

This world conference, a major trade show serving the interests of pharmaceutical lobbies, brought together 18,000 participants and gave rise to around 2,000 oral presentations and posters of very disparate interest. Unfortunately the share of **clinical research** has been systematically declining since its first meeting in favor of prevention, epidemiology, social, legal and human rights. The congress reiterated the commitment to achieve the

### **90-90-90 goal**

(90% of people diagnosed, 90% of diagnosed treated, 90% with undetectable viral load). Today 17million diagnosed (less than 50% ), 46% treated and 38% undetectable. The funding needed to reach the 90-90-90 target will reach more than \$ 19 billion next year, but will then drop to \$ 18 billion by 2020. The results presented in the major media have focused, in the absence of major results, on PrEP and on the absence of contamination in cases of undetectable viral load, results already presented previously. It is astonishing that on a plethora of works presented (more than 1000 studies) by thousands of researchers and colossal sums invested, none brings a beginning of answer to the essential wait of the patients, namely the eradication of the virus or an effective preventive or therapeutic vaccine. Overall, everything goes as if the sole objective of the research world driven by the pharmaceutical lobbies and their national and international political allies was to convince the HIV patient to take a triple therapy as soon as he is diagnosed with HIV, and to maintain it. for life, and for any seronegative individual with sexual activity, to make a pre-exposure prophylaxis (PrEP), namely a light antiviral treatment (dual therapy) for life! There is no room for contestation of early initiation of treatment, intermittent structured treatments, light treatments and complementary treatments. We are faced with a total lockdown of medical information for the sole benefit of pharmaceutical lobbies and their accomplices at the level of national and global health authorities (WHO and UNAIDS). Regarding PrEP, by taking Truvada, its adoption was significantly associated with the decline in diagnoses in the United States, although this prevention remains very marginal (77,000 people in the US in 2016 with a decrease of no more than 4.7% in new cases of seropositivity diagnosed in the states most practicing this prevention). In addition, taking Truvada on demand proved to be as effective as the daily intake during the first year of the French PrEP study. This is a costly prevention with side effects inherent to Truvada. It is essential to remember that PrEP is accompanied by an outbreak of other STDs (Syphilis, Gonorrhoea, Chlamydia, Lymphogranuloma venereum, Human papillomavirus, Herpes simplex virus, Hepatitis C). It seems to us regrettable not to focus the prevention effort on the sole use of condoms, which is the safest, most economical and risk-free way. It seems to us that the media hype around PrEP is motivated solely by the desire of pharmaceutical lobbies to considerably increase its clientele (30million additional patients to be treated). Regarding the adverse effects of treatments Alan Go (Abstract / 2778) shows that HIV is associated with a significant increase in the risk of heart failure and stroke. In the study presented, it appears that people living with HIV had a significantly higher rate of heart failure or stroke than HIV-negative participants, although they had fewer cardiovascular risk factors. The researchers concluded that heart failure or stroke in people living with HIV did not seem related to the developmental pathways of arteriosclerosis, or plaque development in the arteries. Unfortunately, the authors have refused to conclude that the only reason for these results is other than the taking of certain antivirals for which studies already exist (Abacavir, ...) An attempt at curative treatment (Abstract / 12977) by Sarah Fidler (randomized RIVER study) based on the Kick-and-Kill strategy, ie activation of reservoirs followed by antiretroviral treatment led to failure . This test drives open doors. A similar failure

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had already been achieved in Texas in 2005 with valproic acid. One can wonder about perseverance in failure!

For antiretroviral treatments, we find surprisingly a study establishing that a dual therapy with dolutegravir works well for a first anti-HIV treatment, whereas as early as 2005 a monotherapy with dolutegravir is preconnected! A clinical trial on a triple therapy (we can wonder about the reasons for the persistence of tritherapies prescriptions today in the era of mono or bitherapies and therapeutic simplifications!) Including doravirine, NNRTI, presented in 2015 to the IAS of Vancouver. This is a multicenter, randomized, double-blind study involving 766 people. Triple therapy (doravirine, tenofovir and lamivudine) appears as effective as (efavirenz, tenofovir, emtricitabine). One third of patients have moderate or severe side effects with discontinuation of the trial. The only interest of this trial could be the possibility of using doravirine in case of multiple resistances. Surprising information in young adults and adolescents who have been infected in utero or after birth has been reported. These patients are 13 times more likely to develop cancer and 9 times more likely to die. The development of cancer is associated with the lack of viral suppression and low nadir CD4 cells, leading researchers to suggest early initiation of antiretroviral therapy to reduce risk.

An important presentation, which did not have the impact that one would have expected, concerned the control of the viral load after interruption of antiretroviral treatment. This presentation gathers 14 studies carried out since the 2000s. Of the patients initiating their treatment early and followed for more than two years, 13% of them can interrupt their treatment and maintain a viral load lower than 400 copies during one year and 9 months and 22% for

at least 5 years. At the same time, the number of CD4 fell only slightly (32 cells / mm<sup>3</sup> / year and 221 cells / mm<sup>3</sup> / year for non-controllers).

In the case of late initiation of treatment and maintenance of antiretroviral therapy for 5 years, the rate of control of the viral load after interruption is only 4%.

These results should prompt practitioners to discontinue antiretroviral therapy after 2 or 5 years to determine both

control and non-controller patients and, where appropriate, provide structured discontinuations or treatment

referrals. Such an option would lead to a reduction in the adverse effects of antivirals and a reduction in costs

Ref:Namazi G et al. *The Control of HIV after Antiretroviral Medication Pause (CHAMP) study: post-treatment*

*controllers identified from 14 clinical studies.* The Journal of Infectious Diseases, <https://doi.org/10.1093/infdis/jiy479>

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An important study (PARTNER) on the risk of transmission of HIV by an HIV-positive person with an undetectable viral load has just confirmed that the risk is zero for both gay men and heterosexuals regardless of sexual practice. Regarding the vaccine 9 works were presented, 2 only on humans with two preliminary clinical trials of phase 1 / 2a. No hope for benefits for patients in the medium or long term. A macaque test (Abstract THAA0105) shows that injection of a single dose of broad-spectrum neutralizing antibody can protect against HIV for a period of 6 to 12 months. This is a temporary immunoprophylaxis. Another study on humanized mice with a neutralizing antibody (PGDM1400) base as a basis for the vaccine fails to establish a sufficient prophylactic or therapeutic effect. The clinical study (Abstracts TUAA0104 and TUAA0105) aims to evaluate a prophylactic vaccine consisting of viral vectors comprising a mosquito of HIV-1 Env, Gag and Pol transgenes and a soluble clade of gp140 trimeric protein envelope. . On 36 uninfected individuals, a strong and sustained immune response is observed up to the 78th week. It is difficult to demonstrate the prophylactic efficacy of this vaccine. Finally, two abstracts (TUAA0203 and TUAA0205) recall the potential of gene therapies.

One can only be surprised by the absence of major results on a vaccine that can give hope to patients. It should be mentioned, however, that **Bigpharma has no reason to fund research on the vaccine let alone accept the arrival of a vaccine on the market that would see the collapse of its huge profits on antivirals.**

However, we must remember the

**discovery of an effective and promising vaccine in 2016 based on the viral protein Tat Oyi**

(C104 - Biosantech-Erwann Loret Loret therapeutic Vaccine - Unjustifiable attacks on our site). **From the moment of its presentation, this discovery was attacked without any scientific basis, in the press notably by J.F Delfraissy, President of the ANRS, and on the judicial plane by the CNRS, and the Public Assistance. These have succeeded by judicial way to block the continuation of the test! It is assassinations or at least endangering the lives of others. After 2 years lost in sordid legal proceedings, the President of the Committee of ethics of the Protection of Person (CPP), gave a favorable opinion to a follow-up of cohort after vaccination of Phase II, on 46 patients seropositive.**

This cohort follow-up is scheduled to start in September 2018, and should validate the preliminary results of at least two patients at the beginning of retroseroconversion, after vaccination with Tat Oyi, on which Dr. Loret, researcher at the CNRS communicated to BERLIN before scientists in January 2017. If, because of the small number of patients per dose injected, the main objective of the clinical trial was not statistically significant, it was nevertheless achieved with 30% of subjects having maintained in the same dose a viral load less than 80 copies for 2 months, without triple therapy. This very promising result is a concrete hope that the Tat Oyi associated with triple therapy can potentiate its effectiveness, and reduce the risk of treatment failure in the case of poor compliance with treatment.

New criteria that have emerged since the end of the trial in 2014 and the analysis of the results of the trial show other points of interest, which are just as important today as a controlled viral load when stopped. triple therapy. The clinical course of an HIV-positive patient to a reported AIDS would be closely related to CD4 cell count, CD4 / CD8 ratio, reflection of immune system

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status and pro-viral DNA, a control of cell size infected, unreachable by triple therapy. Vaccination with Tat Oyi showed in the phase II trial that it had a statistically significant effect on the immune system, increasing CD4 and CD4 / CD8 ratio. Tat Oyi would also act statistically significantly on pro-viral DNA, which is a control of the reservoir of the virus, showing that when one accumulates proviral DNA between M0 and M12, the vaccinated with 33µg X 3 have a smaller reservoir at M12 than the placebos. Knowing that an anti-retroviral treatment acts only very little on the size of the reservoir of infected cells hidden in the body, and on the permanent production of extra cellular Tat by these cells, the implementation of this cohort monitoring has received a favorable opinion to validate that treatment by Oyi State could render undetectable pro-viral DNA, a control of the HIV reservoir in the peripheral blood, only five months after the first injection and increase by 66% the CD4 / CCD8 ratio in patients with HIV infection (Retrovirology 2016). This cohort follow-up could, four years after the release of the trial, bring a functional cure if, at the disappearance of the anti-HIV antibodies (P24-GP120), the undetectability of the pro-viral DNA was associated, which would be a real turning point in the treatment of AIDS. The EvaTat trial seems to show that patients with clades B and C are good responders to the Tat Oyi vaccination, which corresponds to 95% of the global population of patients with HIV. The association of triple therapy with Tat Oyi could initially make a large number of patients eligible for the lightening of triple therapy, which corresponds to a strong demand from HIV-positive people, who suffer the heavy side effects of their treatment. For the southern countries for which the quality of the molecule is less good, the Tat Oyi would reduce the therapeutic failures by improving the observance of the treatments