Patient-reported receptiveness to a HIV therapeutic vaccine (RAVVIH study)

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Background: in developed countries where modern antiretroviral treatments (ART) are available and generalized, more than 90% of people living with HIV/AIDS (PLWHA) have obtained an immunovirological success but this is not the case in the developping world.The need for strict adherence to ART, the potential ART side effects and the emergence of drug –resistant viruses are important challenges to life-long ART. So, there is a need for an HIV cure. There is currently intense research into the development of therapeutic vaccines against HIV and, in the future, PLWHA are expected to benefit directly from such vaccines. A preventive HIV vaccine would also be a great tool to prevent, control and maybe eradicate the pandemic [Puls RL et al 2006].The Thai RV144 phase III vaccine trial showed a modest efficacy. Anticipate the acceptability of vaccines by the public has become an increasingly important factor in considering which vaccines should be given [Rerks-Ngarm et al 2009]. In the recent years, prophylactic vaccinations appear to be less and less accepted by a wider part of the general French population. It is therefore important to study the acceptability of a HIV therapeutic vaccine in PLWHA in France.

Objectives: Measure the acceptability of a future HIV therapeutic vaccine and the willingness to participate to a HIV vaccine trial in HIV-infected patients aged 18-75 followed in 3 French hospitals

Methods

Study design: prospective, non randomized, multicenter, interventional, qualitative and quantitative study. Between December 2013 and may 2014, all consecutive outpatient followed in 3 hospital-based infectious disease departments were sollicited during their semestrial follow up visit for HIV. The 3 participating centers were choosen to be representative of French PLWHA described in the nationally representative VESPA survey.
Ethics: each patient received an information notice about the study. Prior written consent was sought before entering the study. Questionnaires and interviews were anonymous. The study was approved by an Ethics Committee
This study was registered on ClinicalTrails.gov ID: NCT02077101.
Eligibility criteria:
-age between 18 and 75 years old,
-being infected with HIV-1,
-having a French medical insurance.
Exclusion criteria: patients who understood French poorly or were illiterate.

Qualitative analysis: A review of the literature identified HIV vaccine acceptability determinants: trust in doctors, knowledge, perceptions of illness, stigma, quality of life (QoL). Individual interviews were performed by a trained psychologist. The selection of patients was done to reflect the socio-demographic characteristics of the PLWHA population in France. The interviews of 45 to 60 minutes duration were recorded and the verbatim transcribed. The analysis was performed manually by two experienced researchers. Open coding was performed within a framework predefined by the themes in the interview guide. A first list of codes was carried out independently and then pooled together to check for discrepancies. A common list was then used and enriched for further analysis.

Quantitative analysis.
Patients completed 3 self-administered questionnaires: two validated and published (Brief IPQ R and PROQOL HIV) and a specific «RAVVIH questionnaire ».
- The RAVVIH questionnaire contained items identified in several preventive vaccine acceptability studies. Items were assessed by a scientific committee and tested by a group of PLWHA before the beginning of the study. RAVVIH questionnaire contains 72 items : 14 socio-demographics, 8 addiction-related and 50 vaccination-related items.
- The Brief Illness Perception Questionnaire (Brief IPQ R) is a 9-item questionnaire designed to rapidly assess cognitive and emotional representations of illness. The Brief IPQ uses a single-item scale approach to assess perception on a 0–10 response scale. The Brief IPQ comprises 5 items on cognitive representation of illness perception: consequences, timeline, personal control, treatment control, and identity. This questionnaire assesses perceptions on each of the five dimensions by asking patients for their own beliefs about their condition
- The Patient-reported outcomes quality of life HIV instrument (PROQOL-HIV) contains 43 items, reflective of the themes that dominate the experience of HIV patients living in the HAART era. General health perception, social relationships, emotions, energy/fatigue, sleep, cognitive functioning, physical and daily activity, coping, future, symptoms, and treatment. It has been developed simultaneously across 9 countries, following rigorous international standards.
The distribution of acceptability score was summarized using the usual indicators (mean and median) and dispersion (standard deviation, interquartile and range).

KEY RESULTS

Table 1 Clinical characteristics of patients (N=215)

	F N=64			M N=151			Combined N=215		
Age (yrs) (tertiles)	37	42	52	43	51	60	40	49	57
Year of HIV diagnosis (tertiles)	1993	2002	2010	1991	1998	2007	1992	1999	2008
HIV infection transmission category :									
- other	3 %			3 %			3 %		
- heterosexuals	89 %			27 %			45 %		
- MSM	0 %			59 %			42 %		
- Injecting drug users	8 %			11 %			10 %		
Year of initiation of ART (tertiles)	1997	2003	2011	1997	2003	2009	1997	2003	2009
CDC clinical stage : A	80 %			66 %			64 %		
B	12 %			7 %			9 %		
C	28 %			26 %			26 %		
D	0 %			1 %			1 %		
HIV Viral load below detection limit	95 %			97 %			96 %		
CD4 cell count/mm3 (tertiles)	431	620	828	460	630	830	452	628	828
Co morbidities									
Chronic hepatitis B (AgHbs+)	8 %			3 %			5 %		
Hepatitis C (positive HCV serology)	12 %			15 %			14 %		
HBV+HCV	2 %			1 %			1 %		
Treated Diabetes	3 %			9 %			7 %		
Treated Hypertension	20 %			30 %			27 %		
Cancer	6 %			9 %			8 %		
Vaccination coverage									
HBV vaccination : updated	64 %			80 %			75 %		
Not up to date	20 %			9 %			12 %		
Don't know	15 %			11 %			12 %		
Diphtheria-tetanus- inactivated poliovirus vaccination dTp : updated	67 %			75 %			73 %		
Not up to date	14 %			14 %			14 %		
Don't know	19 %			11 %			13 %		
Pneumococcal vaccination : updated	16 %			15 %			15 %		
Not up to date	62 %			70 %			67 %		
Don't know	22 %			23 %			17 %		
Influenza vaccination : updated	19 %			23 %			21 %		
Not up to date	72 %			69 %			70 %		
Don't know	9 %			8 %			9 %		

Table 2. Socio-demographic characteristics

N=215	%
French born	80
Secondary school completed	58
Single	47
Renting	59
Being in couple	45
No children	57
Secure employement	88
Additional private insurance	86
Give up some medical care for financial reasons	11

Qualitative analysis

Clinical and socio-demographic data of the 20 interviewees :
13 men and 7 women, mean age: 46 years old [23 – 66].
14 were French-born, 5 from Sub Saharan Africa 1 from Portugal.
All patients were on ART and had an undetectable viral load.

Table 3. Interviewees: vaccine expected benefits

Expected benefits	Life impact
Suppression of treatment daily constraint	Reduce daily burden
Avoid ART side effects	
Social image	No longer hide
Allay guilt	Relieve the burden of guilt
Recovery of Sexual liberty	
Hope of cure	Back to normal life
Recover more strength/ Vitality	Better perception of future

Some patients (4/20): No change expected from the vaccine : *"the disease is still there" , "I am sick, I am sick, nothing will change"*

Table 4. Interviewees: minimal HIV therapeutic vaccine requirements

Minimal acceptable delay between 2 immunizations	6 months
Minimal efficacy required	80% - 100%.
At least efficacy required as important as ongoing ART	

Quantitative analysis

- 220 patients: 70% men: 49% MSM, 10% IDU, 31% migrants
- 96% of patients were taking ART, 92% had undetectable viral load
- **93% believed vaccines are useful**
- High vaccination coverage (75%) for hepatitis B, diphtheria, tetanus & polio
- Some knowledge about a therapeutic vaccine reported by 54% of patients
- 53% of them considered that an acceptable therapeutic vaccine would fully suppress virus
- ART interruption for at least 3-6 months would be acceptable for 40% of patients and 44% hoped for definitive ART cessation
- High willingness (91%) to receive a HIV therapeutic vaccine if the HIV referent clinician would recommend it.
- Mainly fear were the possible side effects (71%)
- Administration mode (syringe) was not a barrier for 86% of patients
- Willingness to participate to a therapeutic vaccine clinical trial was 74%

BRIEF IPQ R : Patients are rather worried by the duration of their disease. The answers are more positive as regards their ART treatment, the symptomatology and the understanding of their disease. The internal consistency of this questionnaire is unsatisfactory on this sample (alpha Cronbach 0,536)

PROQOL HIV : Participants are more worried about stigma, their sexual life. The quality of their social relationships is considered satisfactory. The average score is >70 (on 100 points) and 50% of the individual scores are between 60 and 90 points indicating an intermediate QoL to good one.

Visual Analog Scale (VAS) of therapeutic vaccine acceptability : The last question of the RAVVIH questionnaire was an analogic visual scale in ten points about the acceptability of a future therapeutic vaccine. The average score was 8.4 ± 2.2. Half of patients (n = 79, 46 %) gave a score of 10. This VAS was well associated with the acceptability : those who where friendly volunteers for therapeutic immunization had an average score of 8.9 ± 1.5 while those who where not (answers « No » and « Don't know ») had a mean score of 5.0 ± 2.7 (Wilcoxon test, p < 0.001).

Multivariate analisis: therapeutic vaccine acceptability was not correlated with gender, (Pearson $\chi 2$, p = 0.487), age (Welch test, p = 0.521), education (Secondary school completed or not , p = 0.688) or disease duration (p = 0.921).

Discussion: To our knowledge, for the first time in France our study provides data about acceptability of a future HIV therapeutic vaccine by the PLWHA in clinical practice. In spite of growing scepticism in the French general population concerning prophylactic vaccination our quantitative and qualitative analysis showed that PLWHA have a high acceptability of HIV therapeutic vaccine. Our study has limitations, we did not included patients who understood French poorly and HIV-2 patients; study acceptability was high but we cannot exclude a recruitment bias. The 3 infectious disease departments who participated in the study are actively inciting updated preventive vaccine coverage which is not the case in all hospitals. The study acceptability was very high (around 90%). This study shows that the individual benefit of the future HIV therapeutic vaccine is so important that its acceptance is no correlated with mode of contamination, age, gender, illness perception, socio demographic characteristics or duration of disease. On the other hand, vaccine acceptability is strongly associated with the confidence in treating physician and vaccine characteristics (efficiency, expected benefits). Our results show a high rate of willingness to participate to a vaccine clinical trial as previously reported by others [Dong et al 2014].

Conclusion: This study explored the perception of therapeutic vaccine by a representative sample of PLWHA in France. Patients are receptive to the idea of receiving a HIV therapeutic vaccine and the confidence in their treating clinician is a key factor of acceptability.

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