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The contribution of immune-based therapy towards functional HIV cure

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HIV infection remains a formidable global health threat with 37 million adults and children living with HIV. Combination antiretroviral therapy (ART) has made a significant impact on HIV morbidity and mortality, but is unable to cure HIV infection due to the reservoir of latently infected cells, particularly long-lived immune memory cells. ART must therefore be taken for life.

The HIV 'Shock and Kill' concept involves latency reversal in the presence of ART to reactivate (shock) latent reservoirs that can then be killed by the lytic effects of the virus, or the immune system. However, it transpires that latency reversal alone is insufficient to reduce HIV reservoirs. The REDUC study (NCT02092116), sponsored by Bionor Pharma ASA, was the first to include therapeutic vaccination inthe HIV 'Shock and Kill' concept. REDUCwas carried out in two parts at Aarhus University Hospital, Denmark. Part A (n=6) tested the effects of a single cycle of 3 romidepsin intravenous (iv) infusions during ART, to confirm safety and the capacity for latency reversal. In Part B (n=20), participants were immunised with the peptide-based therapeutic vaccine, Vacc-4x (1.2mg) administered as 4 weekly intradermal (id) injections followed by 2 weekly booster injections 8 weeks post priming. Recombinant human granulocyte macrophage colony stimulating factor (rhuGM-CSF) administered id was used as a local adjuvant. Three weeks post-immunization, participants received one cycle of romidepsin infusions and nine weeks later, eligible partcipants underwent a monitored antiretroviral pause (MAP). ART was resumed when plasma viral load reached 1000copies/mL. In part A, 5/6 participants showed detectable plasma HIV RNA during latency reversal, but HIV reservoirs (total HIV DNA)remained unchanged. In Part B, in 9/17 participants, there was no detectable plasma HIV RNA at any time-point during the latency reversal period. For the remaining participants, low level virus load was detected after either one or two of the romidepsin infusions. There was a statistically significant reduction of total HIV DNA (39.7%; p=0.012; n=16). Analysis of integrated DNA showed a reduction that was not statistically significant (19.2% p=0.123; n=15). A viral outgrowth assayto measure replication competent virusin part B showed a reduction that was statistically significant (38%; p=0.019; n=6). However, the reduction in HIV reservoirs was not sufficient to delay the time to viral rebound on treatment interruption. These findings support the inclusion of immune-based therapiestowards functional HIV cure, and other clinical studies involving therapeutic vaccination are in progress.

Biography:

Maja A. Sommerfelt is Director of Research and External Innovation at Bionor Pharma ASA. She obtained her PhD degree from the University of London, United Kingdom, at the Institute of Cancer Research where she studied receptors for diverse retroviruses on human cells. She carried out post-doctoral research at the University of Alabama at Birmingham in the United States where she studied retroviral assembly using molecular techniques. She then joined the University of Bergen in Norway where she became Professor in 1996. Maja Sommerfelt joined Bionor Pharma ASA in 2002 and has been involved in clinical research and development of the company's lead product, Vacc-4x.