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RESULTS OF A PHASE 2B STUDY OF VOBARILIZUMAB, AN ANTI-INTERLEUKIN-6 RECEPTOR NANOBODY, AS MONOTHERAPY IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

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Background: Vobarilizumab is a Nanobody® consisting of an anti-IL6 receptor domain and an anti-human serum albumin domain in development for treatment of RA.

Objectives: To assess the efficacy and safety of several dose regimens of vobarilizumab monotherapy administered subcutaneously to patients with active RA.

Methods: Patients with active RA who were intolerant to methotrexate (MTX) or for whom continued MTX treatment was inappropriate were randomized in a 1:1:1:1 ratio to 1 of the 3 blinded dose groups of vobarilizumab or to open-label tocilizumab (TCZ), all of which were given subcutaneously. Efficacy was evaluated descriptively at Week 12 using a number of widely accepted clinical endpoints. Adverse events and routine safety parameters including laboratory assessments were recorded. TCZ administered weekly or biweekly according to local labeling was included to obtain parallel descriptive information.

Results: The study enrolled 251 patients in Europe, Latin America and the United States. Baseline demographics and disease characteristics were well balanced across groups with mean $DAS28_{CRP}$ between 5.9 and 6.2.

Week 12 (% of patients)	Vobarilizumab 150mg q4w (N=62)	Vobarilizumab 150mg q2w (N=62)	Vobarilizumab 225mg q2w (N=63)	Tocilizumab 162mg q1w(N=60) q2w (N=4)
ACR20	73	77	81	78
ACR50	44	37	49	45
ACR70	16	24	21	23
HAQ-DI score decrease ≥0.25	65	68	71	72

$DAS28_{ESR}$ <2.6	34	21	40	25
$DAS28_{CRP}$ <2.6	26	27	41	27
SDAI remission	8	5	8	11
CDAI remission	10	5	6	9

At Week 12, 73% to 81% of the patients assigned to one of the vobarilizumab groups achieved an ACR20 response, while ACR50 and ACR70 response rates between 37 - 49% and 16 - 24%, respectively, were observed (see table). At the end of the 12-week treatment period, clinically meaningful improvement in HAQ-DI scores and remission based on $DAS28_{CRP}$ and $DAS28_{ESR}$ was observed in a substantial number of patients treated with vobarilizumab, either q4w or biweekly. Between 5% and 10% of the patients achieved remission defined by the more stringent CDAI or SDAI criteria. In total, 94% of patients randomized to open-label TCZ received drug weekly. In spite of this disparity in dosing frequency similar efficacy results were obtained in the vobarilizumab and TCZ groups.

One vobarilizumab treated patient (225mg q2w treatment group, 1.6%) experienced a SAE during the treatment period as did 2 patients in the TCZ group (3.1%). Frequencies of treatment-emergent adverse events were similar across the groups. Of the vobarilizumab treated patients, 2.1% discontinued study drug due to TEAEs compared with 6% in the TCZ group. One case of severe hypersensitivity, not considered serious, was reported in the 225mg q2w treatment group. Liver function abnormalities were infrequent across all study groups. Grade 3 neutrophil toxicities were less commonly observed with vobarilizumab (1.1%) than with TCZ (4.3%).

Conclusions: In patients with active RA, treatment with vobarilizumab monotherapy had a positive impact on disease activity with no unexpected safety findings.

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OP0098

REMISSION AND MAINTENANCE OF EFFICACY IN A PHASE 2B STUDY OF VOBARILIZUMAB, AN ANTI-INTERLEUKIN 6 RECEPTOR NANOBODY, IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS DESPITE TREATMENT WITH METHOTREXATE

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Background: Vobarilizumab is a Nanobody® consisting of an anti-IL-6R domain and an anti-human serum albumin domain in development for treatment of RA. The efficacy and safety were assessed in a 24-week double-blind global phase 2b study in patients with active RA on a stable background of MTX. Main efficacy and safety results were previously reported.[Ref1]

Objectives: To report the impact of treatment with vobarilizumab on secondary efficacy endpoints including SDAI and CDAI remission and the sustained response at 4 consecutive visits based on ACR50, ACR70 and $DAS28_{CRP}$.

Methods: Patients were randomized to receive subcutaneously administered placebo or 1 of 4 dose regimens of vobarilizumab in addition to MTX. SDAI and CDAI remission at Week 24 was evaluated, as was maintenance of efficacy as defined by sustained $DAS28_{CRP}$ <2.6 responses at 4 consecutive visits (i.e., at Weeks 12, 16, 20 and 24). In addition, a post-hoc analysis was performed on sustained ACR50 and ACR70 responses from Week 12 through Week 24. Proportions of patients achieving response for these endpoints were summarized by treatment group. Subjects with missing values were analyzed as non-responders.

Results: A total of 345 patients were randomized. Demographics and baseline characteristics were similar across groups with mean baseline $DAS28_{CRP}$ between 5.8 and 6.2. At Week 24, up to 19% and 20% in the vobarilizumab groups reached CDAI and SDAI remission, respectively vs. 10% and 9% who received placebo (Table 1).

Table 1: Percentage of patients with CDAI and SDAI remission at Week 24

	Placebo (N=69)	Vobarilizumab 75mg q4w (N=69)	Vobarilizumab 150mg q4w (N=70)	Vobarilizumab 150mg q2w (N=68)	Vobarilizumab 225mg q2w (N=69)
CDAI remission (≤2.8)	10	15	19	12	19

SDAI remission (≤3.3)	9	10	19	15	20

At Week 24, up to 61% and 45% of the patients in the vobarilizumab groups achieved an ACR50 or ACR70 response, respectively (39% and 17% on placebo). Approximately one third of the randomized patients in the 3 highest treatment groups had a sustained ACR50 response from Week 12 through Week 24 (Table 2). Sustained remission defined by $DAS28_{CRP}$<2.6 at 4 consecutive visits, i.e. at weeks 12, 16, 20 and 24, was observed in 20% to 25% of the patients in the 3 highest dosing arms compared with 3% of those receiving placebo.

Table 2: Percentage of patients with sustained efficacy response at 4 consecutive visits (Weeks 12, 16, 20 and 24)

	Placebo (N=69)	Vobarilizumab 75mg q4w (N=69)	Vobarilizumab 150mg q4w (N=70)	Vobarilizumab 150mg q2w (N=68)	Vobarilizumab 225mg q2w (N=69)
$DAS28_{CRP}$<2.6	3	4	20	25	20
ACR50	16	14	29	31	39
ACR70	4	7	11	13	13

Conclusions: In patients with active RA, treatment with vobarilizumab at the 3 highest dose regimens in addition to MTX had a positive and sustained impact on disease activity through Week 24 as defined by clinically relevant efficacy endpoints.

References: References: [1]Weinblatt et al. (Annual Scientific Meeting, Canadian Rheumatology Association, 2017)

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