London Therapeutic Tender Implementation: Guidance for Clinical Use

4th June 2014

FINAL

Contents

General principles

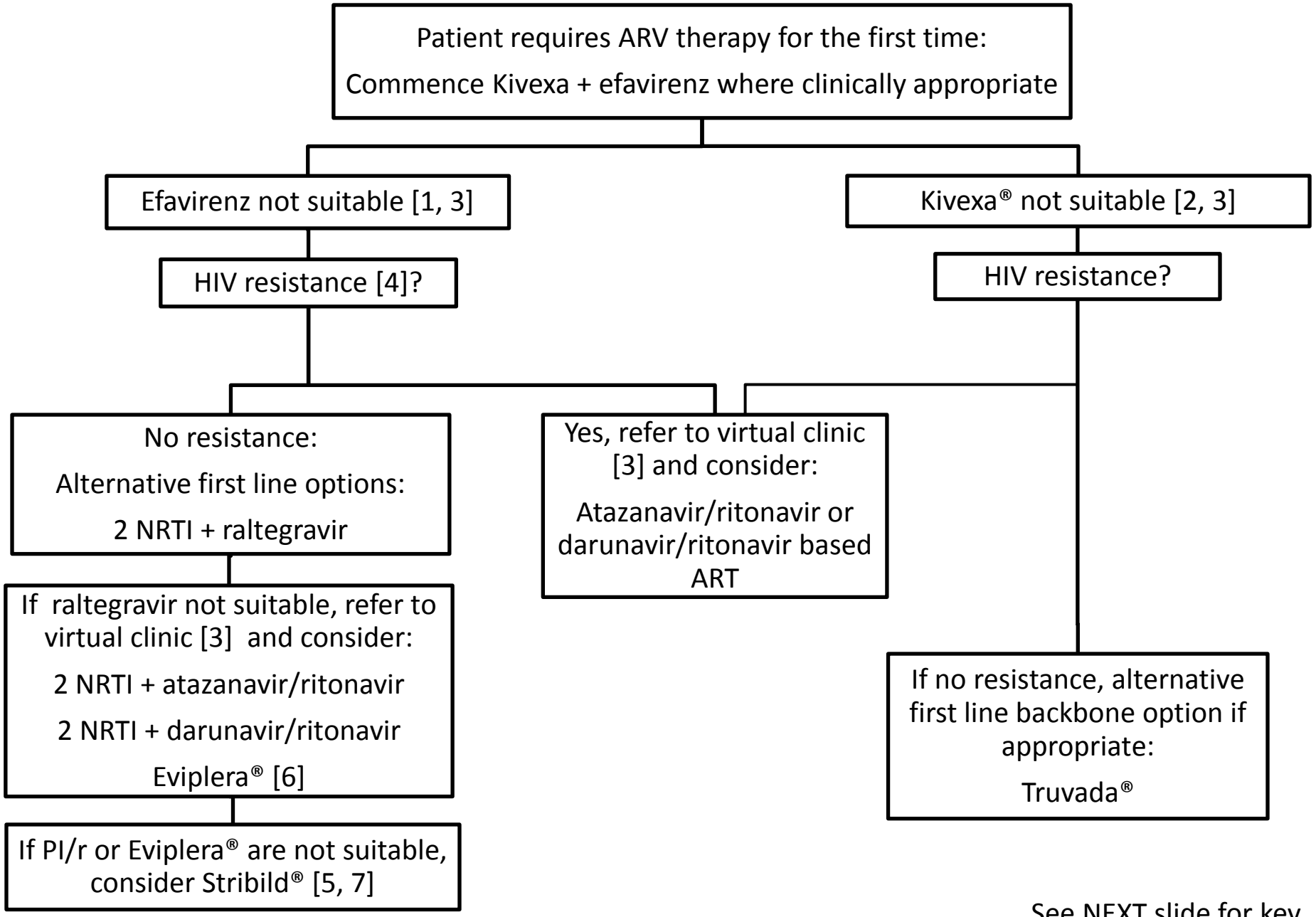
- The tendering process has realised large savings for the NHS.
- Good medicines management remains a cornerstone of cost-effective HIV treatment.
- This guidance strives to achieve best value whilst maintaining access to alternative regimens which may be more tolerable for some patients.
- Current BHIVA guidelines[1] and data from recent conferences/publications has been considered when making decisions (excepting for the caveats for Kivexa® use on slide 10).
- Good communication between clinicians, commissioners and people living with HIV is essential in making effective treatment decisions.
- We recommend patients are given the opportunity to be involved in making decisions about their treatment [1].
- Informed patient choice should be central to all treatment decisions.

1. Churchill D et al. HIV Medicine (2014), 15 (Suppl. 1), 1–85. DOI: 10.1111/hiv.12119.

Financial impact of Therapeutic Tendering for branded ARVs

- Annual expenditure on ARVs in London is currently **£190m.**
- Since 2011, Therapeutic Tendering saved at least **£10.5m** (recurring full year savings).
- This is equivalent to a reduction of about **5.2%** in annual ARV expenditure.
- The new therapeutic contract starting in April 2014 is expected to save at least **£4.8m (2.5%).**

London ARV algorithm: First line therapy



See NEXT slide for key

London ARV algorithm: First line therapy - Key

1. Caution with **efavirenz** where evidence of clinical depression or other significant mental health issues, or where side effects of **efavirenz** are likely to have an impact on the shift work or lifestyle of patients, impacting on adherence.
2. **Kivexa®** not indicated if: HLA-B*5701 positive, baseline VL>100,000c/ml, HBV co-infection, resistance to **abacavir** or **lamivudine**, or patients with higher cardiovascular risk (>10% ten-year risk). See BHIVA treatment guidelines (2014) for definition and assessment. (Churchill D et al. HIV Medicine (2014), 15 (Suppl. 1), 1–85).
3. Virtual review and audit clinic (multi-disciplinary team meeting) referral should be made for all patients who do not fulfil the outlined clinical criteria for exceptions to use of **Kivexa®**, or who require third agents other than **efavirenz** or **raltegravir**, or those with HIV antiretroviral resistance or where **Stribild®** is being considered (see point 7). If there is a clinical need to initiate a non-preferred regimen then local mechanisms should be established to review retrospectively.
4. If treatment is required prior to availability of baseline resistance assay then start PI/r based ART and review in line with guidance when resistance assay available.
5. **Stribild®** should only be considered where **efavirenz**, **raltegravir**, **atazanavir/r, darunavir/r** or **Eviplera®** are not suitable.
6. **Eviplera® (or rilpivirine)** is not indicated where HIV VL>100,000c/ml.
7. In line with NHS England. Clinical Commissioning Policy Statement: **Stribild®** for the treatment of HIV-1 infection in adults: September 2013 Reference NHS England B06/PS/a.

Key points (1)

- First line therapy
  - **Kivexa®** remains the NRTI backbone of choice where clinically appropriate for patients starting ART.
  - **Efavirenz** is the preferred third agent unless there is a clinical contra-indication.

- Patients currently on stable therapy
  - London guidance does not recommend switching treatment for patients who are on stable treatment unless there is a clinical reason.

Key points (2)

- If there is a clinical indication to avoid, or to switch because of **efavirenz** toxicity:
  - Consider use of **raltegravir.**

- If there are potential adherence concerns with twice daily **raltegravir:**
  - Consider **Eviplera®**, or 2NRTIs (preferable **Kivexa**) with **atazanavir/r**, or **darunavir/r** with review by virtual clinic.

- In patients with baseline drug resistance or concerns regarding intermittent adherence.
  - Use boosted **atazanavir** or **darunavir.**

Key points (3)

- Referral to multi-disciplinary team meetings (virtual review and audit clinic) should be made for all patients who:
  - Do not fulfil the outlined clinical criteria for exceptions to use of **Kivexa®**, or require regimens that do not contain **efavirenz** or **raltegravir**.
  - Whenever **Stribild®** is being considered.
- PI monotherapy is not a recommended strategy.

Choice of NRTI backbone

- The London HIV Drugs & Treatment Group has seen no new data to support changing London recommendations made in 2012 on choice of **Kivexa®** vs **Truvada®**.
- Following the 2012 guidance, cost must be taken into consideration when choosing the NRTI backbone.
- Where clinically appropriate, **Kivexa®** remains the NRTI backbone of choice.
- **Truvada®** should be considered where:
  - Baseline HIV viral load is in excess of 100,000 copies/ml, unless there are other clinical considerations (e.g. renal impairment).
  - Co-infection with Hepatitis B.
  - In patients at higher cardiovascular risk (>10% ten-year risk) - see BHIVA treatment guidelines (2014) for definition and assessment. [1]
  - Where patient is HLA-B*5701 positive (**Kivexa®** contraindicated).

1. Churchill D et al. HIV Medicine (2014), 15 (Suppl. 1), 1–85 section 8.6.2. DOI: 10.1111/hiv.12119.

Choice of 3rd agent

- **Efavirenz** is the preferred third drug for first line therapy.
- If efavirenz is not clinically appropriate, **raltegravir** is the recommended alternative.
- In patients with baseline drug resistance or concerns regarding intermittent adherence, ritonavir boosted **atazanavir** or **darunavir** should be used.
- If there are concerns over adherence to twice daily therapy, then **atazanavir/r** or **darunavir/r** (preferably with **Kivexa®**) or **Eviplera®**.
- **Stribild®** should be considered if a **PI/r** or **Eviplera®** are not appropriate.

Exceptions to efavirenz use

- No change to 2012 guidance [1], other than BHIVA pregnancy guidelines now allow the use of **efavirenz**. However, some clinicians and patients will still prefer to use other third drugs.

- It is recommended that clinicians avoid efavirenz in patients with clinical depression or other significant mental health issues or where side effects of efavirenz may have an impact on the work or lifestyle of patients, impacting on adherence.

1. London DTSG 2011 guidance: Efavirenz not suitable if: Patient has baseline resistance, patient wants to become pregnant, concern over central nervous system (CNS) side effects e.g. previous history or current psychological state

Raltegravir

- When **efavirenz** is unsuitable then **raltegravir** is the recommended alternative, except in patients with baseline resistance.

- **Raltegravir** may be advantageous in those with co-morbidities due to:
  - Relatively few drug-drug interactions [1] compared to PI/r.
  - A good side effect profile compared to PI/r.
  - Less impact on lipids.

1. Caution with patients using supplements/antacids/multivitamins containing di or trivalent cations (e.g. Mg/Al/Ca/Zn/Fe) which may chelate raltegravir . Consult SPCs for raltegravir and all integrase inhibitors for advice

Fixed dose combinations (FDC)

- There is no additional evidence of improved virological success for FDCs compared with separate components.
- FDCs should not be prescribed in preference to other appropriate regimens within the guidance.
- FDCs can be prescribed when the individual components of a combination include this option.
- In line with current national policy, there is no requirement to switch patients from **Atripla®** to **Truvada®** plus **generic efavirenz** (see slide 24).

Boosted protease inhibitor choice

- A boosted protease inhibitor (PI/r) is recommended as first-line therapy in the following situations:
  - Primary drug resistance.
  - Where intermittent adherence seems likely and there is concern about the development of drug resistance.
  - If there are concerns over twice-daily therapy, **a boosted-PI** (preferably with **Kivexa®**) can be considered. The recommended PIs are **ritonavir boosted atazanavir** or **darunavir.**
  - If treatment is required prior to availability of baseline resistance assay then start PI/r based ART and review in line with guidance when resistance assay available (or refer to virtual review and audit clinic for review).
- Clinicians should consider drug-drug interactions and the resistance and side effect profile in choosing between PIs.

Stribild® (TDF/FTC/c/EVG)

- **Stribild®** should be considered as an alternative option in patients not suitable for **efavirenz**, **raltegravir**, **atazanavir/r**, **darunavir/r** or **Eviplera®.**
- Within the current pricing framework, **Stribild®** is more expensive than other suggested regimens.
- **Stribild®** contains **cobicistat** which is associated with frequent drug interactions, some of which may be similar to those seen with ritonavir.
- When switching therapy, **Stribild®** may be considered for patients without resistance, in whom **raltegravir,** a PI/r, or **Eviplera®** are not appropriate.
- **Stribild®** should be used in accordance with the NHS England clinical commissioning policy statement. [1]

1. NHS England. Clinical Commissioning Policy Statement: Stribild® for the treatment of HIV-1 infection in adults: September 2013 Reference NHS England B06/PS/a

Eviplera® (TDF/FTC/RPV)

- **Eviplera®** should only be considered as an alternative option in patients not suitable for **efavirenz** or **raltegravir,** with review by the virtual review and audit clinic**.**

- For patients switching therapy **Eviplera®** may be considered for patients without resistance, in whom **raltegravir** is not suitable after review by the virtual clinic.

Switching therapy (1)

- If switching for **efavirenz** toxicity (in absence of viral failure or resistance) the recommended switch option is **raltegravir.**

- If **raltegravir** is not indicated, then **atazanavir/r, darunavir/r** or **Eviplera®** should be considered.

- If **atazanavir/r, darunavir/r** or **Eviplera®** are not suitable, then **Stribild®** should be considered.

Switching therapy (2)

- Patients stable on **atazanavir/r** or **darunavir/r** should not be switched between PIs unless there are clear clinical indications to do so, and these should preferably be discussed at a multi-disciplinary meeting (virtual review and audit clinic

- Those established on PI/r (without resistance) or **Eviplera®** may be offered the switch to **raltegravir** with two NRTIs to improve tolerability, reduce the potential of drug interactions.

- Prescribing of all medicines, including non-ARVs, should be reviewed in all patients at least annually. This is in line with BHIVA 2014 guidelines. [1]

1. Churchill D et al. HIV Medicine (2014), 15 (Suppl. 1), 1–85.

Multi-disciplinary review (virtual review and audit clinic)

- The use of virtual review and audit clinics (VCs) to review patients starting or switching therapy is good clinical practice.
- Patients needing to initiate or switch to a non-preferred regimen [1] should be discussed in a VC as per best practice.
- Where there is urgent need to use a non-preferred regimen, local mechanisms to discuss retrospectively in the VC should be developed.

1. Non preferred regimens include plan to use regimens other than Kivexa® with efavirenz or any first-line regimen not containing efavirenz or raltegravir where the indication for the alternative regimen is not within the guidance (i.e. initiating Atripla® with HIV VL >100,000 copies/mL or HBV co-infection, or use of raltegravir due to clinical depression would not require referral to the virtual review and audit clinic). Switching therapy to non-raltegravir or non-efavirenz containing regimens (with two NRTIs) should be reviewed by the virtual review and audit clinic.

Audit / review of Guidance

- A prospective audit of all patients starting ART and switching within six months will be conducted.

- Centres using higher proportions of non-efavirenz based regimens will have external audit of their virtual review and audit clinic.

Protease Inhibitor monotherapy

- The London group does not recommend PI monotherapy other than in specific clinical situations such as the need to avoid NRTI toxicity with limited options.

- If PI monotherapy is used then **darunavir/r** is the recommended PI.

- **Atazanavir** is not recommended as PI monotherapy.

Dolutegravir

- NHS England are yet to make a funding decision on the place in therapy of **dolutegravir.**

- Once the commissioning statement is released, the London DTSG will consider its place within the prescribing guidance.

Prescribing of generic ARVs

- Where there are contracts for generic ARVs, patients should be switched from the branded equivalent as soon as possible, taking into account the need for the provision of appropriate information and counselling.

- There is no requirement to switch
  - **Atripla®** to **Truvada®** plus generic **efavirenz**
  - **Nevirapine PR 400mg** to the immediate release 200mg formulation.
  - **Kivexa®** to **abacavir** and generic **lamivudine**

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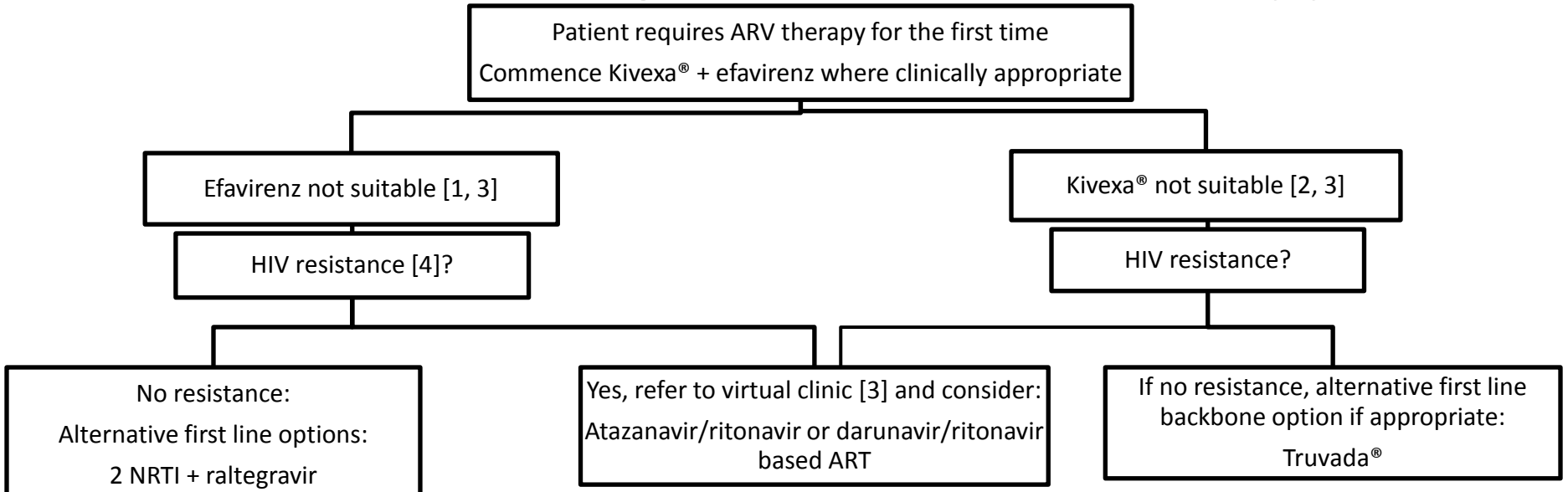

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