Executive summary

Background

Breast cancer is not only the most commonly diagnosed cancer in the world but also highly curable, with 5-year relative survival rates reported to range between 69% and 89% in Europe and North America. Survival rates depend directly on the stage at diagnosis, waiting time to initiate treatment after diagnosis, quality of treatment, and compliance with treatment.

Guided by the National Plan for Cancer Prevention and Control (2010–2019), the Moroccan Ministry of Health has made significant investments in improving diagnostic and therapeutic facilities for common cancer types in Morocco. Initiatives include the introduction of breast and cervical cancer screening programmes nationwide and the establishment of specialized units to manage breast and cervical cancers at the two largest publicly funded oncology centres in the country: Centre Mohammed VI pour le traitement des cancers (CM-VI) in Casablanca and Institut National d'Oncologie Sidi Mohamed Ben Abdellah (INO) in Rabat. The International Agency for Research on Cancer (IARC)/ World Health Organization (WHO), located in Lyon, France, collaborated with the Ministry of Health and the Lalla Salma Foundation for Cancer Prevention and Treatment to implement a **patterns-of-care study on breast cancer** to assess how far state-of-the-art cancer diagnostics and therapy have been disseminated into routine oncology practice. The study also aimed to identify patient-, provider-, and health system-level factors associated with receipt and utilization of cancer care and to measure their impact on cancer-specific survival.

The study was conducted retrospectively at CM-VI and INO and documented the changing patterns of care over a decade, from 2008 to 2017.

Methods

Patients with a confirmed diagnosis of breast cancer who were registered at the two oncology centres between 2008 and 2017 were included in the retrospective study. Patients with recurrence detected at registration were excluded. The records of eligible patients registered during a 2-month period of each year between 2008 and 2017 were scanned, and data were abstracted to fill in a structured questionnaire. The bimonthly sampling cycle started in January and February for 2008 and was shifted to the next 2 months every year until 2017. Data were abstracted from the case records by trained investigators using a structured questionnaire.

A total of **915 patients** from CM-VI and **1205 patients** from INO were included in the analysis.

Key findings

The **median age** at registration of patients with breast cancer was 49 years, and most were premenopausal. No appreciable shift in median age was seen over time.

A **family history of breast cancer** in first- and/or second-degree relatives was reported in 12.5% of the patients with breast cancer.

The median interval between the onset of symptoms and first medical consultation leading to referral for cancer diagnosis (the **access delay**) was 6 months. The interval exceeded 12 months in 30% of the patients. The access delay was significantly shorter in 2013–2017 than in 2008–

2012 for the patients registered at INO, possibly reflecting the benefit of the national screening programme and the awareness campaign associated with the programme.

A significant improvement in levels of **coverage with health insurance** was observed over time. Almost all the patients with breast cancer registered at CM-VI were covered by a health insurance scheme during 2015–2017; 86% were covered by the Régime d'Assistance Médicale (RAMED) scheme, which aimed to protect the most economically disadvantaged populations. At INO during the same period, 88% of the patients were covered by a health insurance scheme and 63% were covered by RAMED alone.

Overall, **adequate information to determine American Joint Committee on Cancer (AJCC) tumour–node–metastasis (TNM) stage** was available for 90% of the patients with breast cancer.

A **complete pathology report** (including tumour type and differentiation) was available for more than 90% of the patients, and **hormone receptor and human epidermal growth factor receptor 2 (HER2) expression status** was recorded for more than 80% of the patients. This not only highlights the high standard of the pathology facilities available but also reflects the high quality of record maintenance and service organization at the oncology centres.

The proportion of patients **presenting with advanced-stage cancer** (stage III or IV) was about 45%, and a decrease in the proportion of advanced-stage cancers was noted over time at INO but not at CM-VI. The interval between the onset of symptoms and first medical consultation (the access delay) was the only statistically significant determinant of advanced stage at presentation and was independent of all sociodemographic parameters.

The proportion of patients diagnosed with **clinically small tumours (≤ 2 cm in diameter)** increased with time both at CM-VI (15.1% in 2008–2010 and 20.0% in 2015–2017) and at INO (14.2% in 2008–2010 and 17.9% in 2015–2017), with a corresponding decline in the proportion of locally advanced cancers. This could be an early impact of the breast cancer screening programme, which was introduced in 2010.

Molecular profiling of breast cancers showed that about 55% of patients had luminal-like (estrogen receptor [ER]- and/or progestogen receptor [PR]-positive; HER2-negative) cancers and approximately 30% of patients had HER2-positive cancers (ER and PR either positive or negative). The proportion of triple-negative breast cancers was about 16%. The prevalence of triple-negative breast cancers in our study is comparable to that reported in studies in the USA and Europe. Earlier studies in Africa reported a much higher proportion of triple-negative breast cancers, most likely because of the failure to detect molecular markers in low-quality immunohistochemistry facilities.

Both oncology centres have a **multidisciplinary tumour board (MTB)** that meets once a week. Whereas all patients with breast cancer are referred to the MTB at INO, only selected cases are referred at CM-VI.

Treatment details were available for 86% of the patients registered at CM-VI and 96% of those registered at INO. Most patients at CM-VI (68%) had received some form of cancer-directed treatment (mostly surgery) before registration at the centre. The proportion of patients treated elsewhere (mostly with surgery) was lower at INO (37%). Patients **who had received all their treatment in settings outside the oncology centres had worse prognosis** (persistence or recurrence) than those treated partially or fully at the oncology centres.

The median interval between diagnosis and initiation of treatment (the **treatment delay**) was 2.7 months for patients registered at CM-VI and 1.6 months for those registered at INO. The interval decreased over time at CM-VI but increased at INO. The median interval between registration and initiation of cancer-directed treatment was also relatively long (1.5 months) at both centres.

Surgery was the mainstay of breast cancer management; 70% of the patients registered at CM-VI and 86% of those at INO underwent surgery. The proportion of patients with stage I–III cancer who were treated with **breast-conserving surgery** (BCS) was 50% at CM-VI and only 26% at INO. Postoperative radiotherapy was administered to only 38% of the patients registered at CM-VI who underwent BCS. The proportion was much higher (74%) in those registered at INO. However, the proportion of patients undergoing postoperative radiotherapy at CM-VI is probably underestimated, because some of them had their records maintained in a separate database in the radiotherapy department.

External beam radiotherapy was completed in 3–4 weeks in 55.1% of patients receiving radiotherapy at CM-VI and 66.2% of patients at INO because of the **use of hypofractionated radiotherapy**. Very few of the patients who received radiotherapy at INO and none of those at CM-VI required hospitalization, because most of them were accommodated in the Houses of Life (*Maisons de Vie*) built especially for this purpose.

The **median interval between surgery and initiation of adjuvant chemotherapy** for patients who did not receive radiotherapy in the intervening period was 3 months for those

registered at CM-VI and 2 months for those registered at INO. Ideally, this interval should not exceed 4 weeks.

Overall, 68% of the patients registered at CM-VI and 85% of those registered at INO received **chemotherapy**. Of the patients treated with chemotherapy, the proportion who received **neoadjuvant chemotherapy** was low, both at CM-VI (11%) and at INO (19%).

Almost all the patients treated with chemotherapy received an **anthracycline-based regimen** (either AC60/600 [four cycles of 60 mg/m^2 doxorubicin and 600 mg/m^2 cyclophosphamide every 3 weeks] or FEC100 [600 mg/m^2 5-fluorouracil, 100 mg/m^2 epirubicin, and 600 mg/m^2 cyclophosphamide]). Overall, 53% of the patients who received chemotherapy at CM-VI and 68% of patients at INO had a **taxane included** in the regimen. Inclusion of all chemotherapy drugs necessary for breast cancer management (including trastuzumab) in the **national list of essential drugs** has facilitated their procurement by public hospitals and ensured high treatment completion rates.

Endocrine therapy was administered to 54% of the patients with ER- and/or PR-positive cancers at CM-VI and 84% of those at INO. The proportion of patients who received hormone therapy might have been underestimated, because many received the drugs through outpatient prescriptions. **Trastuzumab** was administered to 28% of patients with HER2-positive cancers at CM-VI and 46% of those at INO.

Survival analysis could be performed only for those patients registered in 2008–2015, because the follow-up data were incomplete for those registered in 2016–2017. **Disease status at last follow-up** was documented for approximately 80% of the patients registered in 2008–2015. Very few patients were doc-

umented to have died at follow-up. This was essentially because the oncology centres did not have information on the patients dying at other health facilities or at home.

The **5-year disease-free survival (DFS)** was 53% for the patients registered at CM-VI and 70% for those registered at INO. The independent factors that were significantly associated with a higher risk of persistent disease or relapse were: **registration during 2013–2015 (compared with registration in 2008–2012), advanced stage of cancer, poorly differentiated cancer, triple-negative cancer, and treatment type**. Being treated completely outside the oncology centres was an important determinant of poor survival. The 5-year DFS was same for the patients with stage I and II cancer treated with BCS (82.9%) or mastectomy (81.3%).

Summary recommendations for strengthening breast cancer care in Morocco

This patterns-of-care study on breast cancer in Morocco revealed that significant progress has been made over the past decade in reducing the access delay, which has resulted in a modest downstaging of cancer (i.e. a shift in the stage distribution of tumours detected towards a lower stage), in organizing high-quality pathology services, and in offering

treatment tailored to stage and molecular profile to a large number of patients. At the same time, the study highlighted the deficiencies that need to be addressed to optimize breast cancer management. Reducing the delays in the care pathway for women with breast cancer symptoms could significantly improve the quality of care and survival rates (Fig. 1).

- The **access delay should be further reduced** by improving community awareness and ensuring that frontline health-care providers (nurses and general practitioners at the primary care level) are better trained to recognize symptoms of breast cancer and perform clinical breast examination. The breast cancer awareness campaign held every year in October needs to be strengthened. Awareness activities should be spread over the year.

- Several **cancer early detection centres** equipped with radiology (ultrasound and mammography) and core biopsy facilities have been established across Morocco to cater for referrals from the breast cancer screening programme. The services of these early detection centres can be used to examine and investigate women with symptoms of breast cancer as well. A well-coordinated **system of referral** should be established between the primary

Fig. 1. Delays in the care pathway for patients with breast cancer are still too long in Morocco. A concerted effort is needed to reduce these delays.
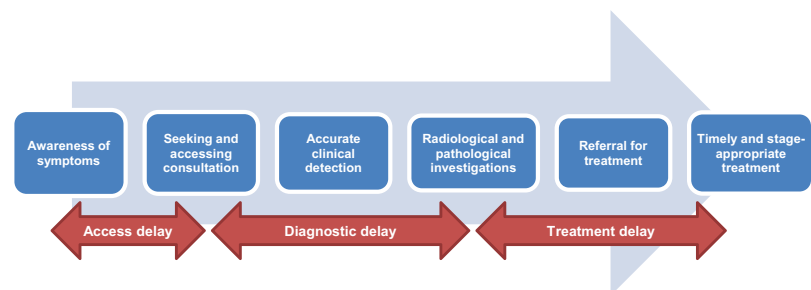
health centres, the cancer early detection centres, and the treatment facilities.

- Most likely because of the screening programme that has been implemented in Morocco, the capacity to diagnose breast cancer has improved in general. Most patients have a diagnosis confirmed on histopathology by the time they reach an oncology centre. Some early impacts of the screening programme on clinical downstaging are also visible. The quality and coverage of the **screening programme should be improved**. Higher compliance with further investigations in screen-positive women is needed.
- The **capacity to detect hormone receptor and HER2 expression** should be further improved at the oncology centres so that the proportion of patients with a complete molecular profile of breast cancer is higher than the current 80%.
- A large number of patients are undergoing surgery in general hospitals and clinics rather than at the oncology centres. **Decentralization of surgical servic-**

es may be a strength if it is appropriately monitored and if the surgeons are adequately trained in the principles and skills of cancer surgery. At present, many of the patients treated in non-oncology specialist settings do not receive standard-of-care treatment (as evidenced by the low proportion of patients receiving neoadjuvant chemotherapy or BCS).

- **Clinical practice guidelines** for managing breast cancer appropriate to the context in Morocco should be drawn up to standardize treatment and harmonize management practices across different facilities. The practice guidelines should be endorsed by the appropriate authorities and disseminated widely through orientation workshops.
- All newly diagnosed cases of breast cancer should be presented at the **MTBs**. Non-oncology settings managing breast cancers (including those in the private sector) could be linked digitally to any of the MTBs at the oncology centres in the region. The surgeons in non-on-

cology specialist settings should be able to discuss their cases before surgery.

- Efforts should be made to further **reduce the treatment delay**. Better counselling of the patients, prioritization of treatment of early-stage cancers, decentralization of treatment services, and improved coordination between different departments may help to reduce the delay.
- The use of **generic brands** and other innovative procurement mechanisms (e.g. direct negotiation with the manufacturers for bulk purchase) should be considered to ensure regular supply of more costly medicines such as taxanes or trastuzumab, which are already included in the national list of essential drugs.
- A **system of quality assurance** should be introduced, focusing on clinical effectiveness, patient safety, and patient experience related to breast cancer care. This will require regular auditing of services and feedback to be gathered from patients. A set of performance indicators and their standards tailored to the national context should be listed.