Rukobia: Binding affinity/dissociation

Summary

- Direct binding affinity/dissociations to gp120 (JRFL HIV strain) were evaluated via competition binding assay/gel filtration with temsavir and BMS-488043 (early attachment inhibitor).[1]
  - The dissociation of temsavir release was slow, with a half-life of ~8 hours.
  - Temsavir binds to gp120 in a reversible fashion.
- Important safety information can be found in the Prescribing Information link and can also be accessed at Our HIV Medicines.

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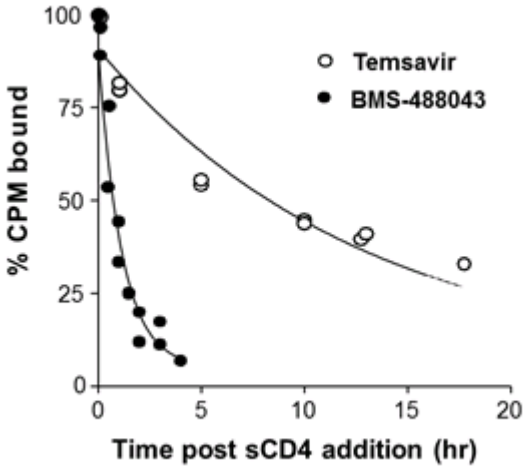
DIRECT BINDING AFFINITIES OF TEMSAVIR TO GP120 STUDY[1]

Binding half-life

A competition binding assay/gel filtration method was used to show that temsavir bound directly to gp120. An earlier attachment inhibitor was used to bind to JRFL gp120 in the presence of various concentrations of unlabeled temsavir or BMS-488043. Temsavir inhibited the binding of BMS-488043 to gp120 with an IC50 of 23 nM, while unlabelled BMS-488043 inhibited with an IC50 of 169 nM.

The ability of temsavir to dissociate from the JRFL gp120 protein was evaluated in a gel filtration assay. The weaker attachment inhibitor BMS-488043, was also analysed for the ability of sCD4 to displace binding to gp120. Figure 2 shows the dissociation of both compounds. Temsavir release was slow, with a half-life of ~8 hours. The weaker attachment inhibitor, BMS-488043, had a much shorter half-life (~0.5 hours) of release. The data conclusively show that temsavir binds to gp120 in a reversible fashion and is competitive with sCD4 binding.

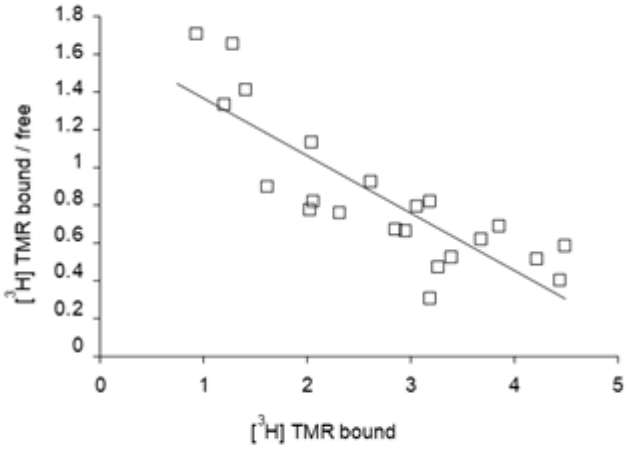
Figure 1 Reversible binding of radiolabelled attachment inhibitors[1]



Binding Affinity

Temsavir was used to determine its direct affinity to the JRFL gp120 protein. A sedimentation equilibrium method was used to produce a Scatchard plot (Figure 1). From this analysis, a KD value of 3.3 nM was determined for the binding of temsavir to purified JRFL gp120.

Figure 2. Scatchard analysis of temsavir binding to JRFL gp120[1]



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Selection of references follows principles of evidence-based medicine and, therefore, references may not be all inclusive.

REFERENCES

1. ViiV Healthcare, Module 2.7.2.4 Clinical Summary of Virology for Fostemsavir, version 2.0, August 8, 2019.