Abstracts

Cuban Research in Current International Journals

The following selection—alphabetical by title—reflects Cuban publishing in international medical and population health journals over the last quarter on an array of topics. Links to these journal articles may be found at www.medicc.org/mediccreview.


CK2 represents an oncology target scientifically validated. However, clinical research with inhibitors of the CK2-mediated phosphorylation event is still insufficient to recognize it as a clinically validated target. CIGB-300, an investigational peptide-based drug that targets the phosphoacceptor site, binds to a CK2 substrate array in vitro but mainly to B23/nucleophosmin in vivo. The CIGB-300 proapoptotic effect is preceded by its nucleolar localization, inhibition of the CK2-mediated phosphorylation on B23/nucleophosmin and nucleolar disassembly. Importantly, CIGB-300 shifted a protein array linked to apoptosis, ribosome biogenesis, cell proliferation, glycolysis, and cell motility in pro- teomic studies which helped to understand its mechanism of action. In the clinical ground, CIGB-300 has proved to be safe and well tolerated in a First-in-Human trial in women with cervical malignancies who also experienced signs of clinical benefit. In a second Phase 1 clinical trial in women with cervical cancer stage IB2/II, the MTD and DLT have been also identified in the clinical setting. Interestingly, in cervical tumors the B23/nucleophosmin protein levels were significantly reduced after CIGB-300 treatment at the nucleus compartment. In addition, expanded use of CIGB-300 in case studies has evidenced antitumor activity when administered as compassionate use. Collectively, our data outline important clues on translational and clinical research from this novel peptide-based drug reinforcing its perspectives to treat cancer and paving the way to validate CK2 as a promising target in oncology.


Objective To assess the economic cost of routine Aedes aegypti control in an at-risk environment without dengue endemicity and the incremental costs incurred during a sporadic outbreak. Methods The study was conducted in 2006 in the city of Guantánamo, Cuba. We took a societal perspective to calculate costs in months without dengue transmission (January–July) and during an outbreak (August–December). Data sources were bookkeeping records, direct observations and interviews. Results The total economic cost per inhabitant (p.i.) per month. (p.m.) increased from 2.76 USD in months without dengue transmission to 6.05 USD during an outbreak. In months without transmission, the routine Aedeses control program cost 1.67 USD p.i. p.m. Incremental costs during the outbreak were mainly incurred by the population and the primary/secondary level of the healthcare system, hardly by the vector control programme (1.64, 1.44 and 0.21 UDS increment p.i. p.m., respectively). The total cost for managing a hospitalized suspected dengue case was 296.60 USD (62.0% direct medical, 9.0% direct non-medical and 29.0% indirect costs). In both periods, the main cost drivers for the Aedes control programme, the healthcare system and the community were the value of personnel and volunteer time or productivity losses. Conclusions Intensive efforts to keep A. aegypti infestation low entail important economic costs for society. When a dengue outbreak does occur eventually, costs increase sharply. In-depth studies should assess which mix of activities and actors could maximize the effectiveness and cost-effectiveness of routine Aedes control and dengue prevention.


Background Evaluation of new therapies for cancer has suffered a paradigm shift in the last years. The use of innovative and more efficient designs is a priority for the scientific community; nevertheless, the use of this kind of design is not yet wide spread. Purpose In this paper will examine the effectiveness of adaptive designs compared with traditional designs in phase II clinical trials. Methods We reviewed a group of abstracts records between 1980 and 2008 and extracted data regarding statistical design, year of publication, kind of evaluated product, localization, sample size and results of the trials. Results Nine hundred and eighty-nine clinical trials were identified and from them 333 traditional designs and 19 adaptive designs were included in the review. Two hundred statistical papers were located and 16 were included in the review. The most frequent designs were Standard up and down designs, continual reassessment methods and its variation and designs with Bayesian approaches. More than 80% of the studies evaluated different schemes of chemotherapy. Adaptive designs evaluated only drugs and not any kind of treatment combination and the most often localizations evaluated in both designs were lung, haematology malignancies, and colon cancers. Conclusions Adaptive designs are more efficient from the statistical point of view but they are not yet widely used because of complex and computationally intensive methods needed, substantial effort for planning the trials and lack of regulatory guidance.


The knowledge of the genetic diversity of HIV-1 constitutes a fundamental premise in the epidemiological surveillance. In the present study, it was analyzed the HIV-1 genetic variability from 142 Cuban patients who were diagnosed of HIV-1 infection during 2009 and 2010. HIV-1 subtypes were determined by partial RT-PCR and sequencing of HIV-1 pol gene. The phylogenetic analysis showed that 47 (33.1%) samples were subtypes B, and 95 (66.9%) non B subtypes, where G, H and C subtypes, as well as the recombinant forms CRF19_cpx, CRF18_cpx and CRFs BG were included. It was detected for the first time in Cuba the circulation of the CRF08_DF. The analyses of recombinants showed the presence of recombinant CRF18_cpx/CRF19_cpx. The study confirms the high genetic diversity of the HIV-1 and the circulation of new genetic variants in the studied population, which indicates the importance of maintaining a constant epidemiological surveillance in Cuba.


Despite promising results in the use of anti-epidermal growth factor receptor (EGFR) Abs for cancer therapy, several issues remain to be addressed. An increasing emphasis is being placed on immune effector mechanisms. It has become clear for other Abs directed to tumor targets that their effects involve the adaptive immunity, mainly by the contribution of Fc region-mediated mechanisms. Given the relevance of EGFR signaling for tumor biology, we wonder whether the oncogene inhibition could contribute to Ab-induced vaccine effect. In a mouse model in which 7A7 (an anti-murine EGFR Ab) and AG1478 (an EGFR-tyrosine kinase inhibitor) displayed potent antitumoral...
disadvantages of the regulatory pyrogen test to assure safety of the end-product Human Serum Albumin (HSA) for parenteral use call for the implementation of an alternative test. In the current study, 16 HSA batches were assayed for pyrogens in parallel with the Rabbit Pyrogen Test, conventional and endotoxin-specific LAL assay and monocyte activation test (MAT). It was found that all HSA batches were contaminated with (1,3)-beta-glucans, which interfere with the conventional LAL. Endotoxin-specific LAL was not suitable to test HSA due to unacceptable endotoxin recovery. Experiments combining polymyxin B and MAT demonstrated that pyrogenic batches were mainly contaminated with endotoxins. However, endotoxin-specific LAL failed to detect one of them. The contaminating (1,3)-beta-glucans enhanced the MAT/IL-6 response to endotoxin, but not that of MAT/over-expressed in many epithelial derived tumors and its role in the development and progression of NSCLC is widely documented. CimaVax-EGF is a therapeutic cancer vaccine composed by human recombinant Epidermal Growth Factor (EGF) conjugated to a carrier protein, P64K from Neisseria Meningitides. The vaccine is intended to induce antibodies against self EGF that would block EGF-EGFR interaction. CimaVax-EGF has been evaluated so far in more than 1000 advanced NSCLC patients, as second line therapy. Two separate studies were compared to assess the impact of high dose vaccination at multiple anatomic sites in terms of immunogenicity, safety and preliminary efficacy in stage IIIb/IV NSCLC patients. In both clinical trials, patients started vaccination 1 month after chemotherapy. Vaccination at 4 sites with 2.4 mg of EGF (high dose) was very safe. The most frequent adverse events were grade 1 or 2 injection site reactions, fever, headache and vomiting. Patients had a trend toward higher antibody responses. The percentage of patients showing a level of antibodies was similar to other vaccines. Disadvantages of the regulatory pyrogen test to assure safety of the end-product Human Serum Albumin (HSA) for parenteral use call for the implementation of an alternative test. In the current study, 16 HSA batches were assayed for pyrogens in parallel with the Rabbit Pyrogen Test, conventional and endotoxin-specific LAL assay and monocyte activation test (MAT). It was found that all HSA batches were contaminated with (1,3)-beta-glucans, which interfere with the conventional LAL. Endotoxin-specific LAL was not suitable to test HSA due to unacceptable endotoxin recovery. Experiments combining polymyxin B and MAT demonstrated that pyrogenic batches were mainly contaminated with endotoxins. However, endotoxin-specific LAL failed to detect one of them. The contaminating (1,3)-beta-glucans enhanced the MAT/IL-6 response to endotoxin, but not that of MAT/over-expressed in many epithelial derived tumors and its role in the development and progression of NSCLC is widely documented. CimaVax-EGF is a therapeutic cancer vaccine composed by human recombinant Epidermal Growth Factor (EGF) conjugated to a carrier protein, P64K from Neisseria Meningitides. The vaccine is intended to induce antibodies against self EGF that would block EGF-EGFR interaction. CimaVax-EGF has been evaluated so far in more than 1000 advanced NSCLC patients, as second line therapy. Two separate studies were compared to assess the impact of high dose vaccination at multiple anatomic sites in terms of immunogenicity, safety and preliminary efficacy in stage IIIb/IV NSCLC patients. In both clinical trials, patients started vaccination 1 month after finishing first line chemotherapy. Vaccination at 4 sites with 2.4 mg of EGF (high dose) was very safe. The most frequent adverse events were grade 1 or 2 injection site reactions, fever, headache and vomiting. Patients had a trend toward higher antibody responses. The percentage of patients showing a level of antibodies was similar to other vaccines.

The Trivers-Willard hypothesis suggests that populations respond to scarcity by decreasing the ratio of males to females at livebirth. Cuba experienced an extreme economic depression in the 1990s called the “special period.” Using time-series analysis, the authors studied the impact of this event on the male:female sex ratio at birth in Cuba from 1960 to 2008. From 1990 to 1993, the per capita gross domestic product in Cuba decreased by 36%. By use of a definition of the special period from 1991 to 1998, there was a prolonged increase in the male:female ratio of livebirths during this period of economic depression ($P < 0.001$), from 1.06 at baseline to a peak of 1.18. This association persisted when using alternative definitions of the duration of economic depression in sensitivity analyses. Once the period of economic depression was over, the male:female ratio returned to the baseline value. These data suggest that, in Cuba, contrary to the Trivers-Willard hypothesis, the human population responded to conditions of scarcity by increasing the ratio of males to females at livebirth. These data may be relevant in the modeling of demographic projections in countries that experience prolonged economic depression and in understanding adaptive human reproductive responses to environmental change.


Human erythropoietin (hEpo) production requires mammalian cells able to make complex post-translational modifications to guaranty its biological activity. As mammalian cell can be reservoir of pathogenic viruses and several animal origin components are usually used in the cultivation of mammalian cells, hEpo contamination with viruses is something of great concern. As consequence, this study investigated the viral removal and inactivation capacity of a recombinant-hEpo (rec-hEpo) purification process. Canine parvovirus, Human poliovirus type-2, Bovine viral diarrhea virus and Human immunodeficiency virus type-1 were used for measuring process viral removal and inactivation capacities. In conclusion, this study corroborated that the assessed rec-hEpo purification process has enough capacity (5.0-19.4 Logs) for removing and inactivating these model viruses and sodium hydroxide demonstrated to be a robust sanitization solution for chromatography columns (5.0 (PV-2)-6.7 (CPV) Logs).