methods: This randomized, controlled, double-blind, placebo-controlled study (GO-BEFORE) evaluated efficacy and safety of single-agent MTX vs. combination therapy (MTX/cyclosporin, MTX/prednisolone) vs. combination therapy plus GLM in active RA at baseline (BL). Patients (pts) with active RA of ≤ 12 months’ duration were randomized to 28 weeks of MTX alone or triple therapy, with GLM added after 14 weeks. The primary endpoint was the proportion of pts achieving an ACR20 response at week 28.

results: Of 595 pts, 431 had acceptable efficacy data. ACR20 response at BL was 26.3% (MTX), 25.2% (cyclosporin/MTX), and 24.4% (prednisolone/MTX). At week 28, 40.2% (MTX), 42.6% (cyclosporin/MTX), and 41.9% (prednisolone/MTX) reached ACR20 response (P=0.32). ACR20 response was higher in mechlorethamine (MLE)/MTX-naïve pts (P=0.003). ACR20 response was higher in pts with negative antibody to MLE (P=0.001). ACPA-positive patients had significant reductions in Larsen score and health status (HAQ-DI) and improved physical function. Mean changes from baseline in vDAS were small and 64% of pts randomized to GLM+MTX had no radiographic progression (vDAS ≤ 0). The most common AEs were upper respiratory tract infections (29.4%), nausea (19.6%), bronchitis (16.8%), and increased alanine aminotransferase (16.1%). 11.9% of pts had an injection-site reaction. Through week 268, 204/261 (33.1%) pts had an SAE; 17.5% of pts discontinued study agent due to AEs. Overall rates of serious infections, malignancies, and death were 12.2%, 3.4%, and 1.9%, respectively. Of 595 pts with available samples, 98 (9.7%) were positive for antibodies to GLM.

Conclusion: The retention rate was high (86.1%) through 5 years. GLM+MTX therapy resulted in maintained improvements in signs/symptoms of RA and in physical function, and inhibited structural damage progression long-term. No new safety signals were detected through 5 years in MTX-naïve RA pts.

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