

Session: RA Treatment: Biologic Efficacy RCT's

Monday, Oct 27, 2008, 2:30 PM - 4:00 PM

Presentation: 1210 - **The AMBITION Study: Superiority of Tocilizumab (TCZ) vs Methotrexate (MTX) Monotherapy in Patients with Rheumatoid Arthritis (RA)**

Pres. Time: Monday, Oct 27, 2008, 3:00 PM - 3:15 PM

Location: Room 307

Category: 18. RA treatment: small molecules

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Abstract: **Background:** Despite the recognized role of biologic agents in the treatment of RA, methotrexate remains the gold-standard. The Actemra versus **Methotrexate double-Blind Investigative Trial In mONotherapy (AMBITION)** study compared the efficacy and safety of monotherapy with the novel anti-interleukin-6 receptor monoclonal antibody, TCZ, versus MTX monotherapy in patients with active RA.

Methods:

International multicenter, randomized, double-blind trial. All patients (n=572) had moderate to severe active RA and had not failed prior MTX or biologic therapy. Over a 24-wk period, patients received either TCZ 8 mg/kg every 4 wk, or MTX 7.5 mg/wk titrated up to 20 mg/wk within 8 wk. Primary efficacy analysis examined non-inferiority of TCZ ACR20 response at Wk 24 vs MTX in the PP population (n=524). If non-inferiority was established, secondary analyses investigated the superiority of TCZ over MTX for other

efficacy outcomes in the ITT population (n=570).

Results:

TCZ non-inferiority vs MTX was established: 70.6% of TCZ and 52.1% of MTX patients achieved an ACR20 response by Wk 24 (PP population; weighted difference 0.21, 95% CI 0.13, 0.29). In the ITT population, TCZ was superior to MTX, with a significantly higher proportion of TCZ patients achieving Wk 24 ACR20/50/70 responses (table). The odds of achieving DAS28 remission were >5 times higher, and good/moderate EULAR response was >4 times higher, with TCZ vs MTX in this population. Mean change from baseline to Wk 24 in CRP level was -2.6 mg/dL for TCZ vs -1.9 mg/dL for MTX; CRP normalisation (hsCRP <0.3 mg/dL) occurred in 88.5% of TCZ and 31.0% of MTX patients. Hemoglobin levels improved in the TCZ arm by Wk 24 (adjusted mean change from baseline +1.2 g/dL vs +0.1 g/dL with MTX). Adverse event (AE) rates were similar: 79.9% with TCZ and 77.5% with MTX. Serious AEs occurred in 3.8% of TCZ vs 2.8% of MTX patients, while serious infections occurred in 1.4 vs 0.7% of patients.

Conclusions:

After 24 wk of treatment, TCZ monotherapy was superior to MTX monotherapy for alleviating symptoms in patients with RA who had not failed prior MTX or biologic therapy. TCZ was safe and well tolerated in these patients.

	MTX n=284	TCZ n=286
ITT population results at Wk 24		
ACR20, n (%)	149 (52.5)	200 (69.9)*
ACR50, n (%)	95 (33.5)	126 (44.1)**
ACR70, n (%)	43 (15.1)	80 (28.0)***
DAS28 remission†, n (%)	30 (12.1)	85 (33.6)
Adjusted mean change in DAS28 score	-2.05	-3.31
Adjusted mean CRP level, mg/dL	-1.87	-2.76
Adverse lab events (safety population)	n=284	n=288
Single shifts in ALT to >3x ULN, % patients	3.5	1.7
Shifts in AST to >3x ULN, % patients	2.1	1.0
Neutrophil count CTC grade -2, % patients	2.1	10.4
Shift in Total cholesterol from <200 mg/dL at baseline to ≥240 mg/dL at last observation, % patients	<1	13.2

Shift in LDL cholesterol from <100 mg/dL at baseline to ≥160 mg/dL at last observation, % patients	0	3.1
†DAS28 <2.6; *p<0.0001 vs MTX; **p=0.0023 vs MTX; ***p=0.0002 vs MTX.		

Research Method: Clinical

Type of Trial: Other

Phase: Phase III

Disclosures: **G. Jones**, MSD, 8; Servier, 8; Roche, 8; Novartis, 8; Servier, 9; MSD, 9; Amgen, 9; Roche, 9; Genzyme, 9; Novartis, 9; Centocor, 9; Abbott, 9; Eli Lilly, 9; Pfizer, 9; BMS, 9; Auxilium, 9; **J. Gu**, None; **M. Lowenstein**, None; **A. Calvo**, None; **J. Gomez-Reino**, BMS, 5; Wyeth, 5; Schering-Plough, 5; Roche, 5; UCB, 5; BMS, 8; Wyeth, 8; Schering-Plough, 8; Roche, 8; Abbott, 8; **D. Siri**, None; **M. Tomsic**, None; **R. Blackburn**, Roche, 3; **T. Woodworth**, Roche, 3; **A. Sebba**, Roche, 5; Amgen, 5; Roche, 8; **M. Genovese**, Roche, 2; Roche, 5.