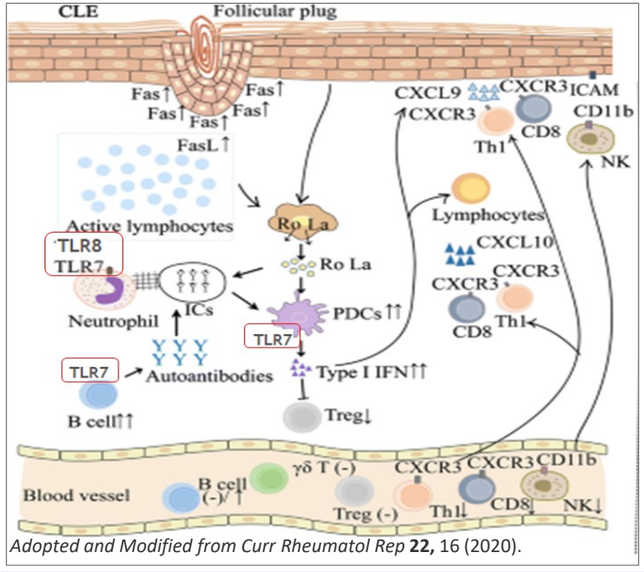
TLR7 INHIBITION WITH BMS-986256, A POTENT AND SELECTIVE INHIBITOR OF HUMAN TLR7/8, PROVIDES ROBUST EFFICACY IN THE MRL/LPR FEMALE MOUSE MODEL OF CUTANEOUS LUPUS

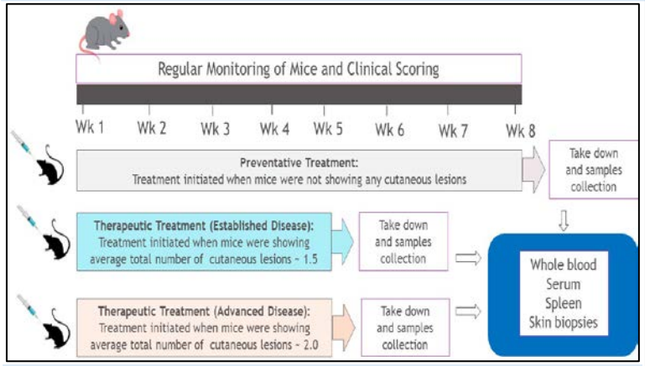
Shailesh Dudhgaonkar[1],Puneet Chopra[1] Siva Subramani[1], Sourabh Ranade[1], Priyadeep Bhutani[1], Sushama Basavanthappa[1], Alaric Dyckman[2] and Gary L Schieven[2]
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TLR7 /8 Play Important Roles in the Pathogenesis of Cutaneous Lupus



Adopted and Modified from Curr Rheumatol Rep **22,** 16 (2020).

Study Outline

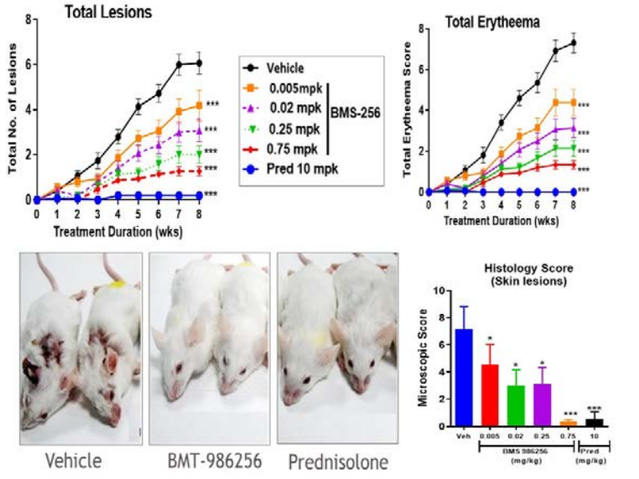


In Vitro Profile of TLR7/8 Antagonist, BMS-986256

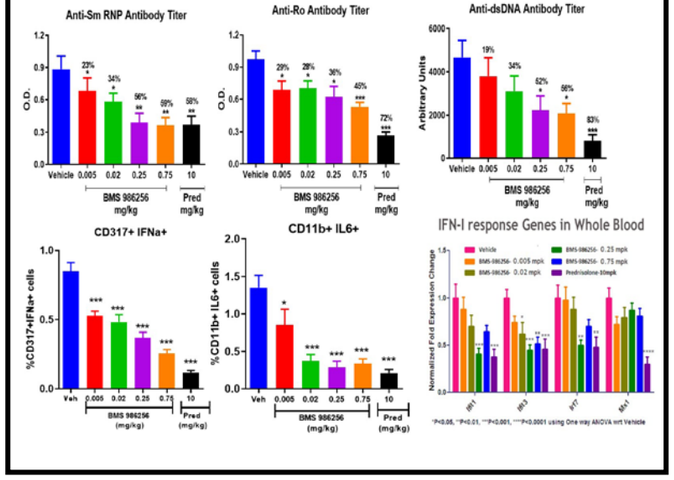
Reporter Assay	IC50 (nM)
TLR7 reporter	0.65 ± 0.24
TLR8 reporter	0.86 ± .53
TLR9 reporter	6400 ± 2470

Whole blood assay	IC50 (nM)
TLR7 hWB IL-6	4.5 ± 0.4
TLR8 hWB IL-6	1.5 ± 0.1
TLR7 mouse blood IL-6	2.4 ± 1

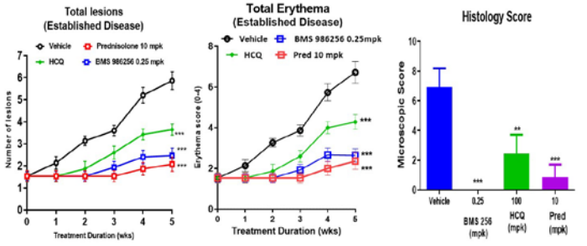
Preventative Treatment of Female MRL/lpr Mice With BMS-986256 Showed Robust Suppression of Cutaneous Manifestations



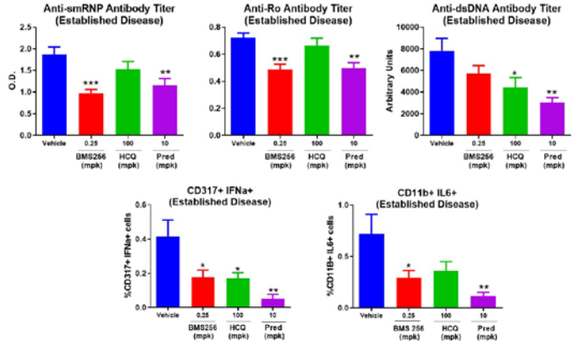
BMS-986256 Showed Significant Reduction in Auto-antibodies, Cytokines Secreting Cells and IFN-I Response Genes in Female MRL/lpr Model of Cutaneous Lupus



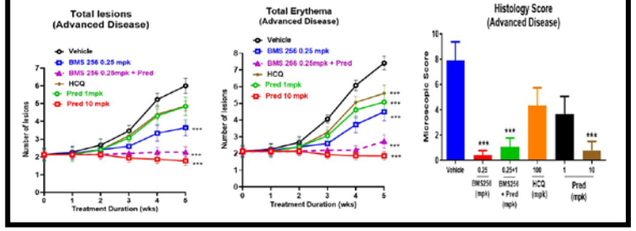
Therapeutic Treatment of Female MRL/lpr Mice With BMS-986256 Showed Robust Suppression of Cutaneous Manifestations: Established Disease



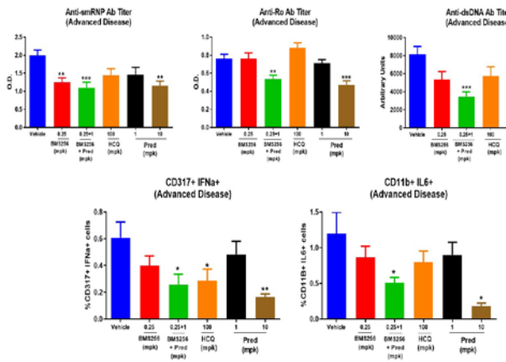
BMS-986256 Showed Significant Reduction in Autoantibodies and Cytokines Secreting Cells in Female MRL/lpr Model of Cutaneous Lupus: Established Disease



Therapeutic Treatment of Female MRL/lpr Mice With BMS-986256 Showed Robust Suppression of Cutaneous Manifestations: Advanced Disease



BMS-986256 Showed Significant Reduction in Autoantibodies and Cytokines Secreting Cells in Female MRL/lpr Model of Cutaneous Lupus: Advanced Disease



Summary

BMS-986256, a highly selective TLR7/8 antagonist, showed robust efficacy in female MRL/lpr model of cutaneous lupus.

In preventative treatment, BMS-986256 demonstrated equivalent efficacy to that of prednisolone and showed –

- robust suppression of cutaneous manifestations
- significant reduction in circulating auto-antibodies and cytokines secreting cells in spleen
- significant reduction in IFN-I response genes in whole blood

In established and advanced disease settings, therapeutic treatment of BMS-986256 showed –

- robust suppression of cutaneous manifestations
- significant reduction in circulating auto-antibodies and cytokines secreting cells in spleen
- superior efficacy than HCQ

In advanced disease settings, therapeutic treatment with combination of BMS-986256 and low dose of prednisolone showed equivalent efficacy to that of high dose prednisolone