Innate rate of p25 cleavage

What is the explanation for improved polymorphic coverage?

Increasing coverage from BMS-A to BMS-

Summary and Conclusions

- BMS-955176 is a 2nd generation MI with a low serum shift and potency toward Gag polymorphic virus resistant to BVM
- 176 has demonstrated proof of concept, entering phase 2b studies 2Q 2015
- CA/SP1 cleavage rates are a function of Gag polymorph; faster rates can result in reduced MI sensitivity
- Persistent inhibition of in vitro CA/SP1 cleavage depends on genotype and MI
- Dissociation rates of MIs from Gag VLPs are a function of polymorph and MI
- BMS-955176 longer dissociation half-lives for polymorphs vs. BVM
- consistent with improved polymorphic potency
- Inhibate CA/SP1 cleavage rates and specific Gag VLP dissociation that allow the modeling of kinetics of MI cleavage inhibition
- Stabilizes viral assembly and reduces overall viral yield in both the presence and absence of Gag polymorphs

The model provides a framework for understanding the kinetics of CA/SP1 cleavage and MI activity against Gag polymorphs.