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COMPETING INTEREST OF FINANCIAL VALUE ≥ £1,000:	
Speaker Name	**Statement**
Ian Williams	None
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BHIVA guidelines for the treatment of HIV-1 positive adults with antiretroviral therapy 2012

Ian Williams

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British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2012

NHS Evidence
accredited provider
NHS Evidence - provided by NICE
www.evidence.nhs.uk

NHS Evidence has accredited the process used by the British HIV Association (BHIVA) to produce guidelines. Accreditation is valid for five years from July 2012 and is applicable to guidance produced using the processes described in the British HIV Association (BHIVA) Guideline Development Manual. More information on accreditation can be viewed at www.evidence.nhs.uk

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Members of ART guidelines writing panel

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GRADE System: Grades of recommendation, assessment, development and evaluation

Grading a recommendation: Two components

1. **Quality of evidence**:
   - extent to which confidence in estimate of effect adequate to support decision
   - High (A), moderate (B), low (C), very low (D)

2. **Strength of recommendation**
   - strong (1) or conditional (2)

   Determined by:

   Quality of evidence

   Balance of desirable/undesirable outcomes

   Values and preferences

   Resource use

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1.2.4 Good practice points (GPP)

- GPPs are recommendations based on the clinical judgment and experience of the working group. GPPs emphasise an area of important clinical practice for which there is not, nor is there likely to be, any significant research evidence. They address an aspect of treatment and care that is regarded as such sound clinical practice that health care professionals are unlikely to question it and where the alternative recommendation is deemed unacceptable.

Patient involvement

3.1 Recommendation:

- We recommend patients are given the opportunity to be involved in making decisions about their treatment. (GPP)

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- When to start
- What to start

Question: Which of these options best describes you?

1. Clinician
2. Nurse
3. Pharmacist
4. Researcher
5. Community representative
6. None of the above

When to start: Chronic infection

Case 1:

45 year old gay man, diagnosed HIV positive 6 months ago, asymptomatic. CD4 count 570 cells/uL, viral load 85,000 copies/ml. HBV immune, HCV negative. Regular partner HIV negative. He asks for your advice on when to start ART?

When to start: Chronic Infection

Question: what advice would you give on when to start ART

1. Immediately to reduce risk of transmission
2. Once CD4 count confirmed <500 cells/µL
3. When CD4 count 350-400 cells/µL
4. When CD4 count ≤350 cells/µl
5. Advise uncertainty: invite him to consider participating in START trial

When to start: Chronic infection

4.1.1 Recommendations

- We recommend patients with chronic infection start ART if the CD4 count is ≤350 cells/µL [1A]: it is important not to delay treatment initiation if the CD4 cell count is close to this threshold.

✓absolute risk of disease progression is significantly higher for a given CD4 count in older people , so consideration should be given to starting at higher CD4 counts in older persons.

✓Evidence from cohort studies suggest that the risk of disease progression is significantly higher once the CD4 count falls below 350 cells/µL, so it is important not to delay unnecessarily the initiation of ART if the CD4 count is close to this threshold.

When to start: Chronic infection

We recommend patients with the following conditions start ART:

- AIDS diagnosis (e.g. Kaposi's sarcoma) irrespective of CD4 cell count [1A];
- HIV-related co-morbidity including HIVAN [1C], ITP, [1C], symptomatic HIV-associated neurocognitive disorders irrespective of CD4 cell count [1C]
- Co-infection with hepatitis B virus if the CD4 count is ≤500 cells/µL [1B]
- Co-infection with hepatitis C virus if the CD4 count is ≤500 cells/µL [1C]
- Non-AIDS defining malignancies requiring immunosuppressive radiotherapy or chemotherapy [1C]

We suggest patients with the following conditions start ART:

- Co-infection with hepatitis B virus if the CD4 count is >500 cells/µL and treatment of hepatitis B is indicated [2B]

Treatment to Reduce transmission

4.4.1 Recommendations

•We recommend the evidence that treatment with ART lowers the risk of transmission is discussed with all patients, and an assessment of the current risk of transmission to others is made at the time of this discussion. (GPP)

•We recommend following discussion, if a patient with a CD4 count above 350 cell/µL wishes to start ART to reduce the risk of transmission to partners, this decision is respected and ART is started. (GPP)

Treatment to reduce transmission

The discussion should include the following:

- The decision to start ART is the patient's choice
- ART lowers rather than eliminates the risk of transmission:
- Uncertain whether any benefits to their own health
- Other prevention strategies including condoms continue to be recommended.
- The evidence that ART lowers the risk of transmission mainly relates to vaginal sex.
- High and consistent adherence to ART is required
- Taking ART does not result in immediate complete viral suppression;

When to start

4.2.1 Recommendation: Advanced disease

- We recommend patients presenting with an AIDS-defining infection, or with a serious bacterial infection and a CD4 count <200 cells/µL, start ART within two weeks of initiation of specific antimicrobial chemotherapy (1B).

4.3.1 Recommendations: Primary Infection

- We recommend patients presenting with primary HIV infection and meeting any one of the following criteria start ART:
    - Neurological involvement [1D]
    - Any AIDS-defining illness [1A]
    - Confirmed CD4 cell count <350 cells/µL (1C]

What to start

Treatment outcome	Ranking
Viral suppression (<50) at week 48	9: critical
Viral suppression at week 96	8: critical
Proportion of all randomised subjects with protocol-defined virological failure at week 48 +/- week 96	9: critical
Proportion of all randomised subjects who develop drug resistance	8: critical
Quality of life	8: critical
Proportion discontinuing for adverse events	7: critical
Proportion with grade 3/4 adverse events (overall)	7: critical
Proportion with grade 3/4 ALT/AST elevation	7: critical

Cost or resource use not considered as an outcome
Separate GRADE analysis for populations defined by base line VL not considered

What to start

Case 2:

35 year old gay man, CD4 count 360 cells/µL, VL 75,000 copies/ml, no transmitted resistance, ART naïve, HLA B5701 negative, HBV and HCV negative, no significant co-morbidity, wants to start ART. Declines participation in a clinical trial. He asks what ART regimen you would advise he starts?

What to start

Question 3: What ART regimen would you advise?

1. Efavirenz + TDF/FTC
2. Efavirenz + ABC/3TC
3. Atazanavir/r + TDF/FTC
4. Atazanavir/r + ABC/3TC
5. Raltegravir + TDF/FTC
6. Rilpivirine +TDF/FTC
7. None of the above

What to start

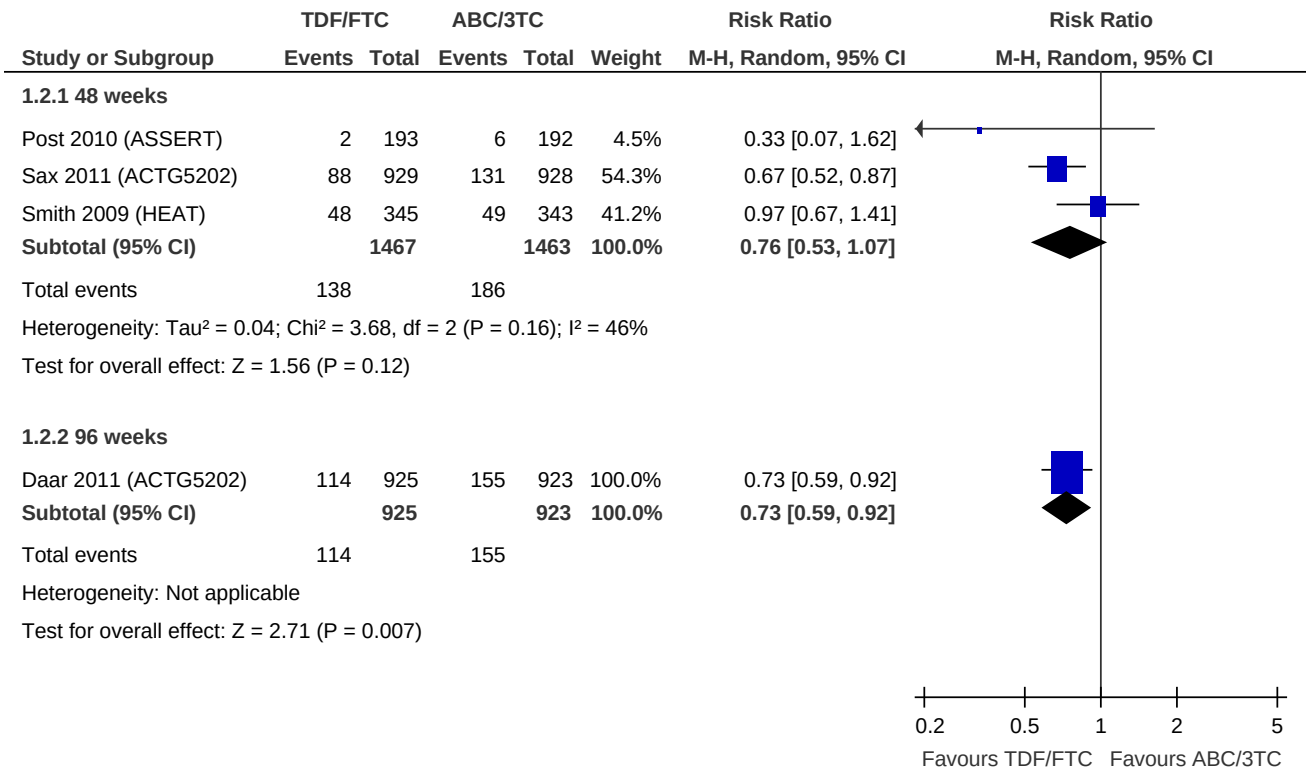
	Preferred	Alternative
NRTI backbone	Tenofovir and Emtricitabine	Abacavir and Lamivudine (1,3)
Third agent	Atazanavir/ritonavir Darunavir/ritonavir Efavirenz Raltegravir	Fosamprenavir/ritonavir Lopinavir/ritonavir Nevirapine (2) Rilpivirine (3)

1. Abacavir is contraindicated if HLA B*5701 positive
2. Nevirapine is contra-indicated if baseline CD4 greater than 250/400 cells/µL in women/men.
3. Use recommended only if baseline viral load less than 100,000 copies/ml: rilpivirine as a third agent, abacavir + lamivudine as NRTI back bone

The presence or future risk of co-morbidities and potential adverse effects need to be considered in the choice of antiretroviral drugs in individual patients.

What to start: NRTI backbone

Proportion of randomised subjects with protocol defined virological failure at 48 +/- 96 weeks



Effect size: 45 fewer per 1000 patients (13 fewer to 69 fewer)

What to start

Case 3:

30 year heterosexual black African women, CD4 count 360 cells/µL, VL 75,000 copies/ml, no transmitted resistance, ART naïve, HLA B5701 negative, HBV and HCV negative, no significant co-morbidity, considering becoming pregnant, wants to start ART.

She asks what ART regimen you would advise she starts?

What to start

Question 4: What ART regimen would you advise?

1. Efavirenz + TDF/FTC
2. Efavirenz + ABC/3TC
3. Atazanavir/r + TDF/FTC
4. Atazanavir/r + ABC/3TC
5. Raltegravir + TDF/FTC
6. Rilpivirine +TDF/FTC
7. None of the above

What to start: Novel strategies

5.5.1 Recommendation

•We recommend against the use of protease inhibitor monotherapy as initial therapy for treatment-naïve patients. (1C)

5.5.4 Recommendation

•We recommend against the use of protease inhibitor-based dual antiretroviral therapy with a single NRTI, NNRTI, CCR5 receptor antagonist, or an integrase inhibitor as an initial therapy for treatment-naïve patients. (1C)

Supporting patients on therapy

- **Adherence:**
  - Adherence support interventions
  - Once daily dosing / Fixed dose combinations
- **Pharmacology**
  - drug interactions / Therapeutic drug monitoring
  - Stopping therapy: pharmacological considerations
  - Switching therapy: pharmacological considerations
- **Switching ART in virological suppression**
  - switching ARVs in combination ART
  - PI/r monotherapy
- **Stopping therapy**

Managing virological failure

- **Blips, low level viraemia, virological failure**
- **Patients with no or limited drug resistance**
- **Patients with triple class (NNRTI, NRTI, PI) virological failure with or without triple class resistance**
- **Patients with limited or no therapeutic options when a fully viral supressive regimen cannot be constructed**

ART in specific populations

When to start, what to start

- **Tb co-infection**
- **Viral hepatitis co-infection**
- **HIV-related cancers**
- **HIV associated neurocognitive impairment**
- **Chronic kidney disease**
- **Cardiovascular disease**
- **Women**

BHIVA ART guidelines 2012

Dissemination:

- HIV Medicine (2012), 13 (suppl 2), 1-85
- Online: www.bhiva.org
- Patient friendly version (NAM)
- Summary/quick reference version
- Slide set
- e-Learning module

Guidelines review

Schedule:

December 2012

- selected review of new evidence
- update GRADE analysis

January/February 2013

- update selected recommendations

2014: Full revision