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NEWS

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Scientific Formal (Paper) Presentations

CODE: SSK12-03
SESSION: SSK12
Radiolabeled Antibody to gp41 HIV Glycoprotein Kills ART-treated Lymphocytes from HIV Patients and HIV-infected Monocytes in Human Blood Brain Barrier Model

Date/Times

- **DATE: Wednesday**
- **TIME: 10:50 -11:00 AM**
- **LOCATION: S504CD**

PARTICIPANTS

- Ekaterina Dadachova PhD - Nothing to disclose.
- Dina Tsukrov undefined - Nothing to disclose.
- Alicia McFarren undefined - Nothing to disclose.

SUBSPECIALTY CONTENT

- Molecular Imaging

PURPOSE
Eliminating virally infected cells is an essential component of HIV eradication strategy. In addition, many patients on antiretroviral therapy (ART) suffer from HIV-associated neurocognitive disorders as the brain becomes a reservoir for infection. Thus, the drugs that can enter into the CNS and eradicate the infection are needed.

METHOD AND MATERIALS
Radioimmunotherapy (RIT), a clinically established method to kill cells using radiolabeled monoclonal antibodies (mAbs), was recently used to target the HIV gp41 glycoprotein expressed on the surface of infected cells. As gp41 expression by the infected cells is downregulated in patients on ART, we evaluated the ability of RIT to kill infected cells treated with ART in vitro using patients lymphocytes. We also tested the ability of the same radiolabeled mAb 2556 to gp41 to cross the blood brain barrier (BBB) and kill HIV infected monocytes in the CNS.

RESULTS
We found that RIT was able to specifically kill ART-treated lymphocytes and to reduce HIV p24 to undetectable levels. ART and RIT worked in concert to decrease viral production when compared to ART or RIT alone, indicating that expression of gp41 under ART was still sufficient to allow 2556 mAb binding and killing infected cells. A 4 µCi dose of 213Bi-2556 successfully killed over 80% of PBMCs ($p<0.05$), even in patients with well-controlled viremia. The isoelectric point (pI) of 2556 mAb was >9 compared to isotype control 1418 mAb pI of 8. 213Bi-2556 killed significantly more HIV infected than uninfected monocytes on the astrocyte side of the BBB in dose response manner ($p<0.05$). Confocal microscopy staining for tight junction proteins did not demonstrate any significant damage to the barrier integrity.

CONCLUSION
In conclusion, RIT in concert with ART eliminated infected cells. Co-treatment was effective in both Atripla and tenofovir/emtricitabine/atazanavir cohorts. We demonstrated the unique ability of 213Bi-2556 mAb to cross the BBB and specifically kill HIV infected monocytes. These findings demonstrate the feasibility of an RIT-based strategy for use with ART to achieve HIV eradication systemically and in CNS.

CLINICAL RELEVANCE/APPLICATION
HIV/AIDS remains an incurable disease. Our goal is to develop RIT-based strategies for therapy of systemic and CNS HIV for use with other anti-retroviral strategies to achieve complete HIV eradication.