Vilobelimab demonstrates significant improvement in reduction of draining tunnels, total lesion count, IHS4 and the newly introduced modified-HiSCR: a post hoc analysis of the Phase IIb SHINE study

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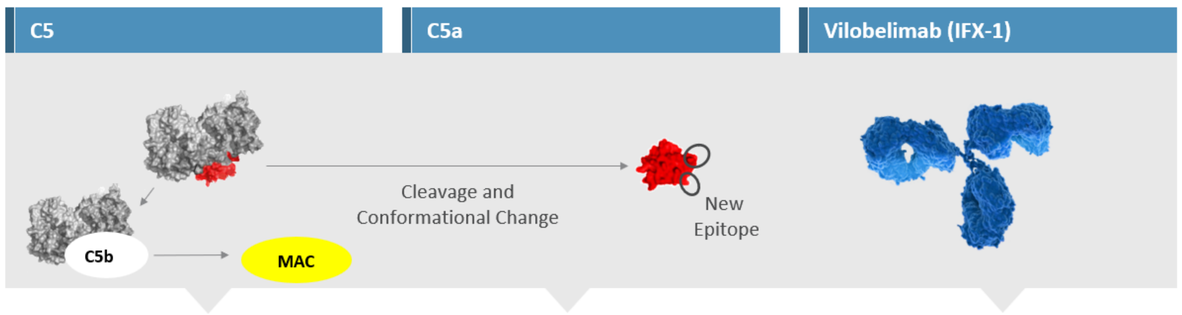
Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory disease characterized by abscesses, nodules and draining tunnels (dTs) with purulent and bloody drainage in sites such as axillae, groin, buttocks, and breasts. Flares are unpredictable and cause permanent disfigurement and disability with need for surgery. Despite availability of biologics, many patients' responses are limited and wane over time. There is increased systemic complement C5a levels and local expression of C5a receptor1 (C5aR1). Skin microbiota express a C5-cleaving enzyme leading to generation of C5a. Yet, C5a cannot be blocked fully by upstream inhibitors such as those for C3 or C5. Therefore, a targeted C5a inhibitor could decrease HS lesions.

SHINE was a prospective, randomized, placebo-controlled, double-blind multicenter study in subjects with moderate to severe hidradenitis suppurativa (HS). Although the primary endpoint (HiSCR50) was not met due to a high placebo response rate, post-hoc analyses demonstrated a significant improvement in HS patients to vilobelimab in the highest dose treatment arm, 1200mg, using additional endpoints that account for reductions in draining tunnels. The purpose of this post-hoc analysis of the Phase IIb SHINE study was to explore additional efficacy endpoints.

C5a Generation and Anti-C5a Vilobelimab[1]

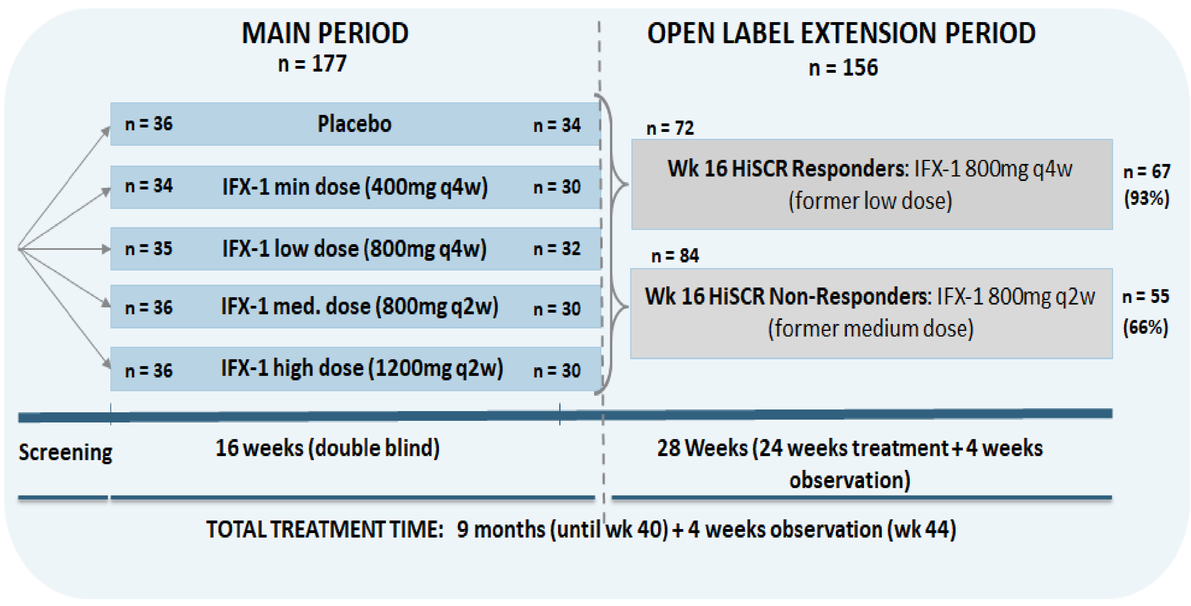


Production of C5a occurs by cleavage of C5 *via*:
- Complement pathway activation, or;
- Directly via enzymes (*e.g.*, thrombin, trypsin and elastase)

C5a is a key chemo-attractant and a strong activator of neutrophils leading to Neutrophil Extracellular Traps (NET) which are believed to be a disease driver in HS; Vilobelimab targets this key mechanism

Key Features:
- Fully selective, binds with high affinity
- Blocks C5a biological effects up to 100% in human blood
- Leaves MAC intact (preserves body's protection against infection)

SHINE Study Design

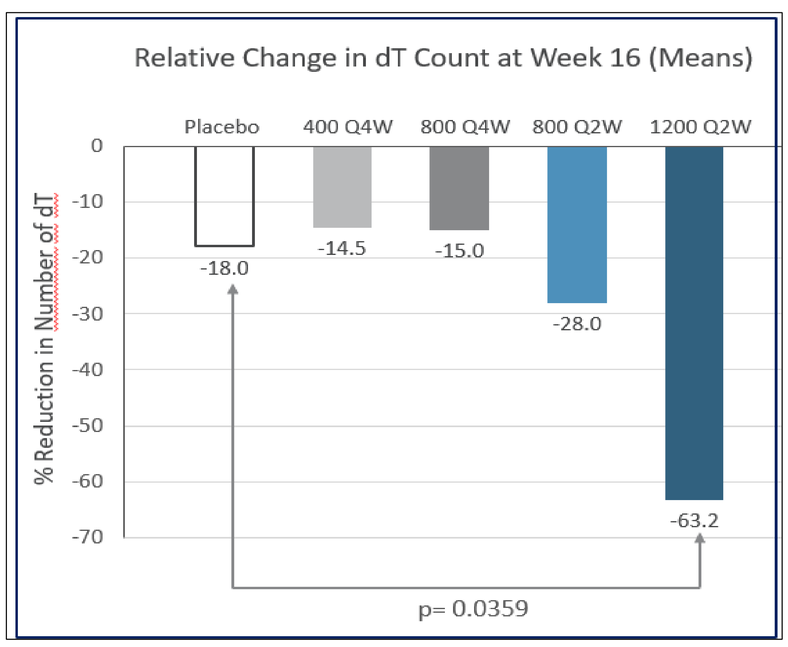


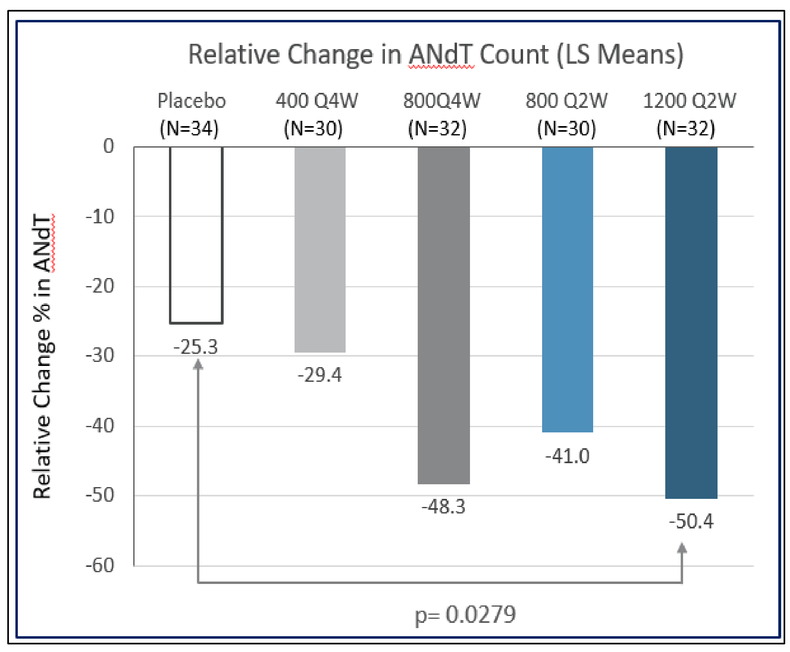
Methods

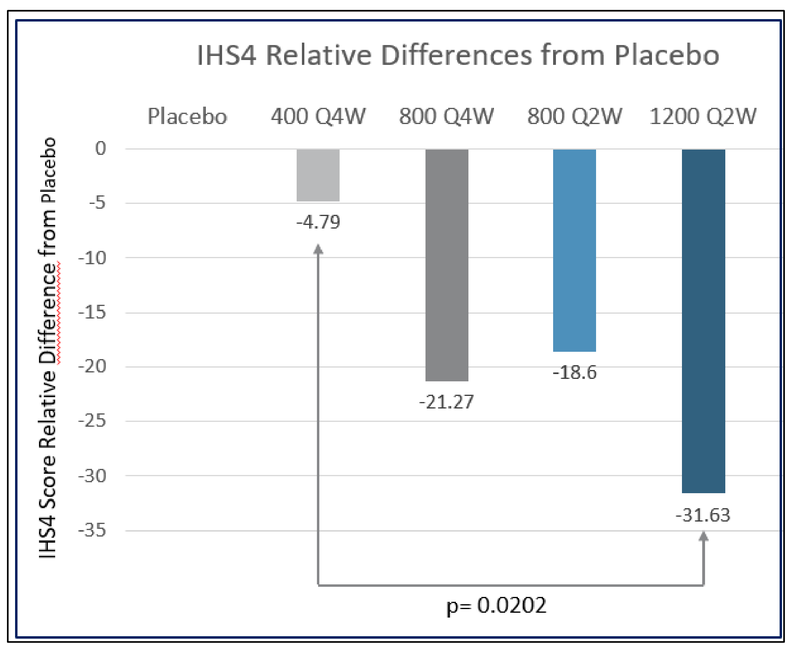
- 177 subjects were randomized into 5 treatment arms: vilobelimab (400mg Q4W, 800mg Q4W, 800mg Q2W, 1200mg Q2W) and placebo.
- Post-hoc analysis for efficacy at week 16 assessing the percentage reduction of draining tunnels (dT), reduction of total lesion counts (abscesses + nodules + draining tunnels (ANdT)) and the International Hidradenitis Suppurativa Score 4 (IHS4)[2] compared to placebo.
- The modified-HiSCR (m-HiSCR defined as at least 50% reduction of ANdT count with 50% reduction of dT count) was also evaluated as part of this post-hoc analysis for the patient population having at least one dT at baseline.

Results

At week 16, Vilobelimab 1200mg Q2W showed a significant reduction of dT, ANdT and IHS4 *vs* placebo. The percentage of responders utilizing the m-HiSCR in patients with at least one dT at baseline was 54.5% for vilobelimab 1200 mg Q2W compared to 26.2% for placebo.







Discussion

Draining tunnels are indicative of severe, chronic inflammatory disease, while abscesses and nodules are acute inflammatory lesions which usually fluctuate. HiSCR50 does not count the reduction in dT, but only considers no increase in dT relative to baseline.[3] The m-HiSCR, however, considers the effect on all 3 lesions with an emphasis on the reduction of dT which greatly impacts HS patients' quality of life. Based on mechanism in targeted blocking of C5a, vilobelimab caused a reduction of all three inflammatory lesion counts with a significant impact on dT. A 1200mg Q2W dose of vilobelimab showed a significant reduction of dT and ANdT counts as well as improvement in IHS4 score compared to placebo. Vilobelimab 1200mg Q2W efficacy in HS is also reflected in a significantly higher responder rate measured by the m-HiSCR compared to placebo.

The observed results suggest that vilobelimab treatment may lead to significant benefit to patients suffering from moderate to severe HS disease and that a dose at or higher than 1200mg Q2W may be required for future studies. The m-HiSCR is suggested as a new tool to be considered when examining the effectiveness of therapeutic intervention for patients with draining tunnels. Additional research will be required to validate this tool.

References: 1. Riedemann et al. *Clin Immunol*. 2017;180:25-32; 2. Zouboulis et al. *Br J Dermatol*. 2017;177:1401-9; 3. Kimball et al. *J Eur Acad Dermatol Venereol*. 2016; 30(6): 989-94

Conflicts of Interest: NCR, CC and HT are employees of InflaRx GmbH.