Experimental Treatment of Ebola Virus Disease with TKM-130803: A Single-Arm Phase 2 Clinical Trial - DTU Orbit (20/10/2019)

**BACKGROUND:**
TKM-130803, a small interfering RNA lipid nanoparticle product, has been developed for the treatment of Ebola virus disease (EVD), but its efficacy and safety in humans has not been evaluated.

**METHODS AND FINDINGS:**
In this single-arm phase 2 trial, adults with laboratory-confirmed EVD received 0.3 mg/kg of TKM-130803 by intravenous infusion once daily for up to 7 d. On days when trial enrolment capacity was reached, patients were enrolled into a concurrent observational cohort. The primary outcome was survival to day 14 after admission, excluding patients who died within 48 h of admission. After 14 adults with EVD had received TKM-130803, the pre-specified futility boundary was reached, indicating a probability of survival to day 14 of ≤0.55, and enrolment was stopped. Pre-treatment geometric mean Ebola virus load in the 14 TKM-130803 recipients was $2.24 \times 10^9$ RNA copies/ml plasma (95% CI $7.52 \times 10^8$, $6.66 \times 10^9$). Two of the TKM-130803 recipients died within 48 h of admission and were therefore excluded from the primary outcome analysis. Of the remaining 12 TKM-130803 recipients, nine died and three survived. The probability that a TKM-130803 recipient who survived for 48 h will subsequently survive to day 14 was estimated to be 0.27 (95% CI 0.06, 0.58). TKM-130803 infusions were well tolerated, with 56 doses administered and only one possible infusion-related reaction observed. Three patients were enrolled in the observational cohort, of whom two died.

**CONCLUSIONS:**
Administration of TKM-130803 at a dose of 0.3 mg/kg/d by intravenous infusion to adult patients with severe EVD was not shown to improve survival when compared to historic controls.

**TRIAL REGISTRATION:**
Pan African Clinical Trials Registry PACTR201501000997429.