelizumab 120 mg SD (N = 42) | Total (N = 382) | Ligelizumab 240 mg q4w (N = 226) |
| | 24 mg (N = 43) | 72 mg (N = 84) | 240 mg (N = 85) | | | | | |
| At least one AE | 36 (83.7) | 63 (75.0) | 63 (74.1) | 62 (72.9) | 34 (79.1) | 37 (88.1) | 295 (77.2) | 190 (84.1) |
| Mild | 16 (37.2) | 31 (36.9) | 32 (37.6) | 36 (42.4) | 15 (34.9) | 22 (52.4) | 152 (39.8) | 100 (44.2) |
| Moderate | 16 (37.2) | 27 (32.1) | 28 (32.9) | 21 (24.7) | 12 (27.9) | 13 (31.0) | 117 (30.6) | 77 (34.1) |
| Severe | 4 (9.3) | 5 (6.0) | 3 (3.5) | 5 (5.9) | 7 (16.3) | 2 (4.8) | 26 (6.8) | 13 (5.8) |
| At least one serious AE | 3 (7.0) | 2 (2.4) | 2 (2.4) | 3 (3.5) | 4 (9.3) | 4 (9.5) | 18 (4.7) | 13 (5.8)* |
| AEs leading to discontinuation | 0 (0.0) | 1 (1.2) | 1 (1.2) | 2 (2.4) | 2 (4.7) | 2 (4.8) | 8 (2.1) | 8 (3.5) |
| ≥ 1 AE possibly related to treatment | 5 (11.6) | 18 (21.4) | 24 (28.2) | 7 (8.2) | 12 (27.9) | 6 (14.3) | 72 (18.8) | 54 (23.9) |

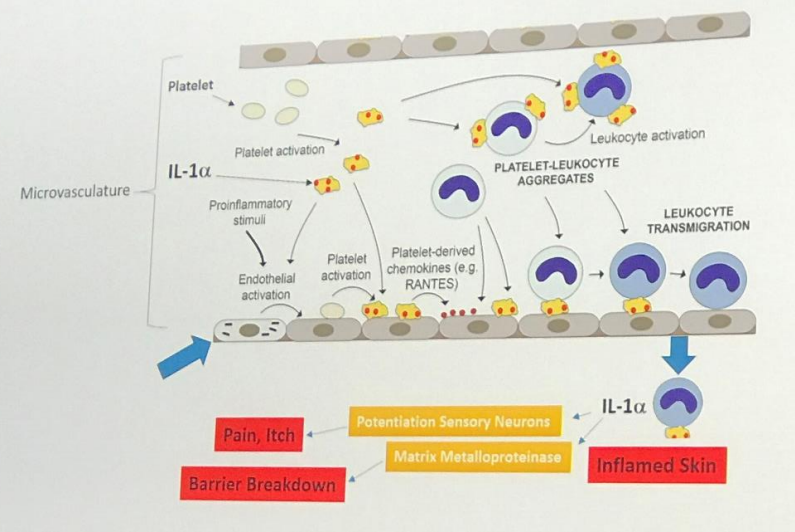
Data presented as n (%)

*One serious AE (hypersensitivity) reported related to ligelizumab (re-assessment ongoing with adjudication committee)

Ligelizumab was well tolerated with no unexpected safety signals

# HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: ROLE OF IL-1∝






- Precursor IL-1 ∝ protein made constitutively by keratinocytes, some epitelial cells and CNS cells
- Binds to Il-1 receptor present on all cells
- Upon stimulation, most inflammatory cells (e.g. Platelets, macrophages, neutrophils, dendritic cells and others) can produce Il-1 ∝
- Synergizes with TNF ∝ to produce cytokines, Il-8, PDGE, and others...

**Biologic effects include:**

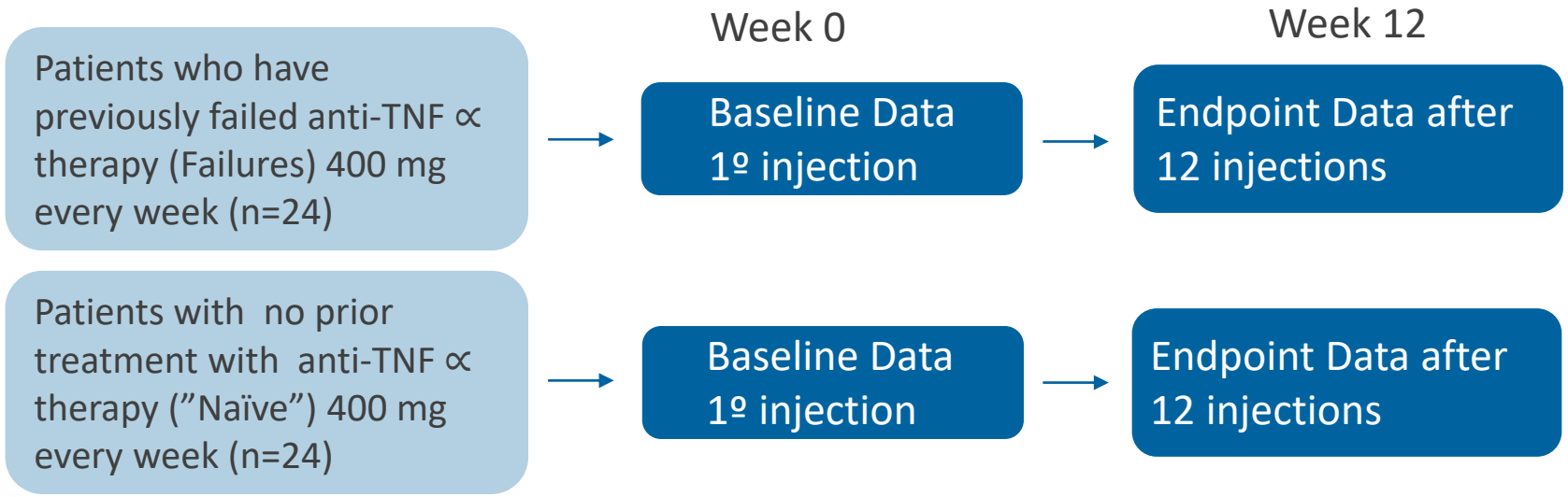
- Induces pro-collagen I and III, fibroblast proliferation and collagen synthesis
- Induces TNF release
- Stimulates hepatocytes to make acute phase reactants
- Increases protease production
- Potentiates pain perception
- Drives neo-angiogénesis

# HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: ANTI IL-1- ∝ : BERMEKIMAB



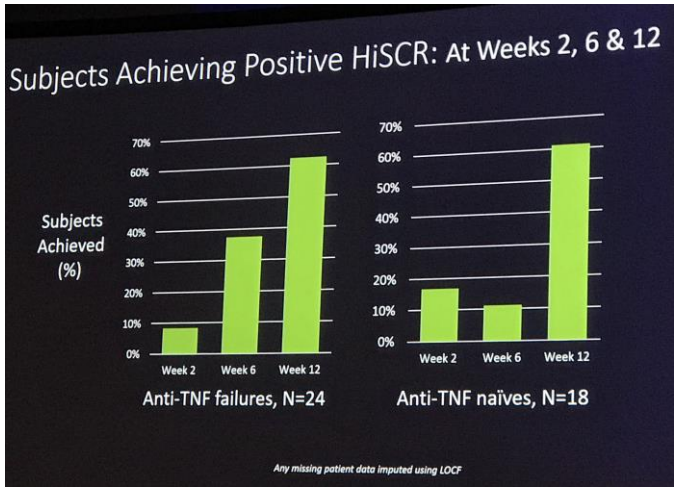
**Phase II Open Label Study of Bermekimab in patients with moderate to severe hidradenitis suppurativa**

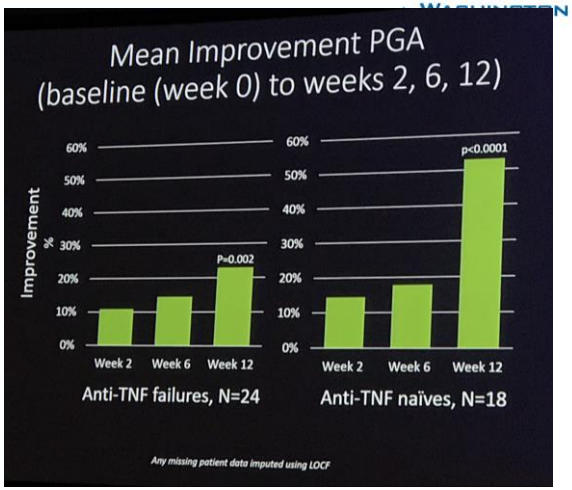
- $IgG_1$ subclass
- Derived from a natural human humoral response against IL-1 ∝
- Binds and neutralizes Il-1 ∝
- Does not bind Il-1b
- Binds all forms of Il-1 ∝ : full, processed, membrane-bound, soluble

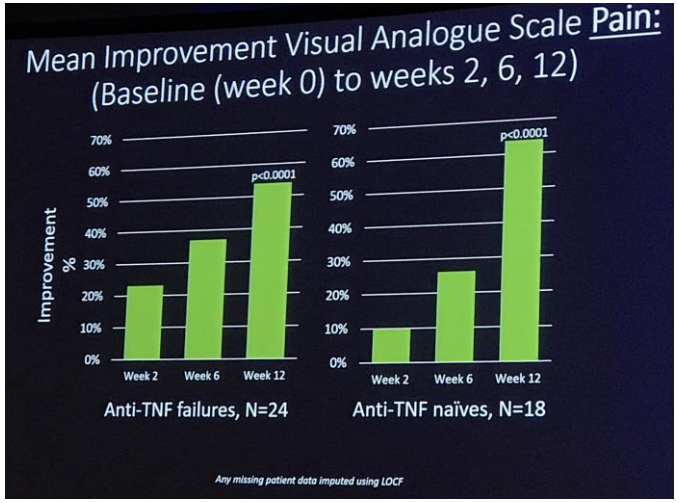


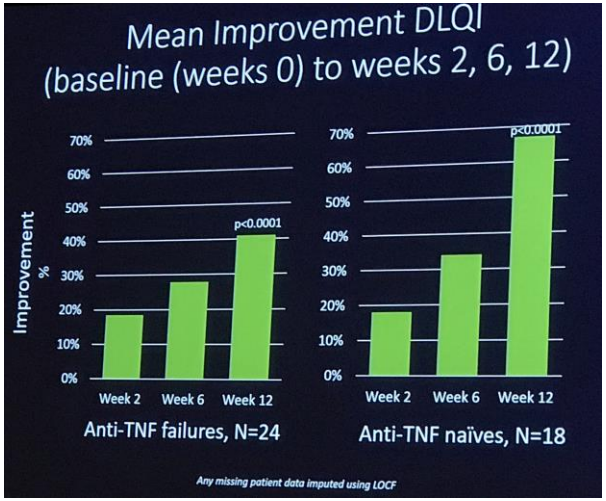
# HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: ANTI IL-1- ∝ : BERMEKIMAB





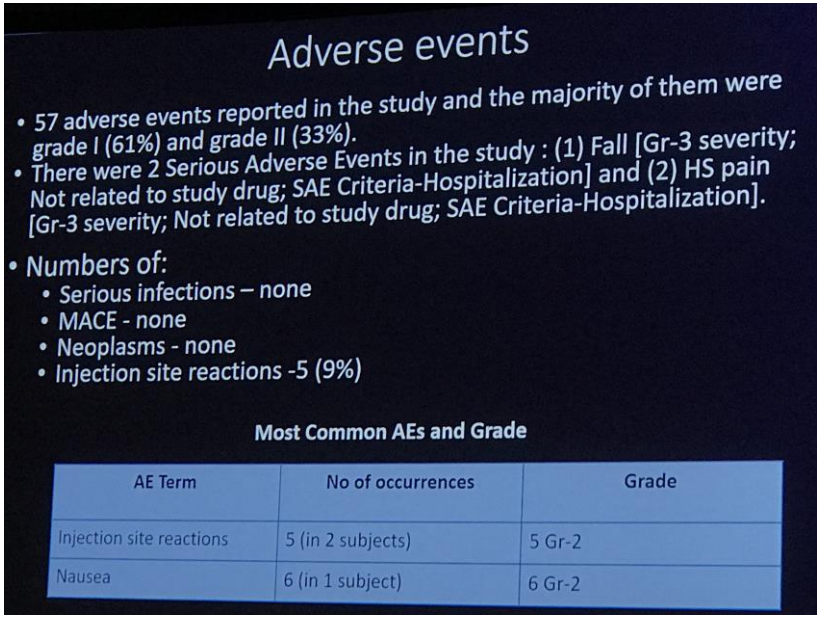
# HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: CURRENTLY ONGOING CLINICAL TRIALS



## Phase II Open Label Study of Bermekimab in patients with moderate to severe hidradenitis suppurativa

**There are now clinical trials in hidradenitis for:**

- IL-17 inhibitor
- IL-23 inhibitor
- Anti-CD-40 monoclonal antibody
- C5a receptor inhibitor
- JAK inhibitor




**Results are expected for the nex year!**

# HIGHLIGHTS IN HIDRADENITIS SUPPURATIVA: NEW INSIGHTS IN COMORBIDITIES

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1. Evaluate the odds of stroke, coronary artery disease, peripheral artery disease, and heart failure in patients with HS compared to the general population (patients without a chronic inflammatory skin disease).
2. Evaluate the odds of stroke, coronary artery disease, peripheral artery disease, and heart failure in patients with HS compared to patients with psoriasis.

- Retrospective cohort study
- 4,914 HS patients, 4,641 psoriasis patients, and 23,266 controls.

**Hidradenitis Suppurativa is Associated with Increased Odds of Stroke, Coronary Artery Disease, Heart Failure, and PAD**

**Table 1: HS vs. Controls**

| | Odds Ratio | Confidence Interval | P-value |
|---|---|---|---|
| Stroke | 1.45 | 1.11-1.90 | 0.0065 |
| PAD | 1.77 | 1.31-2.40 | 0.0002 |
| CAD | 1.41 | 1.10-1.80 | 0.0064 |
| Heart Failure | 1.15 | 0.86-1.54 | 0.3484 |

Table 1: Multivariate analysis using logistic regression to study the odds of stroke, PAD, CAD, and heart failure after adjustment for gender, race, age, hypertension, hyperlipidemia, diabetes, smoking and BMI in patients with HS vs. controls.

**Table 2: HS vs. Psoriasis**

| | Odds Ratio | Confidence Interval | P-value |
|---|---|---|---|
| Stroke | 1.14 | 0.82-1.60 | 0.4259 |
| PAD | 1.04 | 0.74-1.48 | 0.8088 |
| CAD | 1.15 | 0.86-1.53 | 0.3626 |
| Heart Failure | 0.92 | 0.64-1.33 | 0.6587 |

Table 2: Multivariate analysis using logistic regression to study the odds of stroke, PAD, CAD, and heart failure after adjustment for gender, race, age, hypertension, hyperlipidemia, diabetes, smoking and BMI in patients with HS vs. patients with psoriasis.