HOT TOPICS IN HIV

Vaccines, immune recovery and eradication

Clinical experiences on HIV remission in absence of ART

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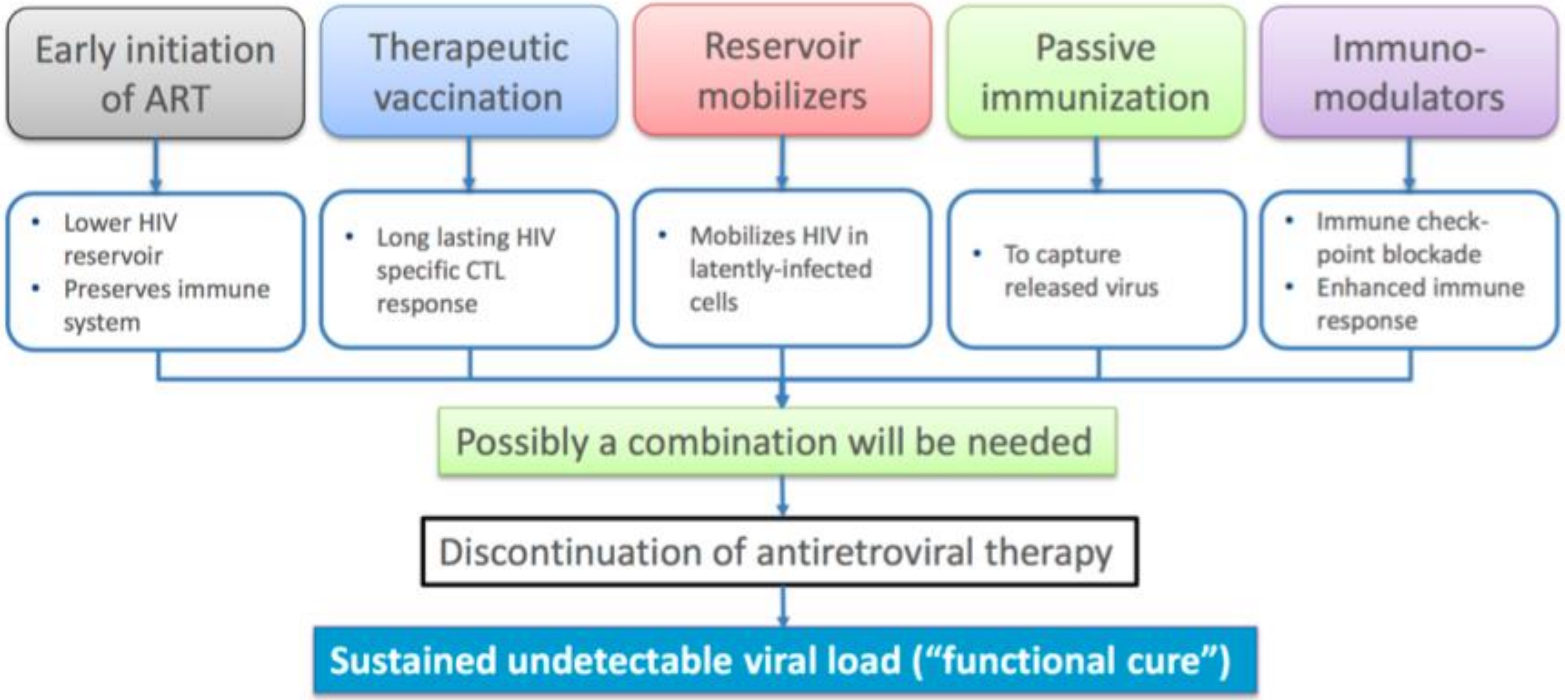
Cure / Remission trials with ATI

- ET: BCN01 (HIVconsv); AELIX002 (HTI vax)
- CT : iHIVARNA (mRNA)

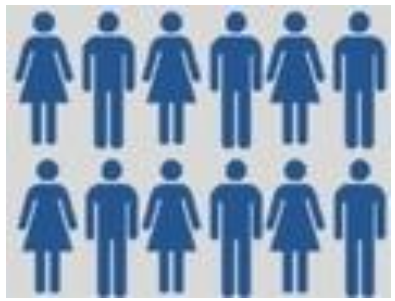
- BCN02 – HTI vax + HIVconsv vax + Romidepsin
- RISVAC03 – MVA-B + Disulfiram

- AELIX003 – HTI vax + TLR7a
- BCN03 – HTI vax + SOSIP

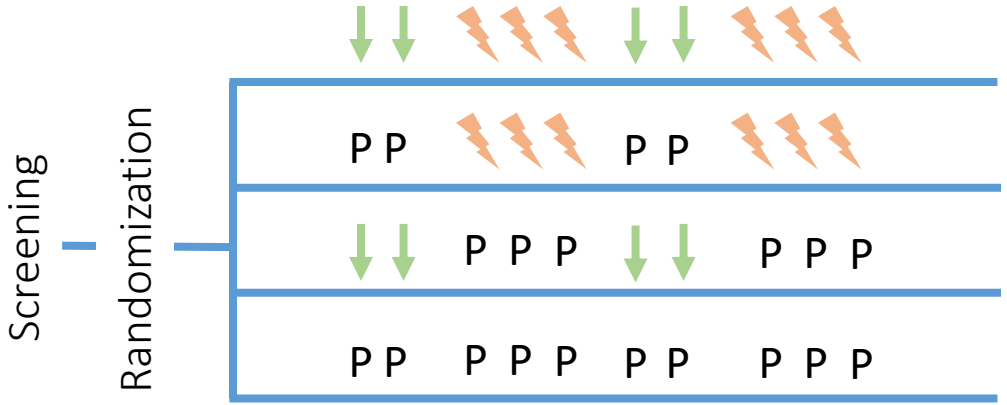


Mothe 2019; Mothe, Rosas 2020; Jong 2019; Mothe 2015; NCT03204617 & NCT04364035 ongoing

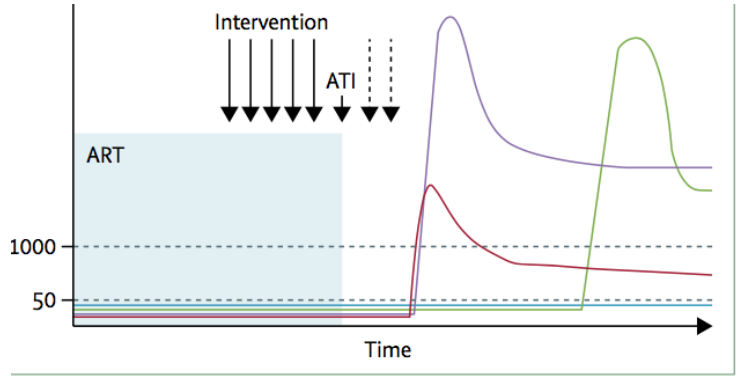
Main Challenges of HIV remission trials



POPULATION



TRIAL DESIGN



ATI ENDPOINTS

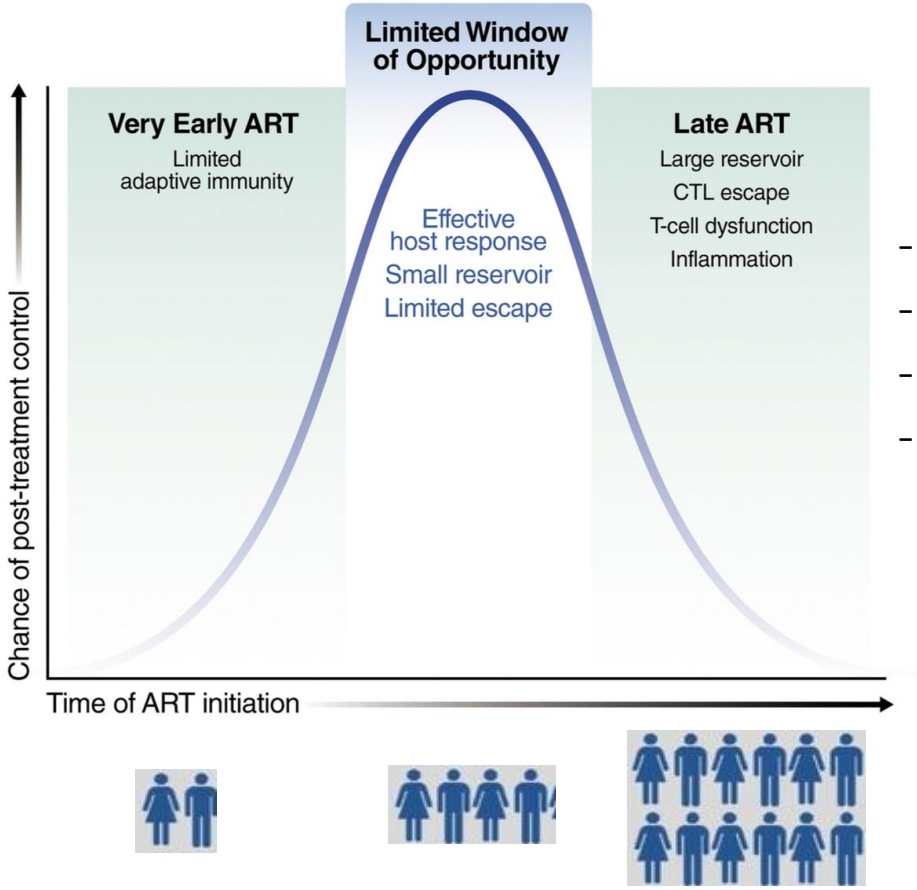
1: Study population

PROs

- limited exhaustion and escape
- limited reservoir
-↑ 'homogenous' population
-↑ responsiveness to vaccination
-↑ chances to success? Early signal

CONs

- limited availability
- women poorly represented
- High rate of PTC (up to 14%?)
- not the target population
- High risk population (implications of STI in ATI)



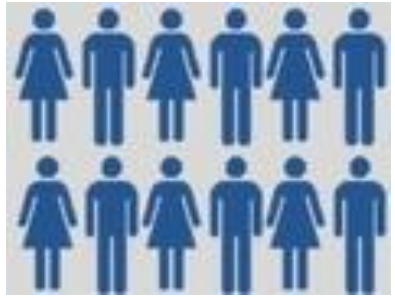
PROs

- easier to recruit (more pt)
- closer to the global target population
- inclusion more heterogenous pop
- less expected PTC (<4%)

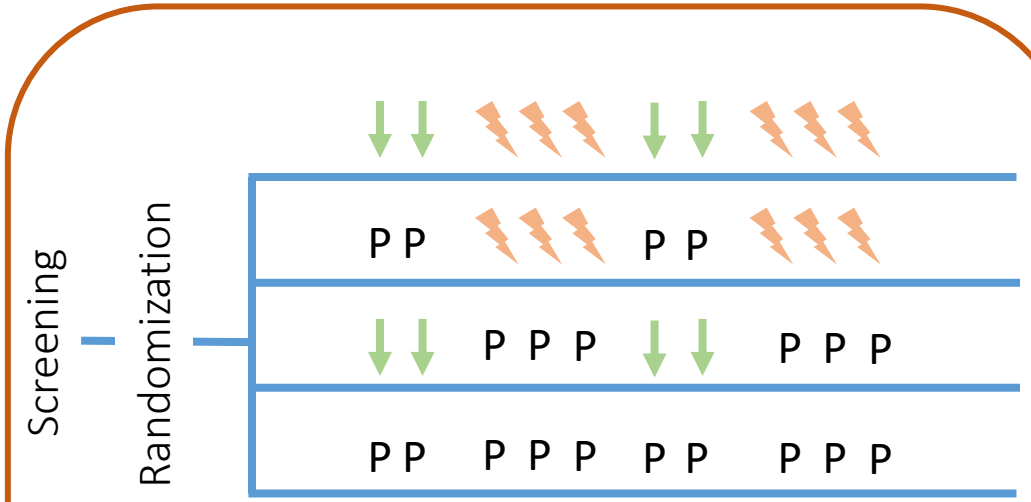
CONs

- more confounding factors
- less chances to success?

Main Challenges



POPULATION



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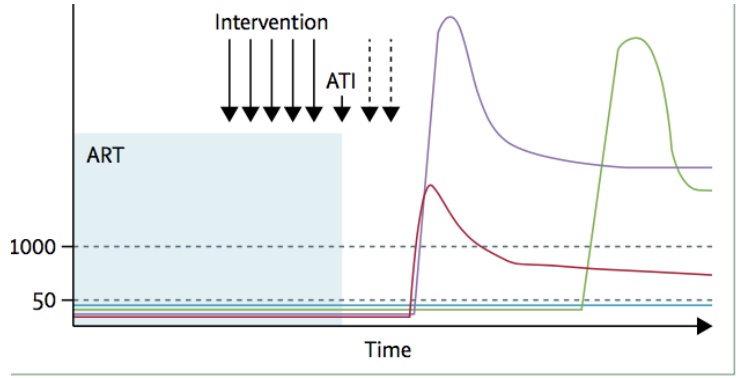
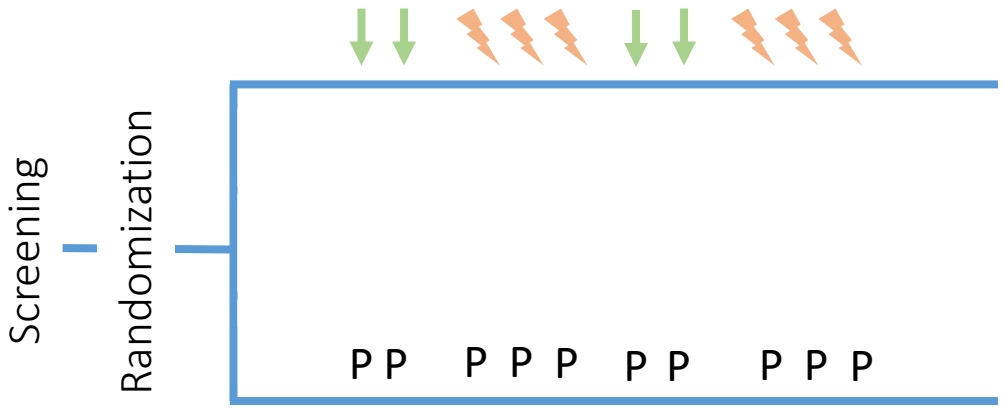


ATI ENDPOINTS

2-Study arms

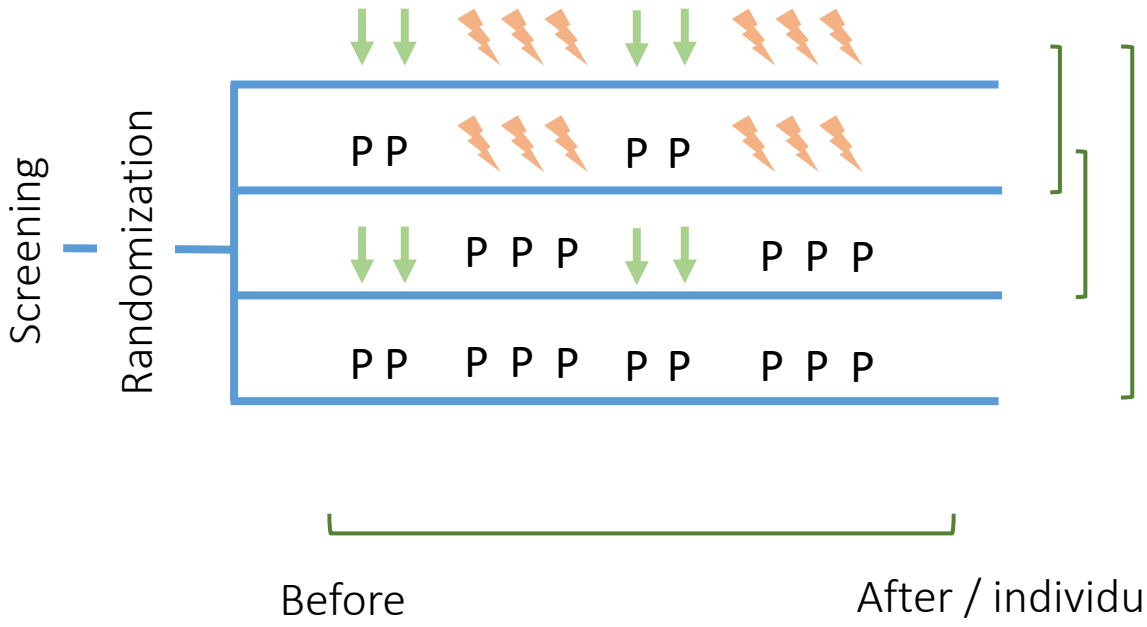
- Which are the questions to be answered ?



Double blind, placebo-control
Best for assessing safety (↓ subjectivity bias)
↑ sample size to detect less frequent adverse events
↑ **sample size to see efficacy signal (accounting for PTC, HLA biases…)**

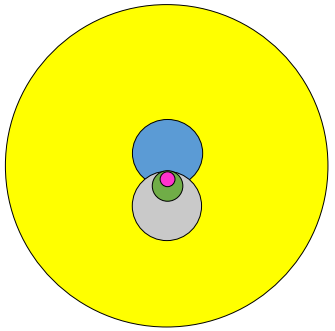
- Which are the resources & timelines you have?

2- Study arms

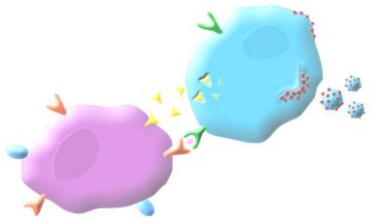


Reactivation

Reservoir
(multiple assays)



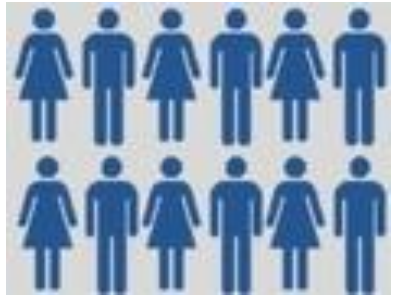
Immune responses
(Q, phenotype, functionality…)

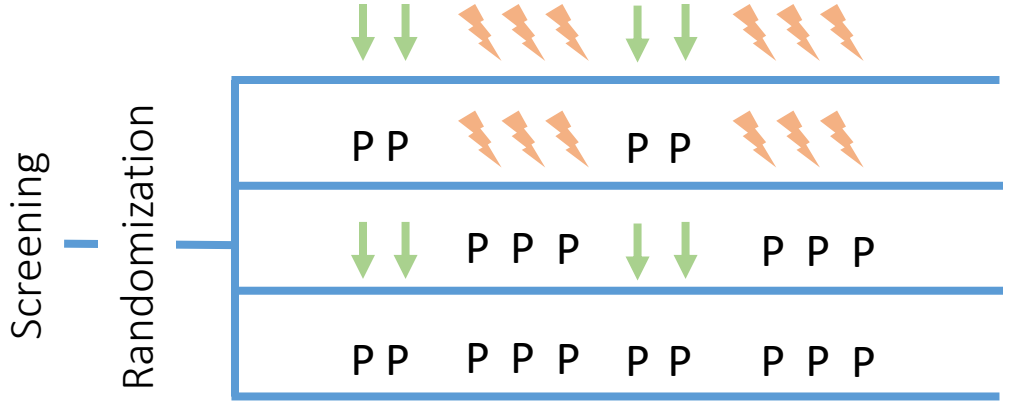


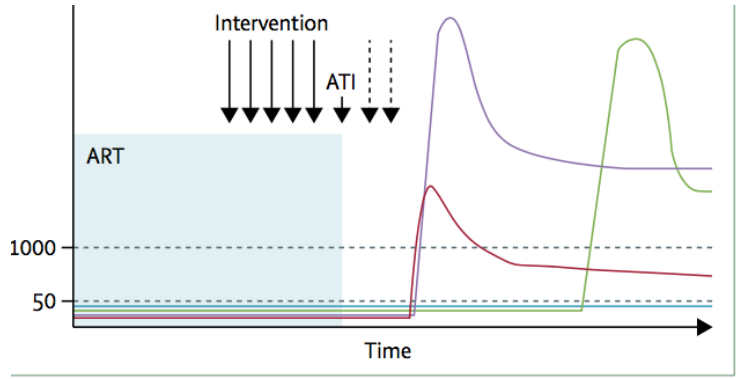
→ Very intense and complex trials to decipher mechanisms of actions, Pk, PD, etc → how feasible will be?
→ 'sample storage' not always an answer (fresh assays, High volumes, special collection tubes, etc)
→ Prioritize the objectives and optimize the design accordingly with the available resources

→ Balance between risks / benefits for both the trial outcomes and the particpants

Main Challenges





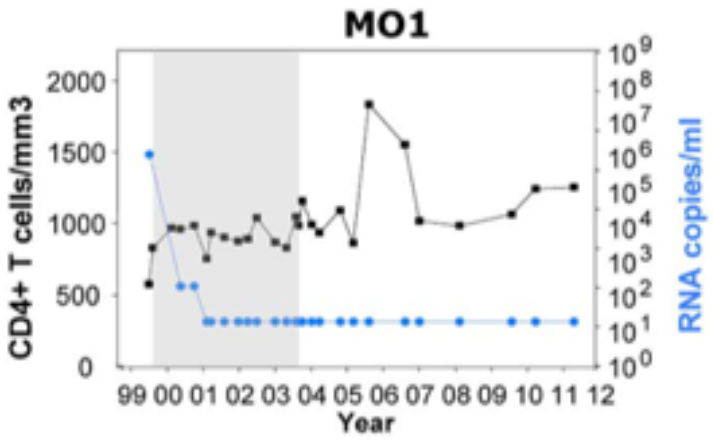


POPULATION

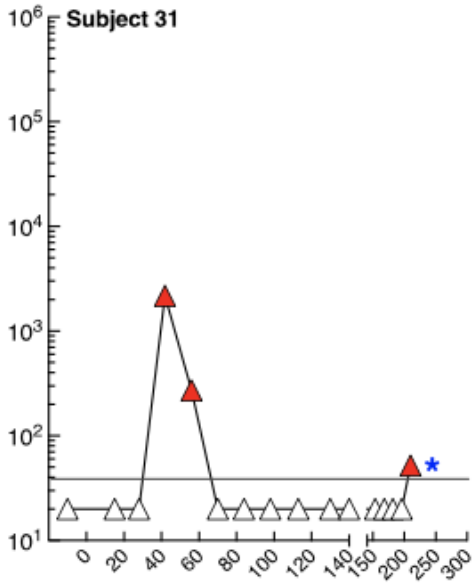
TRIAL DESIGN

ATI ENDPOINTS

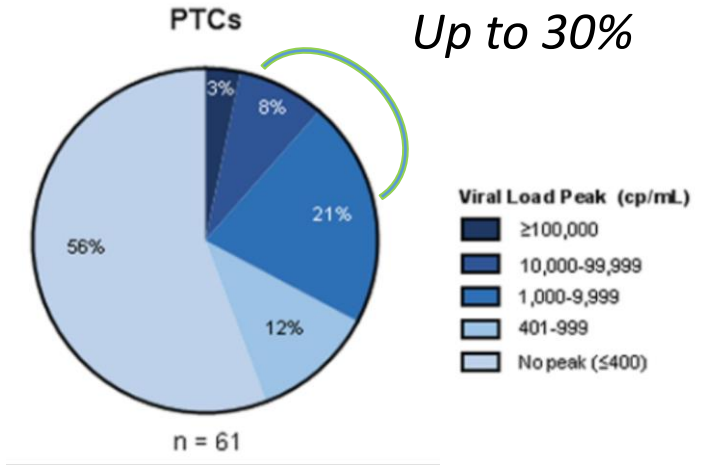
ATI design : safe & useful!



'Non-rebounders'



'Post-rebound controllers'

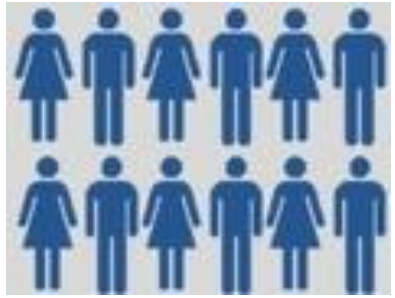


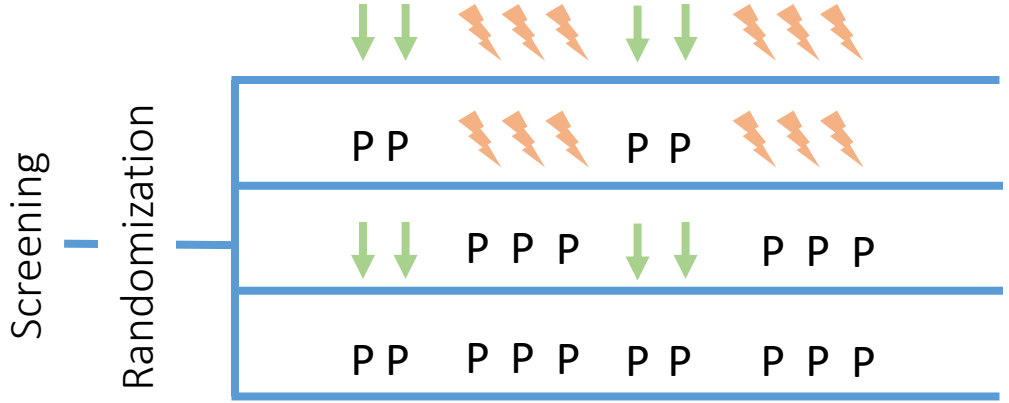
→ **Consensus on design:** Allowed for up to 24 weeks, close monitoring, strict IC, etc → accepted but recuitment challenging
→ Endpoints: time to X vs kinetic profile to rule out an immune pressure effects
→ If outcome is an immune-mediated post-intervention control : higher pVL thresholds & time are needed
→ If outcome is reduction of the reservoir, time to viral rebound might be enough…or even no ATI if reservoirs are detectable ?

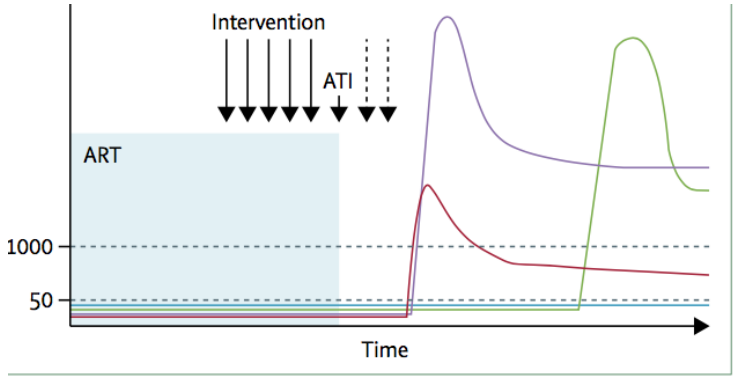
→ Risk-mitigation plan!!! (disclosure, transmission, psychological impact, etc)

Salgado 2011, Saez-Cirion 2013, Sneller 2018, Namazi 2018, Julg 2019

++ challenge : COVID19







POPULATION

- Is it safe?
- Account for risk factors for covid severity?

TRIAL DESIGN

- Include testing, when? How?
- Defer IMP?

ATI ENDPOINTS

- It is safe?
- Include testing, when?
- Resume ART if COVID19?

Conclusions / Summary for Community

- Cure field is still in a very early stage clinical development.
- Experimental medicine / Phase I / Proof of concept trials in the HIV cure field are generally small but very complex, long and very heterogeneous in their design.
- Early-treated individuals (although not the final target population) seems to be the best study population to test new interventions at an early stage (because of a potentially higher success rate) but have also instrinsecal challenges.
- ATI still needed for testing efficacy of immune-interventions.
- There is NO a perfect trial desing in the cure field : One (trial) does not fits all (needs)
- Correlates of remission / control & PTC are crucial to improve CT design
- Impact of COVID-19 pandemic into cure trials

ALL STUDY PARTICIPANTS!!!

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