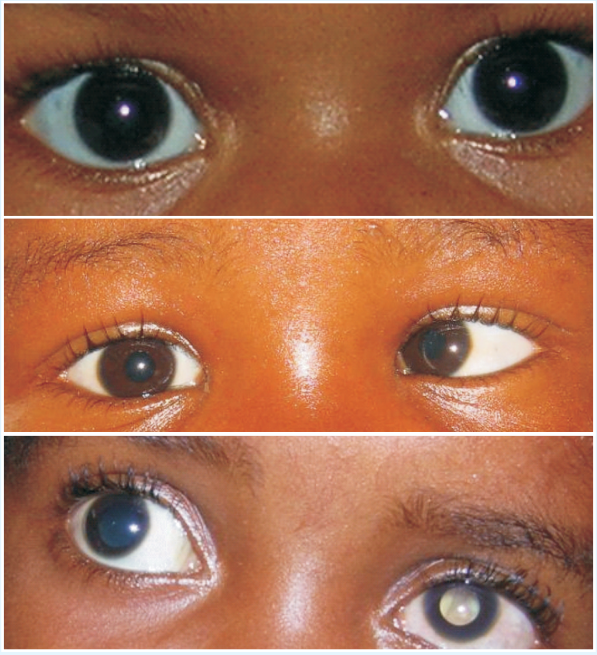
MINISTRY OF HEALTH

RETINOBLASTOMA

BEST PRACTICE GUIDELINES 2019



KENYA NATIONAL RETINOBLASTOMA STRATEGY

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ACKNOWLEDGMENT

This is the first revision of the Kenya National Retinoblastoma Strategy Best Practice Guidelines and has drawn from the expertise of many individuals from medical and social sciences.

As the guidelines continue to assure good quality of care for children with retinoblastoma, they embrace and emphasize the multidisciplinary approach in retinoblastoma care.

The continued learning over the last 5 years from the different disciplines involved has been instrumental in this revision.

The Ministry of Health wishes to extend appreciation to all who contributed and supported the revision and production of this document for quality improvement in retinoblastoma care.

We are sincerely grateful to our heroes; the survivors of retinoblastoma and their families who inspire for best possible care.

The value of experience and insight from individuals with clinical, laboratory, pharmaceutical and non-technical backgrounds cannot be underestimated and indeed greatly enriched the revision of these guidelines.

The process of revising these guidelines was guided by the Ministry of Health; Ophthalmic Services Unit with close collaboration of the University of Nairobi; Department of Ophthalmology and with support from the College of Ophthalmology East Central and Southern Africa (COECSA).

We thank all team members who participated in the revision of these guidelines (see annex 5). It is with deep commitment to the cause that culminated in these revised guidelines and it is our sincere hope that the same commitment will remain to see through the continued improvement of the survival of children with retinoblastoma and the realization of Universal Health Coverage.

DR MICHAEL M. GICHANGI

HEAD: OPHTHALMIC SERVICES UNIT

FOREWORD

Best Practice Guidelines are key tools in the realization of Universal Health Coverage. Retinoblastoma, a curable cancer of the eye mainly affects children under the age of five years. The survival of children afflicted by this cancer remains low in Kenya while we know that it is completely curable if diagnosed and treated early. This has been demonstrated by the high cure and survival rate in developed where survival is over 95%.

These Best Practice Guidelines have been revised in response to the felt needs, improvement in the health system, changing patterns in the practice of retinoblastoma care, and overall National development. The revision process involved gathering relevant evidence and building consensus, agreeing on what is feasible in Kenya.

The document outlines cardinal characteristics of the disease and best approach to the management at different levels of care. The management herein referred to includes timely referral and communication within the health system. It stipulates clearly what should be done in different circumstances and is recommended for use at all levels of care.

Over the last five years, following the implementation of the Best Practice Guidelines, we have observed significant improvement in the outcome of children managed for retinoblastoma with an estimated doubling of survival from 26% to over 50%.

The revision of these **Best Practice Guidelines** took in to account the already existing umbrella National cancer policy and strategy, with emphasis on early detection of cancer. They are incorporated in the National Cancer strategy 2018-2022 and also clearly relates to the "Mother and Child Health (MCH) booklet" in early identification of eye problems in the infant, including retinoblastoma.

We encourage that all children accessing immunization also receive a spot eye check by the Primary Health care worker as required by the MCH booklet.

We recommend that all health workers continue to familiarize themselves with these revised guidelines so that all children may live and see to adulthood.

We also recommend that relevant training institutions give more attention to clinical practice guidelines like this one, at these professional formative stage as we journey towards sustained Universal Health Coverage in Kenya.

DR PACIFICA K. ONYANCHA
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INTRODUCTION

Retinoblastoma is the most important primary cancer of the retina and affects young children mostly under the age of 5 years with over 90% of cases being diagnosed by the third birthday. The retinoblastoma story provides not only a model for what can be achieved in the conquest of cancer through research and education but also provides a model of oncogenesis with exciting insights into specific genetic alterations required to transform normal cells into cancerous cells.

The incidence of retinoblastoma is 1:15,000-20,000 live births and has a fairly uniform worldwide distribution with no sexual or racial predilection; Nyamori *et al* found the incidence in Kenya to be 1:17200 live births[1]. Retinoblastoma is curable if detected and treated early. In the developed world most children treated for retinoblastoma survive, but in Africa most of them die from advanced disease. In Kenya Nyawira *et al* demonstrated the mortality of children diagnosed with retinoblastoma to be greater than 60% and found this to be due to late presentation[2].

The Kenya National Retinoblastoma Strategy was established in 2008 with aim of improving the survival of children with retinoblastoma in Kenya through:

1. Creating awareness about retinoblastoma among the health care workers as well as the general population to ensure early diagnosis;
2. Improving the quality of medical treatment of children with retinoblastoma through access to standard treatments and quality histopathology reports;
3. Family psychosocial support; and
4. Resource mobilization.

These Best Practice Guidelines are a milestone in the clinical care of children with retinoblastoma in Kenya. It is the culmination of three years of deliberations and consultations with different professionals involved in the care of children with retinoblastoma and included ophthalmologists, paediatric oncologists, histopathologists, ophthalmic clinical officers, nurses, parents and child life specialist drawn from all over Kenya. A team from Canada assisted in the process and these Guidelines have borrowed heavily from the Canadian Guidelines but with modifications to suit the situation in Kenya. The purpose of these guidelines is to ensure common standards of evidence-based care to improve the quality of care for children with retinoblastoma Kenya, in a bid to improve their survival.

DEFINITIONS

Level of Evidence

Level 1	Randomized controlled trials (RCTs) (or meta-analyses) *without* important limitations
Level 2	RCTs (or meta-analyses) *with* important limitations; Observational studies (non-RCTs or cohort studies) with overwhelming evidence
Level 3	Other observational studies (prospective cohort studies, case-control studies, case series)ConsensusInadequate or no data in population of interest Anecdotal evidence or clinical experience; 100% agreement of KNRbS members

ACRONYMS

CPS	Canadian Paediatric Society
CT	Computerised Tomography
EBR	External Beam Radiation
EUA	Examination Under Anaesthesia
IIRC	International Intraocular Retinoblastoma Classsification
KNRbS	Kenya National Retinoblastoma Strategy
MCH	Maternal and Child Health
MRI	Magnetic Resonance Imaging
Rb	Retinoblastoma
RbCoLab	Retinoblastoma Collaborative Laboratory
RCT	Randomized Clinical Trial

SCREENING-RECOMMENDATIONS

1. We recommend that all infants and children in whom someone has observed a white pupil (either in person or in a photograph) have a full dilated-eye examination including red reflex test within 72 hours by an ophthalmologist, or medical practitioner who is fully aware of the importance of leukocoria as a sign of Rb. *[Consensus]*

2. We recommend that any child with strabismus or suspected strabismus be seen by their primary doctor:

a. We recommend that the red reflex test be applied to any child with strabismus or suspected strabismus. *[Consensus]*

b. We recommend urgent referral (within 72 hours) to an ophthalmologist of any child with strabismus / suspected strabismus and an abnormal red reflex. *[Consensus]*

c. We recommend that the child in (b) above be seen by secondary or tertiary Rb centres within 72 hours for the above signs of abnormality, which constitutes an emergency. *[Consensus]*

3. We adapt the recommendations of the Canadian Paediatric Society[3] with respect to the suggested timing of vision screening for the general population. *[Consensus]*

4. We recommend consulting with the Kenyan Mother and Child Health booklet for information related to retinoblastoma screening. *[Consensus]*

Table 1. Vision screening guidelines from the CPS[3].

Age	Screening Guideline
Newborn to 3 months	■ A complete examination of the skin and external eye structures including the conjunctiva, cornea, iris, and pupils. ■ An inspection of the red reflex to rule out lenticular opacities or major posterior eye disease. ■ Failure of visualization or abnormalities of the reflex are indications for an urgent referral to an ophthalmologist. ■ High-risk newborns (at risk of retinopathy of prematurity and family histories of hereditary ocular diseases) should be examined by an ophthalmologist.
6 to 12 months	■ Conduct examination as above. ■ Ocular alignment should again be observed to detect strabismus. The corneal light reflex should be central and the cover-uncover test for strabismus normal. ■ Fixation and following a target are observed.
3 to 5 years	■ Conduct examination as above. ■ Visual acuity testing should be completed with an age- appropriate tool.
6 to 18 years	■ Screen as above whenever routine health examinations are conducted. ■ Examine whenever complaints occur.

All children should be screened in their preschool years for amblyopia or its risk factors, as well as for ocular diseases that may have serious consequences, such as retinoblastoma and cataracts. It remains the responsibility of the child's pediatrician to ensure that these tests are performed by the most qualified personnel[4].

FEATURES AND CLASSIFICATION OF RETINOBLASTOMA CENTRES - RECOMMENDATION

We recommend that Rb treatment centres in Kenya be classified as follows:

Primary — able to make a preliminary diagnosis of retinoblastoma.

Secondary — able to make a clinical diagnosis and treat by enucleation & send eye for pathological exam by a qualified pathologist (preferably an ocular pathologist)

Tertiary — able to confirm diagnosis of retinoblastoma with ultrasound and/or CT/MRI, treat retinoblastoma by enucleation and more complex cases by chemotherapy, focal therapy and radiation.

[Consensus]

REFERRAL AND DIAGNOSIS - RECOMMENDATIONS

1. We recommend that any child with signs consistent with Rb be referred to an ophthalmologist to receive a full retinal examination with dilated pupil. A detailed history must be taken to confirm a diagnosis of Rb. *[Consensus]*

2. We recommend that secondary and tertiary Rb centres accept direct referrals of patients with suspected Rb from primary healthcare providers, such as clinical officers, nurses and general practitioners. *[Consensus]*

3. We recommend that primary healthcare providers obtain and record complete contact details including telephone contacts, and immediately refer all Rb cases to a secondary or tertiary Rb centre. *[Consensus]*

4. We recommend that all children referred with any possibility of Rb be seen within 72 hours, or as soon as possible, at the secondary or tertiary Rb centre for thorough ocular and systemic examination. It is the responsibility of the referring clinician to make person-to-person contact, to emphasize the urgency to the parents. *[Consensus]*

5. We recommend that difficult unilateral cases (e.g. very young child; potential to save the eye; unilateral multifocal and/or germline *RB1* mutation), positive family history, or risk for extraocular disease and bilateral cases be referred from a secondary centre to a tertiary centre. *[Consensus]*

6. We recommend that any child with high-risk pathological features (see “Follow-up” chapter) be referred to tertiary centre. *[Consensus]*

7. We recommend that the receiving Rb centre promptly inform the referring physician of the diagnosis, management and outcome of the referral, and invite the referring physician to remain involved with the care and follow-up of the child, as appropriate. *[Consensus]*

8. We recommend that in order to reduce risks associated with radiation exposure, if possible all children with Rb requiring imaging have an MRI of the head and orbits at diagnosis, rather than a CT scan to check for evidence of intracranial cancer and the extent of the disease, but this should not delay treatment (see Treatment chapter). *[Consensus]*

GENETIC COUNSELLING – RECOMMENDATIONS

1. We recommend antenatal history include a detailed family history of eye disease, and referral to an ophthalmologist when this history is positive. *[Consensus]*

For all individuals with Rb and/or family history of Rb, except those excluded by genetic testing (see recommendation #9):

2. We recommend that expectant couples undergo early prenatal counselling and their infants undergo perinatal management to facilitate the earliest possible treatment of tumours. *[Level 2]*[5,6]

3. We recommend counselling for patients, parents and other relatives to discuss Rb, the risk and hereditary pattern of Rb, pregnancy options, post-delivery surveillance screening protocols to diagnose tumors early in infants at risk, and treatment options. *[Level 3]*[7,8]

4. We recommend that each at-risk family member be screened as soon as possible after birth frequently until age 7 years, according to the empiric risk of developing Rb *[Level 2]*[5,6,8]

5. We recommend awareness counselling about the risk of other cancers in adult survivors and relatives. *[Level 2]*[6,9,10]

6. We recommend that children with Rb be offered repeated genetic counselling as they grow up, so that they completely understand their options and appropriate care for themselves and their children. *[Consensus]*

When *RB1* gene mutation identification is available:

7. We recommend RB1 gene mutation identification testing for the first affected person (proband) in each Rb family. *[Level 2]*

8. When the RB1 gene mutation in a proband/family becomes known, we recommend genetic testing for all at-risk relatives. *[Level 2]*

9. We recommend that surveillance be discontinued for relatives determined to be NOT at risk by genetic testing. *[Level 2]*

HISTOPATHLOGY – RECOMMENDATIONS

1. We recommend that the ophthalmologist who enucleates the eye of a child with retinoblastoma communicates with the pathologist who will report the histopathology of the enucleated eye at the time the eye is submitted to the laboratory.*[Consensus]*

2. We recommend that the ophthalmologist who enucleates an eye of a child with retinoblastoma uses the standard request form recommended by the Kenya National Retinoblastoma Strategy Working Group when submitting the specimen for histopathology (Annex 3).*[Consensus]*

3. We recommend that the enucleated eye be fixed in at least 100mls of buffered formalin for at least 24 hours before grossing.*[Consensus]*

4. We recommend that the grossing of the enucleated eye be done by a trained pathologist and the processing should be done by a trained histotechnologist under the supervision of a pathologist experienced in ocular pathology. *[Consensus]*

5. We recommend that the sections include the pupil-optic nerve section as well as superior and inferior calottes.*[Consensus]*

6. We recommend that pathologist reporting the pathology of an eye enucleated for retinoblastoma uses the standard reporting format recommended by the Kenya National Retinoblastoma Strategy Working Group (Annex 4).*[Consensus]*

7. We recommend that the ophthalmologist involved in the child's case review the pathology of every enucleated eye together with the involved pathologist.*[Consensus]*

8. We recommend that the turnaround time for eyes enucleated for retinoblastoma be not more than two weeks.*[Consensus]*

TREATMENT– RECOMMENDATIONS

1. We recommend that children with Rb be cared for by a multidisciplinary team, that provides coordinated and collaborative care in and shared between specialized centres, with expertise and up-to-date protocols and equipment for optimal management of Rb. *[Consensus]*

2. We recommend that tertiary Rb centres work together to assure optimal care for each child. This might include cross-referrals and cross-consultations to access specific technical or human resources. *[Consensus]*

Ocular treatments

3. We recommend that enucleation be performed for IIRC Groups D and E eyes when the other eye is normal or Group A. *[Consensus]*

4. We recommend that unilaterally affected eyes be enucleated unless that unilateral eye is Group A. *[Consensus]*

5. We recommend considering enucleation of any affected eye when optimal salvage treatment and follow up are not possible.

6. We recommend that upfront enucleation WITHOUT pre-enucleation chemotherapy be performed for any IIRC Group E eyes, which pose a risk for systemic metastases. Pre-enucleation chemotherapy is dangerous, since it may mask features of extraocular extension causing understaging and undertreating of systemic disease. *[Level 2]*[12,13]

6. We recommend that pathologist reporting the pathology of an eye enucleated for retinoblastoma uses the standard reporting format recommended by the Kenya National Retinoblastoma Strategy Working Group (Annex 4).*[Consensus]*

7. We recommend that the ophthalmologist involved in the child's case review the pathology of every enucleated eye together with the involved pathologist.*[Consensus]*

8. We recommend that the turnaround time for eyes enucleated for retinoblastoma be not more than two weeks.*[Consensus]*

9. We recommend chemo reduction for tumors in group B, C and D eyes in bilateral disease, or for recurrences after other therapy prior to focal therapy. *[Consensus]*

10. We recommend that cryotherapy through a conjunctival incision may be used for posterior Rb refractory to laser focal therapy. *[Consensus]*

11. We recommend the use of pre-chemotherapy cryotherapy 24–72 hours before chemotherapy to increase drug penetration into the eye, particularly for vitreous seeding, but not in the presence of retinal detachment.*[Consensus]*

12. We recommend systemic chemotherapy with focal therapy for the primary treatment of bilateral IIRC Group B, C or D eyes, but not Group A. If the better eye is group A, B or C, we recommend enucleation of group D eyes. If both eyes are group D we recommend chemoreduction and focal therapy for both eyes in an attempt to save vision as much as possible. *[Consensus]*

13. We recommend the use of Intravitreal chemotherapy for eyes that have vitreous seeds refractory to systemic chemotherapy *[Consensus]*

Radiotherapy

14. We recommend that ocular radiotherapy be used only as salvage therapy for the only remaining eye after chemotherapy and focal therapy have failed to control the tumour. *[Consensus]*

Extraocular disease

For the purpose of decision making for treatment:

15. We recommend that patients be categorized to intention to cure, or intention to palliate. Patients with high risk features on histology, or patients who present with proptosis without evidence of systemic metastasis, should be categorized as intention to cure. Those with evidence of metastasis clinically or on investigations should be categorized as palliation.*[Consensus]*

16. We do not recommend exenteration of the orbit for Rb, since chemotherapy will provide more effective palliation, even for massive proptosis. *[Level 2]*[16]

17. We recommend that the ophthalmologist involved in the child's case review the pathology of every enucleated eye for high-risk features, including invasion of optic nerve, sclera, choroid or anterior segment, that could predispose to extraocular disease or metastasis. *[Level 2]*

18. When high-risk features are observed, including invasion of optic nerve, sclera, choroid or anterior segment, we recommend treatment with prophylactic chemotherapy. *[Level 2]*

19. We recommend that for extraocular Rb (in absence of systemic metastasis) treatment protocols generally include, but not be limited to: orbital radiation for orbital recurrence postenucleation and systemic chemotherapy. *[Level 2]*

20. We recommend that metastatic disease be treated palliatively, with 2 to 3 courses of chemotherapy as per national guidelines or spot radiotherapy for symptoms relief. We recommend abandoning chemotherapy if there is no response after 3 courses. Where possible, hospice care should be included early in the management of these patients. These patients should be kept as close to their families as possible. *[Consensus]*

FOLLOW-UP - RECOMMENDATIONS

1. We recommend that all survivors of Rb receive individualised, lifelong follow-up and surveillance, counselling and interventions for late effects of disease and treatment, delivered by a multidisciplinary team. *[Consensus]*

Ophthalmology follow-up

2. We recommend that following completion of treatment, EUAs for children at risk of developing new Rb tumours continue as often as every 3 weeks, or at longer intervals as tumour activity decreases, until risk of new tumours and recurrences is low, and the child is able to cooperate in clinic. The frequency of examinations will be highest when the child has a proven RB1 germline mutation, family history of disease and/or bilateral Rb. *[Level 2]* [5,11,17]

3. We recommend that EUA or clinic visits for retinal exam continue every 6 months to age 5 and thereafter annually for life. *[Consensus]*

4. We recommend that children shown to not carry the RB1 mutant allele of their family through a blood test do not require EUA or intense surveillance. *[Consensus]*

5. We recommend the examination of an enucleated socket for infection, fit of prosthesis and implant exposure or extrusion at every EUA and clinic visit. *[Consensus]*

6. We recommend prescribing and monitoring the use of protective eyewear for children who are functionally uniocular. *[Consensus]*

7. We recommend that Rb survivors of school age with significantly reduced visual fields or visual acuity less than 6/12 undergo visual assessment and referral to a low vision centre for additional assistance when appropriate. *[Consensus]*

Oncology follow-up

8. We recommend that RB survivors treated with chemotherapy or EBR , undergo oncology clinic follow up every 6 months or as per national guidelines. *[Consensus]*

9. We recommend that persons known to be carrying an RB1 germline mutation or

have bilateral Rb, or non-germline Rb survivors treated with chemotherapy or EBR, be seen in oncology clinic for for comprehensive follow-up including counseling for life. *[Consensus]*

10. We recommend that MRI replace CT scan if possible, for all patients unless proven not to have RB1 germline mutations since diagnostic radiation may increase their already significant risk of secondary non-Rb malignancies. *[Level 2]*[18]

PSYCHOSOCIAL CARE AND ACCESS TO SERVICES - RECOMMENDATIONS

1. We recommend that ongoing psychosocial support and timely and equal access to care is important for all Rb children and their families. *[Consensus]*
2. We recommend that Rb families have easy and equitable access to *[Consensus]*:
    - A social worker or clinical psychologist with expertise in Rb or childhood cancer, from the time of diagnosis onwards.
    - ` Structured psychosocial and developmental assessments at diagnosis and key points during treatment.
    - A child life health worker from diagnosis onwards.
    - Accurate, understandable, as-needed information in a variety of formats.
    - Risk/informed consent information meeting parent language/age/education level.
    - Advocacy services by professionals or community agencies for parents requiring additional support to access appropriate services.
    - A centralized referral source providing links to hospital and community support groups.
    - Long-term psychosocial support from diagnosis through adulthood.
    - Genetic counselling for all family members.
    - Molecular diagnosis when available.
    - Financial support for costs related to treatment.
    - Visual rehabilitation services.
    - Aids for low vision
    - Prosthetic eye service.
    - Paediatric palliative care and bereavement services.

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ANNEX 1

MANAGEMENT FOR RETINOBLASTOMA

All E eyes	Enucleate
Unilateral RB Group B-D	Enucleate
Bilateral RB Group A-D	Salvage
Group A	Focal Laser or Cryoptherapy
Group B-D	Chemoreduction + focal treatment
Pathology pT2a	No Chemotherapy
Pathology pT2b-PT3a	4 courses of chemotherapy
Pathology pT3b and worse	6 courses of Chemotherapy + Radiotherapy
Proptosis without metastasis	Chemotherapy before enucleation
Metastasis	Palliative chemotherapy/radiotherapy

ANNEX 2

RETINOBLASTOMA CHEMO PROTOCOLS

DATE: _____ CYCLE: _____

Weight: _____ kg. Height: _____cm. Surface area: _____ m^2

Day 1 = _____/_____/_____ (dd/mm/yy)

INDICATIONS:

1. **PROPTOSIS:**
   a. **Metastatic workup negative:** Use TREAT-TO-CURE CEV PROTOCAL (Pre-Chemotherapy CT head/orbits; lumbar puncture; bone marrow if abnormal CBC/Differentiate/Platelet; bone scan optional): May give 1-2 cycles CEV for shrinkage prior eye enucleation (not orbital exenteration); Give a total 4-cycle CEV; Orbit radiation as soon as possible (may give concurrent to chemotherapy except on the CEV day).
   b. **Metastatic workup positive:** Use PALLIATIVE PROTOCOL.

2. **UNFAVORABLE HISTOLOGY** (sclera involvement/massive choroid disease/post-laminar tumor in optic nerve/large volume anterior chamber tumor/ciliary body infiltration):
   a. **Metastatic workup negative:** Use TREAT-TO-CURE CEV PROTOCOL (Pre-Chemotherapy CT head/orbits; lumbar puncture; bone marrow if abnormal CBC/Differentiate/Platelet; bone scan optional): Give a total 4-cycle CEV; Orbit radiation if residue tumor after enucleation (tumor at cut margin of optic nerve or long post-laminar tumor involvement).
   b. **Metastatic workup positive or optic chiasm involvement:** Use PALLIATIVE PROTOCOL.

3. **BILATERAL RETINOBLASTOMA:**
   a. One IIRC Group E or D eye: Enucleation at diagnosis.
   b. Both Group E eyes: Bilateral enucleation at diagnosis.
   c. One or both IIRC Group A eyes: Give 2-cycle CEV only on failing repeated focal laser/cryotherapy.
   d. One or both IIRC Group B eyes: Give 2-cycle CEV at diagnosis (may repeat 2-cycle CEV later if needed; if necessary more than once).
   e. One or both IIRC Group C eyes: Give 4-cycle CEV at diagnosis (may repeat 2-cycle CEV later if needed; if necessary more than once).
   f. Both IIRC Group D eyes: Give 4-cycle CEV at diagnosis (may repeat 2-cycle CEV later if needed; if necessary more than once).
4. UNILATERAL RETINOBLASTOMA: Enucleation at diagnosis, except for IIRC Group A eyes that are treated with focal laser/cryotherapy. NO CHEMOTHERAPY INDICATED TO TRY TO SAVE UNILATERALLY INVOLVED EYES.
5. METASTATIC DISEASE: Use dosages as in treat to cure but number of courses should be determined by comfort and pain relieve for the patient. Keep the patient as close to the family as possible.

RETINOBLASTOMA CEV CHEMO PROTOCOL ORDER SHEETS

DATE: _____ CYCLE: _____

Weight: _____ kg. Height: _____cm. Surface area: _____ m^2

Day 1 = ____/_____/_____ (dd/mm/yy)

TREAT-TO-CURE CEV PROTOCAL: PRE-CYCLE 1:

- ☐ CBC, differential count, platelet count
- ☐ Urea, creatinine, sodium, potassium, chloride, calcium, magnesium, phosphate
- ☐ ALT, AST, alkaline phosphatase, bilirubin conjugated & unconjugated
- ☐ Audiogram
- ☐ If under age 1 years, do 12-hour creatinine clearance (12-hour urine collection with Foley catheter & serum creatinine taken with the 12 hours):
- ☐ IF creatinine clearance >100 ml/min/1.73 m^2: carboplatin 28 mg/kg per dose
- ☐ IF creatinine clearance 76-99 ml/min/1.73 m^2: carboplatin 600 mg/m2 per dose
- ☐ IF creatinine clearance 50-75 ml/min/1.73 m^2: carboplatin 420 mg/m2 per dose
- ☐ IF creatinine clearance 25-49 ml/min/1.73 m^2: carboplatin 280 mg/m2/dose
- ☐ IF creatinine clearance ≤24 ml/min/1.73 m^2: NO carboplatin

TREAT-TO-CURE CEV PROTOCAL: PRE-EACH CYCLE:

- ☐ CBC, differential count, platelet count

  If possible, EUA day before chemotherapy for 3-spot single freeze/thaw pre-chemotherapy cryotherapy to increase drug penetration into vitreous (for eyes without retinal detachment)

TREAT-TO-CURE CEV PROTOCAL: PRE-MEDICATIONS & POST-MEDICATIONS:

1. IV Dimenhydrinate (Gravol/Dramamine) ___ mg (2 mg/kg/dose; maximum 50 mg/dose)
2. IV Ondansetron ___ mg (5 mg/m2/dose):
   - ☐ First dose (Dimenhydrinate+Ondansetron) prior to chemotherapy.
   - ☐ Second dose (Dimenhydrinate only) at 3-hours.
   - ☐ Third dose (Dimenhydrinate+Ondansetron) at 6-hours.

TREAT-TO-CURE CEV PROTOCAL DRUGS:

A. 3 years old or YOUNGER:

1. Carboplatin ___ mg (28 mg/kg/dose) in ___ ml (9 ml/kg) 5% dextrose water IV over 30 minutes.
2. Vincristine ___ mg (0.05 mg/kg/dose; maximum of 2.0 mg/dose) IV push
3. Etoposide ___ mg (12 mg/kg/dose), mix well, in ___ ml 0.9% NaCl (30 ml/kg/dose) IV over 30 minutes.
4. Post-chemo, run IV fluid of choice at ___ ml/hr (10 ml/kg/hr) [we use D5W 0.45 saline with KCl 20 mmol/Liter] for 5 hours.

B. OLDER THAN 3 years:

1. Carboplatin ___ mg (600 mg/m2/dose) in ___ ml (9 ml/kg) 5% dextrose water IV over 30 minutes.
2. Vincristine ___ mg (2 mg/kg/dose; maximum of 2.0 mg/dose) IV push
3. 8Etoposide ___ mg (300 mg/m2/dose), mix well, in ___ ml 0.9% NaCl (30 ml/kg/dose) IV over 30 minutes.
4. Post-chemo, run IV fluid of choice at ___ ml/hr (10 ml/kg/hr) [we use D5W 0.45 saline with KCl 20 mmol/Liter] for 5 hours.

C. IF ALLERGIC TO ETOPOSIDE:

1. 3 YEARS OLD OR YOUNGER: Substitute Teniposide ___ mg (12 mg/kg/dose), mix well, in ___ ml 0.9% NaCl (30 ml/kg/dose) IV over not more than 30 minutes.
2. OLDER THAN 3 years: Substitute Teniposide ___ mg (300 mg/m2/dose), mix well, in ___ ml 0.9% NaCl (30 ml/kg/dose) IV over not more than 30 minutes.

ANNEX 3
RETINOBLASTOMA PATHOLOGY REQUEST PROFORMA (version 2019)

Patient name: Lab specimen number:

Date of birth: (dd/mmm/yyyy): / / Sex: Female Male

Hospital: Ward: OP/IP number:

Date of procedure: (dd/mmm/yyyy): / / Time of collection: am pm

Surgeon's name:

Telephone: Email:

CLINICAL INFORMATION PROVIDED BY DOCTOR (as per request form)

Laterality: Right Left Bilateral Trilateral

Previous treatment: None Chemotherapy Other (specify):

Clinical assessment: Optic nerve involvement

Extra-orbital involvement

Recurrence (specify): _____

Metastasis (specify): _____

Other notes (e.g. nodal involvement, etc) : _____

Family history of retinoblastoma? Yes No Unknown

Sign: _____

ANNEX 4

RETINOBLASTOMA PATHOLOGY REPORT PROFORMA (version 2019)

Patient name: Lab specimen number:

Date of birth (dd/mmm/yyyy): / / Sex: Female Male

Hospital: Ward: OP/IP number:

Date of procedure: / / Date received: / /

Time of collection: : am pm

Doctor's name:

CLINICAL INFORMATION PROVIDED BY DOCTOR (as per request form)

Laterality: Right Left Bilateral Trilateral

Previous treatment: None Chemotherapy Other (specify):_____

Clinical assessment: Optic nerve involvement Extra-orbital involvement

Recurrence (specify): _____

Metastasis (specify): _____

Other notes (e.g. nodal involvement, etc): _____

Family history of retinoblastoma? Yes No Unknown

MACROSCOPIC EXAMINATION

Type of specimen: Eye Orbital biopsy Other (specify): _____

Side: Left Right

Structures included: Medial rectus Other:

Extra-ocular muscle marked for orientation: Medial rectus Other: None

Specimen dimensions: Anteroposterior: cm Horizontal: cm

Vertical: cm Optic nerve length: cm

Optic nerve thickness/diameter:

Distal end: mm cannot determine (specify):

Proximal end: mm cannot determine (specify):

Tumour dimensions after grossing: Base at cut edge: mm

Height at cut edge: cm

Cannot determine (specify):

Growth pattern: Endophytic Exophytic Diffuse

Cannot determine (specify):

RETINOBLASTOMA PATHOLOGY REPORT

MICROSCOPIC EXAMINATION

Percentage of retinal involvement: ☐ %

Microscopic involvement of ocular structures.

☐ None	☐ Sclera	☐ Optic disc
☐ Vitreous	☐ Extrascleral extension	☐ Vortex veins
☐ Ciliary body	☐ Iris	☐ Anterior chamber
☐ Angle/Schlemm's canal	☐ Cornea	☐ Lens
☐ Other (specify):	☐	☐

☐ Choroid; maximum extent of choroidal invasion ☐ mm Notes: ☐

Optic Nerve
- ☐ within lamina cribrosa
- ☐ prelaminar
- ☐ retrolaminar ; specify extent of involvement: ☐ mm

Status of tumour at resection margin: ☐ Present ☐ Absent

Surgical margins
- ☐ Cannot be assessed
- ☐ Tumour at margins.
- ☐ None

pT STAGING (EYE)

☐ pTX	Unknown evidence of intraocular tumor
☐ pT0	No evidence of intraocular tumor
☐ pT1	Intraocular tumor(s) without any local invasion, choroidal invasion or pre- or intralaminar involvement of the optic nerve head
☐ pT2	intraocular tumor(s) with local invasion
☐ pT2a	concomitant focal choroidal invasion pre- or intralaminar involvement of the optic nerve head
☐ pT2b	Tumor superficially invasion of stroma of iris and/or trabecular meshwork and/or Schlemm's canal
☐ pT3a	Massive choroidal invasion (>3mm in largest diameter, or multiple focal choroidal involvement totaling >3mm, or any full-thickness choroidal involvement)
☐ pT3b	Retrolaminar invasion of optic nerve head, not involving the transected end of optic nerve
☐ pT3c	Any partial thickness involvement of the sclera within the inner two thirds
☐ pT3d	Full-thickness invasion into outer third of the sclera and/or around emissary channels
☐ pT4	Evidence of extraocular tumour: Tumour at the transected end of optic nerve, tumour in meningeal spaces around optic nerve, full-thickness invasion of the sclera with invasion of episclera, adjacent adipose tissue, extra ocular muscle, bone, conjunctiva or eyelid

Heritable trait (H)

- HX Unknown or insufficient evidence of a constitutional RB1 gene mutation
- H0 Normal RB1 allele in blood tested with demonstrated high-sensitivity assays
- H1 Bilateral retinoblastoma, retinoblastoma with an intracranial primitive neuroectodermal tumour (i.e. trilateral retinoblastoma), patient with family history of retinoblastoma, or molecular definition of a constitutional RB1 gene mutation

FINAL REPORT

- Right/left eye enucleation .....differentiated retinoblastoma showing choroid invasion(<3mm/>3mm) and no/prelaminar/laminar/post laminar optic nerve invasion: optic nerve resection marginis Postive/Negative of tumour.

Stage pT.....(TNM 8th Edition)

Name of Pathologist:

Date (dd/mmm/yyyy): / /

Signature:

ANNEX 5:
PARTICIPANTS IN REVISION OF THE KENYA NATIONAL RETINOBLASTOMA STRATEGY BEST PRACTICE GUIDELINES

1.	Kahaki Kimani	University of Nairobi (Facilitator)
2.	Edna C. Mutai	Kenyatta National Hospital
3.	Ann Makena	PCEA Kikuyu Eye Hospital
4.	Dr. Faith Vata	PCEA Kikuyu Eye Hospital
5.	Nalyanya Wekesa	Moi Teaching & Referral Hospital
6.	Dr. Claric Onyango	Kisii Teaching & Referral Hospital
7.	Mr. Jones Makori	Coast Provincial General Hospital
8.	Dr. Lucy Njambi	University of Nairobi
9.	Margaret Musila	Kenyatta National Hospital
10.	Dr. Kennedy Wabwile	Moi Teaching & Referral Hospital
11.	Wilson Githinji	Kenyatta National Hospital
12.	Dr. Ibrahim Matende	Lighthouse/ Coast Provincial General Hospital
13.	Dr. Joy Kabiru	PCEA Kikuyu Eye Hospital
14.	Dr. Wairimu Waweru	University of Nairobi
15.	Truphosa Chidzuga	Coast Provincial General Hospital
16.	Dr. Jamilla Rajab	University of Nairobi
17.	Dr. Irene Muramba	Coast Provincial General Hospital
18.	Phenny Kanchoro	Lighthouse for Christ
19.	Rose Atsiaya	Lighthouse for Christ
20.	Dr Mary Mugania	Kenyatta National Hospital
21.	Wekesa Nchienya	Moi Teaching & Referral Hospital
22.	Dr. Jean Claude	Sabatia Eye Hospital
23.	Dr. Micheal Gichangi	MOH
24.	Dr. Benjamin Biwott	Moi Teaching & Referral Hospital
25.	Dr. Zahra Mohamed	Coast Provincial General Hospital
26.	Dr. Wata David	Kenyatta National Hospital

NOTES

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