Tel: 0800 227 700 or +27 (0)21 514 1700
Fax: 0800 600 773 or +27 (0)21 514 1744
Address: P. O. Box 38597, Howard Place,
Cape Town, South Africa, 7450
Email: afa@afadm.co.za
Website: www.aidforaids.co.za

SERVICE PROVIDER NEWSLETTER
February 2005 - Issue 10

Management of HIV - Associated Kaposi's Sarcoma (KS)

Background

- KS is a malignancy of lymphatic endothelial origin.
- Almost 100% of cases are associated with Human Herpes Virus-8 (HHV-8) also known as KS Herpes Virus (KSHV).
- KS may involve the skin, oral cavity, lymph nodes or viscera (lung, intestines and rarely other organs such as the liver and bone marrow). Lymphoedema is a potential complication.
- 80-90% of cases of visceral KS will have oral or skin involvement.
- The typical CXR appearance of pulmonary KS is a reticulonodular appearance spreading from the hilar regions bilaterally. The diagnosis is confirmed by visualizing endobronchial KS lesions on bronchoscopy (biopsy poses a high risk of haemorrhage). Pulmonary KS may be associated with intrathoracic adenopathy and/or pleural effusions which are typically bloody or serosanguinous.
- CXR is a useful screen for pulmonary KS. Faecal occult blood is a useful screen for GIT involvement. Proceed to endoscopy for definitive diagnosis.
- KS is a WHO Stage 4 defining illness, regardless of CD4.
- The incidence of KS has been dramatically reduced by HAART (92% reduction in Swiss cohort).
- Although most cases are diagnosed on the typical macroscopic appearance of skin and oral lesions certain cases should have biopsy confirmation. Atypical skin lesions should be biopsied (punch biopsy or excision biopsy) to differentiate from angiomas, dermatofibromas, etc. Nodular lesions that enlarge rapidly should be biopsied to exclude bacillary angiomatosis that is due to *Bartonella* infection.
- Lymph nodes >2cm should be biopsied to exclude TB and lymphoma.
- Atypical oral lesions should be biopsied to exclude other malignancies such as lymphoma, squamous carcinoma and salivary gland tumours.

Treatment principles

- All patients with KS should be pre-test counselled and have HIV testing done after obtaining informed consent.
- All HIV + patients with KS should be commenced on HAART regardless of CD4, as KS is an AIDS-defining illness. **This should always be the first-line therapeutic intervention.**
- Regression and resolution of mucocutaneous KS on HAART alone is well described. There are also case reports of regression of pulmonary KS lesions on HAART alone.
- HAART prolongs the time to treatment failure of KS chemotherapy.
- Co-trimoxazole prophylaxis should be commenced given that this is a Stage 4 defining illness.
- It is important to investigate for and exclude co-existent opportunistic infections (particularly TB), especially if the patient is going to receive chemotherapy, which will immunosuppress, them further.
- Treatment decisions need to be individualized and are based on: extent of disease, rate of growth of lesions, symptoms, CD4 count and general condition. Quality of life is an important factor in decision-making regarding intensity of chemotherapy and decisions as to when palliative therapy becomes appropriate.
- Local therapy is appropriate for localized skin and oral lesions and options include:
  - Intralesional chemotherapy (vinblastine)
  - Local radiotherapy
  - Liquid nitrogen cryotherapy for small lesions
  - Topical alitretinoin gel 0.1%.
- Systemic chemotherapy is preferred in the following patients:
  - > 25 skin lesions
  - Rapidly progressive disease
  - Visceral involvement with symptoms
  - Extensive oedema
  - "B"symptoms (fever, night sweats, significant constitutional symptoms)
  - Failure to respond to local therapy and HAART
- Patients who have a poor performance status and/or very low CD4 tend to tolerate chemotherapy less well. If their poor performance status is due to a factor that is remediable in the short term such as an opportunistic infection then chemotherapy should be delayed until after this has been addressed. However, if it is related to disseminated KS then obviously chemotherapy cannot be delayed. In patients with poor performance status and/or CD4<100 it may be appropriate to adopt a low intensity chemotherapy regimen for initial therapy. And in certain patients who are too ill to tolerate any chemotherapy palliative therapy alone may be more appropriate.

Prognosis

Prognosis depends on the extent of KS at diagnosis. In patients with limited disease 3 year-survival in the HAART era is 88%, but even those patients with disseminated disease have a fair medium term prognosis. Patients with pulmonary KS have a 46% 3 year-survival when treated with chemotherapy and HAART (Nasti, et al, J Clin Onc 21(15): 2876-2882).

Practice point OF THE MONTH

Drug induced hepatitis in patients on rifampicin being treated with ritonavir and saquinavir

We would like to draw your attention to the important medicine safety information document circulated recently by Roche Pharmaceuticals where drug induced hepatitis has been reported in healthy volunteers receiving rifampicin in combination with ritonavir 100mg bd and saquinavir 1000mg bd. Roche have recommended that rifampicin should not be used in patients receiving saquinavir boosted with ritonavir. It is not clear if a similar risk of hepatitis also applies to the current CDC recommendations of 400mg ritonavir/saquinavir BD. If this dose is used, liver function should be carefully monitored.

Generic Antiretrovirals (ARVs)

AfA recommends the use of generic ARVs which have been registered in SA by the MCC. Generic substitution of antiretroviral agents for patients who are stable on therapy is required - if patients or clinicians do not want to substitute, the patient has to pay the difference between the generic and the ethical agent (this is in keeping with the current AfA and broader Medscheme approach to generic substitution).

A number of doctors have expressed concern about the quality of the generic ARVs. The fact that several generic ARVs have recently been withdrawn from the market should give us confidence that the MCC is vigilant and sets high standards, rather than undermining all generic ARVs.

The following generic ARVs are currently available in SA:

Generic Name	Trade Name	SEP for an OP incl. VAT	Comments
Zidovudine	Retrovir® 300mg (GSK) **Aspen Zidovudine® 300mg** Zidovir 300mg (Cipla)	R320.45 **R240.31** R228.91	Not on MPL*.
Zidovudine	Retrovir® 100mg (GSK) **Cipla-Zidovudine® 100mg**	R214.32 **R110.12**	On MPL from 1 Mar 2005.
Zidovudine	Retrovir® S syr (GSK) **Aspen Zidovudine® syr** Zidovir®** syr (Cipla)	R83.85 **R66.78** R66.78	On MPL since 1 Dec 2004.
Lamivudine	3TC® 150mg (GSK) **Aspen Lamivudine® 150mg** Cipla-Lamivudine 150mg	R112.18 **R85.51** R102.57	On MPL from 1 Feb 2005.
Lamivudine	3TC® syr (GSK) **Aspen Lamivudine® syr** Lamivir®** syr (Cipla)	R79.62 **R62.89** R62.89	On MPL since 1 Dec 2004.
Zidovudine/ Lamivudine	Combivir® (GSK) **Aspen Lamzid®**	R365.94 **R296.38**	On MPL since 1 Nov 2004.
Stavudine	Zerit® 40mg (BMS) **Aspen Stavudine® 40mg** Stavir® 40mg (Cipla)	R46.22 **R38.30** R38.30	On MPL since 1 Feb 2004.
Stavudine	Zerit® 30mg (BMS) **Aspen Stavudine® 30mg** Stavir® 30mg (Cipla)	R46.22 **R32.49** R33.09	On MPL since 1 Feb 2004.
Stavudine	Zerit® 20mg (BMS) **Aspen Stavudine® 20mg**	R46.22 **R27.36**	On MPL since 1 Feb 2004.
Didanosine	Videx® 150mg (BMS) **Aspen Didanosine® 150mg**	R196.50 **R157.30**	On MPL from 1 Apr 2005.
Didanosine	Videx® 100mg (BMS) **Aspen Didanosine® 100mg**	R130.95 **R104.86**	On MPL from 1 Apr 2005.
Didanosine	Videx® 50mg (BMS) **Aspen Didanosine® 50mg**	R130.95 **R95.74**	On MPL from 1 Apr 2005.
Didanosine	Videx® 25mg (BMS) **Aspen Didanosine® 25mg**	R130.95 **R85.48**	On MPL from 1 Apr 2005.
Nevirapine	Viramune® 200mg (BI) **Aspen Nevirapine® 200mg** Nevimune® 200mg (Cipla)	R410.40 **R194.60** R159.60	On MPL since 1 Dec 2004.
Nevirapine	Viramune® susp (BI) **Nevimune® susp (Cipla)**	R228.00 **R101.46**	On MPL from 1 Mar 2005.

Prices as at 24 February 2005.

GSK: GlaxoSmithKline
BMS: Bristol-Myers Squibb
Cipla: Cipla Medpro
BI: Boehringer Ingelheim

The product listed first in each block is the branded product.
The products in bold are the MPL (Medicine Price List) reference products i.e. these products and any cheaper generic equivalents will be covered in full by medical schemes whih apply MPL. If a more expensive generic equivalent is used the patient will have to make a co-payment.

*Zidovudine 300mg tablets are not on MPL as none of the generic tablets are scored and you therefore can't use a generic equivalent if the dose is half a tablet bd. (This dose is sometimes used for paediatric patients.)

Lamivir® and Zidovir® are also available in a smaller pack size (100ml). The cost / ml is the same for both pack sizes and both pack sizes will therefore be paid in full.

Scheme Changes for 2005

New schemes contracted to AfA:
Protector Health

Schemes which have been discontinued:
ABI medical scheme merged into SA Breweries / Castellion medical scheme from 1 January 2005. SA Breweries / Castellion medical scheme is also contracted to AfA. Patients who were on ABI medical scheme are still manged by AfA.

Schemes which have left AfA:
Aacmed medical scheme and OmniHealth medical scheme are no longer contracted to AfA (as of 31 December 2004).

NB: Most schemes are now including the HIV related out of hospital pathology costs in the AfA benefit. There are limitations on the number of tests allowed per year. This is advantageous for patients as they shouldn't run out of benefits for HIV pathology (provided that they don't exceed the number of tests allowed per year).

FDA Public Health Advisory for Nevirapine

The FDA has recommended against initiating nevirapine as part of antiretroviral treatment in women with CD4 counts greater than 250, "unless benefits clearly outweigh risks". This recommendation is based on a higher observed risk of serious liver toxicity in females and patients with higher CD4 cell counts prior to initiation of therapy. Females have a three fold higher risk of symptomatic nevirapine liver toxicity than males, and females with CD4 counts >250 have a 12 fold higher risk of symptomatic liver tocixity than females with CD4 counts <250. Males with CD4 counts >400 have a 5 fold higher risk of symptomatic liver toxicity than males with CD4 counts <400.

See: http://www.fda.gov/cder/drug/advisory/nevirapine.htm for the full report.

Drug interaction OF THE MONTH

Rifampicin and lopinavir/ritonavir (Kaletra®)

Case Study
35year old male. 1st line ARV regimen was zidovudine, lamivudine and efavirenz. After failing this regimen ART was changed to stavudine, didanosine and lopinavir/ritonavir in Sept 04. July 04 viral load was 189 832copies/ml - 5.27logs. After approximately 6 months on the new regimen the viral load was checked. The viral load in Feb 05 was 480 699copies/ml - 5.68logs. The doctor contacted AfA and asked if a resistance test would be funded. Compliance was checked. The patient was submitting claims for his ART every month and when we spoke to him he assured us that he was taking all medicines correctly. On further investigation we discovered that he had started TB therapy (including rifampicin) in Jan 05. Rifampicin is a potent inducer of lopinavir metabolism. Coadministration of rifampicin and Kaletra® is contraindicated as it will result in large decreases in lopinavir concentrations which will significantly decrease the lopinavir therapeutic effect. The doctor was advised to add ritonavir 300mg bd to the regimen until 1 week after stopping rifampicin. Using an increased dose of ritonavir allows concurrent use of rifampicin and Kaletra®.