

Data and Safety Monitoring Boards – Responsibility for Stopping or Modifying Trial

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Responsibility of DSMB

- Primary responsibility is to trial participants
 - Reviews unmasked data to verify balance of risks and benefits still relevant and appropriate
 - Consider risks and benefits to individual (side effects, safety of product, disadvantage of being in inferior arm, ...)
- DSMB has NO responsibility to other trials nor to individual participants in those trials



Factors in weighing whether to stop early for benefit

- DSMB should stop trial when
 - No longer ethical to randomize volunteers
 - No longer ethical to withhold better product or intervention from those randomized to inferior arm
- BUT, if stop early for benefit
 - Biased result
 - Observed effect is greater than true effect, but not known how much greater
 - Even if evidence convinces DSMB, evidence may not convince wider community
 - Wasted resources, wasted risks that volunteers took on, abused their willingness to allow experimentation in return for greater good
- Do NOT stop too early, even if DSMB uncomfortable
 - Guidelines on stopping helpful, but no more than a guideline



Responsibility Regarding Evolving Standard of Care (or Prevention)

- Kesho Bora randomized trial (pMTCT)
 - Triple-ARV prophylaxis compared with short-course regimen to prevent transmission during late pregnancy and in first 6 months of breastfeeding
 - Randomized, not masked
 - Control arm
 - (sd-NVP)
 - 4 wk AZT + sd-NVP
 - 14 wk AZT + sd-NVP
 - 14 wk AZT + sd-NVP + 1 wk “tail” (AZT + 3TC)



Factors Driving Decisions on Control Arm – Evolving Standard of Care (or Prevention)

• Pro

- Evolving WHO pMTCT guidelines
- Evolving national contexts
- Ability to deliver the intervention within context of RCT infrastructure and resources
- Wanted to (and expected to) “lead from the front”
- Add pressure on national and local programmes to improve SoC

• Con

- Loss of study power (longer time to produce final result, may never show benefit even if true, ...)
- Over-incentivize benefits of participation in context where only sd-NVP available to women who decline enrolment

