antimalarial safety studies and of integrating pooled individual level safety analyses into WWARN's global efficacy data platform, as a powerful standardised process for dose optimisation.

PA-030 THE IMPACT PROJECT: IMPROVING THE IMPACT OF EXISTING MALARIA PRODUCTS – ACTS

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Background The antimalarial dihydroartemisinin-piperaquine (DHA-PPQ) is one of the recommended drugs to treat uncomplicated *Plasmodium falciparum* malaria. However, DHA-PPQ has a relatively narrow, poorly defined therapeutic dose range and it is unclear whether PPQ concentration-dependent cardiotoxicity (QTc prolongation) poses a clinical risk for specific subgroups. Uncertainty about the exact safe upper PPQ concentration threshold and recognition of the vulnerability of children has led WHO to consider a complex weight-based dosing regimen. These complex dosing schemes may challenge DHA-PPQ introduction into national control programmes. It also highlights the urgent need to standardise the dose optimisation process.

Methods The IMPACT project aims to determine the frequency and severity of DHA-PPQ cardio-toxicity, and its correlation with dose and drug concentration through WWARN-pooled patient-level pharmacokinetic-pharmaco-dynamic safety analysis, and antiretroviral drug interactions using all available data. Using the established WWARN platform, an open study group has been established to allow data sharing and joint analyses by data contributors and other key stakeholders.

Results We will present a progress update of the IMPACT project and associated WWARN DHA-PPQ safety group. Findings will inform an up-to-date safety profile and upper PPQ dose thresholds across key risk groups and identify remaining research priorities. DHA-PPQ dosing challenges, lessons learnt, and opportunities to address these through a more standardised process for antimalarial dose optimisation will be reviewed, and awareness of dose optimisation research priorities will be raised among researchers, funders and control programmes.

Conclusions This work will help inform policy decisions on DHA-PPQ dosing regimens and help demonstrate the importance of identifying global research priorities for targeted