

Future Prevention Trials

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MTN PI

Optimizing Adherence
After VOICE 9/1/2015





Future HIV Prevention Trials

- Vaccines: multiple injections over several months
- Injectable PrEP: lessons from DMPA; requirement for consistent injections; drug “tail” following injections may require use of daily oral PrEP
- Monthly or quarterly rings: new populations
- On demand non-coital products
- Contraceptive ARV products: MPTs

Lessons from Contraception

Failure rates (first year)

Perfect use 0.2%^[1]

Typical use 6%^[1]



Usage

Duration effect 3 months
(12–14 weeks)

Depo-Provera



- The difference between “perfect use” and “typical use” is due to whether women return on time for their injections
- “Forgiveness window”: pregnancy rates in the month following a missed injection is still incredibly low (0.4%)

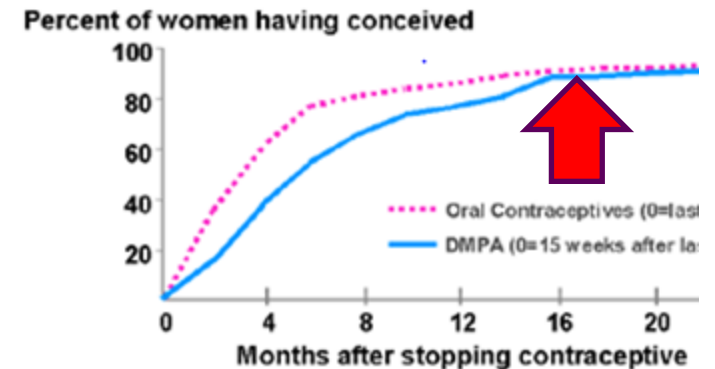
Lessons from Contraception

- Window of forgiveness is due to long “tail”
- Compared to implants or oral contraceptives, return to fertility is longer in women receiving DMPA
- Some women have detectable levels of DMPA 10-12 months after an injection

Depo-Provera



DMPA: Return to Fertility



PrEP by injection

The idea:

Receive an ARV injection that lasts 2-3 months

Status:

Two Phase II trials of safety, tolerability and acceptability just started – results likely early 2018



- HPTN 077 (GSK1265744 – Cabotegravir)
 - 176 men and women at low-minimal HIV risk, ages 18- 65
 - 8 sites: Brazil, Malawi, South Africa, Thailand and 4 US (George Washington, UCLA, UNC , San Francisco Dept of Public Health)
- HPTN 076 (TMC278 – Rilpivirine)
 - 132 women, ages 18-45
 - 4 sites: South Africa, Zimbabwe and 2 US (Bronx - Columbia University, Newark -

Injectable PrEP

- There have been limited clinical studies of injectable ARVs in HIV uninfected people
- The emerging data following people who received a SINGLE rilpivirine injections a year ago show that some people have detectable drug a year later
- The question: is this level of drug adequate to lead to selection of NNRTI resistant virus in people who become infected?

Injectable PrEP: Adherence Issues

- How do we ensure adherence to quarterly or bi-monthly injections?
- How do we counsel people who have received injections regarding
 - how long they are protected?
 - how long they will have low levels of drug which are not high enough for protection but may be high enough to select for resistance?
- What if we provide daily oral PrEP to keep people “safe” during the long injectable “tail”?

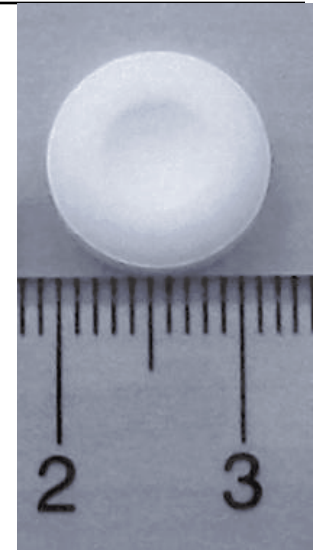
Monthly or Quarterly Rings



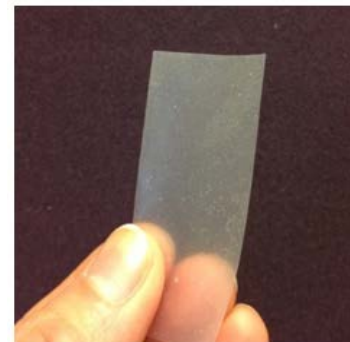
- Using a ring is not like taking a pill: it takes some learning before it is easy
- Next studies with rings will need to reach new populations:
 - Adolescents
 - Pregnant or breastfeeding women
 - Sex workers
- Each of these populations will have somewhat different adherence challenges

On demand products

- An alternative to sustained delivery products
- Adherence was suboptimal in FACTS; hard to assess in 017
- Could be used at the time of sex
- Could be used to provide protection over several days depending on the active pharmaceutical agent and the formulation
- What do we need to do to enhance adherence to these products?



Fast-dissolving tablet



Extended release film

Combination Products in Development

The idea:

Many women at risk of HIV also want family planning. Why not combine HIV prevention with contraception?

- Rings would be worn 90 days at a time
 - 4 rings would provide HIV prevention and contraception for a year
- Vaginal rings in development
 - Tenofovir / levonorgestrol ring (CONRAD)
 - Dapivirine / levonorgestrol ring (IPM)



Status:

Phase I study (CONRAD 128) ongoing at Eastern Va Med School and in Dominican Republic; Phase I study (MTN-030/IPM 041) in development, to take place in Pittsburgh and Birmingham)

Combination HIV Prevention/ Contraceptive Rings

- Adherence to combination products may provide rapid feedback to participants who remove the rings: removal of ring will result in drop in LNG levels which will cause bleeding
- Bleeding associated with ring removal may make the product less acceptable or it could be an attribute that will enhance adherence
- What should we do to understand this?



10 mm LNG
segment



Future HIV Prevention Trials

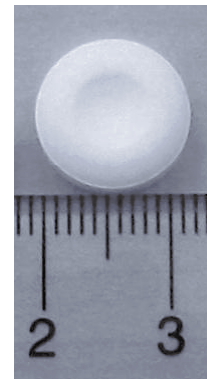
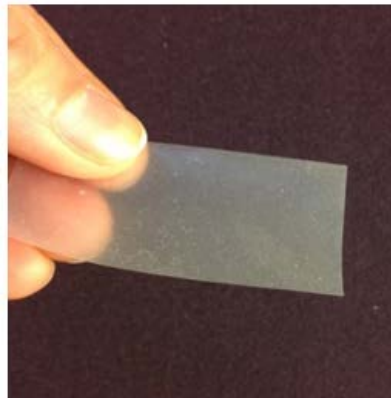
- Adherence is the key to efficacy
- New platforms for HIV prevention are being developed, but
 - Injectable PrEP will present different challenges with adherence
 - If the dapivirine ring is found to be effective, still need to expand into new populations
 - More research needed for improving adherence to on demand products
 - Enhancing adherence to MPTs will be complex and may present other challenges



We Must Not Assume.....

- That injectables will solve the problems with adherence to oral PrEP.
- That vaginal rings will solve all of the problems of adherence with vaginal gels.
- That on demand products will always have lower adherence than sustained release products for all women.
- That providing contraceptives with HIV prevention will increase adherence.

Method Mix will be Key



10 mm LNG
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