

THE ICCARRE¹ LETTER

UPDATED INVENTORY AND PROJECTIONS ON LONG TERM SUSTAINABLE TREATMENT OF HIV INFECTION

November 2018

DESPITE ANTI RETROVIRALS, THE EPIDEMIC IS NOT TURNED OFF

under ARV combinations effective for one or two semesters, HIV carriers can no longer transmit their virus to intimate partners... A fair if only an already ancient (2008) state of matters.

And yet in our favored countries, 3 to 5 % new HIV infections are still registered each year, notably so in men who have sexual relations, occasional or regular, with other men (HSH); in formerly Soviet countries, the epidemic tends to spread within the general population ... HIV counts in Washington DC USA are hardly less pejorative than ...in Zimbabwe.

Within the realm of medical history, HIV infection would not seem fundamentally or biologically programmed to wane off under the sole means of antiretroviral chemotherapy. The fact is that no other chronic infections - sexually or otherwise transmissible- which by nature do not evolve spontaneously towards healing (pulmonary tuberculosis, Leprae, syphilis, etc..), have ever been eradicated by targeted chemotherapies².

TREATMENT OF ESTABLISHED HIV INFECTION COULD LAST DECADES

For lack of a likely cure in sight - nor of its least distant substitute (*long-lasting functional remissions*, where omitting ARV treatment would no longer be plagued by imminent HIV resurgence), long term suspensions of ARVs without HIV rebounding have yet to come to the clinical fore³.

AND AS SO LONG LASTS, LET IT WEIGH AS LITTLE AS CAN BE

What will the cumulative toxicity of non-vitamin C products taken along 10 20 30 years or more be? Also at more than 10,000 euros per person year over decades (within European socialized health care systems), will national solidarities afford treating everyone at all times for ever ?

ICCARRE APPROACHES FUNCTIONAL REMISSION

Who must treat long and far spares his/her patient's mind ...and body's water-tables. In these regards, short cycles of intermittent ARVs is approaching a strategic position in the sustainable management of persons with HIV. Indeed...

1 *Intermittent in short Close Cycles, Anti Retrovirals Retain Efficacy*

2 Seventy years into the life-saving availability of anti mycobacterial antibiotics, WHO still counts each year 7 to 8 millions new cases of lung tuberculosis.

3 As reported in *NATURE* October 2018, broadly neutralizing anti HIV antibodies injected to 11 patients may have paved a new way to allaying ARV treatment. A glimmering glint, still not quite auspicious of a coming spring.

From 2006 to 2018 at Raymond-Poincaré Hospital, Garches, France, 102 patients have successfully reduced their weekly ARV intakes to *three days* over 9 000 weeks; 82 have been down on a *two days /week* regime over 16 000 weeks, half of whom for > 2 years ; 26 eventually took their combined ARV weekly intakes medicines to JUST ONE Day for > 2 000 weeks - over 7 years with the most ancient volunteers. One day of ARV intakes per week over a year nearly amounts to 45 weeks *without chemistry nor a transmissible retrovirus !*

HIV, *Rex Tremendae* of the embers years, has so been tackled under triple ARV combinations (1996), snared in with ICCARRE (2010-2015) and now with QUATUOR (2017 onwards) ... A whole symbolic representation to be recomposed, presented, taught, *explained*.

WHY IS IT ? BECAUSE HIV WANTS IT WELL

One or two semesters continuously passed under suppressive ARV combinations, and the time of maintenance treatment relief has come up. In that second treatment period, HIV will regularly have slowed its rebounding momentum, so much that it will take from *5 to 21 days* and more for it to resurge upon momentary ARVs interruption. Whatever is going on during such *pauses, eclipses, respirations*, may not be clear. Yet the noted *delays in rebounds off ARVs* entice ARVs to be adjusted to *barely less intermittent prescription counterpoints* .

FRENCH ACADEMIA COMMITTED TO THE ICCARRE FRONT ...WHICH IT CONSOLIDATES

The French National Agency for AIDS Research (ANRS) has been pursuing since 14 months its first large controlled *QUATUOR* clinical trial - on 640 volunteers from 62 university hospital centers, all under standard triple combinations for 4 days or (randomized) 7 days a week catches, *with no pejorative returns at this time*.

Results and pertinent recommendations are expected early 2020, namely, a commanding registration en scripting the 4 days of weekly maintenance regime as performing as well as the current 7 day dogma. For French and other sero-positive people, a breathing liberation in the coming...And for France AHP University, an object of national pride⁴.

SAVING DIDANOSINE⁵ FOR THE SAKE OF QUADRIX, THE SERO-POSITIVE PEOPLE'S PILL

In our patients under maintenance treatment 3 days 2 days 1 day a week, 52, 60, and 17 will have taken a unique, AHP FRANCE UNIVERSITE-sponsored, quadruple ARV combination made of widely prescribed now *vintage* ARVs devoid of intellectual property rights (QUADRIX ©).

Over 294 cumulative years of intermittent treatment three two one day per week - and not even FOUR viral escapes per 100 treatment-years - QUADRIX has shown its qualities of *tolerance, efficacy, desirability*

ICCARRE ONTO FURTHER PULL UPS... ALONG A SOON PROXIMATE MAINSTREAM

4 Time to invite an inspired industrialist to try a *first in class* Pharma-Soothing pose, Great Renderer of a new Humanist Paradigm ? *Not on your nelly !* Big pharma is not intent on changing the rule commanding *uninterrupted* ARVs. All to the contrary since megaphone announcements of long-lived injectable ARVs: one or two trimestrial injections, and patients ' body and souls will be under continuous anti-retroviral immersion.

5 Didanosine is one of the 4 ARV components of the out-of-compass QUADRIX combination; the industrial manufacturer of Didanosine has suspended the monopolistic production of its ARV since March 2018.

Buoying behind the unfettered QUATUOR bow wave, sailing towards the legitimization of short cycles of intermittent treatment, it will take some good ICCARRE diplomacy to animate networks of influence and weave alliances meant to:

1. Attract interest of philanthropist pharma professional retakers⁶, so as to set up a *temporary importation authorization* for Didanosine, in line with requirements by the National Agency for the Safety of Medicinal Products ANSM;

2. selling the benefits of the 3 days 2 days 1 day project at colleges of ARVs prescribers via conferences, presentations-discussions, documents, memos...

A Missi Dominici Mission inaugurated at Salpêtrière, a French infectiology sanctuary where *adjusting posologies, reducing chemistry, letting patients breathe*, was pleaded before a complacent full medical audience. Touring some 60 university hospital chapels will require resilience, luck, audacity...and supportive grants!

3. invite the benevolent ANSM to pursue its guidance through the regulatory maze required to properly seat the 3.2, 1 project ...

4. gather a panel of sympathetic experts to form an advisory directory for the elaboration of a demonstrative clinical trial protocol;

5. ultimately create a philanthropic ICCARRE endowment fund, to help initiate private / public fundings for the 3 2 1 clinical trial.

ONCE A WEAKER, ICCARRE MAY EVENTUALLY PREVAIL...IF NOT ON ITS SOLE OWN⁷

6 A professional re-taker philanthropist...? The QUADRIX combination only costs today, at current France ARV market price only 1450 euros per year for three two one day catches. Reformating the 4 vintage ARVs in *Rainbow-colored* (patentable) blistered boxes, especially indicated for a 3 2 1 day dosing schedule, could be proposed to the market for less than 1000 euros per year - while still ensuring sumptuous profits to the manufacturer-distributor of the *sero-positive people's pill with a worldwide vocation* !

7 In 11 patients submitted to 3 injections of a pair of broad spectrum anti HIV-1 antibodies, the observed median time to HIV rebound off ARVs (21 weeks...) was impressive!...A glimmering anticipation of a future clinical trial, with patient volunteers *under a one day a week combination schedule*, to whom would be – or would not be - injected 2 to 3 double doses of broadly neutralizing antibodies ... In expectation of a 45 weeks off ARVS per year, without a transmissible retrovirus, at the consolidating price of 2 to 3 antibody injections ... Looking like future ?