Background: S/GSK1349572 is a potent next generation HIV integrase inhibitor (IN) under clinical development. Previous studies with a subset of clinically relevant IN mutants demonstrated that S/GSK1349572 had highly reduced resistance, while wildtype IN was not. However, studies conducted before its release as a clinical candidate had not included wildtype IN as a control. To properly assess the resistance profile of S/GSK1349572, a panel of wildtype IN (WT) and IN-resistant IN were constructed and their resistance was measured against WT and an optimized INI-resistant IN (S/GSK1349572-resistant IN). We demonstrate S/GSK1349572’s profile against a panel of clinically relevant integrase mutants.

Methods: Activity in the INI-resistant double/triple mutant (S/GSK1349572-resistant IN) was measured by a chemical assay and also included a single-round infection assay (S/GSK1349572-resistant IN) and included double mutants in the S/GSK1349572-resistant IN panel. The results were compared to the resistance to S/GSK1349572 and S/GSK1349572-resistant IN.

Results: S/GSK1349572 had a significant resistance in all the INI-resistant IN. In the single-round infection assay, resistance was measured against S/GSK1349572-resistant IN and S/GSK1349572-resistant IN-resistant IN. The results showed that S/GSK1349572 had a moderate resistance in all the INI-resistant IN. The results also showed that the resistance to S/GSK1349572-resistant IN and S/GSK1349572-resistant IN-resistant IN was higher than the resistance to S/GSK1349572-resistant IN-resistant IN-resistant IN.

Discussion: S/GSK1349572 demonstrated low resistance across all clinically relevant IN mutants. These results highlight the potential of S/GSK1349572 as a novel INI-resistant IN.

Conclusions: S/GSK1349572 demonstrates low resistance across all clinically relevant IN mutants. These results highlight the potential of S/GSK1349572 as a novel INI-resistant IN.