Retinoblastoma programme 2019–2029 in Niger

Adam Nouhou Diori, Hôpital National Amirou Boubacar Diallo, Niamey, Niger; **Yakoura Abba Kaka,** Hôpital National de Niamey, Niger; **Laminou Laouali,** Hôpital National de Zinder; **Aïchatou Mahamadou,** Centre National de Lutte Contre le Cancer, Niger; **Amadou Bouba Hassane Traore,** Centre Hospitalier Régional de Maradi, Niger; **Pierre Bey,** Alliance Mondiale Contre le Cancer; **Youssoufou Souley Abdoul Salam,** Hôpital National Amirou Boubacar Diallo, Niamey, Niger; **Amza Abdou,** Hôpital National Amirou Boubacar Diallo, Niamey, Niger; **Laurence Desjardins,** Alliance Mondiale Contre le Cancer; and **Karim Assani,** Alliance Mondiale Contre le Cancer and University of Kinshasa, RD Congo


ADAM NOUHOU DIORI


YAKOURA ABBA KAKA


LAMINOU LAOUALI


AÏCHATOU MAHAMADOU

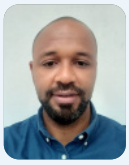

AMADOU BOUBA HASSANE TRAORE


PIERRE BEY


AMZA ABDOU


LAURENCE DESJARDINS


YOUSSOUFOU SOULEY ABDOUL SALAM

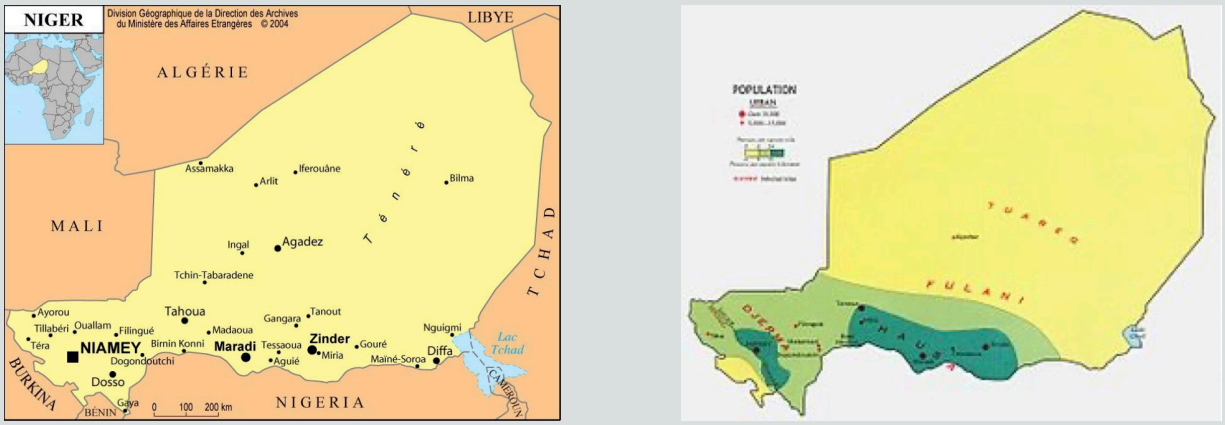

KARIM ASSANI

Retinoblastoma (RB) is a rare intraocular cancer. It can be unilateral or bilateral and affects young children before the age of five years. Early diagnosis and rapid management by a specialized multidisciplinary team achieves a 95% cure rate in developed countries, whereas in low- and middle-income countries mortality remains high. The Alliance Mondiale Contre le Cancer (AMCC), in partnership with the Franco African Group of Paediatric Oncology (GFAOP) and multidisciplinary African teams, has supported an RB programme in sub-Saharan Africa since 2011 to improve training of ophthalmologists and ocularists, equipment for conservative management, and programmes for early diagnosis and data collection. In 2019, this programme was extended to all French-speaking, and to some English-speaking and Lusophone teams".The programme was implemented in Niger in 2021 and a retrospective study of children with RB was recently conducted in Niamey. A total of 127 eyes with RB were observed, with 58 extraocular diseases at presentation. Three children with bilateral disease had one eye with conservative management. Early diagnosis campaigns are detailed. Retinoblastoma is still a diagnosis challenge in sub-Saharan Africa, and the creation of secondary centres is one way to facilitate early diagnosis. Local multidisciplinary teams face specific problems, such as socioeconomic difficulties, travelling problems, refusal of enucleation, and treatment abandonment.

Retinoblastoma (RB) is a rare type of eye cancer that affects young children under five years of age, affecting both eyes in approximately one-third of cases, and often appearing during the first year of life *(1)*. Approximately 8,500 new cases occur worldwide each year (of 8 billion inhabitants, 25% of whom are under 15 years of age), including 2,000 cases in sub-Saharan Africa, which has a population of approximately 1.2 billion, of which 40% are under 15 years of age *(2)*. A retrospective analysis of RB diagnosed in 40 European countries and 43 African countries shows that considering the frequency of RB to be one case for every 17,000 births, only 42% of expected cases are diagnosed in Africa versus almost 100% in Europe *(3)*. These facts were demonstrated in a larger study of 153 countries showing a further 49.1% of extraocular forms in low-income countries *(4)*. In these countries, such as Niger, survival remains below 20% due to late diagnosis or even no diagnosis, the small number of teams trained and equipped for treatment, training and equipment being costly for a limited number of cases, and countries having to face multiple other priorities *(5)*. Although it is not a public health problem, RB is exemplary today because it is easily curable in high-income countries (a 98% cure rate for more than 20 years, but for only 15% of global cases) with, for bilateral cases, preservation of at least one eye and useful visual acuity thanks to early diagnosis from the initial symptoms, rapid access to a competent team, well-codified treatments (enucleation + chemotherapy +/- local ophthalmological treatments) applied without delay, and complete insurance coverage with rehabilitation by prosthesis after enucleation *(2)*.

It is in view of this observation that the World Alliance Against Cancer (Alliance Mondiale Contre le Cancer [AMCC], cancer-amcc.org), in partnership with the African Francophone

Figure 1: Xxxxxxxxxx



Group for Paediatric Oncology (GFAOP, www.gfaop.org) for French-speaking countries and the multidisciplinary team in Bamako, Mali, has led successive programmes since 2011 to "support early diagnosis, access to treatment, and rehabilitation for children with RB in French-speaking sub-Saharan Africa". A demonstration was provided by the dynamic team in Mali that the cure rate could exceed 80% in unilateral intraocular forms with prostheses manufactured locally, thanks to training (ophthalmologist and ocularist), the provision of additional equipment for ophthalmological procedures and anticancer drugs, assistance with early diagnosis campaigns, and support for the most deprived families *(6)*.

In 2019, a 2019–2028 programme was implemented on the same basis as the previous programmes but this time extended to most French-speaking sub-Saharan countries (Benin, Burkina Faso, Cameroon, Congo, Ivory Coast, Gabon, Guinea, Madagascar, Mali, Mauritania, Niger, Central African Republic, DR Congo, Togo, and Senegal), to some English-speaking countries (Ethiopia, Ghana, Kenya, Rwanda, Tanzania, and Uganda), and Portuguese-speaking countries (Mozambique and Angola), with a total of 1,400 new cases of RB expected in 2024 in the 23 countries concerned *(7)*. The objective of the programme is to contribute to curing at least 800 children with RB each year from 2030, in line with the World Health Organization's objective of curing 60% of childhood cancers. The Niamey team joined the programme coordinated by the AMCC in 2021.

Patients and methods

This is a retrospective study of children with RB in Niamey, Niger. Niger is a Central African country, covering 1.26 million km². It is home to 28 million inhabitants, with a high fertility rate (6 children/woman) and a projected population of 80 million by 2050. Currently, 47% of the population is under 15 years of age, and the number of new annual cases of RB, estimated at between 55 and 60 in 2024, will more than double by 2050. Routine care is free for children under five years of age, the age group at which RB is diagnosed (8).

Niger and its population: The population is mainly concentrated in the southwest of the country, with the capital, Niamey (nearly 2 million inhabitants), very remote. INS report, 2023 *(9)*.

- The implementation of the conservative treatment system and prostheses after enucleation was made possible thanks to the additional training in Bamako in 2021 and at the Curie Institute in 2024 of Dr Adam Nouhou Diori, an ophthalmologist at the Amirou Boubacar Diallo National Hospital (HNABD), which houses the referral ophthalmology department; and the training of an ocularist in Bamako in 2021. The paediatric oncologist at the National Cancer Centre in Niamey (CNLC), Dr Aîchatou Mahamadou, heads the paediatric oncological unit, which provides assessment and chemotherapy, and has been a member of the GFAOP since 2015 and a pillar of the multidisciplinary paediatric oncological team.
- Training has been supplemented by the allocation of equipment by the AMCC in recent years, including an enucleation box, indirect ophthalmoscope, diode laser plus helmet, cryode, fundus camera, prosthesis equipment; and the supply by the GFAOP of anticancer drugs for RB chemotherapy.

Thus, since the end of 2022, a dynamic and progressively well-equipped multidisciplinary team has been operational in Niamey. Enucleated children benefit from a prosthesis manufactured on site. Conservative treatments have been possible since 2023.

We conducted a retrospective study from 1 January 2022 to the end of December 2024 in the ophthalmology department of the HNABD in Niamey.

All children admitted to the HNABD and the Paediatric Oncology Department of the CNLC, diagnosed with retinoblastoma during the study period, were included.

Table 1: **Characteristics of eyes with retinoblastoma by year**

Year	2022	2023	2024
Number of children	35	35	35
Unilateral	31	26	26
Bilateral	4	9	9
Stage (number of eyes)	Intraocular: 24 Extraocular: 15	Intraocular: 17 Extraocular: 27	Intraocular: 28 Extraocular:16
Chemotherapy	Yes	Yes	Yes
Enucleation	23	13	14
Thermotherapy	0	2	1
Prosthesis	0	3	13

Of a total of 127 eyes with retinoblastoma over a 3-year period, the following were noted:
- 22 bilateral cases (44 eyes);
- 69 eyes with an intraocular stage; and
- 50 enucleated eyes, 16 of which were fitted with an ocular prosthesis.

A multidisciplinary consultation process was established: the team participates in a web conference coordinated by the AMCC every two weeks, where RB cases are discussed within the network of teams participating in the AMCC's RB programme using the RB-NET platform.

Actions are essential to promote early diagnosis. These actions must be repeated annually and involve training healthcare professionals and informing parents. Actions already taken are described in the results.

The 2029 objective is for at least 80% of incident RB cases in the country to reach the multidisciplinary team in Niamey, with most cases occurring at the early intraocular stage. The creation of a WhatsApp alert group including all ophthalmologists in Niger, extended to senior technicians, facilitates the arrival of cases in Niamey.

Data collection includes age, unilateral or bilateral form, stage at diagnosis, treatments used, and survival.

For conservative treatments, fundoscopy is performed at the start of active treatment every four weeks under general anaesthesia until complete response, then every month or every two months until one year of follow-up. All children, including unilaterally enucleated children, are followed every three months until two years of age, every four months until three years of age, then every six months until five years of age, and finally every year from the age of five.

The registries include consultation data, physical and electronic patient records from the paediatric oncology unit, as well as those from the ophthalmology department of the HNABD.

Respect for anonymity and confidentiality of patient identities, as per the Declaration of Helsinki, guarantees the ethics of our database.

Results

The actions carried out for early diagnosis are as follows:

- Training of general practitioners and paediatricians from

Table 2: **: Conservative management of three eyes**

Clinical cases	Case 1	Case 2	Case 3
Age	17 months	6 years	11 months
Gender	Female	Female	Female
Group of RB	OD: group A–B OG: group E	OD: group E OG: group C	OD: group A OG: group D
Results	OD: complete remission OG: enucleation	OD: Enucleation OG: complete remission of the main lesion with several recurrences producing a large retinal ischaemia	OG: complete remission OG: enucleation
Ocular prosthesis	Yes	Yes	Yes

all eight regions of Niger (25 participants) with the support of the Bamako team and the AMCC programme manager from 8–13 November 2021;

- Postgraduate Education Sessions (EPUs) organized in collaboration with the Nigerien Society of Ophthalmology (SNO): SNO Congress in 2022 with approximately 300 participants and EPUs on 23 February and 27 May 2023 and 1 June and 5 October 2024, which reached approximately 200 healthcare professionals;
- Local awareness-raising for healthcare practitioners in major referral hospitals in the capital (Niamey). In 2023, the National Hospital of Niamey brought together approximately 30 students, paediatricians, paediatric oncologists, and ophthalmologists in the paediatric staff room; and on 7 and 15 June 2023, the HNABD brought together approximately 50 participants, respectively, in their paediatric staff room.
- Training workshop for ophthalmology practitioners (ophthalmologists and senior ophthalmology technicians) from all regions in the recognition and referral of suspected cases of RB on 1–2 November 2023, with approximately 45 participants.

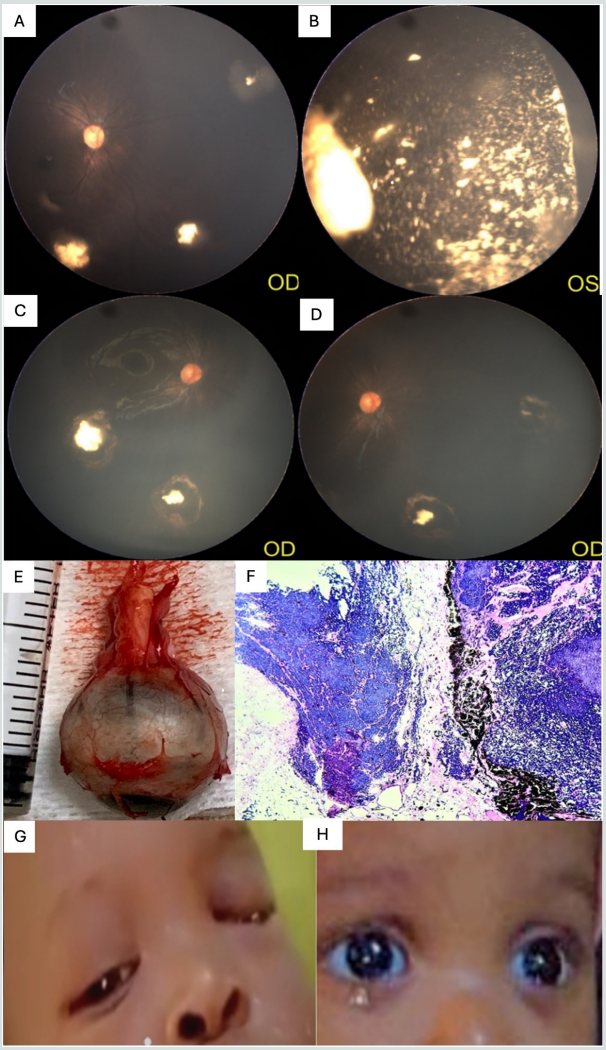
Children with extraocular forms (58 eyes) received palliative treatment following tumour spread, either orbital or cerebral.

Three children with bilateral retinoblastomas underwent conservative treatment of one eye with thermochemotherapy.

This treatment consisted of a combination of intravenous chemotherapy and local ophthalmic treatments (trans-pupillary diode laser thermotherapy and cryotherapy).

All three eyes were cured, although one eye experienced several local relapses after stopping chemotherapy, which required local ophthalmic treatment. (Figure 1, 2, and 3)

Figure 1: Clinical case number 1



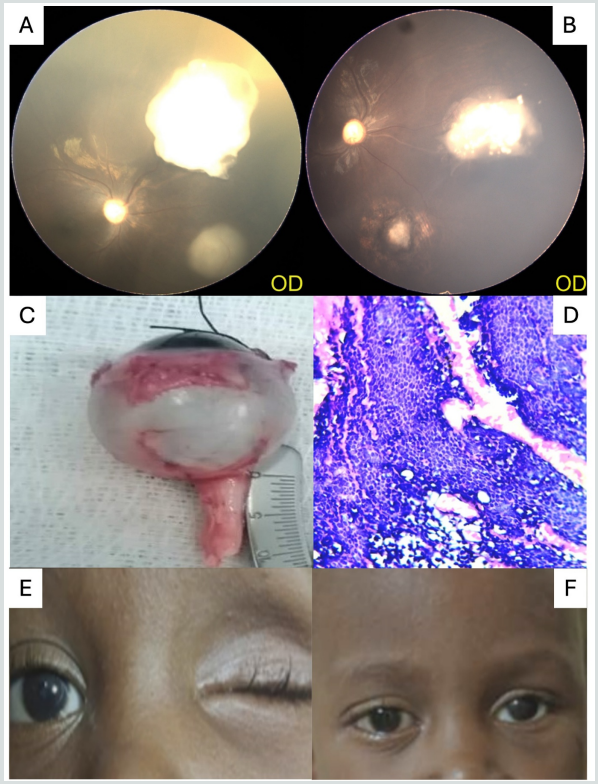
A. Fundus photography of the right eye at diagnosis. Two tumours are in the nasal part of the eye. B. Fundus photography of the same right eye after treatment by thermochemotherapy (six cycles of intravenous chemotherapy [vincristine, etoposide, carboplatin] and diode laser), showing calcified scars. C. Photography of the left enucleated eye. D. Histopathology sample of the left enucleated eye demonstrating the tumoral cells (hematoxylin and eosin staining). E. Aspect of the left orbit after enucleation, without ocular prosthesis. F. Satisfactory aesthetic rehabilitation after placement of the left ocular prosthesis.

Discussion

Retinoblastoma is a rare but highly curable tumour, which justifies the action taken by the AMCC since 2011 through a programme to support the management of RB in sub-Saharan Africa *(10)*. The possibility of rapid improvement in outcomes was demonstrated in Mali in 2018 thanks to support through training, additional equipment, and early diagnosis actions *(6)*. In Niger, in a recent study tracing the results of the service's activities from January 2016 to October 2022 (6 years 10 months), we found that most children arriving at the referral service are at a late stage that no longer allows for cure *(5)*. The conservative referral treatment centre in Niger was established in 2021, but it was not until May 2023 that the first case of bilateral RB meeting the criteria for conservative treatment was recorded. It should be noted that several challenges were overcome at different levels (logistics, training, etc.). Children with RB were able to benefit from free care for children under five years of age for certain aspects of treatment, even though the lack of financial means of parents of children with RB and the distance of localities from the reference centre were causes of delays in treatment *(11)*. Malnutrition and malaria were the main comorbidities among the children treated. Faced with all these challenges, it is sometimes necessary to know how to use personal relationships to facilitate the entry of equipment into the country, or to know how to innovate in order to adapt the equipment for our use.

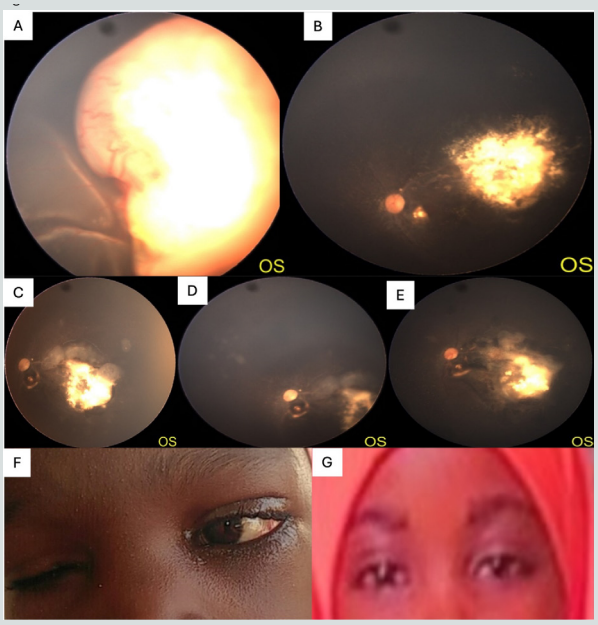
To facilitate early diagnosis, it was decided with AMCC to develop two secondary centres (Zinder and Maradi) in Niger so that a greater number of children can have access to early diagnosis.

Figure 2: Clinical case number 2



A. Fundus photography of the left eye at diagnosis, demonstrating a voluminous tumour at the posterior pole and a complete retinal detachment. B. Fundus photography of the same left eye after two cycles of intravenous chemotherapy (vincristine, etoposide, carboplatin), showing a retinal scar, without active disease. C and D. Fundus photography of the same left eye after initial treatment, demonstrating retinal recurrences and new lesions. E. Aspect of the fundus of the same eye after treatment of the active tumours by thermotherapy. E. Aspect of the right orbit after enucleation, without ocular prosthesis. F. Satisfactory aesthetic rehabilitation after placement of the right ocular prosthesis.

Figure 3: Clinical case number 3



A. Fundus photography of the right eye at diagnosis, demonstrating three retinal tumours. B. Fundus photography of the left eye at diagnosis, demonstrating a large retinal tumoral and a diffuse dense vitreous seeding. C and D. Fundus photography of the right eye after thermochemotherapy, demonstrating three retinal scars. E. Photography of the left enucleated eye. F. Histopathology sample of the left enucleated eye demonstrating the tumoral cells (hematoxylin and eosin staining). G. Aspect of the left orbit after enucleation, without ocular prosthesis. H. Satisfactory aesthetic rehabilitation after placement of the left ocular prosthesis.

Several actions are underway in 2025 including:

- Strengthening the multidisciplinary team in Niamey with the training of a second ophthalmologist at the IOTA University Hospital in Bamako to ensure continuity of conservative treatment, which was successfully initiated in 2023;
- Training ophthalmologists and senior ophthalmology technicians in Niamey on the diagnosis of RB, which is purely clinical, and on referral to the Niamey team;
- Informing primary health centre staff, who are the first point of contact for the population when faced with signs suggestive of RB (leukocoria, strabismus), and the appropriate actions to take within the framework of Ministry of Health programmes; and
- Identifying and training ophthalmologists (in Niamey) and senior ophthalmology technicians (onsite) in the two secondary centres in Zinder and Maradi.

Retinoblastoma is a rare malignant tumour of the retina that mainly affects young children *(12,13)*. In 90% of cases, the diagnosis is made before the age of five years, as in all three cases we report, even though cases of RB in older children have been reported in the literature *(12, 14,15)*. On the other hand, bilateral or multifocal retinoblastomas are all hereditary, with autosomal dominant transmission. Retinoblastoma is unilateral in 70% of cases; the average age at diagnosis is approximately two years *(16)*. One of the cases we report became bilateral after five years of evolution in a unilateral form. In synchronous bilateral forms, the average age at diagnosis is about one year and tends to decrease in industrialized countries thanks to the screening of children in at-risk families by systematic examination of the back of the eye *(17)*. About two-thirds of stage A–C eyes can be saved by reduction chemotherapy alone coupled with focal treatments, compared to 25–30% of stage D eyes *(18)*.

Our three cases treated with this procedure healed. Hyperthermia is delivered by transpupillary infrared irradiation using a diode laser, at cytotoxic temperatures. It can destroy small tumours without vitreous swarming or subretinal fluid *(19)*. We performed transpupillary thermotherapy using a helmet and a 20-diopter lens, delivering continuous power calibrated to 350 mW for an average of 20 minutes on the tumours.

In the case of enucleation, the optic nerve must be severed as far as possible, over a length of at least 10mm for histopathological examination *(20)*. The most affected

eye was enucleated in all patients with a good section of the optic nerve of approximately 10mm. Very close specialized ophthalmological monitoring is necessary, because the reappearance of new tumour foci is part of the normal evolution of RB, especially the hereditary form *(21)*. One of the cases we followed had manifested several recurrences and relapses during his follow-up. Thanks to close and regular monitoring, the new tumours were able to be controlled.

Conclusion

Thanks to the considerable support of the AMCC, Niger, a low-income French-speaking sub-Saharan country, has been able to consolidate a multidisciplinary team for the organized care of children with RB, including conservative treatment allowing the preservation of one eye and useful vision in cases of bilateral RB. This is a young treatment centre, so several challenges remain to be addressed over time, especially in terms of early diagnosis as part of the public health actions of the country's health authorities. ■

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Declaration of Competing Interests

The authors declare no competing interests.

Dr Adam Nouhou Diori is an ophthalmologist and Deputy Chief Medical Officer of the Ophthalmology Department of Amirou Boubacar Diallo National Hospital in Niamey, Niger. He is the CAMES Assistant Professor at the Faculty of Health Sciences at Abdou Moumouni University in Niamey and the Coordinator of the sixth year of medical studies at FSS/UAM. He is also Head of the Retinoblastoma Conservative Treatment Unit in Niger, AMCC focal point for Niger and a member of the GFAOP Retinoblastoma Committee.

Dr Abba Kaka H Yakoura is an ophthalmologist and Head Physician of the Ophthalmology Department of the National Hospital of Niamey, Niger. She is CAMES Associate Professor at the Faculty of Health Sciences at Abdou Moumouni University in Niamey, Niger and Coordinator of the Bachelor's Degree in Ophthalmology at FSS/UAM.

Dr Laouali Laminou is an ophthalmologist and Chief Physician of the Ophthalmology Department of Zinder National Hospital, Niger. He is CAMES Assistant Professor at the Faculty of Health Sciences at André Salifou University in Zinder and the regional focal point for retinoblastoma management in Zinder.

Dr Aichatou Mahamadou is a paediatric oncologist and Head of the Paediatric Oncology Unit at the National Cancer Centre (CNLC) in Niamey, Niger. She is a member of the GFAOP Retinoblastoma Committee.

Amandou Boube Traore Hassane is an ophthalmologist and Head Physician of the Ophthalmology Department of the Regional Hospital Centre in Maradi. He is the CAMES Assistant Professor at the Faculty of Health Sciences at Dan Dicko Dankoulodo University in Maradi. He is also Deputy Director of the Niger Institute for Comprehensive Eye Health and the Maradi regional focal point for retinoblastoma management in Maradi.

Dr Pierre Bey is Professor Emeritus of Radiation Oncology with 30 years of practice in paediatric radiotherapy. He is Medical Director of AMCC and was Director of the Institut Curie (Paris) Hospital, which is the reference centre for retinoblastoma in France. He has published 160 articles in peer-reviewed journals.

Dr Abdoul Salam Youssoufou Souley is an ophthalmologist, in the Ophthalmology Department of the Amirou Boubacar Diallo National Hospital in Niamey, Niger. He is also the Medical Commander of the Niger Armed Forces (FAN).

Professor Abdou Amza is an ophthalmologist and Chief Physician of the Ophthalmology Department of the Amirou Boubacar Diallo National Hospital in Niamey, Niger. He is CAMES Full Professor at the Faculty of Health Sciences of Abdou Moumouni University in Niamey, and Coordinator of the Specialist Diploma in Ophthalmology at FSS/UAM.

Dr Laurence Desjardins is an ophthalmologist and President of the Alliance Mondial Contre le Cancer (AMCC). Among many roles, she has been Head of the Opthalmic Oncology and Surgical Departments at the Curie Institute in Paris, as well as being site Director in Paris, President of the Opthalmic Oncology Group (OOG) and Vice President of EVER. She has published 235 artilces in peer-reviewed journals and worked extensively on African projects.

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