Republic of Zambia

Ministry of Health

NON-COMMUNICABLE DISEASES GUIDELINES

CANCER

04

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CANCER

Volume 4

CHAPTER FOUR

CANCER

DEFINITION:

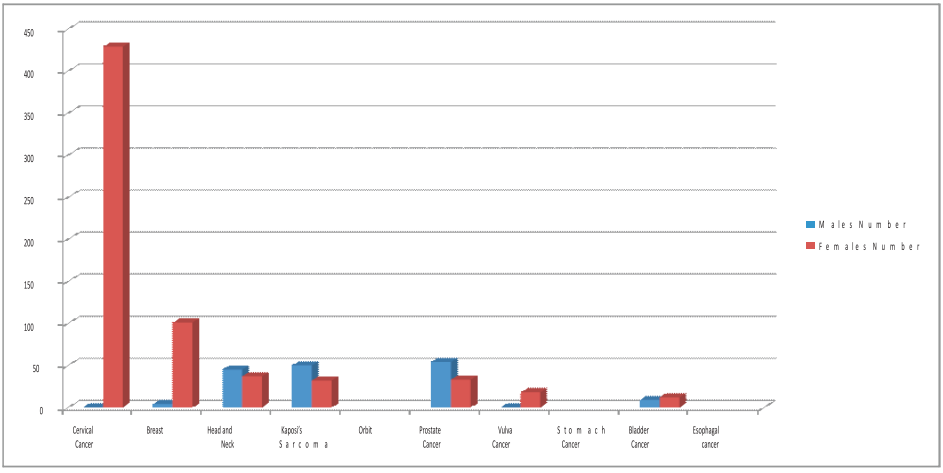
Cancer is a group of disorders characterised by uncontrolled, abnormal cell division that arises from one cell in any part of the human body and has the potential of spreading to nearby tissues and distant organs.

EPIDEMIOLOGY:

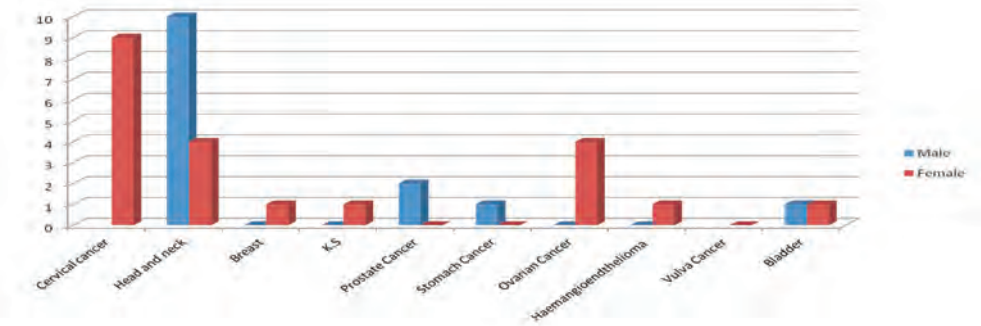
The cancer burden worldwide is expected to increase from 11million cases in the 2000 to 22million cases by the year 2020, with 70% of these cases occurring in Africa. Every year more people die from cancer than HIV/AIDS, TB, malaria combined. In 2005 cancer killed 7.6 million people. This number by 2015 will increase by 9million and 11.5 million by 2030 if nothing is done. More than 30% of these cancer deaths are preventable and a further 40% are curable for as long as they are detected early.

In Zambia today, the cancer burden is increasing and has two peaks at presentation in Zambian adults. The first is seen in those ages between 25-45years and the second is in those over 50years. The first peak affects the reproductive age group and is the same age that is highly affected by HIV and other virus like human papilloma virus, hepatitis b and c, ebstein bar virus, human herpes virus type 8, bacteria like *helicobacter pylori*, and parasites like schistosoma. The cancer registry report on Cancer incidence 2009

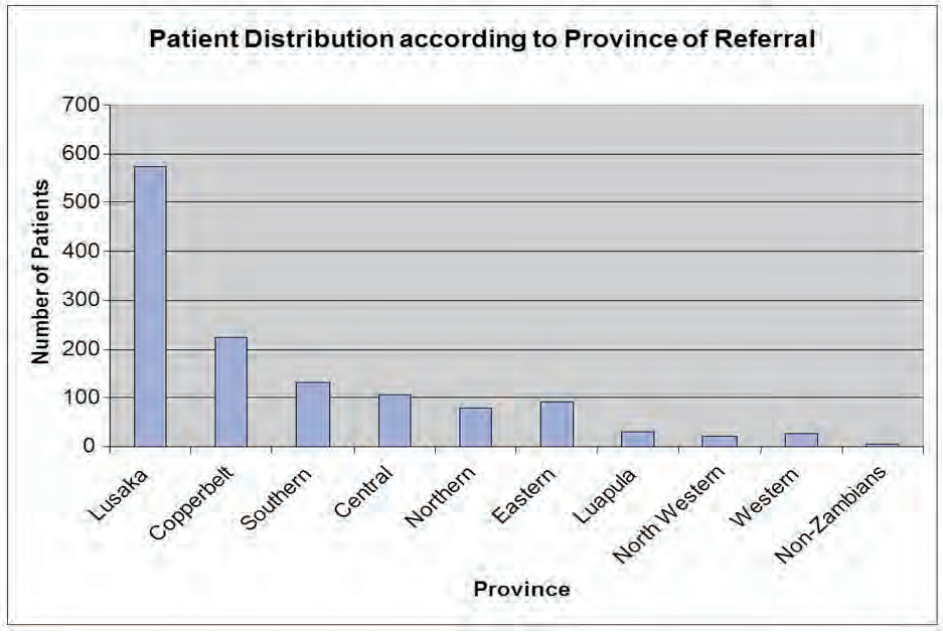
Cancer Mortality 2009



The cancer cases referred from provinces are as shown in the table below



Western, Northwestern and Luapula Provinces refer the least number of cases.



The commonest cancers in adults for both sexes put together are shown in the table below.

Type of cancer	2007	%	Type of cancer	2008	%
cervical	238	33	Cervical	304	25.23
Head and neck	94	13.09	Breast	205	17.02
breast	93	12.93	Head and neck	70	5.81
lymphoma	35	4.86	SCC	58	4.82
SCC	35	4.86	GIT	55	4.57
KS	30	4.17	KS	51	4.24
Prostate	25	3.47	Lymphoma	42	3.48
GIT	23	5.19	Prostate	34	2.82
Sarcoma	16	2.22	Bladder	17	1.41
Bladder	9	1.25	Sarcoma	9	0.74
Melanoma	6	0.83	Melanoma	5	0.41
Wilm's	3	0.41	Vulva	4	0.33
Lung	2	0.27	Lung	2	0.16
Vulva	2	0.27	Myeloma	1	0.08
Myeloma	1	0.13	Others	347	28.82
Others	107	14.87			

60-70% of cancers in Zambia present at stage III and IV. This is as a result of noo National Cancer Control Programmes. However, in Lusaka Province cervical and breast cancer screening started in 2006 and it has been demonstrated that patients referred from the screening programme present at stage I and II to the hospital. The Ministry of Health has embarked on a programme of scaling up cancer prevention and early detection.

CANCER RISK FACTORS:

In this document only risk factor for those cancers that are preventable in Zambia shall be discussed:

Cervical cancer:

- Human Papiloma Virus infection
- Immunosuppression
- Smoking
- Diet with less fibre and high fat content
- Multiparity
- Young age at first sexual intercourse
- Family history
- Age >45years

Breast cancer:

- Age >45 years
- Early menarche and late menopause
- Nulliparity
- Never breastfed
- Personal history of breast cancer
- Family history of breast cancer
- Exposure to ionising radiation
- Obesity
- Long term use of hormone replacement therapy
- Smoking
- Diet with less fibre and high fat content
- Physical inactivity

Prostate cancer:

- Age >45 in black
- Ethnicity and race; Afro American were more prone than the Caucasian
- Diet
- Obesity
- Physical inactivity
- Family history

Colorectal cancer:

- Gender; more common in women than in men
- Polyps in the colon or the rectum (familial adenomatous polipossis (FAP)syndrome)
- Chronic inflammation of the colon or recurrence
- Family history of ovarian, breast and uterine cancer
- Diabetes
- Diet
- Alcohol
- Smoking
- Physical inactivity
- Obesity

Lung cancer:

- Passive and active smoking
- Exposure to radon gas
- Exposure to asbestos and other chemicals
- Family history
- Excessive alcohol use

Kaposis Sarcoma:

- AIDS related conditions
- Homosexual or bisexual men
- Multiple sexual partners
- Exposure to STIs (HHV8)

PREVENTION:

Prevention is defined as the reduction of cancer mortality via reduction in the incidence of cancer. This can be accomplished by taking a holistic approach targeting all levels of prevention i.e. primary and secondary as well making facilities for treatment of the cases diagnosed early.

- Primary Prevention: these are interventions that are applied in the community to prevent people from disease before they are exposed to risk factors.
- Secondary prevention: these are interventions applied in communities that have already been exposed to the risk factor but have not yet developed the disease.

Primary Prevention

- Community Mobilisation and Education
- Increasing avoidance of risk factors listed above, especially tobacco and alcohol use.
- Good sexual hygiene and safe sexual behavior.
- Eating proper diets
- Regular exercise
- Avoid being overweight
- Avoiding a carcinogen or altering its metabolism and controlling occupational hazards.
- Pursuing lifestyles or dietary practices that modify cancer causing factors or genetic predispositions.
- Medical interventions such as vaccination against Human Papilloma Virus (HPV) and Hepatitis B virus (HBV)

Primary prevention are the most cost effective interventions for cancer control.

Secondary Prevention

Secondary prevention aims at diagnosing the condition at a very early, preferably asymptomatic stage and effectively treating it. This can be achieved through:

- Community Education and Awareness
- Screening for cervical, breast and prostate cancers
- Screening of other cancers

CERVICAL CANCER

Primary prevention:

- Immunisation of all pre-pubertal girls (7-12 years) who have not yet been exposed to sexual intercourse
- Community sensitisation
- IEC material distribution
- Training of health care workers on counselling on cervical cancer

Secondary prevention:

- Community sensitisation and education
- Screening for pre-malignant lesion at the cervix using either visual inspection with acetic acid and immediate cryotherapy or pap smear
- Making available facilities for LEEP and biopsy

BREAST CANCER

Primary prevention:

- Education and training of communities and health care workers
- IEC materials on self breast examination

Secondary prevention:

- Monthly self breast examination
- Yearly clinical breast examination
- Yearly mammography for women ≥40years
- Make available facility for breast core or fine needle aspiration biopsy

PROSTATE CANCER

Primary prevention:

- Education and training of communities and health care workers
- IEC materials on digital rectal examination for all men above 45years

Secondary prevention:

- Yearly PSA for all men 45years and above
- Yearly digital rectal examination
- Optional trans-rectal ultrasound
- Make available facility for prostate core biopsy

SCREENING FOR OTHER CANCERS

Oral Cancer:

Oral cancer and its precancerous lesions, including leukoplakia, can be readily detected by visual inspection of the oral cavity not only by trained heath workers and doctors, but to a large extent by the subject himself.

1. **Self-Examination of oral cavity:**
   This is important for detecting oral lesions at an early stage. All habitual tobacco users should do it once a month. The following procedure should be followed:
   Rinse the mouth with water and stand before a mirror in adequate light.
   Look in the mirror for any abnormal white or red patch, ulcer or roughened area, or granular area or swelling in the mouth.
   If any such area is seen, the suspicious area should be felt with the fingers (normal oral mucosal is soft and pink).

Consult a doctor if any abnormal area is found

2. **Examination by a Health Professional:**
   Health care providers should utilize every opportunity to examine the oral cavities of tobacco users. All parts of the oral cavity should be examined; oral cavity includes lip, anterior 2/3 of tongue, floor of mouth, buccal mucosa, gingival mucosa, hard palate and retromolar area.

   1. Population Screening:
   2. Population screening for oral cancer results in the diagnosis of large numbers of oral pre-cancers and early stage tumours.

Colorectal Cancer:

- Faecal occult blood test (FOBT) is a very cost-effective and quite applicable screening method available, but its specificity and sensitivity are limited.
- Colonoscopy and biopsy provides the definitive method for detecting colorectal cancer and its precursor lesions, e.g., polyps.

TUMOUR MARKERS:

Certain cancers release biological products into the circulation, which can be measured for increasing the level of diagnostic suspicion. The common ones are:

- *Alpha Feto protein (α - FP)*: This is increased in Liver cancer and certain tumours of testis and ovary. It is also increased in cirrhosis and hepatitis.

- *Beta Human Chorionic Gonadotrophin (β - hCG)*: Increased in choriocarcinoma and testicular tumours. Also increased in hypogonadism and hydatiform mole.
- *Carcino Embroyonic Antigen (CEA)*: Increased in colorectal, breast and stomach cancers and Cholangiocarcinoma. Also raised in liver disease and among smokers.
- *CA - 125*: Raised in epithelial ovarian cancers. Also raised during pregnancy, menstruation, endometriosis, ascites and pleural effusion.

Tertiary Prevention

Tertiary prevention is also quite important in cancers. It consists of proper treatment of diseases. The available options are Surgery, Radiotherapy and Chemotherapy. It also involves specialized issues as palliative care, terminal care and pain relief and reassurance / advise to the patient and family.

CERVICAL CANCER TREATMENT GUIDELINES

Definition: This is a cancer of the cervix.

1. Symptoms and Signs

- Abnormal Vagina bleeding
- Abnormal vaginal discharge
- Lower abdominal pain
- Backache
- Dyspareunia
- Nodule, ulcer or fungating growth
- Complications
- Anaemia
- Sciatic pain
- Incontinence of urine or faeces
- Sepsis
- Uraemia

2. Diagnosis

Diagnosis	1st level	2nd level	3rd level
History and physical findings	E	E	E
CXR	E	E	E
FBC,U/Es, LFTs, HIV, CD4	D	E	E
Cervical biopsy	D	E	E
IVP	D	E	E
EUA, Cystoscopy, Proctoscopy	D	D	D
Screening	E	E	E
Abdominal ultrasound (to rule out abdominal Metastasis and hydronephrosis	D	E	E

Key: E - Essential, D - Desirable

3. Treatment

This depends on the stage of the cancer
Non-invasive lesions can be managed by

- Electrocautery
- Cryotherapy
- Laser therapy
- Surgery for stage IB1 or less. Note surgery **should not** be done in cases with stage IB2 and above.

Chemoradiation for stages IB2 IVA
Metastatic disease: palliative treatment depends on presentation. Need for local symptoms control with radiotherapy for bleeding and pain control. The first-line combination chemotherapy include:

- carboplatin/paclitaxel
- cisplatin/paclitaxel
- cisplatin/topotecan

The first-line single agent therapy includes:

- cisplatin
- carboplatin
- paclitaxel

Some patients may require best supportive care
There is no role of chemotherapy alone in stage IB2 IVA and therefore all these patients need to be referred to the Cancer Diseases Hospital via UTH for chemoradiotherapy.

Radiotherapy 2Gy per fraction to 46 50Gy of External beam radiation therapy (EBRT) with Brachytherapy to a total of 75 85GY to point A. chemotherapy is given concurrent with the radiation using Cisplatinum 80mg/m2 iv 3 weekly.
Adjuvant radiotherapy: after radical hysterectomy depend on surgical findings and disease stage.

Indications include:

- Cervical tumour diameter > 4cm
- Lymphovascular invasion (LVI)
- Positive surgical margins
- Treatment involves chemoradiotherapy.

FOLLOW-UP AFTER PRIMARY THERAPY

Eighty to 90% of recurrences occur in the first 2 years following treatment. After treatment, periodic follow-up testing and examination are recommended. This

usually involves a physical examination and Pap smear. The general follow-up schedule is as follows:

- 3 to 4 monthly for the first 2 years.
- 6 monthly from year 3 to 5.
- Annually after year 5.

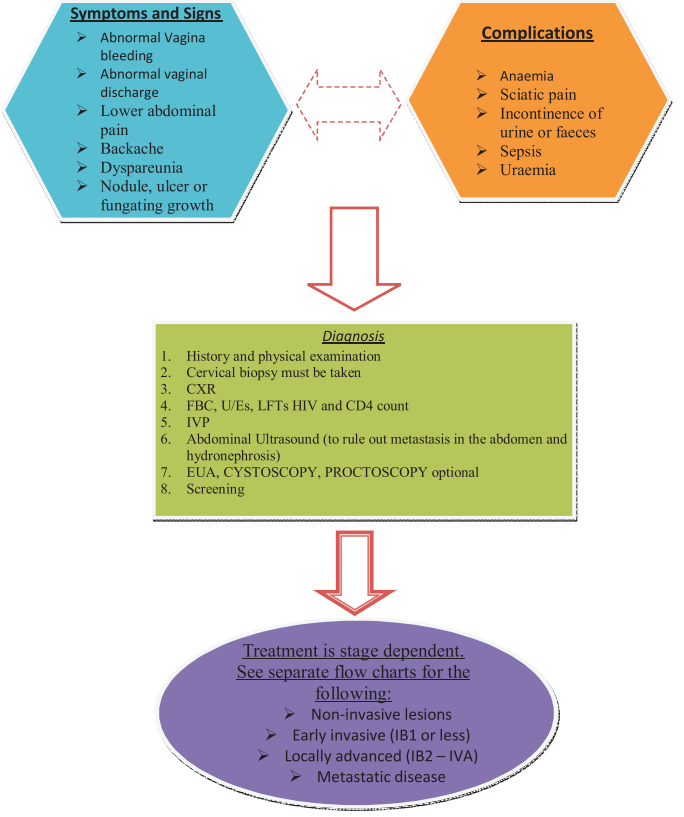
Post-radiotherapy follow-up is as follows:

- The first examination for response is at 6 weeks.
- Pap smear at 6 months
- Then 6 monthly to yearly pap smears
- Use of vaginal dilators and lubricants for women who wish to remain sexually active.

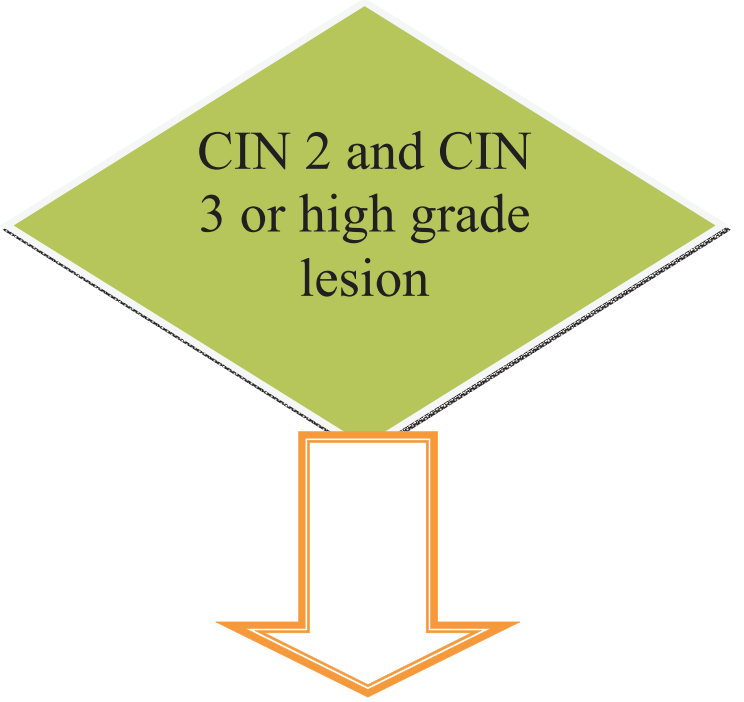
Hormone replacement post-radiotherapy treat:

- Kliogest or conjugase I tablet OD for women less than 50 years old
- Premarine cream those 50 years and above.

CERVICAL CANCER TREATMENT GUIDELINES (flow chart)

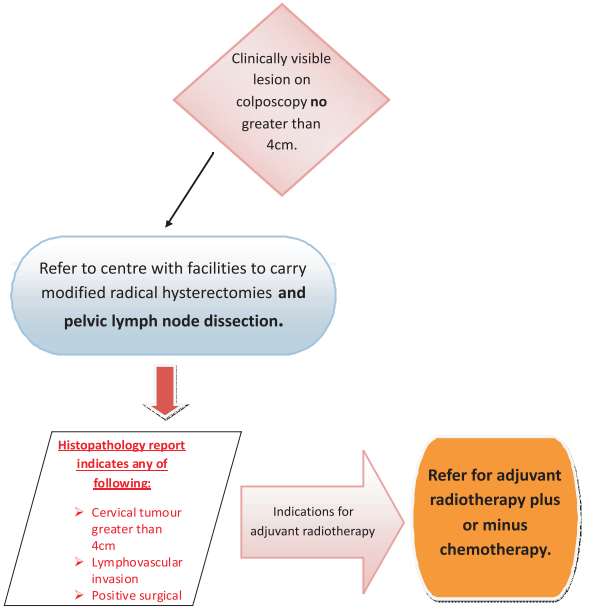


Referral and follow-up criteria for non-invasive cervical lesions

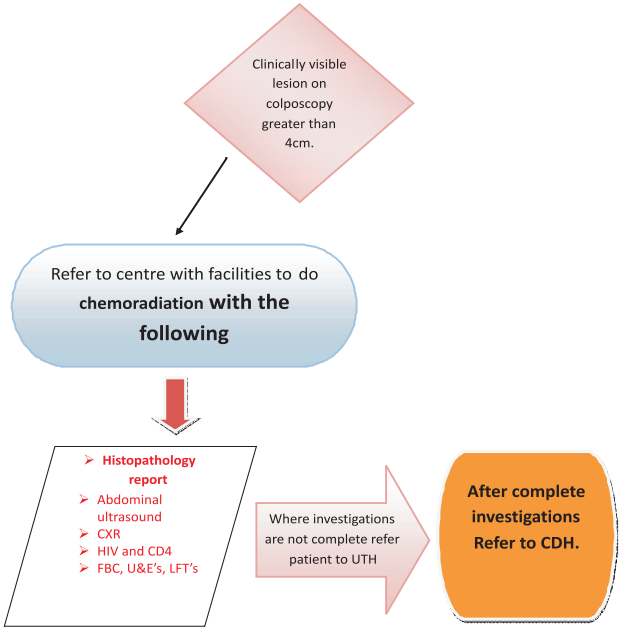


1. Refer to centres with by electrocautery, cryotherapy, or laser therapy.
2. For advanced lesions refer for conisation or LEEP (or biopsy). If pathology report indicates presence of lesion at margin, repeat biopsy procedure.

Referral and follow-up criteria for early invasive (stage IA - B1) cervical lesions



Referral and Treatment of patients with Stage IBii - IVA Cervical Cancer



Referral and follow-up criteria for metastatic cervical cancer (stage IVB).

Unequivocal clinical evidence of distant metastases, e.g. cannon balls on chest x-ray

Performance status WHO or ECOG 0 – 2

(zero to two).

- Need for local symptoms control with radiotherapy for bleeding and pain control.
- Palliative chemotherapy (see text).

Performance status WHO or ECOG 3 and above.

FOLLOW-UP AFTER PRIMARY THERAPY

The general follow-up schedule is as follows:

- 3 to 4 monthly for the first 2 years.
- 6 monthly from year 3 to 5.

Post-radiotherapy follow-up is as follows:

- The first examination for response is at 6 weeks.
- Pap smear at 6 months
- Then 6 monthly to yearly pap smears
- Use of vaginal dilators and lubricants for women who wish to remain sexuallv active.

Hormone replacement post-radiotherapy treat:

- Kliogest or conjugase 1tablet OD for women less than 50 years old

BREAST CANCER TREATMENT GUIDELINES

Assessment for Breast Cancer

The general approach to evaluation of breast cancer has become formalized as triple assessment:

- clinical examination,
- imaging (usually mammography and/or ultrasonography)
- and needle biopsy

However, this should always be performed as part of a more general assessment beginning with clinical history.

Symptoms and signs

- Breast lump
- Skin thickening or alteration
- Dimpling of skin (Peau d 'orange)
- Nipple inversion or nipple abnormalities (e.g. ulceration, retraction)
- Unilateral nipple discharge
- Dilated veins
- Axillary lump

Signs & symptoms of metastatic disease

- Breathing difficulties
- Bone pain
- Symptoms of hypercalcemia
- Abdominal distention
- Jaundice
- Localizing neurologic signs
- Altered cognitive function

Diagnosis

History and physical examination

The following features in a breast lump should raise concern:

- Hardness
- Irregularity
- Focal nodularity
- Asymmetry with the other breast
- Fixation to skin or muscle
- Bilateral mammogram

Biopsy preferably a core biopsy

Laboratory studies FBC, LFTs, U&Es
Pathology review tumour grade, margins, receptor status
Radiographic studies dependant on basis of history, physical findings and screening blood tests:
CT scan / MRI
Bone scan
Chest x-ray
Cardiac function (ECHO) for left sided breast cancer and those on anthracycline.

Treatment

1. Surgery

Surgery is considered primary treatment for breast cancer, as many patients with early-stage disease are cured with surgery alone. The goals of breast cancer surgery include complete resection of the primary tumor with negative margins to reduce the risk of local recurrences, and pathologic staging of the tumour and axillary lymph nodes for providing necessary prognostic information. Several different types of operations are available for the treatment of breast cancer.

Adjuvant treatment for breast cancer involves radiation therapy and a variety of chemotherapeutic and biologic agents.

Dependent on stage, receptor status, age as per details below.
Early Breast cancer

Breast Conserving Treatment:- wide local excision with axillary dissection, then Adjuvant Radiation therapy and/or chemotherapy

Modified Radical Mastectomy with an axillary dissection. Adjuvant Chemotherapy and radiotherapy will depend on the histopathological findings (stage).

Locally Advanced Breast Cancer - must be treated with all modalities (Surgery, Chemotherapy and Radiation therapy)

Metastatic Breast Cancer Chemotherapy and where indicated hormonal therapy

2. Chemotherapy Regimens

Adjuvant therapy has been estimated to be responsible for 35-72% of the reduction in mortality rate. Adjuvant treatment of breast cancer is designed to treat micrometastatic disease, or breast cancer cells that have escaped the breast

and regional lymph nodes but which have not yet had an established identifiable metastasis. Treatment is aimed at reducing the risk of future recurrence, thereby reducing breast cancer-related morbidity and mortality. Various chemotherapeutic agents and combinations are available

- AC - Doxorubicin 60mg/m^2 IV D1and cyclophosphamide 600mg/m^2 IV D1 repeat every 21 days for 4 cycles OR
- CAF - Oral cyclophosphamide 100mg/m^2 D1 - 14, Doxorubicin 30mg/m^2 IV D1 and D8, and 5 Fluorouracil 500mg/m^2 IV D1 and D8. Repeat every 28 days for 6 cycles OR
- FAC - 5 Fluorouracil 500mg/m^2 IV D1 &8, Doxorubicin 50mg/m^2 IV D1, and cyclophosphamide 500mg/m^2 IV D1. Repeat every 21 days for 6 cycles OR
- CMF Cyclophosphamide 100mg/m^2 PO D1 - 14, Methotrexate 40mg/m^2 IV D1 & 8, and 5 Fluorouracil 600mg/m^2 IV D1 & 8 every 28 days for 6 cycles
- TAC - Docetaxel 75mg/m^2 D1 IV, Doxorubicin 50mg/m^2 IV D1, and cyclophosphamide 500mg/m^2 D1 IV every 21 days for 6 cycles.

3. Radiotherapy

Usual dose in the curative setting is 2Gy per fraction to 50Gy with a boost of 2Gy per fraction to 12 - 16Gy. Radiotherapy can also be used in treatment of painful local bone metastasis, spinal cord compression, and brain metastasis and for local disease on the chest wall, etc.

Breast Cancer Screening

Early detection remains the primary defense available to patients in preventing the development of life-threatening breast cancer. Breast tumors that are smaller or nonpalpable are more treatable when detected and thus have a more favorable prognosis.

4. Screening

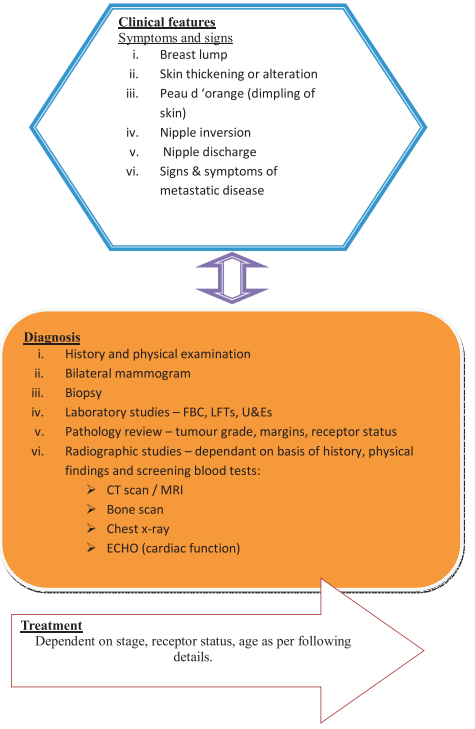
Screening modalities for breast cancer include

- breast self-examination
- clinical breast examination
- Mammography
- Ultrasonography
- Magnetic resonance imaging.

TABLE 1: Breast Cancer

Resources	Facility level			
	Community	Level 1	Level 2	Level 3
Awareness of symptoms	E	E	E	E
Breast examination skills	E	E	E	E
Full clinical assessment	D	E	E	E
Facilities for mammogram	I	I	E	E
Ultrasound	I	I	E	E
Biopsy facilities	I	I	E	E
Histopathology service	I	I	D	E
CT Scan facilities	I	I	D	E
MRI facilities	I	I	D	E
Skills and equipment for surgery	I	I	D	E
Skills and equipment for chemotherapy	I	I	D	E
Skills and equipment for radiotherapy	I	I	D	E
Skills and equipment for managing metastatic disease	I	I	D	E

BREAST CANCER TREATMENT GUIDELINES (flow chart version)

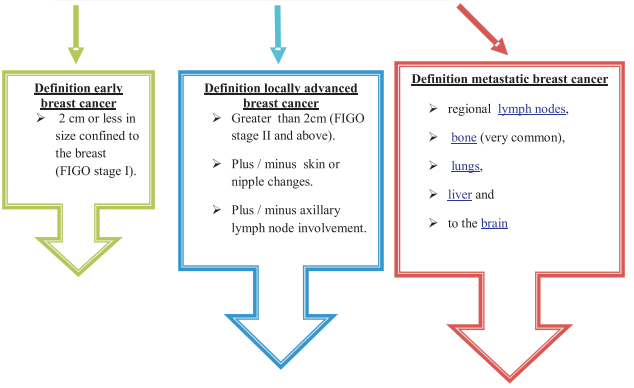


TREATMENT

i) Early Breast cancer
- Breast Conserving Treatment:- wide local excision with axillary dissection, then Adjuvant Radiation therapy and/or chemotherapy
- Modified Radical Mastectomy with an axillary dissection. Adjuvant Chemotherapy and radiotherapy will depend on the histopathological findings (stage).

ii) Locally Advanced Breast Cancer - must be treated with all modalities (Surgery, Chemotherapy and Radiation therapy)

iii) Metastatic Breast Cancer – Chemotherapy and where indicated hormonal therapy



1. **Chemotherapy**
   - AC – Doxorubicin 60mg/m^2 IV D1and cyclophosphamide 600mg/m^2 IV D1 repeat every 21 days for 4 cycles OR
   - CAF – Oral cyclophosphamide 100mg/m^2 D1 – 14, Doxorubicin 30mg/m^2 IV D1 and D8, and 5 Fluorouracil 500mg/m^2 IV D1 and D8. Repeat every 28 days for 6 cycles OR
   - FAC – 5 Fluorouracil 500mg/m^2 IV D1 &8, Doxorubicin 50mg/m^2 IV D1, and cyclophosphamide 500mg/m^2 IV D1. Repeat every 21 days for 6 cycles OR
   - CMF Cyclophosphamide 100mg/m2 PO D1 – 14, Methotrexate 40mg/m^2 IV D1 & 8, and 5 Fluorouracil 600mg/m^2 IV D1 & 8 every 28 days for 6 cycles
   - TAC – Docetaxel 75mg/m^2 D1 IV, Doxorubicin 50mg/m^2 IV D1, and cyclophosphamide 500mg/m^2 D1 IV every 21 days for 6 cycles.

2. **Radiotherapy** – usual dose in the curative setting is 2Gy per fraction to 50Gy with a boost of 2Gy per fraction to 12 – 16Gy. Radiotherapy can also be used in treatment of painful local bone metastasis, spinal cord compression, brain metastasis and for local disease on the chest wall, etc.

Follow up
- First two years quarterly (3-4 months)
- Next three years every six months
- After years, once yearly
- The patient can be followed up at the local clinic and each visit history and physical examination should be done.
- Do yearly mammography
- Maintain on tamoxifen

PROSTATE CANCER TREATMENT GUIDELINES

Signs and symptoms

A. Local disease

Asymptomatic or lower urinary tract symptoms similar to those of benign prostatic hypertrophy (BPH) e.g.

- Urinary frequency
- Decreased urine stream
- Urinary urgency
- Haematuria.

B. Advanced/metastatic disease

- Weight loss and loss of appetite
- Anaemia
- Bone marrow suppression
- Bone pain, with or without pathologic fracture
- Spinal cord compression
- Lower extremity pain and edema due to obstruction of venous and lymphatic tributaries by nodal metastasis
- Uremic symptoms can occur from ureteric obstruction caused by local prostate growth or retroperitoneal adenopathy secondary to nodal metastasis.

Diagnosis

- Digital rectal exam (DRE)- An irregular firm prostate or nodule is typical, but many cancers are found in prostates that feel normal. Pay careful attention to the prostate consistency, regard nodules or changes in the texture or the level of asymmetry with a high index of suspicion.
- Abnormal PSA (> 4ng per ml) The upper limit of normal for PSA is 4 ng/mL. With a PSA level of 4-10 ng/mL, the likelihood of prostate cancer is about 25%; with a level above 10 ng/mL, the likelihood is over 50%.
- Biopsy
- FBC, LFTs, U&Es
- Radio-Isotope bone scan

Treatment

Dependent on stage, age, Gleason score and PSA level.

For treatment purposes, four categories are recognised.

Table 1 Risk stratification for men with localised prostate cancer

Risk	PSA	Gleason Score	Clinical Stage
Low Risk	< 10 ng/ml	6	T1-T2a
Intermediate Risk	10–20 ng/ml	7	T2b-T2c
High Risk	> 20 ng/ml	8-10	T3-T4

Low risk
T stage up to T2b, PSA up to 10 ng/ml, Gleason score up to 6

Four options of treatment in this group
- Curative Radiotherapy,
- Brachytherapy,
- Radical Prostatectomy, and
- Active Surveillance.

Neo adjuvant Androgen deprivation.

Intermediate risk

T stage T2c, PSA 10 20 ng/ml, Gleason score 7

Curative Radiotherapy with neoadjuvant androgen deprivation for 3 months prior to radiotherapy. Some patients may require a transurethral resection of the prostate to relieve symptoms of urinary retention

High risk
T stage above T2c, PSA > 20ng/ml, Gleason score 8 to 10
Radiotherapy to whole pelvis plus adjuvant androgen deprivation for a period of 2 3 years. Some patients may require a transurethral resection of the prostate

Metastatic disease

Options include
- Surgical castration (Bilateral Subcapsular Orchidectomy) and some patients may require a transurethral resection of the prostate.
- Medical castration with LHRH agonists Goseriline plus antiandrogen given two weeks before Goseriline is commenced.

Antiandrogens:- Cyproterone acetate 50 100mg TDS po daily for 2 3 years.
Chemotherapy with Docetaxel 75mg/m2 IV repeat 21 days for 6 cycles with or without estramustine or prednisolone, in those patients who have failed after adequate androgen deprivation therapy.

Radiotherapy to treat painful bony metastasis including spinal cord compression.

Follow Up

- Quarterly for the first two years
- Twice yearly for three years
- Yearly after five years

But for stage 4 cancer with bone metastasis see monthly for zolidronic acid
At each visit take history and do physical examination and PSA every three months
Other investigations will depend on the history and physical examination findings

Prostate Cancer Screening
DRE and PSA evaluation are the 2 components used in prostate cancer screening.

TABLE 2: Prostate Cance

Resources	Facility level			
	Community	Level 1	Level 2	Level 3
Awareness of symptoms	E	E	E	E
Clinical Assessment	I	E	E	E
Digital Rectal Examination	I	I	E	E
PSA	I	I	E	E
Ultrasound	I	I	E	E
Biopsy facilities	I	I	E	E
Histopathology service	I	I	D	E
CT Scan facilities	I	I	D	E
MRI facilities	I	I	D	E
Skills and equipment for surgery	I	I	D	E
Skills and equipment for chemotherapy	I	I	D	E
Skills and equipment for radiotherapy	I	I	D	E
Skills and equipment for managing metastatic disease	I	I	D	E

Clinical features

Signs and symptoms

i. Asymptomatic or lower urinary tract symptoms similar to those of benign prostatic hypertrophy (BPH).
ii. Haematuria.
iii. Metastatic symptoms including bone pain, weight loss and spinal cord compression.

Diagnosis

i. Abnormal PSA (> 4ng per ml)
ii. Digital rectal exam (DRE)
iii. Biopsy
iv. FBC, LFTs, U&Es
v. Bone scan

Treatment

Dependent on stage, age, Gleason score and PSA level. For treatment purposes, **four** categories are recognised.

Low risk

T stage up to T2b, PSA up to 10 ng/ml, Gleason score up to 6

Intermediate risk

T stage T2c, PSA 10 – 20 ng/ml, Gleason score 7

High risk

T stage above T2c, PSA > 20ng/ml, Gleason score 8 to 10

Metastatic disease

Favourable risk group → Four options of treatment in this group

- Curative Radiotherapy,
- Brachytherapy,
- Radical prostatectomy, and
- Active Surveillance.

No adjuvant androgen deprivation.

Intermediate risk group

- Curative Radiotherapy with neoadjuvant androgen deprivation for 3 months prior to radiotherapy. Some patients may require a transurethral resection of the prostate to relieve symptoms of urinary retention.

High risk group but still organ confined

- Radiotherapy to whole pelvis plus adjuvant androgen deprivation for a period of 2 – 3 years. Some patients may require a transurethral resection of the prostate.

Metastatic disease:- options include

1) Surgical castration (Bilateral Subcapsular Orchidectomy) and some patients may require a transurethral resection of the prostate.
2) Medical castration with LHRH agonists Goseriline plus antiandrogen given two weeks before Goseriline is commenced.
3) Antiandrogens:- Cyproterone acetate 50 –100mg TDS po daily for 2 – 3 years.
4) Chemotherapy with Docetaxel 75mg/m^2 IV repeat 21 days for 6 cycles with or without estramustine or prednisolone, in those patients who have failed after adequate androgen deprivation therapy.
5) Radiotherapy to treat painful bony metastasis including spinal cord compression.

LYMPHOMAS

Definition

Lymphomas are malignant tumors of the lymphoreticular system and are classified into Hodgkin's disease and non-Hodgkin's lymphoma.

1. Hodgkin's Disease (HD)

The lymphoid tissue on biopsy shows malignant lymphoid cells with Reed - Sternberg cells.

Classification

- Nodular Lymphocyte predominant HD
- Classic HD
- Nodular Sclerosing
- Mixed Cellularity
- Lymphocyte depleted
- Lymphocyte rich

Symptoms and Signs

- Fever, weight loss, and night sweats
- Loss of appetite
- Pruritis
- Pallor
- Pain in the infiltrated tissue (Alcohol induced)
- Enlarged lymph nodes
- Hepatosplenomegaly
- Weight loss.

Diagnosis

- History and physical examination
- Excision biopsy
- FBC, ESR, LDH, LFTs, U/Es
- CXR
- Abdominal Ultrasound
- CT chest abdomen and Pelvis
- HIV and CD4 count
- For advanced stage disease bone marrow aspiration and trephine

Treatment

The choice of treatment is determined by the stage of the disease. It consists a combination of radiotherapy and chemotherapy

Stage I & II 4 cycles of chemotherapy plus involved field radiation therapy
Stage III & IV 6 8 cycles of combination chemotherapy plus radiotherapy for residual localized disease.

Chemotherapy

ABVD regimen
- Doxorubicin 25mg/m2 D1 & 15 IV
- Bleomycin 10 units/m2 D1 & 15 IV
- Vinblastine 6mg/m2 D1 & 15 IV
- Darcabazine 375mg/m2 D1 & 15 IV

Repeat every 28 days

MOPP regimen
- Mechlorethamine 6mg/m2 IV
- Vincristine 1 1.4mg/m2 IV D1 & 8
- Procarbazine 100mg/m2 orally from D1 14
- Prednisolone 40mg/m2 orally from D1 14

Repeat cycle every 28 days

NB: ABVD is the standard chemotherapy regimen and must be used as first line.

2. Non-Hodgkin's Lymphoma (NHL)

This is heterogeneous group of lymphoreticular malignancies. These lymphomas may be associated with HIV/AIDS.

Symptoms and signs

*See under Hodgkin's disease.

Classification
- Low grade
- Aggressive
- Highly Aggressive

Diagnosis

As for Hodgkin's Lymphoma
HIV and CD4 count
Do immunohistochemistry and flow cytometry where possible
Lumbar puncture for the highly aggressive

Treatment
- Low grade Stage I & II - curative radiotherapy or watchful waiting, if they are HIV negative.

- Low grade Stage III & IV watchful waiting or with single or combination chemotherapy and radiotherapy

Single agents
- Fludarabine 25mg/m2 IV D1-5 for every 28 days OR
- Chlorambucil 2 4 mg orally daily or 30 60mg orally every 2 weeks

Combination chemotherapy
- CVP
- CHOP

Aggressive Disease
- Stage I & II 3 cycles CHOP chemotherapy chemotherapy plus consolidation radiotherapy to 30 36Gy
- Stage III & IV CHOP chemotherapy 6 8 cycles and radiotherapy to local residual disease

Regimens

CHOP
- Cyclophosphamide 750mg/m2 D1 IV
- Doxorubicin 50mg/m2 D1 IV
- Vincristine 1.4mg/m2 D1 IV (maximum of 2mg)
- Prednisolone 100mg PO D1 5

Repeat every 21 days

CVP
- Cyclophosphamide 400 600mg/m2 D1 IV
- Vincristine 1.4mg/m2 D1 IV (maximum of 2mg)
- Prednisolone 100mg PO D1 5

Repeat every 21 days.

Highly Aggressive NHL

Burkitt's Lymphoma

Definition

This is a highly aggressive NHL, which presents mainly in children, with a jaw swelling, abdominal mass, ovarian mass and CNS involvement. It is discussed here as it is an AIDS defining disease whose presentation is not restricted to the paediatric age group.

Diagnosis

Diagnosis	1st level	2nd level	3rd level
History and physical examination	E	E	E
FBC+ESR, LFTs,U/Es, LDH	E	E	E
CXR	E	E	E
CT scan (abdomen and pelvis)	D	D	E
HIV, CD4	E	E	E
CSF examination done at first treatment	D	D	E
Biopsy of tumour plus lymph node	D	E	E
Bone marrow aspiration and/or trephine biopsy	D	E	E

Key: D Desirable, E Essential

Treatment

This is associated with tumour lysis syndrome, so IV pre-hydration and allopurinol must be given before starting chemotherapy

Regimen

Patients with localised disease receive 3 cycles of CODOX-M.
Patients with multiple site involvement are treated with CODOX-M alternating with IVAC and intrathecal therapy for 4 cycles each.

CODOX-M and CODOX-M alternating with IVAC

CODOX-M

- Cyclophosphamide 800mg/m2 D1 and 200mg/m2 D2-5 IV
- Vincristine 1.5mg/m2 D1 IV (max 2mg)
- Doxorubicin 40mg/m2 D1 & 8 IV
- Methotrexate 1.2g/m2 continuous IV infusion on D10, then 240mg/m2 IV each hour over 23hrs
- Folinic Acid 192mg/m2 IV D11 starting from the 12th hour of methotrexate infusion, then 12mg/m2 IV every 6hrs for next 48hrs
- G-CSF (Filgastrim) support starting on day 13 until granulocyte count is above 1X109/L

CNS prophylaxis

- Cytarabine 30mg/m2 IT D1 & 3
- Methotrxate 12mg/m2 IT D15 (Not more than 20mg total dose)
- Hydrocortisone 20mg/m2 D1, 3 and 15
- Folinic Acid

IVAC

- Ifosphamide 1.5g/m2 IV D1 5
- Etoposide 60mg/m2 IV D1 5
- Cytarabine 2g/m2 IV every 12hrs for D1 and 2
- Filgastrim start on D7 till absolute granulocyte count is over 1X109/L

CNS prophylaxis

- Methotrexate 12mg/m2 IT D5
- Folinic Acid 15mg orally stat on D6

LYMPHOMA TREATMENT GUIDELINES
(flow chart format).

Hodgkin's Disease (HD)
Characterised by presence of
Reed - Sternberg cells.

Classification

- Nodular Lymphocyte predominant HD
- Classic HD
  1. Nodular Sclerosing
  2. Mixed Cellularity
  3. Lymphocyte depleted
  4. Lymphocyte rich

Non-Hodgkin's Lymphoma (NHL)
Heterogeneous group of lymphoreticular malignancies. These lymphomas may be associated with HIV/AIDS.

Classification

- Low grade
- Aggressive
- Highly Aggressive

Diagnosis

- History and physical examination
- Excision biopsy.
- FBC, ESR, LDH, LFTs, U/Es.
- CXR
- Abdominal ultrasound.
- CT chest abdomen and Pelvis
- HIV and CD4 count.
- For advanced stage disease bone marrow aspirate and trephine.

Symptoms and Signs

- Fever, weight loss, and night sweats
- Loss of appetite
- Pruritis
- Pallor
- Pain in the infiltrated tissue (alcohol induced)
- Enlarged lymph nodes
- Hepatosplenomegaly
- Weight loss.

Diagnosis

- As for Hodgkin's Lymphoma
- HIV and CD4 count
- Do immunohisto-chemistry and flow cytometry where possible
- Lumbar puncture for the highly aggressive disease (histopathology)

TREATMENT GUIDELINES for
Hodgkin's Disease (HD) & Non-Hodgkin's Lymphoma (NHL)

Hodgkin's Disease (HD) Treatment

The choice of treatment is determined by the stage of the disease. It consists a combination of radiotherapy and chemotherapy.
Stage I & II – 4 cycles of chemotherapy plus involved field radiation therapy.
Stage III & IV – 6 – 8 cycles of combination chemotherapy plus radiotherapy for residual localized disease.

Chemotherapy

ABVD regimen

- Doxorubicin 25mg/m^2 D1 & 15 IV
- Bleomycin 10 units/m^2 D1 & 15 IV
- Vinblastine 6mg/m^2 D1 & 15 IV
- Darcabazine 375mg/m^2 D1 & 15 IV

Repeat every 28 days

MOPP regimen

- Mechlorethamine 6mg/m^2 IV
- Vincristine 1 – 1.4mg/m^2 IV D1 & 8
- Procarbazine 100mg/m^2 orally from D1 – 14
- Prednisolone 40mg/m^2 orally from D1 – 14

Repeat cycle every 28 days

NB: ABVD regimen is the standard treatment regimen.

Non-Hodgkin's Lymphoma (NHL) Treatment

Low grade Stage I & II - curative radiotherapy or watchful waiting, if they are HIV negative.
Low grade Stage III & IV – watchful waiting or with single or combination chemotherapy and radiotherapy.
Single agents

- Fludarabine 25mg/m2 IV D1-5 for every 28 days OR
- Chlorambucil 2 –4 mg orally daily or 30 – 60mg orally every 2 weeks

Combination chemotherapy

- CVP
- CHOP

Aggressive Disease

Stage I & II – 3 cycles CHOP chemotherapy chemotherapy plus consolidation radiotherapy to 30 – 36Gy
Stage III & IV – CHOP chemotherapy 6 –8 cycles and radiotherapy to local residual disease

Regimens

CHOP

- Cyclophosphamide 750mg/m2 D1 IV
- Doxorubicin 50mg/m2 D1 IV
- Vincristine 1.4mg/m2 D1 IV (maximum of 2mg)
- Prednisolone 100mg PO D1 – 5

Repeat every 21 days.

CVP

- Cyclophosphamide 400 – 600mg/m2 D1 IV
- Vincristine 1.4mg/m2 D1 IV (maximum of 2mg)
- Prednisolone 100mg PO D1 – 5

Repeat every 21 days.

TREATMENT GUIDELINE for Highly Aggressive NHL
Burkitt's Lymphoma
(see paediatric protocol for HIV negative children)

Diagnosis

i) History and physical examination
ii) Biopsy of the tumour **plus** of Lymph node
iii) FBC, ESR, LFTs, U/Es, LDH
iv) Bone Marrow Aspiration and/or Trephine biopsy
v) CXR
vi) CT scan of the abdomen and pelvis
vii) HIV testing and CD4 especially in adults
viii) CSF examination done at the first intrathecal treatment

Treatment (Burkitt's Lymphoma)

This is associated with tumour lysis syndrome, so IV pre-hydration and allopurinol must be given before starting chemotherapy.

Regimen

Patients with localised disease receive 3 cycles of CODOX-M.

Patients with multiple site involvement are treated with CODOX-M alternating with IVAC and intrathecal therapy for 4 cycles each.

CODOX-M and CODOX-M alternating with IVAC

CODOX-M

- Cyclophosphamide 800mg/m2 D1 and 200mg/m2 D2-5 IV
- Vincristine 1.5mg/m2 D1 IV (max 2mg)
- Doxorubicin 40mg/m2 D1 & 8 IV
- Methotrexate 1.2g/m2 continuous IV infusion on D10, then 240mg/m2 IV each hour over 23hrs
- Folinic Acid 192mg/m2 IV D11 starting from the 12^{th} hour of methotrexate infusion, then 12mg/m2 IV every 6hrs for next 48hrs
- G-CSF (Filgastrim) support starting on day 13 until granulocyte count is above $1X10^9/L$

CNS prophylaxis

- Cytarabine 30mg/m2 IT D1 & 3
- Methotrxate 12mg/m2 IT D15 (Not more than 20mg total dose)
- Hydrocortisone 20mg/m2 D1, 3 and 15
- Folinic Acid

IVAC

- Ifosphamide 1.5g/m2 IV D1 – 5
- Etoposide 60mg/m2 IV D1 – 5
- Cytarabine 2g/m2 IV every 12hrs for D1 and 2
- Filgastrim start on D7 till absolute granulocyte count is over $1X10^9/L$

CNS prophylaxis

- Methotrexate 12mg/m2 IT D5
- Folinic Acid 15mg orally stat on D6

FOLLOW UP: Follow up at Cancer Diseases Hospital.

CANCER REGISTRY

Cancer Notification

All Cancer Cases should be notified to ZNCR Private Bag RW IX Lusaka or email zncr@moh.gov.zm using the form below:

CONFIDENTIAL

ZAMBIA NATIONAL CANCER REGISTRY
Private Bag RW1X Lusaka, Zambia.
Tel: 260211251200 Fax: 260211250305
E-mail:zncr@moh.gov.zm

CANCER NOTIFICATION FORM
(Explanatory notes on cover page)
Reg No. _____
Registry Use

I. PATIENTS DETAILS (Please tick appropriate box where applicable)

Name of Patient in Block Letters)(Start with Surname)

Date of Birth :* _____
If DOB Unknown, Specify Age _____

NRC/ Foreign Identification No.* _____ / _____ / _____

PLACE OF BIRTH: _____ TRIBE: _____
CHIEF: _____
GENDER: 1 MALE ☐ 2 FEMALE ☐ 9 NOT KNOWN ☐
OCCUPATION:

NATIONALITY:
1 Zambian ☐
8 Other Specify ☐ _____
9 Not Known ☐

ETHNIC GROUP:
1 African ☐ 4 African Albino ☐
2 Caucasian ☐ 5 Other Albino ☐
3 Colored ☐ 6 Other Specify: ☐
4 Asian ☐ 9 Not Known ☐

Permanent or Usual Address:

Contact Address:

MARITAL STATUS: 1 Single ☐ 2 Married ☐ 3 Divorced ☐ 4 Separated ☐ 5 Widow ☐ 9 Not Known ☐
REACHED MENOPAUSE 1 Yes ☐ 2 No ☐ 9 Not Known ☐
HIV STATUS: 1 Positive ☐ 2 Negative ☐ 9 Not Known ☐

II. RISK FACTORS:
A. Alcohol 1 Now ☐ 2 Past ☐ 9 Not Known ☐ If Alcohol yes, Specify type: _____
B. Tobacco 1 Now ☐ 2 Past ☐ 9 Not Known ☐ Other Specify:
If Tobacco is Now or Past type 1 Cigarettes ☐ 2 Snuff ☐ If cigarettes, number per day ☐☐ Years of Smoking ☐☐

III. HOSPITAL / CLINICAL DETAILS

Referring Hospital/Clinic: _____
Patient Number: _____ Ward: _____

Hospital / Facility Referred to: _____
Patient Number: _____ Ward: _____

Doctor/ Consultant In-Charge

Hospital / Facility responsible for subsequent Treatment and Follow-ups:
1 Same as Above ☐ 2 Other Specify: ☐

IV. TUMOUR (Please specify primary organ or site of Cancer and exact location if possible)

Date of Diagnosis * _____

Primary Site:
Histological / Clinical Diagnosis: _____

Basis of Diagnosis (Check one or more as applicable)
1 Death Certificate Only ☐
2 Clinical Only ☐
3 Clinical Investigation ☐
4 Specific Tumor Marker ☐
5 Cytology ☐ (Lab No._____)
6 Metastasis ☐ (Lab No._____)
7 Primary Tumor ☐ (Lab No.)
9 Not Known ☐

Extent of Disease:
0 In Situ ☐
1 Localised ☐
2 Local Extension Only ☐
3 Local Extension + Regional Nodes ☐
4 Regional Nodes ☐
5 Distant Metastasis ☐
8 Not Applicable ☐
9 Not Known ☐

PRESENT STATUS:
1 ALIVE ☐ Date of Last Contact: _____
2 DEAD ☐ Date of Death: _____

If Dead Cause of Death
1 Cancer ☐ 9 Not Known ☐
2 Others Specify: ☐

V. CLINICAL STAGING & TREATMENT

Clinical Staging (cTNM)
T _____
N _____
M _____

Staging Group

0	In Situ	☐	5	3A ☐
1	1A	☐	6	3B ☐
2	1B	☐	7	4A ☐
3	2A	☐	8	4B ☐
4	2B	☐	9	Not Known ☐

Treatment (Check one or more as applicable)
1 Other Treatment ☐
2 Surgery ☐
3 Radiotherapy ☐
4 Chemotherapy ☐
5 Hormones ☐
6 Anti-Retrovirals ☐
7 Palliative Care ☐
9 Not Known ☐

VI. SOURCE OF INFORMATION

1st Notification	Province	Facility Name	Date Seen:
2nd Notification	Province	Facility Name	Date Seen:
3rd Notification	Province	Facility Name	Date Seen:

Other Remarks:

Notification Date: *

* Mandatory fields

REFERENCES

Krupski, T L, Theodorescu D, Kim E D (2012), Prostate Cancer http://emedicine.medscape.com/article/1967731-clinical accessed 24/01/12
National Institute for Health and Clinical Excellence (2008); CG58 Prostate Cancer Diagnosis and Treatment, http://guidance.nice.org.uk/CG58/Guidance/pdf/English accessed 24/01/12

Perez L Text Book of Radiation Oncology

Libel and Philips Text Book of Radiation Oncology

NCCN guidelines 2011

Cancer.gov/nci guidelines

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