syringes) by PWID likely to transmit HIV (who are HIV seropositive and not on antiretroviral treatment)?
(3) Are the problems in sharing injection equipment concentrated in recent migrants to France? Recent migrants may be coming from areas without traditions of harm reduction, and may thus not be fully informed about HIV/AIDS, safer injection, and safer sex.
(4) What are the reasons for the difficulties in obtaining sterile injection equipment? Are PWID as a community aware of these difficulties, and are PWID and public health authorities working collaboratively to overcome these problems?

In our article, we discussed not only instances wherein combined prevention has led to the 'end' of HIV epidemics among PWID, but also recent outbreaks of HIV infection among PWID. Although there was considerable variation among these outbreaks, a common component of all of them was change in local patterns of drug use and injection behavior. We noted that ending HIV epidemics among PWID requires not only public health scale implementation of evidence-based interventions but also continued monitoring of local patterns of drug use and risk behavior. We believe that France has the needed scientific expertise, resources, political will, and collaborative relationships between public health workers and people who use drugs to maintain an end of the HIV epidemic among PWID in the country.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

Don C. Des Jarlais[a] and Patrizia Carrieri[b], *[a]Icahn School of Medicine at Mount Sinai, New York, NY, USA, and [b]INSERM, U912 (SESSTIM), Marseille, France.*

Correspondence to Don C. Des Jarlais, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
E-mail: DDesjarlais@chpnet.org

Received: 29 March 2016; accepted: 6 April 2016.

References

1. Cazein F, Pillonel J, Barin F, Jauffret-Roustide M. **HIV infection among persons who inject drugs: ending old epidemics and addressing new outbreaks.** *AIDS* 2016; **30**:1857–1858.
2. Des Jarlais DC, Kerr T, Carrieri P, Feelemyer J, Arasteh K. **HIV infection among persons who inject drugs: ending old epidemics and addressing new outbreaks.** *AIDS* 2016; **30**:815–826.

DOI:10.1097/QAD.0000000000001117

Unite forces to validate biomarkers in the quest for lasting HIV remission

With interest, we have read the article by Li *et al.* [1] on the pooled analysis aiming to identify predictors of viral rebound. By reexamining the aggregated data, the authors convincingly show that lower levels of cell-associated HIV DNA and HIV RNA are associated with longer time to HIV rebound following analytical treatment interruption (ATI). This is in line with predictions on time to virological rebound from earlier modelling studies [2]. This important and clinically relevant finding aids the search for biomarkers for lasting HIV remission.

The ability to identify patients who can control HIV in the absence of treatment, either spontaneous or after eradication interventions, will have a global impact. The study of Li *et al.* [1] unfortunately also shows that the vast majority of participants are still unable to control viraemia. Rebound viraemia can be associated with a retroviral syndrome, additional immune damage, and forward transmission. The improved identification of patients unlikely to remain aviraemic will prevent an unnecessary and potentially hazardous ATI in these patients. Nonetheless, patient-based ATI studies remain necessary to identify biomarkers associated with viral rebound. Sharing data will, however, greatly aid this goal for two principle reasons.

First, collaborative research would better support the patients' sacrifices for the greater good. The justification for researchers to ask their patients to participate in potentially dangerous ATI studies is only appropriate when the nature of the study has been weighed against the importance of the expected outcome. Alternative and less invasive approaches to test a hypothesis should have been considered and excluded as realistic possibilities. These considerations are a moral obligation of every researcher and a pivotal part of ethical committee procedures. Collaborations will further honour the patients' risks greater than individual projects.

Second, collaborations will improve the power to find relevant biomarkers in ATI studies. This helps finding meaningful differences and reduces the risk of false negative results. A biomarker could also facilitate the follow-up after therapy interruption in patients, similar to the correlation between a suppressed plasma HIV-RNA and clinical outcomes. The identification of a validated biomarker for lasting HIV remission will eventually render future ATI studies obsolete.

The quest for lasting HIV remission by the identification and validation of biomarkers to replace ATI studies would benefit greatly from a collaboration between investigators,

individuals, the pharmaceutical industry, and regulatory authorities. Challenges of this approach can be foreseen. Retrospective analyses must incorporate methods to deal with inconsistencies and differences between studies. Future studies in the field should ideally be a prospectively initiated collaboration, and the design should be shaped to optimally answer the research questions. As a research community, we should define codes of good conduct to prevent inappropriate data abuse.

We propose an international collaboration to share the datasets of published work, perform meta-analyses, and initiate well designed prospective studies to validate possible biomarkers. Examples of innovative collaborative research projects that result in relevant findings from other research fields are progressively emerging [3], and are also expanding within the HIV research field [1,4]. HIV researchers from various continents have already gathered together to discuss the future management of HIV [5]. These incentives are increasingly applauded by prominent researchers [6,7]. Future collaborative studies should be conducted between trustworthy pioneering researchers who will acknowledge each other's input by relevant coauthorships. Combining knowledge will further shape hypothesis driven studies to fill important knowledge gaps in the HIV cure research. Together, we have a better and unique chance of finding validated biomarkers that will help us to identify patients who can be given a chance to live antiretroviral free lives, outside the spectrum of clinical ATI trials.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

Casper Rokx[a], Stefano Vella[b], Guiseppe Pantaleo[c], Yves Lévy[d,e,f] and Charles A.B. Boucher[a], *[a]Department of Viroscience, Erasmus MC University Medical Center, Rotterdam, the Netherlands, [b]Department of Pharmacology and Therapeutic Research, The Italian National Institute of Health, Rome, Italy, [c]Department of Immunology and Allergy. University of Lausanne, Switzerland, [d]INSERM U955, Institut Mondor de Recherche Biomédicale, [e]Faculté de Médecine, Université Paris Est Créteil, and [f]Vaccine Research Institute, Créteil, France.*

Correspondence to Casper Rokx, MD, Department of Viroscience, Room Ee1671, Erasmus MC University Medical Center, Wytemaweg 80, 3015 CN, Rotterdam, The Netherlands.
Tel: +31 (0)6 813 363 28; fax: +31 (0)10 703 3875; e-mail: c.rokx@erasmusmc.nl

Received: 22 March 2016; accepted: 3 April 2016.

References

1. Li JZ, Etemad B, Ahmed H, Aga E, Bosch RJ, Mellors JW, *et al*. **The size of the expressed HIV reservoir predicts timing of viral rebound after treatment interruption.** *AIDS* 2016; **30**:343–353.
2. Hill AL, Rosenbloom DI, Fu F, Nowak MA, Siliciano RF. **Predicting the outcomes of treatment to eradicate the latent reservoir for HIV-1.** *Proc Natl Acad Sci U S A* 2014; **111**:13475–13480.
3. Dalerba P, Sahoo D, Paik S, Guo X, Yothers G, Song N, *et al*. **CDX2 as a prognostic biomarker in Stage II and Stage III colon cancer.** *N Engl J Med* 2016; **374**:211–222.
4. TenoRes Study Group. **Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study.** *Lancet Infect Dis* 2016; **3099**:00536–00538.
5. Rokx C, Richman DD, Müller-Trutwin M, Silvestri G, van Lunzen J, Khoo S, *et al*. **Second European round table on the future management of HIV 10–11 October 2014, Barcelona, Spain.** *J Virus Erad* 2015; **1**:211–220.
6. Longo DL, Drazen JM. **Data Sharing.** *N Engl J Med* 2016; **374**:276–277.
7. Taichman DB, Backus J, Baethge C, Bauchner H, de Leeuw PW, Drazen JM, *et al*. **Sharing clinical trial data: a proposal from the International Committee of Medical Journal Editors.** *N Engl J Med* 2016; **374**:384–386.

DOI:10.1097/QAD.0000000000001118