Press Release Title: Study Suggests Targeting B Cells May Help with MS

Abstract Title: #006 The Relationship Between Peripheral B-Cell Levels and MRI Disease Activity in Relapsing Remitting Multiple Sclerosis (RRMS)

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Objective: To evaluate the relationship between peripheral B-cells and brain MRI gadolinium-enhancing (GdE) lesions in RRMS subjects.

Background: B-cells have been implicated in the pathogenesis of disease in RRMS. Studies of supra-pharmacological anti-CD20 B-cell depletion have shown reduced disease activity but no relationship between B-cells and efficacy. OMS112831 is an ongoing Phase 2B placebo-controlled dose-ranging study of subcutaneous (SC) ofatumumab in RRMS. Headline safety and efficacy data are presented elsewhere (Presentations: S23.006, I7.1.007). The wide range of studied doses (3-180 mg) modulates B-cell depletion providing additional opportunities to explore relationships between B-cells and disease activity.

Design/Methods: Study OMS112831 is evaluating the inhibition of new GdE lesions during a 12-week placebo controlled period. Weighted mean CD19 B-cell count for the period 4-12 weeks were correlated to the number of new GdE lesions on an individual patient basis (n=231). A non-parametric analysis was used to identify threshold effects and generalized linear models used to identify relationships between peripheral B-cell levels and MRI disease activity.

Results: Analysis of cumulative new GdE lesions showed disease activity was significantly reduced below a threshold CD19 count of 64 cells/uL for the period 4-12 weeks. A generalized linear model with underlying negative-binomial distribution accounting for over-dispersion of lesions across patients showed a highly significant linear relationship (P<0.001) with residual annualized disease activity of one new lesion per year and a threshold of approximately 32-64 cells/uL.

Conclusions: This dose-response study of anti-CD20 therapy in RRMS demonstrates modulation of pharmacological and clinical effects. Relating peripheral B-cell pharmacology to appearance of new GdE lesions reveals a potential threshold of 32-64 cells/uL for significantly reducing MRI lesion activity. These results present a possible new target threshold for exploration of therapeutic benefit in RRMS patients undergoing anti-CD20 therapy.

Study Supported By: GlaxoSmithKline, Inc.