A mechanistic study of anti-HIV activity and cancer registry match investigation in laboratory drug 2- Indolinones show record linkage among them many interesting leads evaluation.

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Statement of Purpose: It is well documented that HIV infection dramatically increases the risk for various cancers. However the risks for cancers overall and specifically by different types among HIV-positive individuals in India are largely unknown and it is generally felt that these risks are lower than that reported in other populations. The little that is known about the association of HIV and malignancies in India stems from case reports and hospital based studies. There have been very few cases reported of Kaposis’ sarcoma and hospital based prevalence studies of HIV in cancers have found rates ranging from 1 to 4%. One hospital based study which analysed data on testing of cancer patients (Cancer Causes and Control 2008; 19: 147-153) has provided some preliminary estimates in the form of Proportional Incidence Ratios (PIRs) which confirmed the preliminary impression that Kaposis’s sarcoma is rarely observed in HIV infected individuals in India. The study found increased PIRs for non-Hodgkin’s lymphoma (NHL) and anal cancer in males and females, increased PIR for cervical and vaginal cancer in females and Hodgkin’s disease, testicular cancer, colon cancer, and several head and neck cancer sites in men. However there have been no populations based studies to assess the risk of different cancers in HIV. It is well accepted that such studies which minimize selection, response and referral biases would be able to provide better estimates of cancer risk for different anatomical sites among HIV infected persons in a region. Systematic monitoring of cancer burden is therefore important both from a public health and from a clinical management perspective to maximize the benefits of a resource intensive intervention. Record linkage is a well-recognized tool to study the morbidity and mortality patterns in a population in general or in a particular area. Matching of HIV and Cancer registry’s has been found to be a useful tool for understanding HIV and Cancer epidemiology in many developed countries of the world (USA, UK, Australia, Italy) and also in Uganda. It was felt however that this kind of a linkage study would not be possible in India due to lack of unique identification number for matching and databases (especially small molecule drug discovery part). The approach can be used in bioinformatics practices, to take this study further, a laboratory work focused on interesting finding novel lead molecule of 2- Indolinones showed such record-linkage in multiple anti cancerous and HIV-1 activity.

Methods: Laboratory R & D and trial batches of novel 2- Indolinones were carried out by using auto parallel synthesizer. Total 97 derivatives of 2-indolinones have been synthesized, medical drugs raw material N-methyl morpholine, substituted benzylchlorides, isoniazid, substituted benzoilhydrazide, quinazoline, orthophenylenediamine, halogens and alkyl groups as substituent and compounds were recrystallized by using ethanol-chloroform mixture. Structures of compounds were confirmed by FTIR, 1HNMR and Mass spectra. IR spectra were recorded in KBr disk on Nicolate IR-Instrument and reported in cm-1. Synthesized compounds checked for anti-cancer study and melphalan as a standard were also evaluated for their in vitro activity against human Non-Small Cell Lung Cancer. Synthesized compounds were screened for anti-cancer activity at National Cancer Institute, Maryland, USA and Rega Institute, Belgium respectively. Anti-HIV-1 activity checked and it has been displays low cytotoxicity (CC50>1mM) to cell lines, TZM-bl and displayed potent anti-HIV-1 activity found against laboratory adapted strains UG070, 7 th PID.

Results: In vitro anti- cancer activity of lead compound 5-(morpholin-4-ylmethyl)-8-nitro-4,4a,5,9b-tetrahydro-1H-pyrazino[2,3-b]indole-2,3-dicarbonitrile it has found good quality of anticancer activity against most of the cancer cell line with ranges from -77.23 to 55.85% growth. Lead compound display -77.23 to 7.31% growth against non-small cell-lung cancer (HOP-62). Same lead compound in vitro anti-HIV-1 activity has very low cytotoxicity (CC50>1mM) and it has been displays 65.35 ug/ml to cell lines, TZM-bl. Also it displayed potent anti-HIV-1 activity and found 5.02 µg/ml against laboratory adapted strains UG070, 7 th PID. Conclusions: Some anticancer drugs, but not all, inhibit replication of human immunodeficiency virus (HIV) and thus, exhibit a therapeutic potential. Thus, they may be an effective adjunct therapy or perhaps result in a cure. One possibility is the development of potent anticancer drugs that exhibit anti-HIV activities. These drugs, at high doses are used for cancer therapy; at lower concentrations they exhibit anti-HIV activities in cultured cells.