Abstract #438

Central Nervous System (CNS) Safety of a Kick&Kill Strategy with Romidepsin

Sara Carrillo-Molina,1 Ignacio Martínez-Zalacain,2 Beatriz Mothe,3 José Moltó,1 Christian Manzardo,4 Jose M. Miro,1 Pep Coll,5 Michael Meulbroek,1 Anna Prats,1 Maile Garolera,1 Tomas Hanke,1 Christian Brandner,1 Carles Soriano-Mas,3 Jose A. Munoz-Moreno1 on behalf of the BCN02-Neuro Study Group

1 Fundació Llíria contra la SIDA (FLS), Badalona, Catalonia, Spain / 2 Institut d’Investigació Biomèdica de Bellvitge (IDIBELL), L’Hospital de l’Llobregat, Barcelona, Catalonia, Spain / 3 Institut de Recerca de la SIDA i Cáncer, Badalona, Barcelona, Spain / 4 Hospital Clinic-IDIBAPS-University of Barcelona, Barcelona, Catalonia, Spain / 5 BCN Checkpoint, Barcelona, Catalonia, Spain / 6 Ciències Sanitàries i Hospital de Terrassa (CST), Terrassa, Catalonia, Spain / 7 The Jenner Institute, Oxford, UK

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BACKGROUND

- Research on compounds tested in new kick&kill strategies for HIV eradication should cover different clinical safety levels, including the central nervous system (CNS). That necessity becomes more important considering that reactivation of latent reservoir is aimed to be reached, and, additionally, that antiretroviral therapy cessation is a requirement of HIV eradication strategies currently.
- Romidepsin (RMD) is a potent histone deacetylase inhibitor (HDACi) that has shown efficacy on latent HIV infection in vitro and in vivo studies. However, its CNS effects in HIV-infected individuals are unknown to date.
- We studied the CNS safety of an HIV eradication strategy including the use of RMD in the setting of the BCN02-ROMI study, a trial that assessed the safety and effect of a MAI-HIV infection in combination with RMD in early-treated HIV-infected patients.

RESULTS (I)

METHODS

Design and Study Population
The BCN02-Neuro substudy was an observational prospective study developed as a substudy of the BCN02-ROMI study, a trial that assessed the safety and effect of a MAI-HIV infection in combination with RMD in early-treated HIV-infected patients.

Sample Characteristics
A total of 11 individuals from the main study accepted to participate. Ten patients were recruited as controls. Study participants were randomly (90%), getting infected brains in lieu with other men (90%) (mean SD age of 40 (9)) years. All demographic and clinical variables were balanced between groups. Table 1 shows the characteristics of the study sample.

In the intervention group, all participants underwent Pre and Post assessments. After Post assessment, 1 patient did not fulfill immune criteria to interrupt therapy and entered the MAP stage. Out of them, 3 maintained virological control without requirement of CART resumption and 7 relented therapy. MAP mean (min-max) time was 2.9 (2.3-5.5) weeks. Figure 2 shows the study flowchart in the intervention group.

Cognitive and Functional Outcomes
Baseline cognitive functioning was comparable between groups, as well as functional outcomes. Cognitive change from Pre to Post assessment was equivalent between groups (mean NPZ-6, 20; CI 14.31 to 0.03; p = 0.32; p = 0.45). Intragroup changes also did not show differences. Change in functional outcomes was not significant for any dimension, again considering both-between and intra-group comparisons. Figures 3a, 3b, 3c, and 3d show some of the main cognitive and functional results from Pre to Post assessment.

RESULTS (II)

Regarding Final assessment, cognitive differences were not found between groups or intra groups at the end of the study. With respect to functional outcomes, all scores showed similar results in both groups. All brain regions studied, including subcortical areas involving corticostriatal circuits (i.e., caudate nucleus, ventral striatum/nucleus accumbens, putamen, pallidum, and thalamus) and frontal cortex (i.e., dorsomedial, dorsolateral, cingulate, ventromedial, medial orbitofrontal, and lateral orbitofrontal cortex), showed no statistically significant volumetric or structural discrepancies within the Intervention and Control groups at any of the study timepoints. Figure 5 represents a graphical summary of the cerebral areas included in the neuroimaging analyses.

CONCLUSIONS

- No detrimental effects on cognitive status, functional outcomes, and neuroimaging parameters were observed after the use of 3 weeks infusions of RMD (5 mg/m²) in the setting of a kick&kill eradication strategy for HIV.
- After a short MAP with plasma viral load threshold criteria of >2,000 copies/mL and 24 weeks follow-up of CART resumption, no negative contributing effects were observed in cognitive, functional, or neuroimaging outcomes.
- The HIV cure approach investigated in this small trial, including the use of a MAI-HIV infection, administration of RMD, CART interruption, and posterior 24-week therapy reinstitution, appears to be safe for the CNS.

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