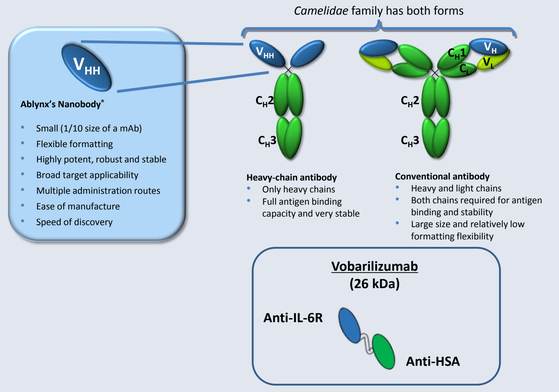
FRI0239

Results of a Phase 2b Study of Vobarilizumab, an Anti-Interleukin 6 Receptor Nanobody®, as Monotherapy in Patients with Moderate-to-Severe Rheumatoid Arthritis

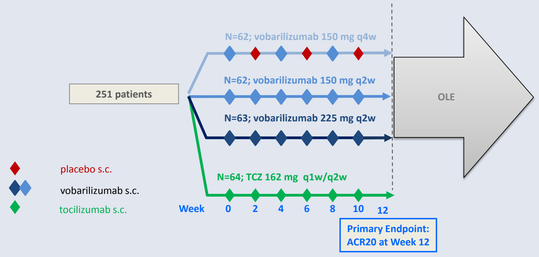
Thomas Dörner[1], Michael E. Weinblatt[2], Katrien Van Beneden[3], Evelyne Dombrecht[3], Kristof De Beuf[3], Pieter Schoen[3] and Robert K. Zeldin[3]

[1]Charité University Hospitals, Berlin, Germany, [2]Brigham and Women's Hospital, Boston, MA, US, [3]Ablynx NV, Zwijnaarde, Belgium

Background: vobarilizumab, an IL-6R targeting Nanobody



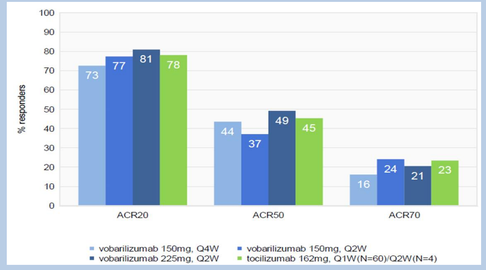
Study Design of the Phase 2b Clinical Trial



- A total of 251 patients were enrolled in Europe, Latin-America and the United States
- In total, 94% of the patients randomized to open-label TCZ received drug weekly
- All 3 vobarilizumab dosing regimens were expected to be efficacious

Efficacy Results: ACR Responses at Week 12

Proportions of Patients achieving ACR20, ACR50 and ACR70 Responses at Week 12



- The primary efficacy analysis indicated that at Week 12, 73% to 81% of the patients assigned to 1 of the vobarilizumab groups achieved an ACR20 response
- The proportion of patients treated with vobarilizumab who achieved ACR50 and ACR70 response rates was between 37-49% and 16-24%, respectively
- Similar efficacy results were obtained in the TCZ group

Safety through Week 12

Number of patients (%) with treatment-emergent adverse events (TEAE)	vobarilizumab 150 mg, q4w N=62	vobarilizumab 150 mg, q2w N= 62	vobarilizumab 225 mg, q2w N=63	TCZ 162 mg, q1w/q2w, N=60/4
Any TEAE	**34 (54.8)**	**33 (53.2)**	**31 (49.2)**	**31 (48.4)**
- treatment-related	21 (33.9)	20 (32.3)	21 (33.3)	20 (31.3)
- leading to study drug discontinuation	1 (1.6)	1 (1.6)	2 (3.2)	4 (6.3)
Any serious TEAE	**0**	**0**	**1 (1.6)**	**2 (3.1)**
- treatment-related	0	0	1 (1.6)	2 (3.1)
- leading to death (not treatment-related)	0	0	0	0

- One case of severe hypersensitivity, not considered serious, was reported in the 225 mg q2w treatment group
- Two vobarilizumab-treated patients experienced a grade 3 liver enzymes toxicity (1 ALT and 1 AST, respectively; both were considered as not related to the study treatment)
- Grade 3 neutrophil toxicities were less commonly observed with vobarilizumab (1.1%) than with TCZ (4.3%)

Objectives and Methods

Objectives

- This **phase 2b** study of vobarilizumab was designed to assess the **efficacy** and **safety** of several dose regimens as monotherapy in adults with **moderate-to-severe RA**

Methods

- **Patients intolerant to MTX** or **for whom continued MTX treatment was inappropriate** were randomized 1:1:1:1 to one of 3 blinded dose regimens of **vobarilizumab** or to **open-label tocilizumab (TCZ)**
- Patients on vobarilizumab who completed the study could enroll in a 2-year open-label extension study
- **Efficacy** was evaluated **descriptively** at Week 12 using a number of widely accepted clinical endpoints
- The **open-label TCZ arm** allowed to obtain **parallel descriptive information** concerning the efficacy and safety of TCZ in the same clinical trial RA population
- **Adverse events** and routine **safety parameters** including laboratory assessments were recorded

Baseline Demographics and Disease Activity – ITT Population

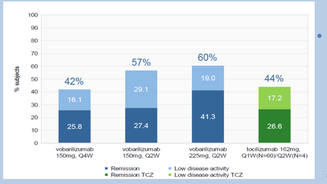
Mean (SD)	vobarilizumab 150 mg, q4w N=62	vobarilizumab 150 mg, q2w N=62	vobarilizumab 225 mg, q2w N=63	TCZ 162 mg, q1w/q2w N=60/4
Age, years	53.0 (12.3)	51.2 (12.1)	51.3 (11.8)	50.0 (12.3)
Females (%)	79.0	85.5	85.7	87.5
Duration of RA, years	8.0 (7.4)	8.4 (6.7)	7.7 (8.0)	6.8 (5.7)
TJC 68	27.9 (16.0)	28.1 (14.3)	25.8 (13.5)	27.3 (13.1)
SJC 66	14.4 (7.7)	17.1 (9.5)	17.3 (8.5)	17.3 (9.8)
CRP, mg/L	17.7 (19.9)	23.6 (22.9)	33.5 (41.6)	22.0 (20.7)
$DAS28_{CRP}$	5.9 (0.9)	6.2 (0.9)	6.1 (1.0)	6.2 (0.9)
$DAS28_{ESR}$	6.4 (0.9)	6.8 (0.9)	6.6 (0.9)	6.8 (1.0)
HAQ-DI score	1.6 (0.7)	1.8 (0.7)	1.8 (0.7)	1.7 (0.8)

- Demographics and baseline disease characteristics were well balanced across groups, and indicated the presence of long-standing disease in patients with moderate-to-severe RA
- Majority of patients discontinued prior MTX because of intolerance (63.7% of all patients)

ITT, intent-to-treat; TJC, tender joint count; SJC, swollen joint count; CRP, C-reactive protein; $DAS28_{CRP/ESR}$, disease activity score in 28 joints using CRP or ESR; HAQ-DI, health assessment questionnaire disability score for RA

Secondary Efficacy Results at Week 12

Proportions of Patients achieving Low Disease Activity (LDA)* and $DAS28_{CRP}$<2.6 at Week 12



- The percentage of patients achieving at least LDA at Week 12 was highest in the 150 mg q2w and 225 mg q2w dosing groups

* 2.6≤ $DAS28_{CRP}$≤ 3.2

Proportions of Patients achieving secondary efficacy endpoints at Week 12

Percentage (%) of patients	vobarilizumab 150 mg, q4w, N=62	vobarilizumab 150 mg, q2w, N=62	vobarilizumab 225 mg, q2w, N=63	TCZ 162 mg, q1w/q2w, N=60/4
$DAS28_{ESR}$< 2.6	34	21	40	25
SDAI remission	8	5	8	11
CDAI remission	10	5	6	9
HAQ-DI score decrease ≥ 0.25	65	68	71	72

- At week 12, clinically meaningful improvement in HAQ-DI scores was observed in a substantial proportion of patients

Conclusions

- This phase 2b study provides evidence that in patients with moderate- to-severe RA, treatment with subcutaneous vobarilizumab monotherapy for 12 weeks, reduced the signs and symptoms and improved the physical function
- 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
- In spite of the disparity in dosing frequency, similar efficacy results were obtained in the vobarilizumab groups and the open-label TCZ group
- Safety findings were in general not dose-related and were consistent with the known safety profile associated with IL-6R blockade. No unexpected safety findings were reported