

# Effect of illicit drugs consumption measured by hair analysis on adherence and efficacy of ravidasvir plus sofosbuvir in Asian adults with chronic HCV

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## Background

Active use of illicit drugs is prevalent in the Hepatitis C (HCV) infected population. This is a risk factor for reduced adherence to chronic treatment regimens<sup>2</sup> and has the potential to impact the efficacy results in clinical studies. Analysis of hair samples allows evaluation of the consumption of opioids, amphetamines, methadone and other drugs.

## Methods

As an exploratory objective in the STORM-C-1 trial<sup>1</sup> (an open label phase II/III, multicenter trial to assess the efficacy, safety, tolerance, and pharmacokinetics of ravidasvir plus sofosbuvir in HCV (+/- HIV) chronically infected adults with no or compensated cirrhosis in Thailand and Malaysia), hair samples were analysed by chromatography coupled to mass spectrometry (Figure 1) with the objective of assessing the usage of illicit drug, and its impact on adherence to the treatment regimen and on treatment efficacy.

Hair samples were collected at baseline and at end of treatment (EOT) for all subjects where possible. Two centimeters of hair sample were collected which corresponds to 2 months of cumulative use. Illicit drugs consumption was based on the hair levels over these 2 months.

Adherence was assessed at each visit during therapy by checking the subject diary card and subsequently by a monthly count of tablets from returned bottles.

An assessment of the impact on efficacy, especially in subjects who failed to meet the primary study endpoint (sustained virologic response 12 weeks after end of treatment (SVR12), considered as "cure"), of illicit drug use during the 12/24-week treatment period of the study (as determined from analysis of hair samples taken at EOT) was performed by drug type (opioid, amphetamine, methadone, other drugs) and by frequency of use (chronic and/or occasional, according to their concentrations).

The subjects were de-identified for this analysis to provide maximum assurance of anonymity for subjects using illicit substances.

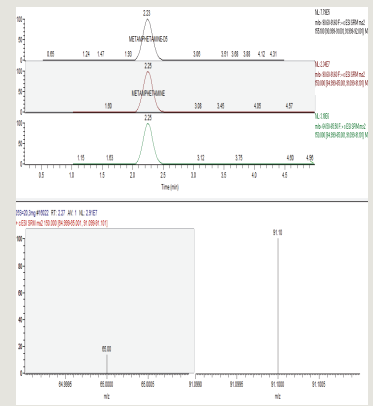


Figure 1: Chromatograph of metamphatamine

## Results

EOT hair samples were obtained for 231/301 subjects (76.7%). Evidence of use of illicit drugs during the study treatment period was observed for 119/231 (51.5%), of whom 59 (25.5%) were shown to be chronic users (Figure 2). Out of the 59 chronic users, 30 used amphetamine (50.8%), 25 methadone (42.4%) and 22 opioid (37.3%) (Figure 3).

Adherence to the study drugs was high among the chronic users (mean 99.5%, standard deviation 2.3%) and similar that in the overall population (Figure 4).

All 59 chronic drug users achieved SVR12 (Figure 4). Of the 9 subjects who did not achieve SVR12 out of the 301 subjects, there were 5 virological failures and 4 non-virological failures. EOT hair samples were provided by 3 of the 5 subjects who experienced virological failure. No illicit substances were detected in the hair samples from 2 of these subjects. The third subject was an occasional user of illicit drug.

The proportion of confirmed chronic drug users who had treatment emergent serious adverse event (7/59, 11.9%) was numerically higher than the corresponding proportion of subjects shown not to be chronic drug users (11/172, 6.4%), however the difference was not statistically significant.

Figure 2: Illicit drugs use during the study treatment period

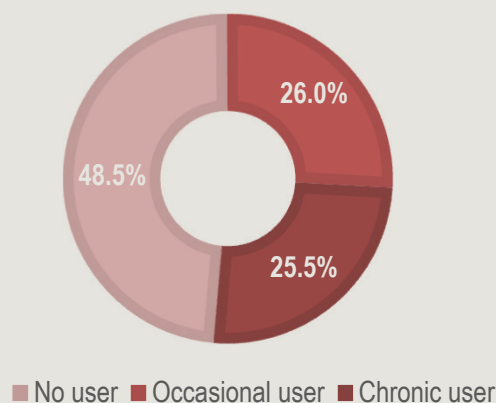


Figure 3: Illicit drugs type use by chronic user

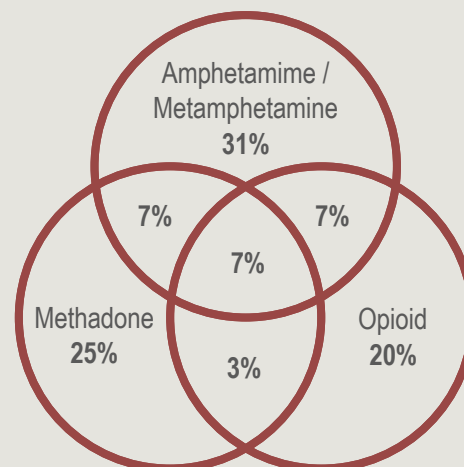
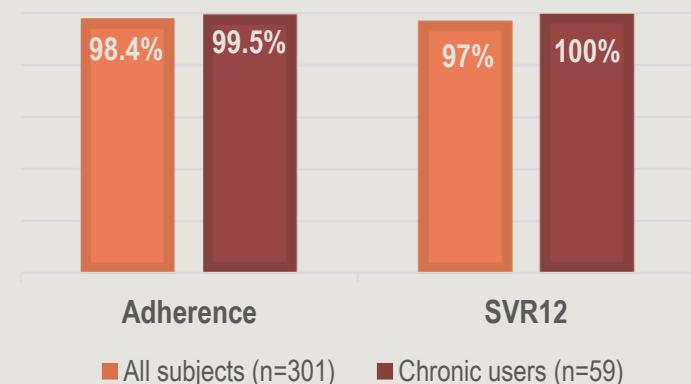


Figure 4: Adherence to study treatments and efficacy outcome (SVR12)



## Conclusions

Adherence to study treatments among chronic users of illicit drugs confirmed by hair analysis was excellent in this population of Asian adults with chronic HCV. Based on available data, cure rate was comparable to non-drug-users and there was no association between chronic use of illicit drugs and failure to achieve SVR12 in this potentially higher risk population.

## References

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