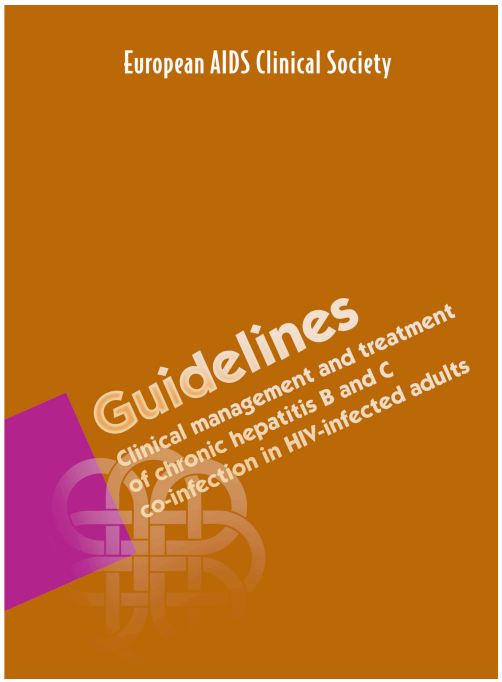

Clinical Management and Treatment of HIV Infected Adults in Europe

Panel Members

Nathan Clumeck, Belgium, Chair
Nikos Dedes, Greece
Anton Pozniak, UK
François Raffi, France

and the EACS Executive Committee

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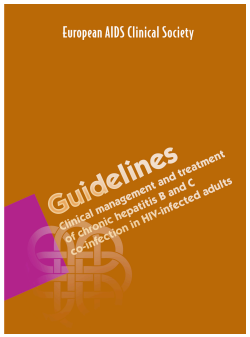


Recommendations for Initiation of Therapy in Naïve HIV-Infected Patients

ASYMPTOMATIC - CD4 350-500

Previously :
Treatment may be offered if VL > 10^5 c/ml and/or CD4 decline >50-100/mm3/year or age >55 or hepatitis C co-infection

Now : Treatment should be considered if VL>10^5 c/ml and/or CD4 decline >50-100/mm^3/ year or age >50 or, pregnancy, high cardiovascular risk, malignancy.

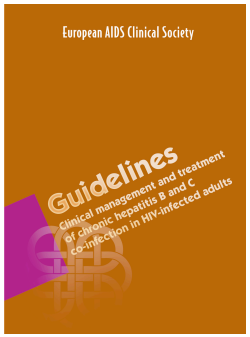
Treatment recommended if hepatitis C co-infection, hepatitis B co-infection requiring therapy, HIV-associated nephropathy or other specific organ deficiency.

ASYMPTOMATIC - CD4 > 500

Previously :
Treatment should be deferred, independently of Plasma HIV RNA; closer follow-up of CD4 if VL > 10^5 c/ml

Now : Treatment should **generally** be deferred, independently of plasma HIV RNA; closer follow-up of CD4 if VL > 105 c/ml.

Treatment can be offered if presence of ≥ 1 of the above co-morbid conditions (CD4 350-500).

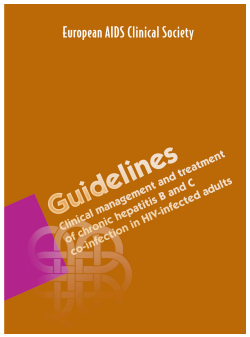


Initial Combination Regimen for Antiretroviral-Naïve patient

Select 1 drug in column A and 1 NRTI combination in column B	A	B	REMARKS
Recommended	NNRTI • EFV[1] • NVP[5] or ritonavir-boosted PI • **ATV/r[6]** • **DRV/r[6]** • LPV/r[7] • SQV/r	TDF/FTC ABC/3TC[2-3-4]	– TDF/FTC co-formulated – ABC/3TC co-formulated – EFV/TDF/FTC co-formulated – ATV/r: 300/100 mg qd – DRV/r: 800/100 mg qd – LPV/r:400/100 mg bid or 800/200 mg qd – SQV/r:1000/100 mg bid
Alternative	SQV/r **FPV/r** **RAL[9]**	• ZDV/3TC[8] • ddI/3TC or FTC[8]	– SQV/r: 2000/100 mg qd – **FPV/r:700/100 mg bid or 1400/200 mg QD** – RAL : 400 mg bid – ZDV/3TC co-formulated

6 Castle study (LPV/r vs ATV/r) has shown better tolerability of ATV/r and Artemis study (LPV/r vs DRV/r) better efficacy and greater tolerability of DRV/r.

9 Raltegravir is indicated in combination with other anti-retroviral medicinal products for the treatment HIV-1 infection in adult patients. It has been studied only in combination with TDF/FTC in naïve patients with limited follow-up (48 weeks).



A NEW TABLE

SWITCH STRATEGIES FOR VIROLOGICALLY SUPPRESSED PATIENTS
(confirmed plasma viral load < 50 c/ml)

Indication:

- Documented toxicity
- Side-effects
- Planned pregnancy
- Wish to simplify regimen
- Actual regimen no longer recommended
- Prevention of long-term toxicity (pre-emptive switch)
- Aging and/or co-morbidity with a possible negative impact of drug(s) in current regimen eg on CVS risk, metabolic parameters.
- Management of potential drug interactions
- Management of TB, HBV or HCV infection

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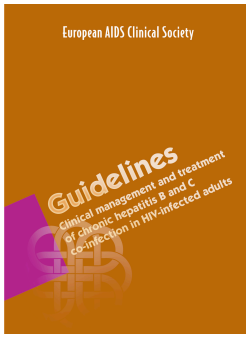

SOMES PRINCIPLES FOR SWITCHING

- PI/r to NNRTI switch for simplification, prevention or improvement of metabolic abnormalities, adherence facilitation. NVP has the advantage of its metabolic profile. EFV has the advantage of possible FDC of 3 drugs (Atripla®).

- Switching from PI/r to NNRTI or raltegravir only possible if 1) no history of prior virological failure; and 2) NRTI backbone fully active.

- PI/r or enfuvirtide to raltegravir switch for simplification, prevention or improvement of metabolic abnormalities, adherence facilitation.

- Simplification of a complex multi-drug regimen in antiretroviral-experienced patients with 1) substitution of drugs difficult to administer (enfuvirtide) and/ or with poor activity (NRTI in case of multiple NRTI resistance) and/or poor tolerability and 2) addition of new well-tolerable, simpler and active agent(s).

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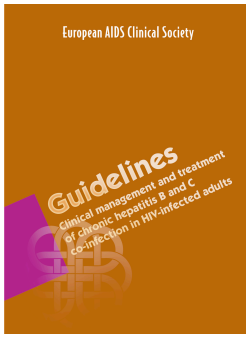

OTHER STRATEGIES OF SWITCHING

PI/r monotherapy with bid LPV/r ,or preferably qd DRV/r, might represent an option in patients with intolerance to NRTI or for treatment simplification. Such strategy only applies to patients without history of failure on prior PI-based therapy and who have had viral load < 50 c/ml in at least the past 6 months.

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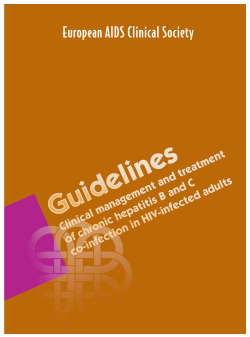

TREATMENT OF HIV PREGNANT WOMEN

Antiretroviral regimen in pregnancy

PREVIOUSLY

- Same as non pregnant,
- Except avoid EFV
- ABC, NVP and TDF not to be initiated but continuation is possible if started before pregnancy
- Among PI/r, prefer LPV/r or SQV/r
- ZDV should be part of the regimen if possible

NOW

- Same as non pregnant,
- Except avoid EFV
- **NVP** not to be initiated but continuation is possible if started before pregnancy
- Among PI/r, prefer LPV/r or SQV/r **or ATV/r**
- **RAL, DRV/r: few data available in pregnant women**
- ZDV should be part of the regimen if possible

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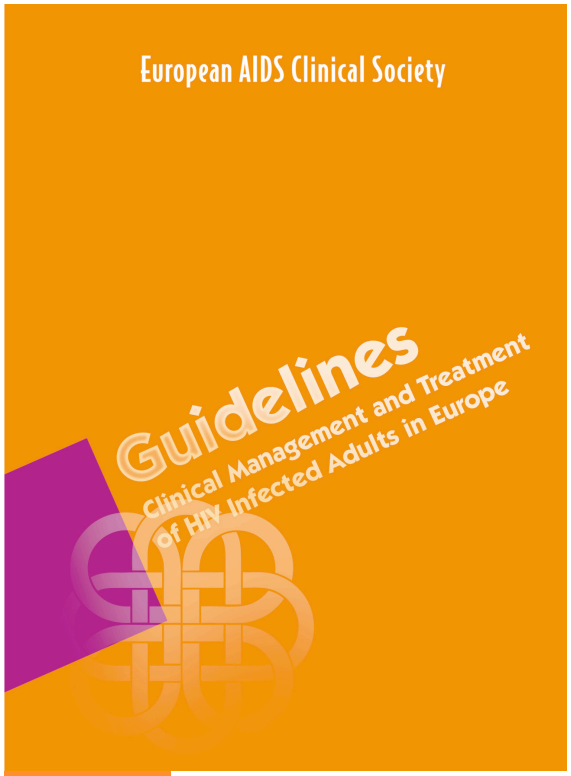

Clinical Management and Treatment of Chronic Hepatitis B and C Co-Infection in HIV-Infected Adults

Panel members

Jürgen Rockstroh, Germany, Chair
Yves Benhamou, France
Sanjay Bhagani, UK
Raffaele Bruno, Italy
Diego Garcia, Spain
Stefan Mauss, Germany
Lars Peters, Denmark
Massimo Puoti, Italy
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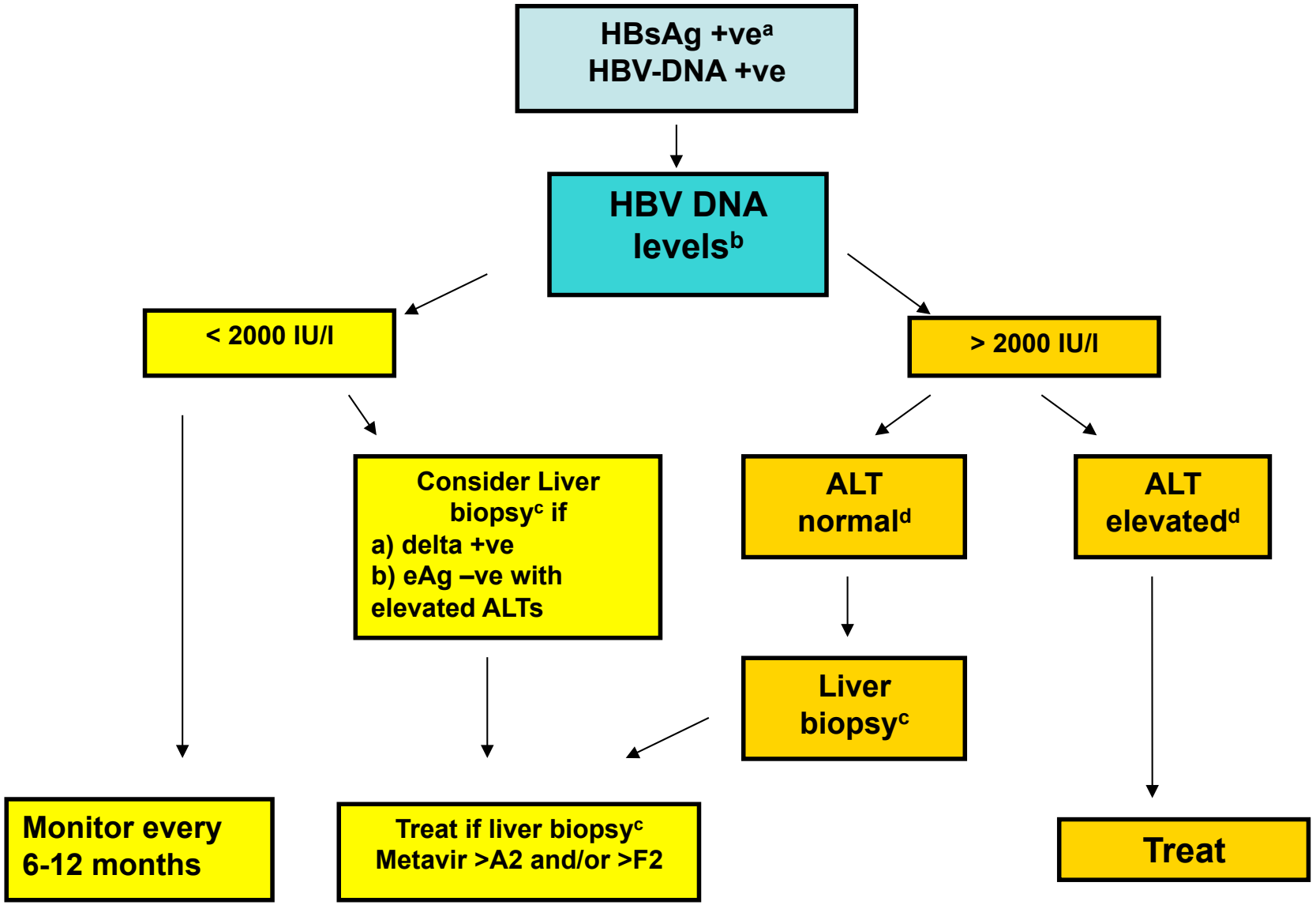
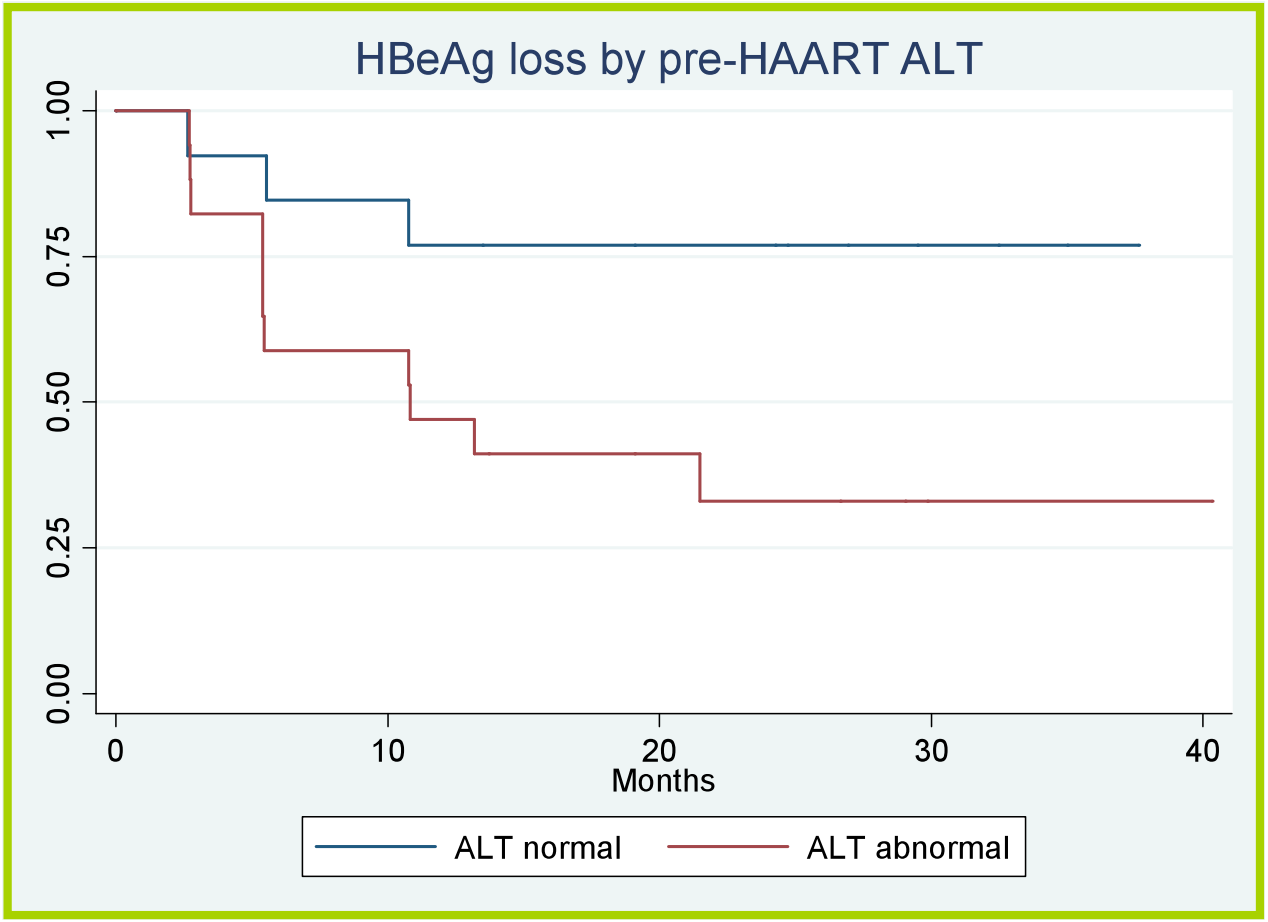
Assessment of treatment indication for HBV



Assessment of treatment indications

- HBV DNA quantitation 1 IU/l = 5 c/ml.
- Patients with replicating HBV and normal liver enzymes may well have significant liver fibrosis therefore always consider fibrosis assessment.
- Note normal ALT is <19 IU/l for women and < 31 IU/l for men.
- Although liver biopsy gives useful additional information on grading and other aetiologies of liver damage, emerging data on the usefulness of non-invasive tests for fibrosis assessment in HBV

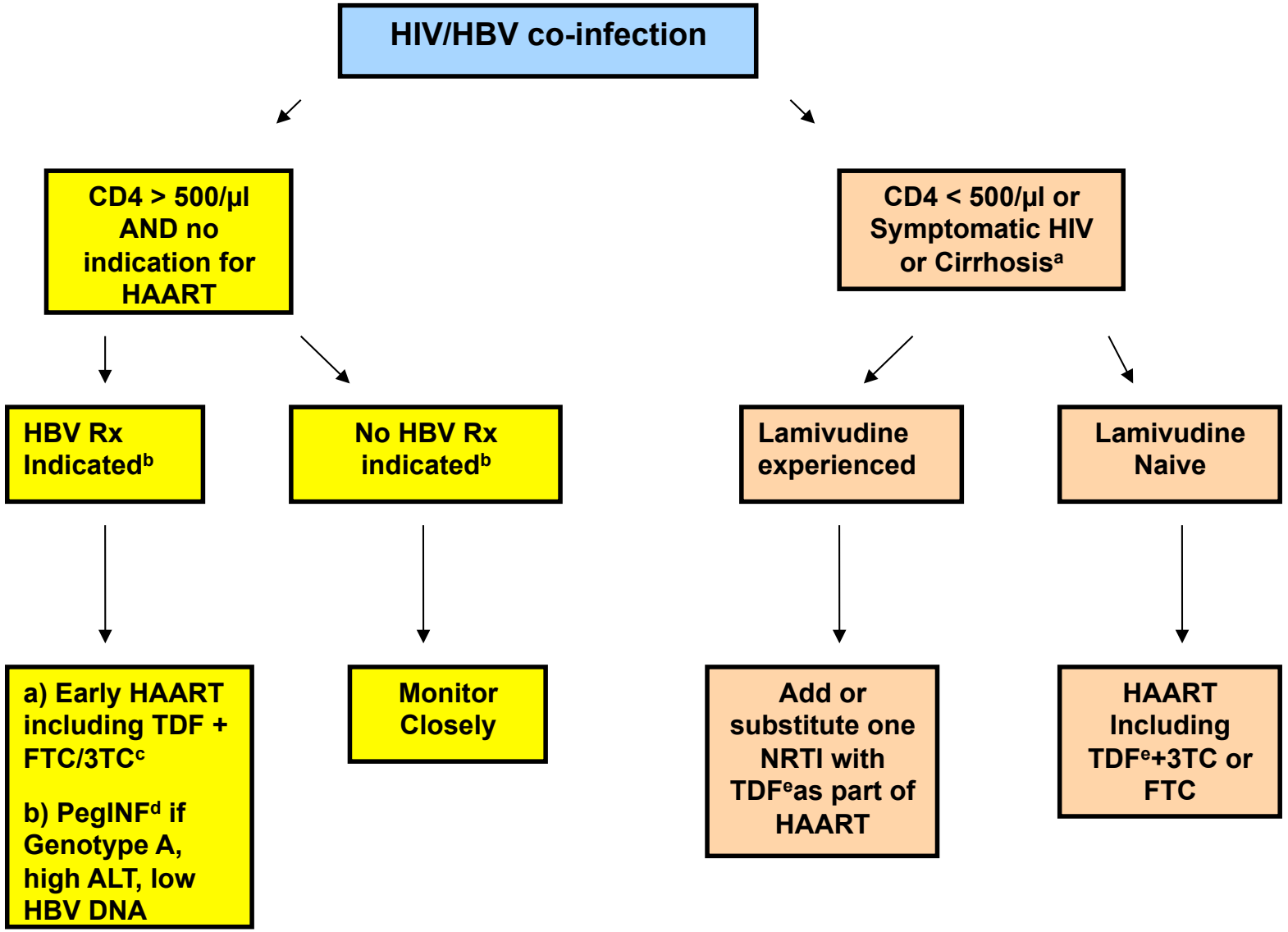
High rates of HBeAg seroconversion following HBV active HAART



Longitudinal Thai cohort (n=47); HBeAg-positive (n=30); median follow up = 27 months HBeAg loss = 46%; HBsAg loss = 13%

Avahingson et al., 5th IAS Conference, Capetown 2009, Poster # WEPEB226

Treatment of chronic HBV in HIV co-infected patients



HBV/HIV Treatment - comments

- Early HAART with TDF + 3TC/FTC strongly advised especially if F3/F4 fibrosis
- If patient unwilling to go on early HAART, adefovir and telbivudine may be used as an alternative to control HBV alone.
- Treatment duration:
  - Not requiring HAART and eAg+, cautiously stop Rc six months post anti-e seroconversion
  - PegIFN – 48 weeks; on-treatment HBsAg levels may help identify those wih likelihood of response
- In some cases of tenofovir intolerance (i.e. renal disease), entecavir ± adefovir or tenofovir in doses adjusted to renal clearance in combination with effective HAART may be advisable.
  - . Caution is warranted to switch from a tenofovir based regimen to drugs with a lower genetic barrier, e.g. FTC/3TC, in particular in lamivudine pretreated cirrhotic patients as viral breakthrough due to archived YMDD mutations has been observed. This has also been described in individuals with previous 3TC HBV-resistance who have been switched from tenofovir to entecavir.