safe antiviral therapeutics. We have identified tetrahydrothienopyridine derivatives from phenotypic screening as a first-in-class pan-serotype dengue virus inhibitor. Resistance analysis showed that mutations in the dengue viral NS4B sequence (nonenzymatic transmembrane protein and a component of the viral replication complex) conferred resistance to compound inhibition, suggesting that the NS4B protein is a molecular target of this scaffold. Extensive SAR studies of this scaffold led to the discovery of new analogs with improved potency in a nanomolar to submicromolar range against all four dengue serotypes. Optimization of physicochemical properties as well as oral *in vivo* pharmacokinetic profile led to a compound showing excellent oral efficacy in the DENV-2 infected AG129 mouse model with >one log viremia reduction when orally dosed at 30 mg/kg once daily for three days. Furthermore, this compound showed good selectivity against off-target safety and cytotoxicity panels. This presentation will discuss our dengue phenotypic screening campaign, medicinal chemistry strategy, SAR, *in vitro* and *in vivo* profile of the optimized compound.

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DENGUE VIRUS INFECTION AND LEISHMANIASIS IN PATIENTS ATTENDING A MEDICAL HEALTH CENTER IN THE RURAL COMMUNITY OF ILARA-MOKIN, ONDO STATE, NIGERIA

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Dengue and leishmaniasis are serious diseases that the World Health Organization (WHO) characterizes as lacking effective control measures. Transmitted by insect vectors and can result in epidemic outbreaks. Sustained control of the vectors are difficult for dengue and leishmaniasis because their high reproductive potential allows the vector populations to recover quickly after intervention wherever adequate breeding conditions exist. Because of their misdiagnosis or underdiagnosed, it is endemic in the tropical countries. Prevalence and epidemiology of these diseases is poorly understood and misdiagnosed in Nigeria, in most cases with malaria. Our study aims to investigate dengue virus and leishmaniasis co-infections in patients visiting a rural community medical center in Elizade University, Ilara Mokin, Ondo State. Blood samples were collected and analyzed for two months. SD Dengue Duo and Bio-rad IT Leish serological test kits was used for the samples analysis. This study examined 101 samples which were simultaneously tested for the target infections. In about 23.76% of the samples (24 samples) were positive for dengue infections. Gender wise, more males (79.17%) than females (20.83%) tested positive to the virus infection. 37.5% of the positive samples were primary infections, 91.6% were past or secondary infections and 33.3% of the samples show late primary infections and early secondary infections. Only 1 sample was positive for Leishmaniasis. The majority of the study population had no pre-knowledge of dengue infection and leishmaniasis as they are carriers of the diseases, providing new insights on both incidence and prevalence. It was discovered that those from villages especially the South-South of Nigeria tested positive the most as carriers of the diseases. Therefore, these areas need special attention for surveillance and treatment for preventive measures. In addition, this study recommends a concerted effort by all stakeholders to enlighten the people about dengue infection and leishmaniasis, and its prevention and eradication from such regions.

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C-REACTIVE PROTEIN AS A POTENTIAL BIOMARKER FOR DISEASE PROGRESSION IN DENGUE: A MULTI-COUNTRY OBSERVATIONAL STUDY

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Dengue infection can cause a wide spectrum of clinical outcomes. The severe clinical manifestations occur late in the disease course, during day 4-6 of illness, allowing a window of opportunity for risk stratification. Markers of inflammation may be useful biomarkers. We investigated the value of CRP measured early on illness days 1-3 to predict dengue disease outcome and the difference in CRP levels between dengue and other febrile illnesses (OFI). We performed a nested case-control study using the clinical data and samples collected from the IDAMS-consortium multi-country study. This was a prospective multi-center observational study that enrolled almost 8000 participants presenting with a dengue-like illness to outpatient facilities in 8 countries across Asia and Latin America. Predefined severity definitions of severe and intermediate dengue were used as the primary outcomes. 378 cases with severe/intermediate dengue were compared to 1134 uncomplicated dengue patients as controls (ratio 1:3), and also 400 patients with OFI. In patients with confirmed dengue, higher CRP levels in the first 3 days of illness were associated with a higher risk of severe outcome (OR 1.64, 95% CI 1.21-2.24), and longer fever clearance time (HR 0.87, 95% CI 0.77-0.99) but not with hospitalization. CRP levels showed a quadratic association between dengue and OFI diagnosis; with levels of approximately 30 mg/dL associated with the highest risk of having dengue. This risk decreased with lower and higher levels of CRPs, likely representing diagnoses with other viral infections with CRP levels <30mg/dL and bacterial infections >30 mg/dL. Antibiotics were given in 6.6% of dengue patients, and these patients had similar outcomes to those not given antibiotics, even those with CRP levels >40mg/dL. CRP had a positive correlation with total white cell count and neutrophils and negative correlation with lymphocytes, but did not correlate with liver transaminases, albumin, or platelet nadir. In summary, CRP measured in the first 3 days of illness is a useful biomarker for early dengue risk prediction and may assist differentiate dengue from other febrile illnesses.

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MITIGATION AND PREVENTION OF DENGUE OUTBREAKS AND SUSTAINING LOW ENDEMICITY THROUGH A COMPREHENSIVE INTEGRATED APPROACH BASED ON BEST PRACTICES: SRI LANKA

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Dengue is a leading public health problem in Sri Lanka where all ages are affected. The aims of the dengue control programme are to carry out proactive integrated vector management based on real-time Dengue surveillance (epidemiological & entomological) data and to strengthen human resource and infrastructure to improve clinical management of Dengue. There has been significant progress in epidemiological and entomological surveillance, clinical management, and active engagement of various ministries through the Presidential Task Force (PTF) on Dengue to enhance community participation. A guideline was developed for *Aedes* vector surveillance and control. Field health officers were trained on vector surveillance and vector control according to the guideline. Field Assistants Mosquito Control (1287) were recruited in a phased manner in 2017 to work at the community level to lead source reduction activities and other vector control and vector surveillance activities. Special Mosquito Control Campaigns (SMCCs) were conducted in 2017 and 2018 for source reduction, with the participation of stakeholders covering 2.7 million and