

# Improving Care for Children With Cancer in Africa: Two Decades of Experience of the French African Pediatric Oncology Group

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## Introduction

In the era of increased interest for pediatric oncology in developing countries and particularly WHO Global Initiative for Childhood Cancer (GICC),<sup>1</sup> it is important to evaluate and learn from various experiences and attempts to improve the care in this field. To bridge the gap between developed countries where overall survival (OS) is reaching 80% and developing countries where it is around 20%, several models have been implemented during the last few decades. International Society of Pediatric Oncology-Pediatric Oncology in Developing Countries advocates twinning and use of adapted regimen.<sup>2</sup>

Trying to put in place care for children suffering from cancer in Africa is probably the most difficult. The health care system is in most parts of sub-Saharan (SS) Africa in difficulties to offer basic care. According to the World Bank<sup>3</sup> among the 30 poorest countries in the world, 26 are in Africa. This continent is also the second most populous after Asia, with 1,032,532,974 estimated inhabitants. The annual population growth rate of African population is twice as high as the global average (2.7% per year). It is thus estimated that by 2025, Africa will have 1.3 billion inhabitants with 500-600 million children under age 15 years. French-speaking Africa consists mainly of North Africa, most of West and Central Africa, and Madagascar. This represents 24 countries where estimated total population is 383,871,000 inhabitants and children under age 15 years represents 23%-50%.<sup>4</sup>

## Group Creation

The Francophone-African Group of Pediatric Oncology (GFAOP) was created in October 2000 by a group of pediatric oncologists from France and Africa who used to meet in Paris at the yearly meeting of Les Journées Parisiennes de Pédiatrie.<sup>5</sup> At that time, no pediatric oncology unit was in place in SS Africa. The group led by Professor Jean Lemerle<sup>6</sup> set out to put in place a comprehensive program aiming at developing childhood cancer program in Africa. This included training doctors and nurses and careful adaptation of treatments tailored to African populations and evaluated

through clinical research program. The group meets at least once a year to evaluate the activity.

The organizational foundations of GFAOP are built around the concept of a pilot unit (PU). The core of a PU is a ward dedicated to the care of children with cancer. PUs have functional links with other complementary structures, including surgery, pathology, and when available (North African units) radiotherapy departments. A commitment from hospital management or ministry of health is required to put in place and support the PU. The program begins with the training of the teams. Up to 2015, a total of 128 health care providers, from 14 African countries, attended the courses. Among them, 72 were nurses, 32 pediatric surgeons, 21 pediatric hemato-oncologists, two pathologists, and one ophthalmologist.<sup>7</sup> A diploma on pediatric oncology has been afterward put in place.<sup>8</sup> The unit is renovated and equipped if needed. A visit of GFAOP delegation is usually organized. The PU is then an integral part of the network and is asked to participate in clinical research programs. Starting with 7 PUs (from six countries), 18 PUs joined the group afterward, and 25 PUs (from 18 African countries) are now integral part of GFAOP African network (Fig 1).

It was decided to start with B-cell lymphoma (BL) and Wilms tumors (WT) to test the efficacy of the program. The impact was measured through the improvement of patients' accrual, survivals, and quality of care. The head of the PU is asked to participate in working groups, make an annual report, and present the activity of his unit during the annual general assembly.

## PU's Support

Active fundraising was put in place by the volunteers to support teams and families. Areas of action were developing workforce training, providing medication and support to the families, and developing clinical research capacity within the group network.

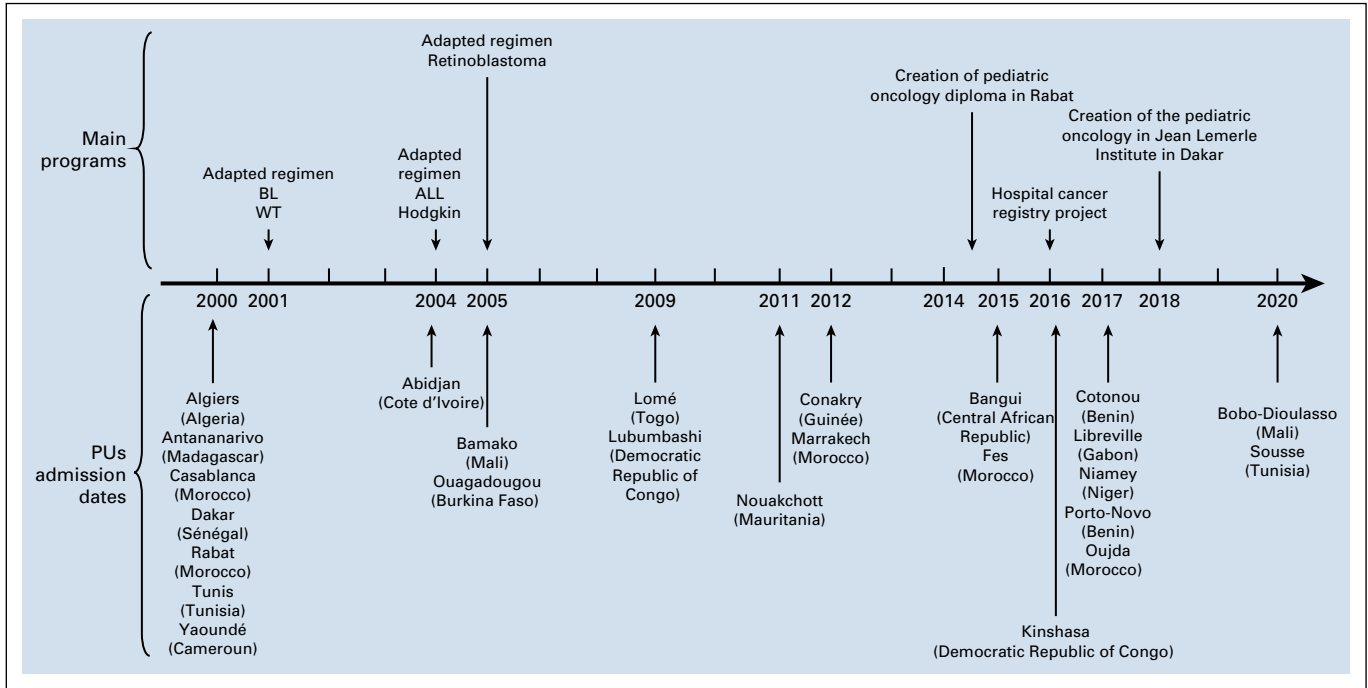
From the start, it appears that patients were in urgent need of drugs as they were not provided by their governments. The group had to provide medication and put in place a system for procurement and dispatching. As the number of patients admitted in PUs

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**FIG 1.** Dates of admission of pediatric oncology PUs in French African Pediatric Oncology Group and dates of initiation of main activities. ALL, acute lymphoblastic leukemia; BL, B-cell lymphoma; PU, pilot unit; WL, Wilms tumor.

increased over the time to reach 1,600 yearly in the SS region, it was needed to raise up to 300,000 € per year to provide support for the patients admitted in this region. This was possible—thanks to the contribution of Moroccan Lalla Salma Foundation<sup>9</sup> and French private donors.

GFAOP developed a network of partnerships with other organizations pursuing common goals. Institute Gustave Roussy in Villejuif (France) contributed in hosting the GFAOP and supporting its activity from the beginnings. Institute Curie in Paris (France) also supported GFAOP activity. Sanofi-Espoir Foundation through My Matters program supported GFAOP in various programs including setting up African School of Pediatric Oncology based in Rabat (Morocco) in 2014. In 2018, Bristol Myers Squibb Foundation supported GFAOP program in putting in place Jean Lemerle Institute in Dakar dedicated to developing nurses' education program, developing early diagnosis, and improving multidisciplinary approach. Alliance Mondiale Contre le Cancer<sup>10</sup> developed a program for retinoblastoma. Moroccan Lalla Salma Foundation contributed significantly by providing medication for most PUs in SS Africa. More recently, Regine Sixt Foundation contributed in the support of the program. The comité de soutien has been during all phases very dynamic in collecting donations from various organizations mainly in France.

Reducing the rate of treatment abandonment by providing housing for parents was considered of major importance. GFAOP initiated a first project with PU of the University Hospital of Treichville in Abidjan. Lalla Salma Foundation<sup>9</sup>

who had experience in putting in place parents' houses in Morocco was helpful in putting in place a house called Akwaba. Soletterre Italian NGO<sup>11</sup> runs the house in Cote d'Ivoire. Another parents' house, set up in Kinshasa (Republic Democratic du Congo), is active since July 2020—thanks to two other NGOs (AB CFAO foundation and Les Jeannots, a local parents' association) who are managing the house. A third house is also set up in Ouagadougou (Burkina Faso)—again thanks to AB CFAO foundation with Soletterre.

**Clinical Research**

The GFAOP's research program can be divided into three periods. The first period (2001-2005) began with two feasibility studies for Burkitt BL and WT. This choice was done because more than 90% survival is achieved in high-income countries using at the time low-inexpensive drugs. The PUs who participated in the study were from Rabat, Casablanca, Tunis, two hospitals in Alger, Dakar, Antananarivo, and Yaoundé. OS rates were higher in North Africa compared with SS units: 70% versus 44% for BL<sup>12</sup> and event-free survival 87% versus 47% for WT, respectively.<sup>13</sup> Interestingly, for the whole PUs participating in BL first study, OS increased from 54% during the first year to 73% during the third year, whereas there was a decrease of toxic death rates from 27% to 10% just by improving supportive care.<sup>12</sup> The results demonstrated that prospective international studies were feasible in Africa. They also identified problems and needs for improvement including supportive care, histological and cytological diagnosis, surgical management, and the structuring and implementation of a multidisciplinary framework.

The second period (2005-2015) began with the establishment of committees specializing in different pathologies on the basis of the International Society of Pediatric Oncology committee system. New therapeutic recommendations were made for three other pathologies (retinoblastoma, Hodgkin's lymphoma [HL], and acute lymphoblastic leukemia [ALL] standard risk) and for BL and WT. Additional SS units included Abidjan, Bamako, Lomé, and Ouagadougou. OS improvements were identifiable in SS units. Therapy with cyclophosphamide alone was a failure for BL.<sup>14</sup> Thus, it was replaced by a B-lymphoma regimen-based therapy without doxorubicin, allowing 60% of the patients to be cured. Interestingly, patients who followed the time schedule achieved an OS of 75%.<sup>15</sup> The OS of patients with unilateral nonmetastatic standard-risk WT was 75%.<sup>16</sup> In Bamako, the OS of children with intraocular retinoblastoma was 85% that decreased to 48% when intraorbital, motivating early diagnosis campaigns.<sup>17</sup> With a COPP-ABV regimen without radiotherapy, 82% OS was observed in 106 patients with HL.<sup>18</sup>

The third period is the current one. Research qualities are being raised to a level equivalent to international standards to better comply with the requirements of clinical research: ethics committees in each country, including the Commission Nationale Informatique et Liberté in France. Data monitoring has been put in place to improve quality in conjunction with the implementation of online registration. In 2016, as part of the Sanofi Espoir Foundation's My Child Matters program, a register, known as Registre Franco-Africain d'Oncologie Pédiatrique (RFAOP), was created. This hospital registry allows registration of all cancer cases seen in the oncology units according to Cancer Registration.<sup>19</sup> The Clinical Research Assistants of the units who record data received initial training and have ongoing training (via e-learning, 1-week face-to-face training, site visits, participation in group meetings, and ongoing individual support via e-mail and visioconferences). The RFAOP permits units to have precise information concerning treatment, outcome, pathology patterns, and pharmaceutical and human resource needs. It provides precise figures to the authorities in the context of advocacy and national cancer plan and can subsequently serve as a basis for the creation of regional and ultimately national registry of childhood cancers. From January 2016 to

December 2018, 13 PUs participated and registered 2,790 cases.<sup>20</sup>

New therapeutic recommendations are progressively implemented. These therapeutic recommendations concern the same five types of tumors (BL, WT, retinoblastoma, HL, and ALL). The group is currently extending the therapeutic recommendations to higher risk forms in the BL and ALL studies on the basis of improvement in supportive care. Three studies have been registered in ClinicalTrials.gov (GFA LMB2019: [NCT04425421](https://clinicaltrials.gov/ct2/show/study/NCT04425421); GFA NEPHRO2020: [NCT4423484](https://clinicaltrials.gov/ct2/show/study/NCT4423484); GFA RB1 2019: [NCT04425434](https://clinicaltrials.gov/ct2/show/study/NCT04425434)) and are recruiting.

### Perspectives and Future Challenges

GFAOP has shown that it is possible to have local teams that are able to provide care to children with cancer, to work as a pluridisciplinary team, and to work with other African teams in building a common program and conducting a clinical research together. Various approaches have been implemented to develop care in developing countries built most of the time around a twinning approach.<sup>2,21,22</sup> A very few efficient initiatives have been implemented in Africa.<sup>23</sup> WHO GICC<sup>1</sup> in partnership with St. Jude Children Research Hospital launched an important initiative with the objective of achieving 60% survival by 2030. The GFAOP approach is similar to the WHO GICC initiative in various aspects.<sup>24</sup> In the Cure-ALLWHO approach, PUs are the countries' centers of excellence, and adapted regimen and clinical evaluation are equally implemented. However, the support does not meet the needs because of the weakness of health care system and lack of governments' engagement. The GFAOP is actively working in putting in place an action plan for the next decade. Each PU contributed to the vision and organization of the program at the country level, including creation of satellite units or new PU and at the network level. GFAOP, after two decades of working in difficult contexts including political instabilities and wars, showed that when African teams are empowered, it is possible to put in place complex pediatric oncology care. This is however far from reaching out to the whole population. With more support, there is an opportunity to get most of African children benefiting from the progress achieved in the developed world. Governments, local authorities, and NGO's engagements are needed to assure the sustainability of the program.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless

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