



POSTER PRESENTATIONS

Session Title: VIRAL HEPATITIS - h) HEPATITIS C – CLINICAL (NEW COMPOUNDS, RESISTANCE)

Presentation Date: Apr 25, 2009

A NEWLY SYNTHESIZED SERINE PALMITOYLTRANSFERASE INHIBITOR, NA 808, HAS THE STRONG EFFECT TO HEPATITIS C VIRUS *IN VITRO* AND *IN VIVO*

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There are many anti-hepatitis C(HCV) drugs under the clinical development. But almost all targets are viral factors, hence these drugs produce the emergence of resistance mutations. To discover new anti-HCV agents, we focused on host factors as the target of anti-HCV agents, which contribute to HCV replication.

We identified serine palmitoyltransferase (SPT) inhibitor as anti-HCV agent through high through-put screening program using HCV replicon cells. Now, we synthesized NA808, a new SPT inhibitor, toward clinical development. Moreover, we evaluated the anti-HCV effect of NA808 *in vivo* using humanized chimeric mice infected with HCV genotype 1a or 2a. In HCV genotype 1a, NA808 led to rapid decline in serum HCV-RNA of about 1-2.5 log within 14 days, while PEG-IFN α -2a dosing at 30ug/kg twice a week achieved less than 1log for 14 day. Furthermore, the combination therapy of NA808 and PEG-IFN achieved over 4 log reduction in serum HCV-RNA. In HCV genotype 2a, NA808 led to rapid decline in serum HCV-RNA of about 3log within 14 days. Also we confirmed the decline of HCV-RNA and the level of HCV core protein in the liver was consistent with the serum level.

Finally, we investigated the mechanism of anti-HCV effect of NA808. It has been reported that sphingolipids and cholesterol compose the lipid raft, in which the replication of HCV occur. We evaluated the influence of NA808 to lipid raft. The analysis proved that NA808 decrease NS5B in lipid raft via decline of sphingomyelin.

Our results indicate that the new SPT inhibitor has strong efficacy to suppress of HCV via affecting the replication machinery.

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