The Abu Dhabi Declaration: Why the Hustle?

Over the past decade, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) have emerged as a very useful tool for supporting and improving the quality of decision-making for oncologists worldwide. Considering that approximately 12 million cancer patients were registered by the WHO during 2008 and that the NCCN Web site (www.NCCN.org) attracts more than 150,000 visitors per month, one can conclude that the NCCN Guidelines program has potentially influenced the management of approximately 15% of all cancer patients worldwide. Although this example shows its far-reaching benefit, it also shows that there is plenty of room for expanding its application. A real need exists within the oncology community to have a reliable evidence-based tool to translate the rapidly accumulating scientific research into practical medical decisions that may offer a better and more consistent treatment outcome for patients.

The NCCN recently launched the NCCN–Middle East and North Africa (NCCN–MENA) Guidelines Congress in an attempt to provide versions of the original NCCN Guidelines tailored for cancer management in this region. However, one may ask whether it is really important to have a revised set of Guidelines specifically dedicated to a certain geographical region, when the original NCCN guidelines are satisfactory and comprehensive. We believe the answer is “YES” for 3 main reasons: differences in race, genetic, and environmental factors; differences in presenting features and stage; and differences in access to technology and drugs.

Differences in Racial, Genetic, and Environmental Factors

The NCCN Guidelines have been generated based on high-level evidence provided by large trials conducted mainly in the United States and Europe (hence predominantly enrolling a Western population) with a limited contribution from the rest of the world, including the Middle East.

Racial and genetic factors are known to play a vital role in the development of cancer. For example, in Europe, the United States, and Australia, people have a higher risk of developing skin cancer because they have fair skin, a characteristic that is uncommonly witnessed in other regions. Although guidelines for prevention and early detection of skin cancer are needed in these countries, they are of lesser importance in the Middle East.

Racial and genetic factors are not only relevant in cancer epidemiology but also can have significant influence on treatment strategies because of varying sensitivities to, and metabolism of, different drugs, resulting in a different prioritization of these approaches. For example, studies recently showed that Asian patients with advanced non–small cell lung cancer have a higher incidence of epidermal growth factor receptor (EGFR) mutations, and therefore experienced a greater benefit from treatment with EGFR inhibitors such as gefitinib and erlotinib. As a result of these findings, these agents were established as first-line therapies for these patients, before platinum-based chemotherapy, unlike in patients with non–small cell lung cancer in Europe and the United States. This raises an important question: can the results from large studies conducted mainly in Caucasian patient populations be accurately applied to the non-Caucasian majority in the rest of the world?

Of course, the pharmacogenomic preferential benefit of EGFR inhibitors reported in the above-mentioned studies does not necessarily exist in the same magnitude in other races or with other types of anticancer drugs. However, one may assume...
that certain differences are likely to emerge from the integrated efforts of experts in the region. The same concept may also be applied to the differences in some environmental factors that may also play a role in the process of carcinogenesis and response to treatment. For example, in contrast to the West, where hepatocellular carcinoma (HCC) is less common and mainly secondary to alcoholic hepatitis and hepatitis B virus, in many Middle East countries, HCC is one of the most common cancers and usually secondary to hepatitis C virus (HCV). In a subgroup analysis of a pivotal sorafenib study, a greater benefit of this drug was seen among patients with HCV-associated HCC. Another example is bladder cancer, which is usually of transitional cell histology in Europe and the United States, but is commonly of squamous cell histology in several countries in the Middle East where schistosomiasis is rampant. These differences may limit the applicability of “West-centric” guidelines in the clinical practice of oncology in other regions of the world.

These issues presented significant challenges for our diverse team while setting the objectives of the NCCN–MENA project, because the geography of our loosely defined region stretches from the west of Morocco to the eastern part of India. Therefore, the so-called MENA cancer patients according to this geographic definition are in fact a large population of racially and environmentally heterogeneous people among whom one might elicit differences rather than similarities. Still, in the current project of NCCN–MENA, we made a thorough review of the available literature generated from cancer patients in our region, seeking any convincing evidence that may suggest a unique therapeutic feature attributable to racial, genetic, or environmental factors.

**Differences in Presenting Features and Stage**

In the Middle East and in other developing regions of the world, cancer is often diagnosed at a younger age and tends to be of more advanced-stage compared with cases reported among the Western populations. For example, in the Middle East, the median age of breast cancer diagnosis is younger (with 25% of patients < 40 years) compared with older than 60 years in the West. The lack of early detection programs in the Middle East has resulted in most breast cancer and other solid tumors presenting at stages III/IV compared with in Western countries. Taken together, the screening policy adopted in the West would certainly miss early detection of breast cancer in many young women, who represent a good proportion of cases in the region.

**Differences in Access to Technology and Drugs**

The Middle East is composed mostly of developing nations with restricted access to advanced technology and novel agents incorporated in current oncology practice. Cost–benefit analysis studies conducted in the West are difficult to apply to this region because of the differences in health systems among the developing and developed nations. Guidelines taking into account these limitations would help optimize the application of novel strategies to best use the limited resources available. Current NCCN Guidelines are cost-blind and do not address these issues, and therefore fall short in a resource-restricted setting.

Despite these limitations, we believe that this project will provide better guidance for oncologists in the MENA region. These regionally targeted projects are likely to stimulate oncologists in the region to not only practice more evidence-based medicine but also conduct local epidemiologic studies and clinical trials to better define the magnitude of the problem and customize solutions for their part of the world. We believe that the MENA region would benefit greatly if they invested in the area of predictive and prognostic biomarkers. Expensive and sophisticated

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technologies can then be channelled to the subsets of patients who are really likely to benefit from them.

Finally, we would like to invite all oncologists in the MENA region to provide feedback on the applicability and usefulness of the first edition of NCCN–MENA Guidelines. It is vital to ensure that this project achieves its primary objective: facilitating the decision-making process in the clinic.

Our hope is that this serves as an NCCN pilot project, and that similar initiatives are launched in other regions of the world, such as Central and South Africa, Latin America, and beyond, which are underrepresented in clinical trials on which most NCCN Guidelines are based.

References