Favipiravir in Patients with Ebola Virus Disease: Early Results of the JIKI trial in Guinea

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Background: The JIKI trial (Inserm C1463) assesses the benefits of high-dose favipiravir in reducing mortality and decreasing Ebola virus (EBOV) viral load in patients with Ebola virus disease (EVD).

Methods: JIKI is a phase II trial conducted in 2 Ebola treatment units run by MSF and ALIMA in Guinea. Inclusion criteria are: positive EBOV RT-PCR (Altona, crossing cycle threshold [CT] for positivity<40), age >1 year, ability to take oral drugs, and informed consent. Participants are prescribed oral favipiravir (adults: 6000mg Day [D]0 [H0 2400mg, H8 2400mg, H16 1200mg], and then 1200mg bid from D1 to 9). The primary endpoint is mortality. Mortality among participants is compared to mortality during the 3 month period preceding trial initiation in the same centers, as recorded in the MSF/EMLab database. On January 22, the DSMB recommended that the investigators present data on the first 69 adults and adolescents.

Results: from Dec 17, 2014 through January 20, 2015, 80 patients received favipiravir, including 69 adults and adolescents >14years (women 64%, mean age 38 years, median duration of illness 5 days). The baseline CT (BCT) was<20 in 42% and >20 in 58%; the baseline creatinine was >110 µM/L in 60% (BCT<20: 79%; BCT>20: 36%), including >300/µM in 27% (BCT<20: 43%; BCT>20: 10%); baseline ASAT level was >1000 IU in 38% (BCT<20: 77%; BCT>20: 17%); and baseline Creatine Kinase level >4000 IU in 18% (BCT<20: 24%; BCT>20: 8%). The figure shows the PCR CT values at baseline (D0) and at D2 and D4 following treatment initiation. Overall, 48% of participants died (BCT<20: 85%; BCT>20: 15%).

The pre-trial mortality was 58% overall (p=0.15), 85% in patients with BCT<20 (p=0.26) and 30% in patients with BCT>20 (p=0.05). Mortality was 100% and 7% in patients with abnormal baseline creatinine values and BCT <20 or >20, respectively. The drug was well tolerated. Results of quantitative virology and PK tests will be available later.

Conclusions: In this non comparative proof of concept trial, most patients with CT< 20 had severe kidney failure and died, with no indication that favipiravir monotherapy improved survival. Patients with CT>20 had a lower mortality rate compared to pre-trial figures in the same settings. These preliminary data encourage continued testing of favipiravir with particular attention to identifying patients earlier in disease course, and to explore other therapeutic options, including combinations, in patients who present at advanced stages