TARGETS FOR DRUG DEVELOPMENT IN HIV NEUROPATHY

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Summary: There are globally ~34 million people infected with HIV. About 40% of those people living with HIV, whose infection is suppressed by antiretroviral therapy (ART) and are often otherwise well, have a length-dependent distal symmetrical sensory polyneuropathy, which in most cases is associated with neuropathic pain. This makes sensory neuropathy 1 of the most prevalent clinical manifestations of HIV in the current era of combined ART and therefore an increasingly major area of therapeutic need. Sensory neuropathy is usually attributable to either viral–neuronal interactions and/or ART neurotoxicity.

Data will be reviewed for:
- the epidemiologic and risk factors of HIV-associated neuropathy
- efficacy of current therapies: a meta-analysis of current randomized controlled trials for neuropathic pain in HIV
- sensory profiles and other clinical characteristics in HIV-positive patients with and without sensory neuropathy
- laboratory animal modeling of HIV GP120-induced neuropathy, including ethologically relevant complex pain behaviors and pharmacologic analysis
- laboratory animal modeling of ART neurotoxicity, including ethologically relevant complex pain behaviors and pharmacologic analysis
- use of gene microarray studies of animals models to reveal novel drug targets

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UPDATE ON THE STATUS OF ARTEMISININ RESISTANCE

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Summary: Drug Resistance and Containment Unit, Global Malaria Programme, World Health Organization, Geneva, Switzerland.

Global malaria control has been threatened by resistance to antimalarial medicines. *P. falciparum* resistance to chloroquine and pyrimethamine both originated in Southeast Asia and subsequently spread to Africa with substantial implications for global public health. Similarly, in the 1980s, resistance to mefloquine emerged rapidly on the western border of Cambodia and on the northwest border of Thailand only a few years after its introduction. In April 2001, WHO recommended the use of artemisinin-based combination therapies (ACTs), combining an artemisinin derivative, known for its rapid action and short elimination from the body, with another drug characterized by a different mechanism of action and slow elimination.

Emerging *P. falciparum* resistance to artemisinin derivatives is a major global public health concern. WHO first issued a warning about the threat of artemisinin resistance in the Greater Mekong subregion in 2005, after routine efficacy studies showed delayed clearance after ACTs. The first cases of confirmed artemisinin resistance were found in western Cambodia, along the Cambodia–Thailand border in late 2006. The 4 countries most affected by the emergence of artemisinin resistance are Cambodia, Myanmar, Thailand, and Vietnam. Despite observed changes in parasite sensitivity to artemisinins, ACTs continue to cure patients, provided the partner drug is efficacious. However, once resistance to artemisinin emerges, it is more likely that resistance to the partner drug will also develop and vice versa. Currently and in absence of a molecular marker, the best available indicator of suspected artemisinin resistance is the proportion of patients who are still parasitemic at day 3 (72 hours) after a full course of an ACT.

In 2010, WHO developed the Global Plan for Artemisinin Resistance Containment (GPARC). The plan was drafted after a consultation with all constituencies of the Roll Back Malaria Partnership, as well as a range of donor organizations and industry partners. WHO is also currently implementing an emergency response plan to scale-up efforts to contain artemisinin resistance in the Greater Mekong subregion. The presentation will provide an update of the current status of artemisinin resistance and containment activities.

Disclosure of Interest: None declared.

COMPLEXITY OF PREDICTING THE MAGNITUDE OF DRUG-DRUG INTERACTIONS IN AN INDIVIDUAL PATIENT: THIS CANNOT FIT TO A POCKET GUIDE; IPAD MAY BE! A. Rostami-Hodjegan
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Summary: The increased prominence of in vitro–in vivo extrapolation (IVIVE) capabilities has helped with recognizing the potential of drug–drug interactions (DDI) at early stages of drug discovery. Latest regulatory guidelines by the EMA and FDA provide recommendations for conduct of IVIVE through modeling. They are designed to protect the public from adverse effects associated with likely DDI by appropriate labeling or preventing the marketing of drugs with unmanageable DDI. However, DDI in an individual patient are determined by a myriad of variables. Prescribers may use labels in the clinical practice; nonetheless, currently, labels do not provide information for all the different permutations of conditions that put certain subgroup of patients at higher risk (eg, comorbid diseases, genetics, age and intake of several drugs). Some recent attempts by both the FDA and EMA have moved the focus from an average individual to a perceived susceptible patient (eg, chronic renal failure).

Creation of user-friendly interface computer programs of DDI prediction, which takes the sources of variability into account, may assist with the prediction and management of DDI in an individual patient. The required information on drugs (ie, affinity to various enzymes, nonenzymatic routes, permeability, protein binding, inhibi-
DEVELOPING A STANDARDISED PRESCRIPTION CHART TO REDUCE ERROR

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Summary: Unfamiliarity is an important contributor to error, including medication errors, some of which result in adverse events. Paper-based inpatient prescription charts differ in different hospitals, and medical trainees move around health care systems, so they may be unfamiliar with such charts initially.

Standards for the design of inpatient prescriptions charts have recently been agreed by the Academy of Medical Royal Colleges in the United Kingdom. In several studies, standardization of prescribing documents has been associated with significantly reduced medication errors in adults in Australia, as well as in some aspects of pediatric medicine. The introduction of a single inpatient prescription chart in Wales in 2004 and its subsequent continuing development will be described. The training resources developed to support the chart will also be discussed.

Standardization of prescribing standards, of acceptable abbreviations, and standardized training in prescribing can also all contribute to a reduction in medication errors and associated adverse events, including when electronic rather than paper-based prescriptions are written.

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References

THE INDIVIDUALISATION OF CANCER THERAPY IN ORGAN DYSFUNCTION

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Summary: Cancer patients with adequate hepatic or renal function are typically studied during drug development. The majority of anticancer agents are cleared by hepatic or renal mechanisms. Therefore, dose adjustments would be anticipated in patients with organ dysfunction. However, when a drug is approved, dosing modification guidelines are often lacking for patients who have varying degrees of hepatic or renal dysfunction, especially moderate or severe dysfunction. In clinical practice, oncologists may start therapy with an empirically derived lower starting dose due to the perception that a patient with organ dysfunction would have poorer tolerability due to increased toxicity. The presentation will summarize: (1) A brief historical perspective of individualization of cancer therapy in organ dysfunction; (2) pathophysiology of organ dysfunction in cancer patients; (3) barriers to the conduct of clinical trials in this population; and (4) recent examples of dosing recommendations for anticancer agents.

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