Switching ARVs for lipodystrophy

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Lipodystrophy: fat redistribution

- **Lipoatrophy:** subcutaneous fat loss
- **Lipohypertrophy:** fat gain
  - Central (visceral)
  - Focal: dorsocervical or breasts
- **Mixed patterns**
Clinical implications

• Common

• Visceral fat accumulation is associated with dyslipidaemia and insulin resistance

• Adherence is compromised when patients believe they have lipodystrophy from ARVs

AIDS 2003; 17(Suppl 1) :S141
NEJM 2005; 352: 48
JAIDS 2002; 31 (Suppl 3): S140
Is lipodystrophy an adverse drug reaction?

- Important to avoid unnecessary drug substitutions with risks of
  - treatment failure
  - new toxicities
  - undermining patient confidence
Systematic review

Is fat loss/gain reversed after switching ARVs?

Eligibility criteria:
• Randomised controlled trials
• Patients on ART with and without lipodystrophy at baseline
• Interventions: switch versus continue current ARV regimen
• Objective measure of fat distribution: MRI, CT or DEXA scan
Does fat loss reverse on switching?
Change from baseline: subcutaneous/limb fat

J Antimicrob Chemother 2009; 63:998
HIV Med 2008; 9:625
JAMA 2002; 288:207
CROI 2011
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Does fat loss reverse on switching?

- Switching away from NRTIs, especially thymidine analogues, led to significantly more fat gain, or less fat loss, over time compared with controls.

Switching is a treatment option
Does fat loss reverse on switching?

• Switching from
  – PI to NNRTI
  – Ritonavir-boosted PI to ritonavir-boosted atazanavir
  – PI to raltegravir

led to no significant between-group differences in limb fat over time.

Switching drugs other than NRTIs does not work

JAIDS 2001; 27:229
Antivir ther 2012; 17:689
AIDS 2012; 26:475
Does fat gain reverse on switching?
Change from baseline: visceral adipose tissue

- NRTI vs PI+NNRTI
- AZT/D4T vs ABC
- PIr vs ATVr

HIV Med 2008; 9:625
JAMA 2002; 288:207
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Change from baseline: visceral adipose tissue

- NRTI vs PI+NNRTI
- AZT/D4T vs ABC
- PIr vs ATVr
- PI vs RAL

HIV Med 2008; 9:625
JAMA 2002; 288:207
Antivir ther 2012; 17:689
AIDS 2012; 26:475
Change from baseline: trunk fat

- p > 0.05
- p = 0.3
- p = 0.1
- p = 0.7

Fat gain
Fat loss

AZT vs TDF
Continue
Switch

JAIDS 2009; 51:562
JAMA 2002; 288:207
Antivir ther 2012; 17:689
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Change from baseline: trunk fat

- p > 0.05
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Fat gain
- AZT vs TDF
- AZT/D4T vs ABC

Fat loss

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<th>AZT vs TDF</th>
<th>Continue</th>
<th>Switch</th>
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Change from baseline: trunk fat

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Fat loss

Fat gain

grams

AZT vs TDF
AZT/D4T vs ABC
PIr vs ATVr

Continue
Switch

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Antivir ther 2012; 17:689
AIDS 2012; 26:475
Does fat gain reverse on switching?

• Similar increases over time in all ARV regimens

Switching to reverse fat gain does not work
Treatment options for central fat gain

• Diet and exercise
  – VAT: modest effect; lipid profile: inconsistent results

• Metformin
  – Trend toward decreased VAT; but decreases LF too

• Growth hormone releasing hormone (tesamorelin)
  – Decreases VAT and improves lipid profile
  – Expensive

AIDS Patient Care STDS 2009; 23: 5
Curr HIV/AIDS Rep 2011; 8: 200
HIV/AIDS (Auckl) 2011; 3: 69
Conclusions

• Lipoatrophy is an adverse drug reaction
• Switching away from NRTIs with mitochondrial toxicity
  – Halts progression
  – Slow, modest improvements over time
Conclusions

• Central fat gain is not an adverse drug reaction, but probably a consequence of treating HIV.

• Treatment options for fat gain are limited, but important to avoid unnecessary ARV switches.