Second Line Antiretroviral Therapy in Aids (NACO Guidelines)

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Introduction

All Patients of AIDS are put on first line ART after they are properly staged(W.H.O STAGING)and they fulfill national &laboratory criteria to start ART.(NACO GUIDELINES).During the treatment period they are followed for drug toxicities, development of O.I.(which may change their clinical staging) and CD4 count. Drug toxicities can be managed by proper replacement by another drug.(substitution as advised by NACO).However frequent development of O.I. thereby changing the clinical staging of the patients to stage 3 or 4 and reduction in their CD4counts alarms the failure of treatment by first line ART and change over to second line ART in these patients. Thus identifying treatment failure is the first step each physician should know before putting the patient on second line ART.NACO has given guidelines to diagnose clinical, immunological & virological failure in these patients of HIV, on first line ART.NACO GUIDELINES are available since April 2011.

Diagnosis of treatment failure

High index of suspicion is needed for this .Failure is suspected in patients who have received proper first line ART for at least 6months,but are deteriorating clinically(occurrence of new O.I) as well as immunologically (decrease in CD4 count),despite good adherence. NACO defines ART failure as follows:

Clinical failure

New or recurrent WHO stage 4 condition, after at least 6 months of ART.

Immunological failure

Fall of CD4 count to pre-therapy or below base line

50% fall from the on treatment peak value (if known)

Persistent CD4 levels below 100celle/mm3

Virological failure

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Plasma viral load>10,000 copies/cc

In spite of above said definitions, every ART center must follow THE NACO protocol before referring the patient for second line ART to SACEP(State AIDS clinical expert panel).

Before referring the patient for 2ND line ART the following investigations should be repeated in every patient.

1. Laboratory tests including Hb, LFT,RFT, and most recent cd4 count should be done before referral.
2. The patient should be counseled for 100% adherence for ART.
3. If patient has OI treat it & give necessary prophylaxis. Treat tuberculosis if present as per RNTCP, repeat CD4 count after 2 weeks OI treatment, and intensive phase (8weeks) treatment of AKT.

The SACEP review will be based on the referral from the ART center providing first line ART. Each COE will have ART centers linked to it and patients from these centers only will be reviewed by particular COE. SACEP will document its decision according whether to provide 2nd line ART or not or re-evaluate. After the decision SACEP will communicate to referring ART center to transfer out the patient to COE. The patient will undergo at least 3 counseling sessions for treatment readiness. All base line and clinical screening is done and recorded before starting the treatment. Only nodal officer of COE is authorized to prescribe ART after approval of SACEP.

Substitute with RIFABUTIN FOR RIFAMPICIN in A.K.T. REGIMEN. After 2 weeks counsel the patient for 2ND line A.R.T.THERAPY

2—Need to initiate 2nd line A.R.T with concurrent detection of T.B.

Counsel for A.R.T and ,initiate A.K.T. with RIFABUTIN. Start A.R.T. after 2 weeks of A.K.T.

3--.Patient already on A.R.T. & then to have T.B.

Counsel &prepare for A.R.T.and initiate treatment with

A.K.T. WITH Rifabutin ON PRIORITY.

Drug interactions

Simvastatin & lovastatin should not be used with LPV/r as it increases levels of these drugs and their side effects. Pravastatin and Fluvastatin are considered to be safest for use with LPV/r. NACO provides annual checkup of fasting blood sugar& lipid profile.

Long term adherence continues to be a challenge in patients who are on ART both 1ST line & 2ND line. The most common reason for drug resistance is non-adherence to drug therapy.100% adherence is required for optimal viral suppression in these patients. Thus initial counseling of patients by doctors is the crucial step before starting 2ND line therapy.

What is SACEP?

NACO has established a State AIDS clinical expert panel (SACEP) for each center of excellence. It consists of

1) Nodal officer of COE/ART center
2) ONE more ART expert(appointed by NACO ,NOT FROM SAME CENTER)
3) Regional coordinator/joint director/consultant at SACS. There would be observers from central level, for monitoring purposes. The SACEP will follow the technical protocols laid out by NACO for selecting the patient for 2nd line ART.ART center at Govt Medical College NAGPUR has been selected for this purpose.

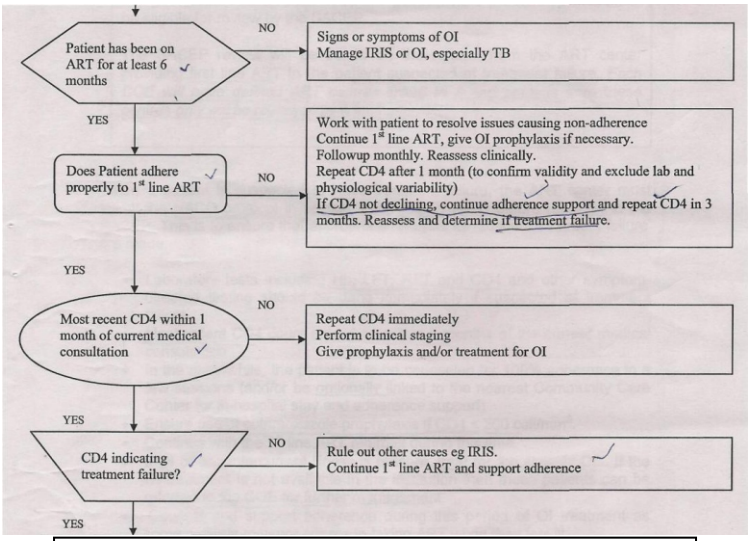
Cost of therapy

According to new NACO guidelines, only kids, widows, and the poor will get free of cost second lIne treatment as the cost is Rs. 8000 /mth as against first line which is only Rs.450/mth .Secondly it is only those who have been in Govt. ART. programme for more than 2 years would be eligible for second line treatment.

Several studies (2,3,4,) available on second line ART in HIV patients in Asia AND Africa have recently reported on the failure of immunologic criteria to appropriately identify virological ART failure.

Rewari, Bharat B.MD, Bachani, Damodar MD et al(5) also reported that for virological failure to start the second line ART it is the viral load estimation which is essential rather than CD4 count as viral load estimation may prevent shifting of many patients from first line to second line ART. Thus there is a urgent need for low cost viral load technologies to guide the detection and clinical management of treatment failure.

PROTOCOL FOR DETERMINING ART FAILURE AT ART CENTERS



Review need for O PROPHY./T/t
Reinforce adherence to1s line ART
Inform to SACEP take appt.

SACEP MANAGEMENT ACCORDING TO VIRAL LOADS

VIRAL LOAD TEST and Treatment		
VL<400COPIES/CC	VL 400-1000COPIES/CC	VL>1000COPIES/CC
CT.1ST LINE ART	CT.1ST LINE ART	VIROLOGICALLY CONFIRMED TREATMENT FAILURE. 1) START 2ND LINE ART 2) FU AT COE FOR 6 MTHS TO STABILISE, ADHERE&VL AT 6MTHS VL<400 REF BACK TO ART CENTERWITH VL>400 FU AT COE REENFORCE ADHERENCE VL AT 12 MONTHS,REVIEW BY SACEP
After SACEP approval patient is put on second line ART.		

NACO SECOND LINE REGIMEN:		
ARV drugs 2ND line	Dosage	DOSING SCHEDULE
TDF+3TC (TENOFOVIR+Lamivudine)	Fixed dose combination TDF 300mg+3TC 300mg	1-0-0
LPV/r (Lopinavir,Ritonavir	LPV 200 mg+ RITONAVIR 50mg	2-0-2
ZDV (Zidovudine)	Zidovudine 300 mg	1-0-1

SIDE EEFECTS RELATED TO NACO SECOND LINE REGIMEN		
ARV drug	**Side effect/toxicity**	**Management**
ZDV	Anemia, neutropenia of acute or slow onset, progressive over months hyperpigmentation of skin	Monitor Hb close for first one monthas per protoco
TDF	Serious s.e. liver &kidney failure Can reduce bone mineral density tests	Monitor Liver & kidney function Calcium supplements
LPV/r	Worsening of liver functions in pts. who have hepatitis Bor C	Monitor LFT IN PTS. Who already have hepatitis & on LPV
3TC	Cough, diarrhea, dizziness, headache, Burning ,tingling, pain in hands, feet, fever, skin rash vomiting, weakness	Symptomatic t/t

Laboratory monitoring of patients on 2ND line A.R.T. TABLE							
TESTS	BASE LINE	DAY 15 IfZDV+INT/t	1	3	6	12	18 24
HB,CBC	√	√	√	√	√	√	ANNUALLY
LFT	√			√	√	√	ANNUALLY
RFT	√			√	√	√	EVERY6MTHS
F.BL.SUGAR	√					√	ANNUALLY
F.LIPID PROFILE	√					√	ANNUALLY
VIRAL LOAD	√						NO MORE VL Unless indicated
CD4	√	THEN EVERY 6 MONTHLY					

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