European Guidelines

for the Clinical Management and Treatment of HIV Infected Adults

2005

These Euroguidelines result from the comparison of guidelines from several European countries and from a discussion with the following panel

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PRIMARY HIV INFECTION (PHI)

Definition : ***Acute primary HIV infection***

- High risk exposure within previous 2-8 weeks
- WB ≤3 bands

Recommend to perform Ag p24 and plasma HIV-RNA

Early HIV infection

- Exposure to HIV or HIV test neg within previous 6 months
- WB > 3 bands

Treatment : Favour clinical trial

Treat if : - OI
or - Severe illness/prolonged symptoms (especially CNS symptoms)
or - Confirmed CD4 < 350 at month 3
or - Confirmed HIV-RNA at M3 > 100000 cp/ml

In the absence of symptoms, wait till month 6 and follow criteria for initiation of treatment in chronic HIV infection.

Duration of treatment : unknown. Close follow up in case of treatment interruption.
Follow up : M1, 3, 6, 9 and 12.

Resistance testing : Recommended.
In case genotyping cannot be performed, store blood for further testing.

Transmission : Recognize PHI and sexually transmitted infections (STIs), including syphilis and hepatitis C ; notify partners.

RECOMMENDATIONS FOR INITIATION OF THERAPY IN NAÏVE PATIENTS

Symptomatic patients : Treatment mandatory.

Asymptomatic patients :

CD4	Treatment
< 200 cells/mm^3 or < 15%	Recommended
201-350 cells/mm^3	Should be initiated in patients : - with rapid CD4 decline independently of viral load Should be considered in patients : - with viral load >10^5 c/ml independently of CD4 count - who are HCV co-infected.
> 350 cells/mm^3	Defer if VL > 10^5 c/ml, closer follow up of CD4 is recommended Treatment should be considered if CD4 decline is rapid

Comment : Whatever the CD4 and VL level, treatment can be offered on an individual basis after evaluation with the patient.

Resistance testing : Recommended
- when prevalence of mutations in naïve patients is > 10%
- in case of high suspicion of transmission of resistance.

Consider resistance testing in other cases.
Store blood if genotyping is not performed.

INITIAL COMBINATION REGIMEN FOR ANTIRETROVIRAL-NAÏVE PATIENT

Select 1 drug in column A, B and C	A	B	C	Comments
Recommended	EFV° NVP* boosted PI : FPV/r LPV/r SQV/r	ABC TDF ZDV	3TC/FTC	• To improve adherence once daily regimen could be preferred and is feasible with FosAPV/r, EFV°, NVP*, ABC, TDF, ddI, 3TC and FTC • ABC/3TC co-formulated as Kivexa® • TDF/FTC co-formulated as Truvada® • FPV/r : 700/100 mg bid or 1400/200 mg qd • LPV/r : 400/100 mg bid • SQV/r : 1000/100 mg bid (hard-gel formulation) • °EFV : contraindicated in pregnant women or women with no reliable and consistent contraception ; not active on HIV-2 and HIV-1 group O. • *NVP : only women with CD4 < 250 and men with CD4 < 400µ/ L ; not active on HIV-2 and HIV-1 group O ; monitor liver tests during the 18 first weeks of treatment ; liver toxicity potentially increased when used in once daily.
Alternative (These drugs may be used as alternatives to the recommended drugs within each of columns A and B in case of contraindication and/or intolerance to the recommended drugs)	ATV/r IDV/r	ddI		• ATV/r : 300/100 mg qd (limited data in naïve patients) • IDV/r : 400/100 mg bid (this dose is chosen based on limited published but extensive clinical experience suggesting preserved virological activity and reduced risk of adverse effects compared to more extensively studies dose of 800/100 mg bid).
Not recommended except in selected patients where a NNRTI or PI is contraindicated and with a VL < 10^5 copies/ml	ABC	ZDV	3TC/FTC	
Not recommended	TDF	ABC	3TC	
Not recommended	TDF	ddI	Any drug	The combination of TDF and ddI may be associated with a decline of CD4, reduced antiviral effect and increased toxicity.
Not recommended	d4T	ddI	Any drug	The combination of d4T and ddI is associated with an increased risk of lactic acidosis and lipodystrophy.
Not recommended	3TC/FTC	ddI	Any drug	Few data available to support this combination as back bone.

MANAGEMENT OF VIROLOGIC TREATMENT FAILURE

Treatment objectives	VL decline > 2 log at W4 ; VL < 400 c/ml at W12 ; VL < 50 c/ml at W24
Definition of failure	VL repeatedly > 50 c/ml 6 months after initiating or changing therapy
Management	General measures : • Evaluation for adherence, compliance, tolerability, drug-drug interactions, drug-food interactions, psychosocial issues, … • Perform resistance testing (usually reliable with plasma VL levels > 500-1000 c/ml) • Consider TDM
Management of first line therapy failure	**If VL < 1000 c/ml** • Check and improve compliance • Check and improve PK • Switch NNRTI's to boosted PI (s) **If VL > 1000 c/ml :** Decision to change will depend on the resistance testing results : • No R+ mutations found : re-check for adherence, perform TDM • R+ mutations found : switch to a suppressive regimen ; multidisciplinary experts discussion advised
Management of subsequent failure(s)	General measures are the same as first line failure ; decision to change will depend on : • VL level, CD4 level and decline • Treatment options remaining - the number of active drugs in each class - ARV's history - factors influencing the tolerability, the adherence - availability of experimental and new mechanistic drugs • Resistance testing results : No R mutations found : re-check for adherence, perform TDM R mutations found : switch to a suppressive regimen ; Multidisciplinary experts discussion advised. In any case consider archived mutations (review treatment history and previous genotypes, if available) General recommendations : • Use > 2-3 active drugs in the new regimen • Defer the change if < 2 active drugs available except in patients with low CD4 count (< 200 cells/mm^3) or with high risk of clinical progression for whom the goal is the preservation of immune function • Favour clinical trials with experimental and new mechanistic drugs (but avoid functional monotherapy) • STI is not recommended except in selected patients (i.e. with tolerability issues) and only for < 8 weeks

TREATMENT OF HIV PREGNANT WOMEN

Criteria for starting HAART in pregnant women :	same as not pregnant
Objective of treatment in pregnant women :	full VL suppression at least at delivery
Resistance testing	Euroguidelines for HIV resistance recommend testing all pregnant women with detectable HIV RNA
SCENARIO	
1- Women becoming pregnant while already treated with HAART :	maintain current treatment except contraindicated drugs
2- Women becoming pregnant while treatment naïve who fulfill the criteria for initiation of HAART :	start HAART at 12 weeks of pregnancy
3- Women becoming pregnant while treatment naïve who do not fulfil the criteria for initiation of HAART :	start HAART at least 12 weeks before delivery
4- Women whose follow up starts very late during pregnancy :	start HAART including ZDV + NVP
Type of combination	Triple therapy recommended ; Zidovudine should be part of the regimen if possible ; Monotherapy with Zidovudine not recommended.
Drugs contra-indicated during pregnancy	Efavirenz, ddI+d4T
IV Zidovudine during labour	Benefit uncertain in women with fully suppressed viral load
Caesarean section	should be advised in women without fully suppressed VL or poor obstetric conditions

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These European Guidelines were supported by an unrestricted educational grant from Hoffmann-La Roche Ltd.