

# Anti-GAGA4 IgM Assay May Distinguish Primary Progressive Multiple Sclerosis from Relapsing Remitting Multiple Sclerosis Patients

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## BACKGROUND

Approximately 10–15% of patients present with slowly evolving progressive disease. Of these, about two-thirds will never experience a relapse, and they therefore have the primary progressive subtype of MS (PPMS).

The gMS<sup>®</sup> Dx diagnostic test is based on the detection of circulating IgM antibodies directed against the glycan antigen Glc(α1,4)Glc(α) (GAGA4).

Various studies demonstrated that relapsing remitting multiple sclerosis (RRMS) patients have significantly higher blood levels of anti-GAGA4 IgM antibodies than patients diagnosed with other neurological diseases and healthy controls. PPMS patients were found to have slightly lower levels of anti-GAGA4 than RRMS patients.<sup>1,2,3,4</sup>

## OBJECTIVES

Investigate the ability of the gMS<sup>®</sup> Dx blood test to differentiate RRMS patients from PPMS patients.

## STUDY TYPE

Cross-sectional retrospective analysis of frozen sera from combined USA and German cohorts (Table 1).

Serum samples were screened by the gMS<sup>®</sup> Dx assay in a blinded fashion without knowledge of diagnosis or other clinical data.

## METHODS

**Total IgM (T-IgM) Levels:** Measured on Roche Modular P800 Automated analyzer using the Roche Tina-quant IgM Gen.2 Turbidometric method; reported in mg/mL.

**Immunoassay:** Sera were diluted 1:1200 and units (EU) of anti-GAGA4 IgM were measured by gMS<sup>®</sup> Dx Immunoassay (Glycominds, Lod, Israel) and normalized by dividing to square root of total IgM levels (T-IgM mg/mL serum)<sup>0.5</sup>.

**Cutoff for gMS<sup>®</sup> Dx Test Positivity:** The gMS<sup>®</sup> Dx cutoff for a positive test was according to manufacturers specifications [50 EU/(mg/mL)<sup>0.5</sup>].

Table 1: Study Population Demographics

	RRMS (n=582)	PPMS (n=26)
USA (n)	497	18
Germany (n)	83	8
Age yrs, mean (SD)	45.3 (11.9)	51.5 (11.9)
Female	77%	35%

## RESULTS

**Comparison of Anti-GAGA4 Levels:** RRMS patients had higher levels (Table 2) of anti-GAGA4 IgM and T-IgM than PPMS patients.

**gMS<sup>®</sup> Dx Test Results:** A proportionally lower number of PPMS patients were positive (Figures 1 and 2) for the gMS<sup>®</sup> Dx test than RRMS patients. Moreover, the 2 positive PPMS patients gMS<sup>®</sup> Dx measurements were at the equivocal cutoff level [52.7 and 54.4 EU/(mg/mL)<sup>0.5</sup>].

**Diagnostic Test:** The gMS<sup>®</sup> Dx test has the ability to differentiate RRMS patients from PPMS patients (Table 3).

Table 2: IgM Antibody Levels

	Median (P25-P75)	
	RRMS (n=582)	PPMS (n=26)
Anti-GAGA4 (EU)	45.8 (25.5-77.0)	33.5 (20.7-44.3)
T-IgM (mg/mL)	1.45 (1.1-2.1)	0.95 (0.7-1.4)
Anti-GAGA4 EU/(mg/mL) <sup>0.5</sup>	36.8 (23.1-59.4)	30.7 (22.8-44.3)

P25-P75: 25th and 75th percentiles

\* PPMS vs. RRMS, p=0.01, Mann Whitney U

† PPMS vs. RRMS, p=0.002, Mann Whitney U

‡ PPMS vs. RRMS, p=0.1, Mann Whitney U

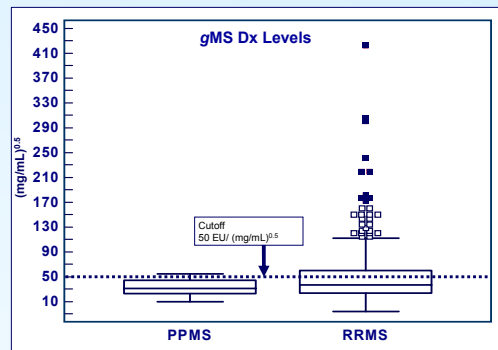


Figure 1: Box plots of gMS<sup>®</sup> Dx levels showing median values, 25% / 75% percentiles, outliers. Unfilled squares are outliers larger than the upper quartile plus 1.5 times the interquartile range. Filled squares are far outliers larger than the upper quartile plus 3 times the interquartile range.

Proportion of Patients Negative/Positive for the gMS Dx Test

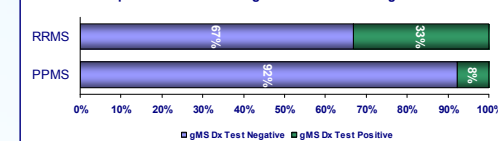


Figure 2: Bar graph depicting proportion of patients positive for the gMS<sup>®</sup> Dx test, p=0.005, Fisher exact test.

Table 3: gMS<sup>®</sup> Dx Test Results

	RRMS (n=582)	PPMS (n=26)
Positive	193	2
Negative	389	24
Sensitivity; 95%CI (%)	33.2 (29.4-37.1)	
Specificity; 95%CI (%)	92.3 (74.9-99.1)	
LR+	4.31	
LR-	0.72	
Fisher exact	p=0.005	

Table 3: Total proportion of patients positive or negative for gMS<sup>®</sup> Dx test and diagnostic accuracy results.

## CONCLUSIONS

This pilot study revealed that MS patients who are positive for the gMS<sup>®</sup> Dx test have a clinical course that is more likely to be RRMS and not PPMS. Intriguingly, RRMS patients are over four times more likely to be positive for the gMS<sup>®</sup> Dx test than PPMS patients. In order to confirm these results further studies will be performed in the near future.

## REFERENCES

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