PROJECT TITLE	Characterization of HIV-1 Drug Resistance to Integrase Inhibitors in Portugal: clinical and economic impact for treatment and drug resistance testing guidelines– Refª. PTDC/SAU-INF/31990/2017
BRIEF DESCRIPTION	HIV-1 first-line treatment regimens include 2 nucleoside reverse transcriptase (RT) inhibitors (NRTIs) combined with one nonnucleoside RT inhibitor (NNRTIs) or one protease inhibitor (PI) or one integrase inhibitor (INIs). Drug resistance (DR) testing before starting the therapy is recommended for NRTI, NNRTI and PI, but not yet for the more recently approved INIs. The increasing first-line use of INIs underscores the importance of evaluating INIs resistance in drug-naive patients (DNs). Herein, we will characterize DR to INIs in Portugal. We will evaluate DR in DN and treated patients, with the ultimate objective of understanding whether it is cost-effective to test for ARV DR to INIs in DNs, as recommended for other drug classes since 2003. The project team has wide experience in viral evolution and ARV DR. Since 2004, we coordinated several projects on the topic of DR in Portugal, Europe and Africa.
OBJECTIVES	To determine the prevalence of INI drug resistance in DN and treated patients; to determine integrase diversity among subtypes for DN and treated patients; to identify natural polymorphisms and mutations implicated in resistance to INIs for DN and treated patients; to determine whether and how frequently Next Generation Sequence identifies minority INI drug-resistant variants not identified by population sequencing; to identify potential risk factors associated with acquisition or transmission of drug resistance to INIs; to determine whether it is cost-effective to use INIs at first-line and whether it is cost-effective to test for INIs drug resistance in DN patients.
IMPLEMENTATION	We will include retrospectively and prospectively DN and TP in VF. DN patients will be included on basis of the BEST HOPE project, which collects data from HIV-1 newly diagnosed patients in 19 hospitals across Portugal. TP will be selected from the database of the Egas Moniz hospital, which includes data from thousands of patients, clinically followed in several Portuguese hospitals since 2001. As conventional DR genotypic tests cannot identify minority viral populations present in less than 20% of the viral quasispecies, we will also use Next-Generation Sequencing (NGS) to analyze minority variants which can compromise the success of HAART. Results generated by NGS can predict treatment outcomes, in cases of therapy failure otherwise not explained by routine DR testing results, and might better guide patient management in clinical practice. Finally, this project will evaluate the economic impact that DR to INIs has on the treatment of DNs and the cost-effectiveness of testing for DR to INIs in DN patients.
FUNDING AGENCY	Fundação para a Ciência e a Tecnologia (FCT)
DURATION	2018-2022
PRINCIPAL INVESTIGATOR	Ana Barroso Abecasis (GHTM/IHMT)
RESEARCH TEAM / INSTITUTION	Instituto de Higiene e Medicina Tropical/ Global Health and Tropical Medicine (Coordinator Institution), GHTM: Ana Abecasis (PI), Marta Pingarilho (Co-PI), Victor Pimentel (Post-doc fellow), Maria do Rosário Oliveira Martins; Ahmed Nabil Shaaban; Patrícia Abrantes Centro Hospitalar Lisboa Ocidental (CHLO)- Lisboa/Portugal: Perpetua Gomes KU Leuven (Belgium): Anne-Mieke Vandamme, Kristof Theys, Ricardo Camacho University of Oxford (UK): Nuno Rodrigues Faria