

Phase III clinical trials of brolocizumab in patients with neovascular age-related macular degeneration

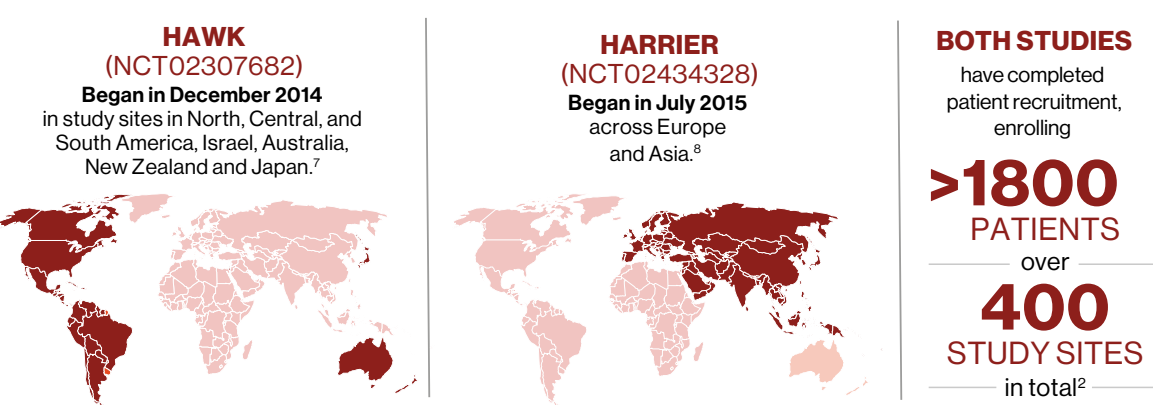
What is brolocizumab (also known as RTH258)?

- A unique, small (26 kDa), humanized, investigational single-chain antibody fragment, which is a potent inhibitor of vascular endothelial growth factor (VEGF)^{1,2,3}
- Abnormally high levels of VEGF are key in the development of neovascular age-related macular degeneration (nAMD), resulting in the formation of abnormal blood vessels in the retina and increased retinal thickness, due to fluid accumulation within or beneath the retinal layers⁴
- nAMD is the leading cause of severe vision loss and legal blindness in people over the age of 65 in North America, Europe, Australia and Asia, impacting an estimated 20 to 25 million people worldwide^{5,6}
- The efficacy and safety of brolocizumab in patients with nAMD is being tested in two pivotal Phase III studies called HAWK and HARRIER^{7,8}

HAWK and HARRIER

Study Overview

HAWK and HARRIER are prospective, randomized, double-masked, 2-year ongoing studies to evaluate the efficacy and safety of brolocizumab for the treatment of nAMD:

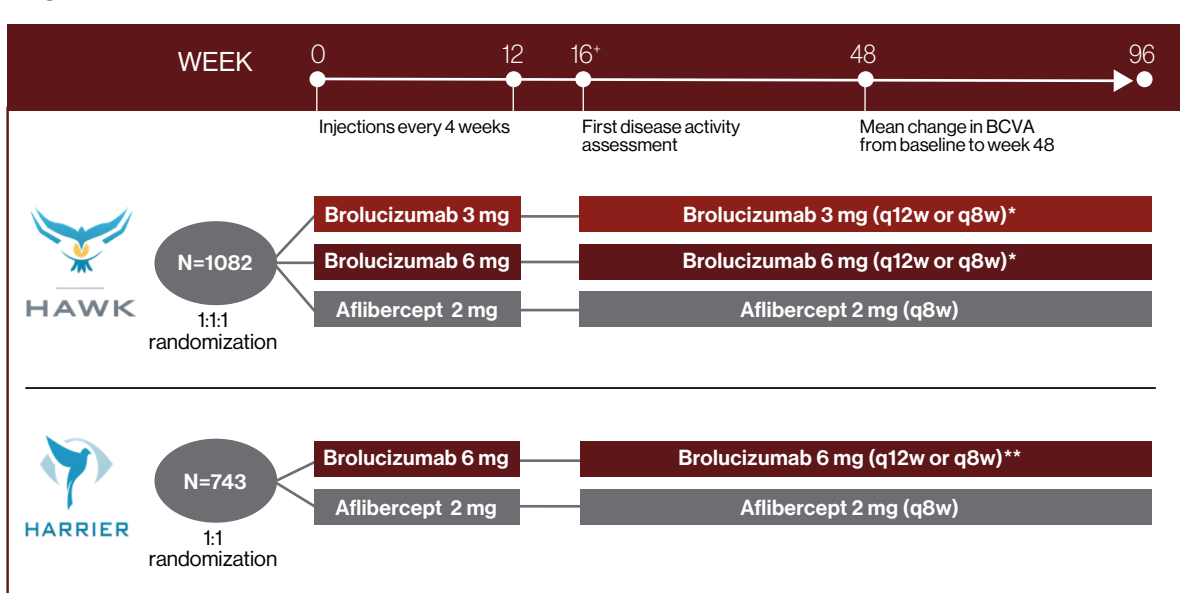


Study Design

What?

Two pivotal trials to test the efficacy and safety of intravitreal injections of brolocizumab 6 mg (HAWK and HARRIER) and brolocizumab 3 mg (HAWK only) versus aflibercept 2 mg in patients with nAMD

How?



+ Matched regimen head-to-head assessment
 * Disease activity assessments were conducted at prespecified visits by the masked investigator supported by protocol guidance based on dynamic functional and anatomical characteristics, at weeks 20, 32, 44, 56, 68, 80 and 92
 ** Additional assessments and potential dosing interval adjustments occurred at weeks 28, 40, 52, 64, 76 and 88 in HARRIER only.

What is the disease activity assessment?

Disease activity assessment (DAA) is the step in which physicians determine which brolocizumab patients are suitable for a 12-week dosing interval and which should be adjusted to an 8-week interval.

In all patients, regardless of treatment arm, disease activity was assessed by the masked investigator. Among patients who received brolocizumab, if the masked investigator determined disease activity to be present, patients were interval adjusted to q8w dosing and they remained at q8w for the remainder of the study.

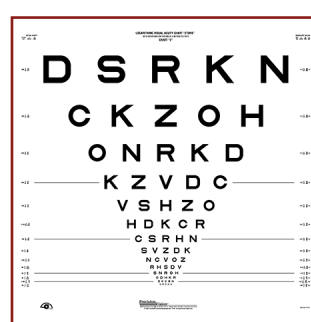


How is the severity of nAMD measured in the HAWK⁷ and HARRIER⁸ trials?

A few key measures:

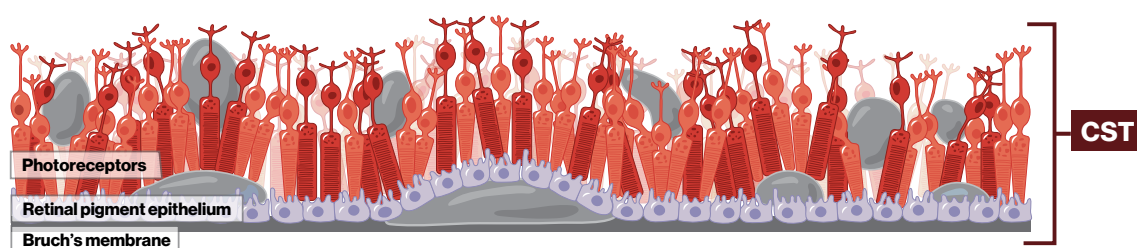
BEST CORRECTED VISUAL ACUITY (BCVA):

BCVA measures the best vision one can achieve with correction (such as glasses), using a standard visual acuity testing chart called the ETDRS chart (Early Treatment Diabetic Retinopathy Study chart)



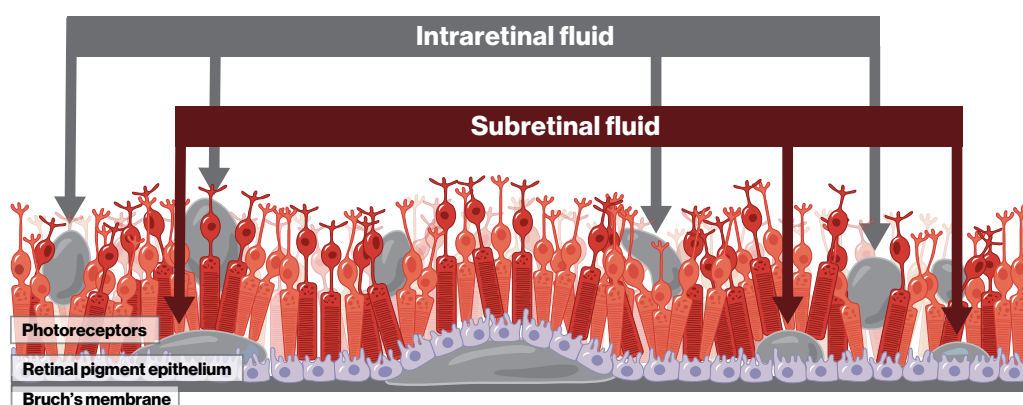
CENTRAL SUBFIELD THICKNESS (CST):

Increases in CST may indicate abnormal fluid accumulation (known as macular edema) in the fovea – the part of the retina responsible for sharp, central vision.



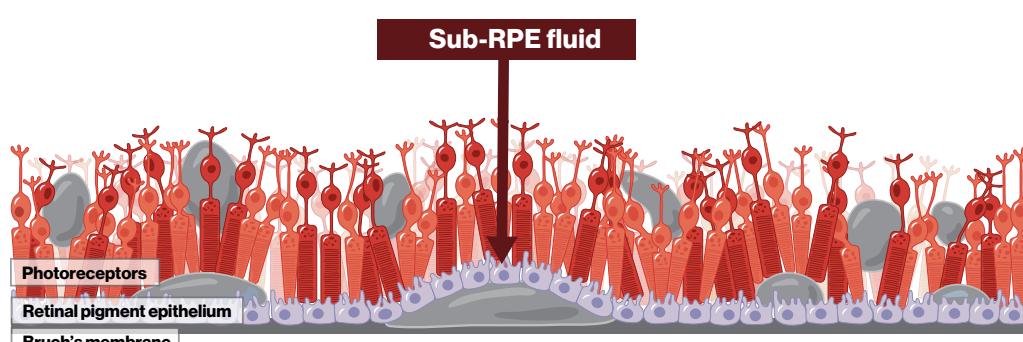
SUB-RETINAL FLUID (SRF) AND INTRA-RETINAL FLUID (IRF):

SRF/IRF is an accumulation of abnormal fluid pockets that may damage cells and surrounding tissue.



SUB-RETINAL PIGMENT EPITHELIUM (RPE) FLUID:

Accumulation of fluid under the RPE may cause a reduction in visual acuity.



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9. Novartis Data on File.



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Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

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