OTR.24 - Clinical, laboratory and sonographic follow-up of Zika virus (ZIKV) infection in Macaca mulatta pregnant rhesus macaque treated with sofosbuvir

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Introduction:
Recent in vivo studies using mice model have shown the antiviral activity of sofosbuvir, as a potential candidate for treatment of ZIKV infection.

Objective:
This study is aimed to evaluate the antiviral effect of sofosbuvir, pre and post inoculation, using the non-human primate (NHP) Macaca mulatta (rhesus macaque) as experimental model.

Methodology:
Nine females rhesus macaques were included, and divided in three groups numbered equally: 1) pregnant macaques, inoculated with ZIKV and orally treated with sofosbuvir 10 days before viral inoculation up to 30 days post inoculation (dpi); 2) pregnant macaques, inoculated and orally treated with sofosbuvir from the 2nd to 30th dpi, and 3) pregnant macaques, inoculated with ZIKV, and not treated. So far, two monkeys (AE62 and AB18) became pregnant and started the experiment. These animals were subcutaneously inoculated with ZIKV Espírito Santo strain at 24-26 (AE62) and 30-32 (AB18) gestational days (gd). Macaque AE62 belonged to the non-treated group 3, while AB18 was allocated in group 2, and started the treatment with sofosbuvir (PO. 15 mg/kg/day) at 2 dpi. Macaque's evaluation were performed daily, and biological samples were collected for laboratorial tests.

Results:
ZIKV RNA was detected in AE62 plasma (at 2, 4 and 8 dpi), urine (from 2 - 9 dpi, and at 12 dpi), and vaginal fluid (2, 4, 8 and 12 dpi) but could not be detected in saliva. Sonographic images obtained at 53-55 gd (29 dpi) revealed fetal death from AE62 macaque. Euthanasia followed by necropsy were performed, and tissues from mother and fetus were collected. Viral RNA was detected in the placenta, uterus, spleen and bladder, as well as in the fetus. Regard to the treated monkey, AB18, viral RNA was detected in plasma (2 and 8 dpi), urine (4 and 6 dpi), and vaginal fluid (2 and 8 dpi). AB18 monkey stopped treatment at 30 dpi and monitoring will continue until birth (scheduled for 20-24 March). The fetus had no evidence of microcephaly or other abnormalities on ultrasound examination.

Conclusion:
At the end of the experiment, we will know if sofosbuvir can be safely used in pregnant monkeys, as experimental model for pregnant women. Results could elucidate whether the drug was able to reduce viremia, as well as to prevent microcephaly and other neurological damages.

Keywords: Zika virus; sofosbuvir; rhesus macaque