Article

## Characterization of Physicians That Might Be Reluctant to Propose HIV Cure-Related Clinical Trials with Treatment Interruption to Their Patients? The ANRS-APSEC Study

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## Supplementary files

Step 1: Qualitative
Sept – Dec 2014

- Observing the production of knowledge allowing to reach representations and collective construction of sense
  - Individual and collective interviews (*Préau et al. 2018, Aids Care*)

Step 2: Mixt June – July 2015

- Eliciting the main viewpoints toward participating in HCRCT
  - Q methodology (Protière et al. 2017, Plos One)

Step 3: Quantitative Oct 2016 – March 2017

- Determining the more pertinent protocols
- Discrete Choice Experiments: comparing 13 pairs of strategies (Protière et al. 2020, JIAS)
- Evaluating adherence with the main viewpoints (Protière et al. 2020 AIDS & present manuscript)

**Figure S1:** Description of the three steps of the ANRS-APSEC study.

Table S1. Description of physicians' characteristics (ANRS-APSEC study, n=164).

	N	%*
Identity and sociodemographic characteristics		
Gender		
Man	80	48.78
Woman	84	51.22
Age (29; 74 years)	164	50 (41; 57)
In a relationship		
Yes	131	79.88
No	33	20.12
Felt part of the LGBT community		
Yes	15	9.15

	N	%*
No	149	90.85
Felt part of the heterosexual community		
Yes	130	79.27
No	34	20.73
Self-identifying as an HIV activist		
Definitely	76	46.34
Somewhat	71	43.29
No	17	10.37
Professional characteristics		
Specialty		
HIV specialist (infectiologist, immunologist)	84	51.22
General practitioner	60	36.59
Other (internist, etc.)	20	12.20
Number of years since graduating (1; 45 years)	164	21 (10; 28
Academic or research involvement	101	21 (10, 20
Yes	64	39.02
No	100	60.98
	164	
Orientation of professional activity (0=care; 10=research)	104	3 (2; 5)
Participated in prevention/information actions organized by HIV associations	(7	40.85
Yes	67	40.85
No	97	59.15
Requested to collaborate in writing National HIV guidelines	26	15.05
Yes	26	15.85
No	138	84.15
Sources of information about HIV cure research		
International conferences		
Yes	108	65.85
No	56	34.15
National conferences		
Yes	139	84.76
No	25	15.24
Meetings of learned societies		
Yes	113	68.90
No	51	31.10
International scientific literature		
Yes	143	87.20
No	21	12.80
HIV associations' journals		
Yes	71	43.29
No	93	56.71
Internet websites (ref. No)		
Yes	97	59.15
No	67	40.85
Participation in multidisciplinary networks		
Yes	110	67.07
No	54	32.93
Number of sources of information used about HIV cure research (0; 7)	164	5 (4; 6)
Experience with clinical trials	101	5 (1,0)
Number of clinical trials physician participated in (0; 99)	164	20 (10; 40
Participated in clinical trials to help advance the work of previous generations	104	<u> -0 (10, 40</u>
• • • • • • • • • • • • • • • • • • • •	106	61.62
Totally agree		64.63
Somewhat agree	46	28.05
Somewhat disagree	12	7.32

	N	%*
General opinion about participating in a clinical trial		
Rather reluctant	2	1.22
Depends of the characteristics of the clinical trial	105	64.02
Deferred to the department head's decision	34	20.73
Favorable	23	14.02
(Most recent clinical trial) Participated in order to advance research		
Yes	129	78.66
No	35	21.34
(Most recent clinical trial) Participated because department head asked them		
Yes	45	27.44
No	119	72.56
(Most recent clinical trial) Participated out of interest		
Yes	110	67.07
No	54	32.93
(Most recent clinical trial) Considered to have adequately informed patients of		
benefits AND risks—6 mv		
Definitely, for both benefits and risks	58	36.71
Somewhat, for benefits and/or risks	90	56.96
Not enough for benefits and/or risks	10	6.33
Viewpoints about HIV cure trials		
Believed that an HIV cure would become available during their career span—6		
mv		
Yes	57	34.76
No	67	40.85
Do not know	40	24.39
Physicians perceptions of their patients' level of concern about HIV-related		
difficulties		
Shorter expected life – 4 mv		
Very (concerned)	31	19.38
A little (concerned)	87	54.38
Not at all (concerned)	42	26.25
Side-effects related to current cART—4 mv		
Very	77	48.13
Not at all or a little	83	51.88
Severe fatigue – 4 mv		
Very	23	14.38
A little	97	60.63
Not at all	40	25.00
Negative impact on health in general—4 mv		
Very	63	39.38
A little	79	49.38
Not at all	18	11.25
Uncertain future – 4 my		
Very	63	39.38
A little	75	46.88
Not at all	22	13.75
Risk of HIV transmission—4 mv	<del></del>	
Very	88	55.00
A little	57	35.63
Not at all	15	9.38
Discrimination—4 mv	10	7.00
Very	136	85.00
Not at all or a little	24	15.00
inot at all of a little	∠ <del>4</del>	13.00

Very         133         83.13           Not at all or a little         27         16.88           Having to live with a secret—4 mv         22         13.75           Very         138         86.25           Not at all or a little         22         13.75           Feeling unable to lead a normal life—4 mv         71         44.38           Very         71         44.38           A little         77         48.13           Not at all         129         80.63           Not at all or A little         31         19.38           Negative impact on sexuality—4 mv         29         80.63           Not at all or A little         106         66.25           Not at all         25         15.63           A little         106         66.25           Not at all         42         26.25           A little         74         42.2           Not at all         42         25.           Out-of-pocket expenses—4 mv         25         15.63           Not at all         42         25.           Physicians perceptions of patients' lives with cART         81         3.35           Physicians perceptions of patients' lives with cART		N	%*
Not at all or a little       27       16.88         Having to live with a secret—4 mv       138       86.25         Very       13       43.35         Feeling unable to lead a normal life—4 mv       71       44.38         Very       71       48.13         Not at all       12       7.50         Negative impact on sexuality—4 mv       29       80.63         Very       19       80.63         Not at all or A little       31       19.38         Negative impact on sexuality—4 mv       29       81.13         Very       29       18.13         A little       106       66.25         Not at all       25       15.63         Cost for society—4 mv       29       18.13         Very       42       26.25         A little       74       46.25         Not at all       42       26.25         A little       74       46.25         Not at all       42       26.25         Physicians perceptions of patients' lives with cART       81       50.63         Solo       77       48.13       80.63         No       83       75.05       80.63 <t< td=""><td>Difficulties constructing a stable relationship with a main partner—4 mv</td><td></td><td></td></t<>	Difficulties constructing a stable relationship with a main partner—4 mv		
Having to live with a secret—4 mv	Very	133	83.13
Very         138         86.25           Not at all or a little         22         13.75           Feeling unable to lead a normal life—4 mv         Very         71         44.38           A little         77         48.13         Not at all         12         7.50           Negative impact on sexuality—4 mv         Very         129         80.63         No.63         No.63         No.63         19.38           Negative impact on professional life—4 mv         Very         29         18.13         A little         106         66.25         No.63         15.63         Cost for society—4 mv         29         18.13         A little         106         66.25         No.63         15.63         Cost for society—4 mv         42         26.25         A little         74         46.25         A little         74         46.25         A little         74         46.25         A little         75         15.63         A little         81         50.63         A little         75         15.63         A little         81         50.63         A little         75         15.63         A little         81         50.63         A little         81         50.63         A little         75         48.13         50.63         A lit	Not at all or a little	27	16.88
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Feeling unable to lead a normal life—4 mv         71         44.38           A little         77         48.13           Not at all         12         7.50           Negative impact on sexuality—4 mv         29         80.63           Not at all or A little         31         19.38           Negative impact on professional life—4 mv         29         18.13           Very         29         18.13           A little         106         66.25           Not at all         25         15.63           Cost for society—4 mv         42         26.25           A little         74         46.25           Not at all         42         25.25           A little         74         46.25           Not at all         54         33.75           Physicians perceptions of patients' lives with cART           Believed that having to take medication on a daily basis is easy for patients—4         81         50.63           No         83         51.88           Opinion of ART-related side effects for patients—4 mv         8         7         48.13           No         83         51.89         2         15.50           A little uncomfortable         2	Very	138	86.25
Very         71         44.38           A little         77         48.13           Not at all         12         7.50           Negative impact on sexuality—4 mv         2         80.63           Not at all or A little         31         19.38           Negative impact on professional life—4 mv         29         18.13           Very         29         18.13           A little         106         66.25           Not at all         106         66.25           A little         106         66.25           Not at all         4         25.05           Very         4         46.25           Not at all         4         27.50           Out-of-pocket expenses—4 mv         25         15.63           Very         25         15.63           A little         81         50.63           Not at all         54         33.75           Physicians perceptions of patients' lives with cART           Believed that having to take medication on a daily basis is easy for patients—4         4           Yes         77         48.13           No         83         51.88           Opinion of ART-related side effects for pati	Not at all or a little	22	13.75
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Very         129         80.63           Not at all or A little         31         19.38           Negative impact on professional life—4 mv         29         18.13           Very         29         18.13           A little         106         66.25           Not at all         25         15.63           Cost for society—4 mv         42         26.25           Very         42         26.25           A little         74         46.25           Not at all         44         27.50           Out-of-pocket expenses—4 mv         25         15.63           Very         25         15.63           A little         81         50.63           No at all         54         33.75           Physicians perceptions of patients' lives with cART           Believed that having to take medication on a daily basis is easy for patients—4         48.13           No         83         51.88           Opinion of ART-related side effects for patients—4 mv         12         7.50           A little uncomfortable         12         7.50           A little uncomfortable         2         13.75           Confidence in current cART—4 mv <tr< td=""><td>Not at all</td><td>12</td><td>7.50</td></tr<>	Not at all	12	7.50
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Cost for society—4 mv       42       26.25         Very       42       26.25         A little       74       46.25         Not at all       44       27.50         Out-of-pocket expenses—4 mv       25       15.63         A little       81       50.63         A little       81       50.63         Not at all       54       33.75         Physicians perceptions of patients' lives with cART         Believed that having to take medication on a daily basis is easy for patients—4         mv         Yes       77       48.13         No       83       51.88         Opinion of ART-related side effects for patients—4 mv       12       7.50         A little uncomfortable       12       7.50         A little uncomfortable       12       7.50         Very uncomfortable       12       7.50         Very uncomfortable       87       53.05         No       77       46.95         No       77       46.95         Believed that current ART would continue to be effective over the long term—4       4         mv       142       86.59         No       22	A little	106	66.25
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Physicians perceptions of patients' lives with cART  Believed that having to take medication on a daily basis is easy for patients—4  mv  Yes 77 48.13  No 83 51.88  Opinion of ART-related side effects for patients—4 mv  Not at all uncomfortable 12 7.50  A little uncomfortable 126 78.75  Very uncomfortable 22 13.75  Confidence in current cART  Very confident in current cART—4 mv  Yes 87 53.05  No 77 46.95  Believed that current ART would continue to be effective over the long term—4  mv  Yes 142 86.59  No 22 13.41	A little	81	50.63
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Opinion of ART-related side effects for patients—4 mv  Not at all uncomfortable A little uncomfortable 12678.75 Very uncomfortable 2213.75  Confidence in current cART  Very confident in current cART—4 mv  Yes No 7746.95  Believed that current ART would continue to be effective over the long term—4  mv  Yes No 14286.59 No 2313.41	Yes	77	48.13
Not at all uncomfortable       12       7.50         A little uncomfortable       126       78.75         Very uncomfortable       22       13.75         Confidence in current cART         Very confident in current cART—4 mv         Yes       87       53.05         No       77       46.95         Believed that current ART would continue to be effective over the long term—4       4         mv       142       86.59         No       22       13.41	No	83	51.88
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Very uncomfortable         22         13.75           Confidence in current cART           Very confident in current cART—4 mv         87         53.05           No         77         46.95           Believed that current ART would continue to be effective over the long term—4         86.59           No         142         86.59           No         22         13.41		12	7.50
Very confident in current cART—4 mv  Yes 87 53.05 No 77 46.95  Believed that current ART would continue to be effective over the long term—4 mv  Yes 142 86.59 No 22 13.41	A little uncomfortable	126	78.75
Very confident in current cART—4 mv  Yes 87 53.05 No 77 46.95  Believed that current ART would continue to be effective over the long term—4 mv  Yes 142 86.59 No 22 13.41	Very uncomfortable	22	13.75
Very confident in current cART—4 mv       87       53.05         No       77       46.95         Believed that current ART would continue to be effective over the long term—4 mv       42       86.59         No       22       13.41	Confidence in current cART		
Yes       87       53.05         No       77       46.95         Believed that current ART would continue to be effective over the long term—4       mv         Yes       142       86.59         No       22       13.41			
No 77 46.95  Believed that current ART would continue to be effective over the long term—4  mv  Yes 142 86.59  No 22 13.41	·	87	53.05
Believed that current ART would continue to be effective over the long term—4 mv Yes 142 86.59 No 22 13.41			
MV Yes 142 86.59 No 22 13.41			10.,0
Yes     142     86.59       No     22     13.41	mv		
No 22 13.41		142	86.59
	* or median (IQR).	<u></u>	10.11

**Table S2.** Factors associated with the reluctance score: results from univariable linear regressions (ANRS-APSEC study, n=164).

β	95% CI	p	p-glob

	β	95% CI	р	p-glob
Gender (ref. Man)			- 1	
Woman	0.03	[-0.28;0.34]	0.87	0.87
Age [29;74 years]	-0.01	[-0.02;0.01]	0.45	0.45
In a relationship (ref. No) Yes	0.03	[-0.35;0.42]	0.86	0.86
Felt part of the LGBT community (ref. No) Yes	0.21	[-0.33;0.74]	0.45	0.45
Felt part of the heterosexual community (ref. No) Yes	-0.08	[-0.46;0.30]	0.67	0.67
Self-identifying as an HIV activist (ref. Definitely) Somewhat No	0.26 0.13	[-0.06;0.59] [-0.40;0.66]	0.11 0.62	0.28
Definitely identifying themselves as an HIV activist (ref. No) Yes	-0.24	[-0.55;0.07]	0.13	0.13
Professional characteristics Specialty (ref. HIV specialist (infectiologist, immunologist))				
General practitioner Other (internist, etc.)	-0.17 -0.26	[-0.51;0.16] [-0.75;0.23]	0.30 0.30	0.43
Number of years since graduating [1;45 years]	-0.01	[-0.02;0.00]	0.14	0.14
Academic or research involvement (ref. No) Yes	-0.12	[-0.44;0.20]	0.45	0.45
Orientation of professional activity [0=care;10=research]	-0.12	[-0.19;-0.05]	0.001	0.001
Participated in prevention/information actions organized by HIV associations (ref. No) Yes	-0.43	[-0.74;-0.12]	0.01	0.01
Requested to collaborate in writing National HIV guidelines (ref. No)			0.10	0.10
Yes	-0.35	[-0.77;0.07]	0.10	
Sources of information used about HIV cure research International conferences (ref. No) Yes	-0.14	[-0.47;0.19]	0.40	0.40
National conferences (ref. No)	0.11	[ 0.17,0.17]	0.10	0.05
Yes	-0.24	[-0.67;0.19]	0.27	0.27
Meetings of learned societies (ref. No) Yes	-0.21	[-0.54;0.12]	0.22	0.22
International scientific literature (ref. No) Yes	-0.48	[-0.94;-0.02]	0.04	0.04
HIV associations' journals (ref. No) Yes	-0.30	[-0.61;0.01]	0.06	0.06
Internet websites (ref. No) Yes	-0.14	[-0.45;0.17]	0.38	0.38
Participation in multidisciplinary networks (ref. No) Yes	-0.13	[-0.46;0.20]	0.43	0.43
Number of sources of information about HIV cure research	-0.15	[-0.26;-0.04]	0.01	0.01
Experience with clinical trials	0.01	500 0 00 0 1	0.01	0.01
Number of clinical trials physician participated in [0;99]	-0.01	[-0.02;0.00]	0.01	0.01
Agreement with statement that participation in clinical trials				
helps to advance the work of previous generations (ref. Totally				0.08
agree) Somewhat agree	0.24	[-0.11;0.58]	0.18	0.08
Somewhat disagree	-0.47	[-0.11,0.38]	0.13	
	J.17	[ =.0.,0.12]	J.24	

	β	95% CI	р	p-glob
General attitude about participating in a clinical trial				
Favorable (ref. No)				0.004
Yes	-0.65	[-1.08;-0.21]	0.004	0.001
Rather reluctant (ref. No)				0.62
Yes	0.36	[-1.05;1.77]	0.62	0.02
Depends on characteristics of the clinical trial				0.40
Yes	0.14	[-0.18;0.46]	0.40	0.10
Deferred to the department head's decision				0.19
Yes	0.25	[-0.12;0.63]	0.19	0.17
Reason for participation in the most recent clinical trial				
In order to advance research (ref. No)				0.202
Yes	-0.24	[-0.62;0.13]	0.20	0.202
Because department head asked them (ref. No)				0.18
Yes	0.23	[-0.11;0.58]	0.18	0.10
Out of interest (ref. No)				0.79
Yes	-0.04	[-0.37;0.28]	0.79	0.7
(Most recent clinical trial) Considered to have adequately				
informed patients of both the benefits and risks of the trial (ref.				
Definitely, for both benefits and risks)—6 mv				0.04
Somewhat, for benefits or/and risks	0.37	[0.04;0.70]	0.03	
Not enough for risks or/and benefits	0.63	[-0.04;1.30]	0.07	
Believed an HIV cure would become available during their career				
span (ref. No)				0.06
Yes	-0.25	[-0.61;0.10]	0.15	0.00
Do not know	0.23	[-0.16;0.62]	0.25	
Physicians' perceptions of their patients' level of concern about				
HIV-related difficulties				
Shorter expected life (ref. Not at all)—4 mv				
A little (concerned)	0.19	[-0.17;0.56]	0.29	0.57
Very (concerned)	0.11	[-0.35;0.56]	0.64	
Side effects related to actual ART (ref. Not at all or a little)—4 mv				0.66
Very	-0.07	[-0.37;0.24]	0.66	0.66
Severe fatigue (ref. Not at all)—4 mv				
A little	-0.23	[-0.59;0.13]	0.22	0.29
Very	0.06	[-0.45;0.56]	0.83	
Negative impact on health in general (ref. Not at all)—4 mv				
A little	0.28	[-0.22;0.79]	0.27	0.50
Very	0.29	[-0.22;0.81]	0.26	
Uncertain future (ref. Not at all)—4 mv				
A little	0.29	[-0.17;0.76]	0.22	0.35
Very	0.35	[-0.13;0.82]	0.15	
Risk of HIV transmission (ref. Not at all)—4 mv				
A little	0.16	[-0.39;0.71]	0.58	0.04
Very	0.51	[-0.02;1.04]	0.06	-
Discrimination (ref. Not at all or a little—4 my	-	. ,		o :-
Very	-0.10	[-0.53;0.33]	0.65	0.65
Difficulties constructing a stable relationship with a main partner		[ 1.22,3.22]	3.30	
(ref. Not at all or a little)—4 mv				0.38
Very	-0.18	[-0.59;0.22]	0.38	0.50
Having to live with a secret (ref. Not at all or a little)—4 mv	0.10	[ 0.07,0.22]	0.00	
Very	-0.34	[-0.78;0.10]	0.13	0.13
vciy	-0.34	[-0.70,0.10]	0.13	

	β	95% CI	р	p-glob
Feeling unable to lead a normal life (ref. Not at all)—4 mv				
A little	0.17	[-0.43; 0.77]	0.57	0.84
Very	0.17	[-0.43; 0.77]	0.58	
Negative impact on sexuality (ref. Not at all or a little)—4 mv				0.51
Very	0.13	[-0.26;0.51]	0.51	0.31
Negative impact on professional life (ref. Not at all) —4 mv				
A little	0.30	[-0.12;0.73]	0.16	0.06
Very	0.63	[0.11;1.15]	0.02	
Cost for society (ref. Not at all)—4 mv				
A little	-0.08	[-0.45;0.29]	0.68	0.91
Very	-0.07	[-0.49;0.34]	0.73	
Out-of-pocket expenses (ref. Not at all)—4 mv				
A little	-0.14	[-0.48;0.20]	0.42	0.72
Very	-0.06	[-0.52;0.41]	0.81	
Perception of patients' life with cART				
Believed that having to take medication on a daily basis is easy				
for patients (ref. No)—4 mv				0.74
Yes	0.05	[-0.25;0.36]	0.74	
Opinion on ART-related side effects for patients (ref. Not at all				
uncomfortable) — 4 mv				0.71
A little uncomfortable	0.00	[-0.58;0.58]	1.00	0.71
Very uncomfortable	-0.19	[-0.88;0.51]	0.60	
Confidence in current cART				
Very confident in current cART (ref. No)				0.05
Yes	-0.31	[-0.62;-0.01]	0.05	0.05
Believed that current cART will continue to be effective over the				
long term (ref. No)				0.11
Yes	-0.37	[-0.82;0.08]	0.11	

mv: missing