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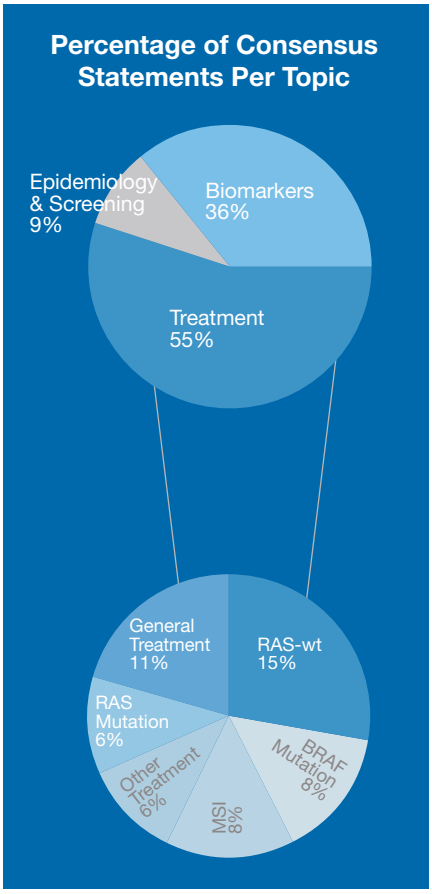
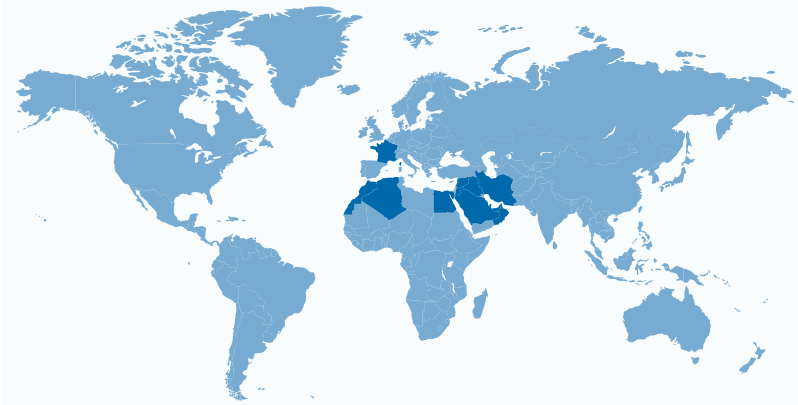
The First Middle East and North Africa Expert Consensus Recommendations for the Management of Advanced Colorectal Cancer

Colorectal cancer (CRC) is the third most common cancer and the second deadliest. Unfortunately, in the Middle East and North Africa (MENA) region, the number of CRC cases has been increasing in recent years and is expected to double by 2030. This is particularly notable in Jordan, Bahrain, and Algeria, where CRC is among the most frequently diagnosed types of cancer. In Jordan, it is the most frequent cancer in men and the second most common in women, while in Bahrain, Qatar, and Algeria, it is the second most common cancer in both sexes. The incidence rate of CRC in Lebanon has increased by 4.36% in males and 4.45% in females between 2005 and 2016, with high age-specific incidence rates observed between the ages of 40 and 49 years, and with 77.4% of patients being aged 50 or above. Tunisia also reported an increase of incidence by 5.3% for males and 2.6% for females between 1993 and 2007.

The absence of recent and clear epidemiological data and guidelines for treating metastatic CRC (mCRC) in the MENA region hinders the management of patients with this form of cancer and makes it difficult to accurately assess its burden. To address this issue, a group of 24 experts in the field of gastrointestinal oncology from the MENA region convened and created the first consensus recommendations for the management of patients with advanced CRC. The panel included experts from Saudi Arabia, Algeria, Jordan, Lebanon, Egypt, United Arab Emirates, Morocco, Qatar, Iran, Iraq, Oman, and Syria, as well as a chairman-expert from France. Together, they formulated 47 statements covering epidemiology, screening, biomarkers, and treatment, in an effort to standardize and unify the screening and management of this cancer in the region, improve outcomes for patients, and help control the burden of CRC.





Participating Countries

- Algeria
- Egypt
- France
- Iran
- Iraq
- Jordan
- Lebanon
- Morocco
- Oman
- Qatar
- Saudi Arabia
- Syria
- United Arab Emirates

The statements are based on the latest international guidelines and best practices and are expected to be widely adopted by healthcare professionals in the MENA region, as they will serve as a valuable resource in the fight against CRC. Highlighted below are some of these statements:

Epidemiology & Screening in the MENA Region

The panel of experts recommended that CRC screening begin for men and women at the age of 45 in the general population. This is in line with the latest American Cancer Society guideline, which recommends starting screening for CRC at age 45 instead of 50. The panel also agreed that both The Fecal Immunochemical Test (FIT) and colonoscopy are valid screening methods, with FIT being the preferred first-line tool due to its cost-effectiveness and better acceptance among the general population.

Biomarkers

This section addresses the topic of biomarkers with 17 statements divided into subsections: RAS, BRAF, microsatellite instability (MSI), and Emerging Biomarkers. The panel concurred that genetic testing for RAS, and BRAF specifically the V600E mutation, should be conducted on all newly diagnosed mCRC patients using NGS or PCR. Additionally, they recommended that all patients with newly diagnosed mCRC undergo universal mismatch repair (MMR) or MSI testing as part of their diagnostic workup.

It is important to note that the statements provided are only a subset of the recommendations put in place by the panel regarding biomarkers in metastatic CRC.

The panel acknowledged that RAS mutational status serves as a negative predictive biomarker for treatment response to anti-epidermal growth factor receptor (anti-EGFR) therapies. They also highlighted that HER2, a well-known oncogenic driver and an important therapeutic target in breast and gastric cancers, is a major emerging predictive biomarker in previously treated mCRC, and its amplification/overexpression may be predictive of resistance to anti-EGFR therapies. As for NTRK fusions in mCRC, they are rare so the panel suggests that NTRK fusion testing be limited to tumors with KRAS wild-type (wt), NRAS-wt and BRAF-wt, and preferably in tumors that are deficient in dMMR or MSI-high previously treated mCRC.

Treatment

The panel pointed out that the sidedness of the tumor in CRC is strongly associated with prognosis. This is due in part to the fact that the right and left colon have different embryological origins. Right-sided tumors are associated with a poorer prognosis when compared to left-sided tumors.

The panel recommends against the use of targeted agents (such as anti-EGFR or antiangiogenic therapy) in patients with upfront resectable metastases during perioperative therapy. As for unresectable mCRC, they recommend the use of biologicals (targeted agents) as first line treatments unless specifically contraindicated. The panel suggests that in RAS-wt unresectable mCRC, bevacizumab be used in combination with chemotherapy as the first-line treatment for right-sided tumors, because anti-EGFR agents do not show clear improvement in progression-free survival and overall survival in this setting. However, for left-sided RAS-wt tumors, the panel agreed that anti-EGFR agents in combination with chemotherapy are the standard of care in the first-line setting.

The panel also highlighted that before administering immune checkpoint inhibitors, MSI-H status should be confirmed by another technique such as molecular biology or IHC. This is because these drugs are expensive, and in cases where the tumor is not MSI-H the drugs would not be active. Additionally, the panel recommends that for first-line treatment of upfront non-resectable MSI-H CRC, single-agent immunotherapy (pembrolizumab) represents the best treatment option.

In conclusion, the panel of experts has reached a consensus on key elements related to biomarkers, diagnostic techniques, initial workup, and the management of advanced CRC that is concordant with international guidelines, with agreement for each recommendation ranging between 50 and 100%.

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