PRESS RELEASE

For UK medical and trade media

AbbVie Data Demonstrate Efficacy and Cost-Effectiveness of Tight Control Approach for Disease Management with HUMIRA® (adalimumab) in Patients with Moderate to Severe Crohn’s Disease

- Phase 3 CALM study shows that closely monitoring disease activity using the tight control approach with adalimumab led to improved endoscopic and clinical outcomes in patients with moderate to severe Crohn’s disease.¹
- A separate economic assessment of the CALM study shows tight control approach was cost-effective due to increased time in remission, decreased Crohn’s disease-related hospitalisations and improvements in quality of life measures compared to clinical management approach.²
- An additional analysis of patients enrolled in CALM assessed major adverse outcomes, such as hospitalisations, surgical procedures, including major surgeries and serious disease-related complications.³
- Tight control is a treatment approach based on regular assessment of disease activity using pre-specified clinical and biological outcome measures and adjusting treatments accordingly.¹,⁴

MAIDENHEAD, UK, November 1, 2017 – AbbVie, a global research and development based biopharmaceutical company, today announced full results from the Phase 3 CALM study evaluating the tight control approach, which closely monitored clinical and biologic disease activity and adjusted a HUMIRA® (adalimumab)-based therapy regimen in patients with moderate to severe Crohn’s disease.

Presented at United European Gastroenterology (UEG) Week® 2017 in Barcelona and recently published in The Lancet, the data show that after 48 weeks, patients using the tight control approach achieved the study’s primary endpoint of mucosal healing (Crohn’s disease Endoscopic Index of Severity [CDEIS] <4), plus absence of deep ulcers and improved clinical outcomes compared with those who underwent the traditional clinical management of symptoms.¹

Additionally, an economic assessment of the CALM study using costs reflecting a United Kingdom (U.K.) setting found that the tight control approach was a cost-effective treatment strategy based on increased time in remission, decreased Crohn’s disease-related hospitalisations and improvements in quality-of-life measures for patients.² These data were also presented at UEG Week 2017.

¹, ², ³, ⁴ Additional supporting data available upon request.
“These results add to the growing body of knowledge supporting the use of a tight control approach to help people manage their Crohn’s disease,” said Isidro Villanueva Torrecillas, vice president, Immunology Medical Affairs, AbbVie. “Building on our deep expertise in serious immune-mediated inflammatory conditions, we are exploring innovative approaches in care with the ultimate goal of improving outcomes for these patients.”

“CALM is the first study to demonstrate that individualising treatment improves outcomes for people with Crohn’s disease, based on objective test results (‘biomarker targets’), rather than traditional, symptom-driven care. This ‘treat-to-target’ approach, where patients are closely monitored so that treatment can be escalated or de-escalated in line with the targets, enables specialists to intervene earlier and to obtain tighter control of this disease which is such a challenge to treat. This improves outcomes: the gut heals better, more patients get off steroids and the need for hospitalisation is reduced without any additional safety concerns. This approach is cost effective and brings discipline to the monitoring and management of Crohn’s disease. It is a real step forward, so I hope there will be widespread adoption of this approach in clinical practice,” said Professor Simon Travis from The Translational Gastroenterology Unit, University of Oxford.

The oral presentation at UEG Week® 2017 (#OP225), titled “Superior endoscopic and deep remission outcomes in adults with moderate to severe Crohn's disease managed with treat to target approach versus clinical symptoms: data from CALM,” evaluated the tight control strategy, which was based on regular assessment of disease activity using both pre-specified clinical and biological outcome measures including serum C-reactive protein (CRP) and fecal calprotectin (FC), Crohn’s disease Activity Index (CDAI) and prednisone use. The clinical management comparator group adjusted treatments according to traditional clinical outcome measures including CDAI and prednisone use. After 48 weeks, significantly more patients using the tight control approach achieved the primary endpoint of mucosal healing (defined as CD Endoscopic Index of Severity [CDEIS] <4) plus the absence of deep ulcers compared with the approach based solely on the clinical management of symptoms (45.9 percent (n=56/122) versus 30.3 percent (n=37/122) respectively, p=0.010). No new safety signals with adalimumab were observed, and the overall rate of adverse events was similar between the tight control and clinical management groups. Please see the publication for additional safety findings.

A second oral presentation (#OP017), titled, “Treat to target for Crohn’s disease with adalimumab treatment is cost effective over 48 weeks: an economic assessment of the CALM trial,” performed an economic assessment of tight control compared to clinical management in a cost-effectiveness model using CALM data from a U.K. setting. Over 48 weeks, the tight control approach was associated with higher average remission rate (62.1 percent versus 47.3 percent), fewer Crohn’s disease-related hospitalisations (mean 0.13 versus 0.28 events/person year), higher quality-adjusted life years (QALYs)
(0.684 versus 0.652) and more adalimumab injections (mean 30.87 versus 24.72) than clinical management of symptoms. While the total medical costs were slightly higher in the tight control group (£13,296) compared to clinical management treatment (£12,627), tight control had 0.032 higher QALYs than clinical management, resulting in an incremental cost-effectiveness ratio (ICER) of £20,913 per QALY. ICER is defined as the difference in cost between two treatments divided by the difference in their effectiveness. The resulting ratio represents the incremental costs associated with the benefits of a therapy. In this study, the ICER amount was within the National Institute for Health and Care Excellence (NICE) threshold of £20,000-£30,000, demonstrating that tight control is cost effective compared to clinical management.

Additional data in a third oral presentation (#OP227) showed that tight control led to a reduction of major adverse outcomes indicative of more serious disease, including Crohn’s disease-related hospitalisations. The rate of hospitalisations was significantly lower in the tight control group compared to clinical management of symptoms (14 events [13.2 events/100 patient years] versus 29 events [28.0 events/100 patient years], p=0.021). The rates of Crohn’s disease-related surgical procedures between treatment arms were not significantly different with 7 events (6.6 events/100 person years, p=0.582) in the tight control group and 9 events (8.7 events/100 person years, p=0.582) in the clinical management group. The proportion of patients with Crohn’s disease-related hospitalisation or serious complication was numerically lower in the tight control group compared with the clinical management group (18 patients [14.8 percent] versus 25 patients [20.5 percent], p=0.240). The tight control group was associated with numerically lower risk of Crohn’s disease-related hospitalisation or serious complication than the clinical management group (hazard ratio=0.7, 95% CI 0.4-1.3, p=0.249). A longer study would needed to confirm these findings.

Notes to editors

About the Phase 3 CALM Study
The “Open-Label, Multi Centre, Efficacy and Safety Study to Evaluate Two Treatment Algorithms in Subjects with Moderate to Severe Crohn’s Disease,” study (CALM) was a prospective, open-label, multicentre, active-controlled, Phase 3 study that assessed the impact of tight control versus standard clinical management of moderate to severe Crohn’s disease. The tight control strategy adjusted treatment based upon stringent criteria of C-reactive protein (CRP), fecal calprotectin (FCP), Crohn’s disease Activity Index (CDAI) and prednisone use, compared to the clinical management of symptoms approach which used CDAI and prednisone use as the basis for treatment optimisation. Patients enrolled in the CALM study were biologic- and immunomodulator-naive. After receiving a prednisone taper, patients were randomised to the clinical management (n=122) or tight control study arms (n=122).
Patients could also be randomised early without receiving prednisone if the patient had already been on prednisone, had a history of intolerance or a contraindication to the use of steroids, or if the investigator felt it was in the patient’s best interest. In both groups, treatment was escalated in a step-wise manner from no treatment to adalimumab 160/80 mg at week zero and two followed by 40 mg every other week, to adalimumab 40 mg weekly, to adalimumab 40 mg weekly plus azathioprine. Escalation was determined by meeting failure criteria. Baseline characteristics between tight control and clinical management groups were similar. The primary endpoint was mucosal healing, defined as a CDEIS of less than 4, plus an absence of deep ulcers at week 48 after randomization. Non-ranked secondary endpoints were evaluated, including deep remission (CDAI< 150, no steroids for 8 weeks or more, no fistula, CDEIS<4 and no deep ulcers) and biologic remission (FCP<250 ug/g, CRP<5 mg/L and CDEIS<4).

About the Economic Assessment of the CALM Study

A cost-effectiveness model was developed to evaluate the economic value of tight control versus clinical management from the CALM study using costs reflecting a U.K. setting. CDAI was used to map patients into four health states (remission: CDAI <150, moderate: CDAI ≥150 to <300, severe: CDAI ≥300 to <450, very severe: CDAI ≥450) weekly over the 48-week trial. Each health state was associated with corresponding health utility from a UK analysis.

About the Crohn’s Disease-related Adverse Outcomes Analysis of the CALM Study

Additionally, a separate analysis of patients enrolled in CALM assessed major adverse outcomes, such as hospitalisations, surgical procedures, including major surgeries and serious disease-related complications. Any hospitalisation on or after randomization and up to 70 days after last dosing were summarized in all randomised patients.

About adalimumab

For further information, please see the Summary of Product Characteristics: https://www.medicines.org.uk/emc/medicine/31860

About AbbVie

AbbVie is a global, research-driven biopharmaceutical company committed to developing innovative advanced therapies for some of the world’s most complex and critical conditions. The company’s mission is to use its expertise, dedicated people and unique approach to innovation to markedly improve treatments across four primary therapeutic areas: immunology, oncology, virology and neuroscience. In more than 75 countries, AbbVie employees are working every day to advance health solutions for people around the world. For more information about AbbVie, please visit us at www.abbvie.co.uk, follow @abbvieuk, on Twitter or YouTube channel.
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3 Colombel, Jean-Frederic, et al. A treat to target approach decreases the rate of CD-related adverse outcomes versus a clinical approach in patients with moderate to severely active Crohn’s disease: data from CALM. United European Gastroenterology Week, Barcelona, October 30, 2017. [Abstract #OP227].

