17. Stomach

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Emerging Prognostic Factors for Clinical Care

Genomic and Molecular Assessments

Genomic and molecular analyses of gastric cancer may provide insights into the underlying pathogenesis, as well as candidate therapeutic approaches. Distinct patterns of genomic alterations may reflect the molecular etiologies of these cancers. Tumors with antecedent infection with the Epstein–Barr virus (EBV) harbor marked DNA methylation.[1] Tumors with inactivation of key DNA mismatch repair proteins undergo hypermutation accompanied by MSI.[1] Both MSI and EBV-positive gastric cancers have been associated with longer survival.[2,3] Many gastric cancers also harbor high rates of genomic instability, with frequent chromosomal amplifications of genes encoding key growth-promoting factors, with the patterns of these alterations highly resembling those seen in esophageal adenocarcinoma.[1,4] Histologic classes of gastric adenocarcinoma also may be associated with genomic features. Diffuse-type gastric cancers often are found to have quieter genomic copy number profiles[1] or more mesenchymal gene expression signatures[3] and to harbor unique gene mutations[5] relative to intestinal tumors.

For patients with resectable disease, the presence of an epithelial-to-mesenchymal gene expression signature is associated with higher rates of relapse and subsequent peritoneal metastases.[3] Profiling of specific genomic alterations also may guide the use of specific biologic or targeted agents. Currently, the use of trastuzumab in metastatic gastric cancer is guided by evaluation of expression and amplification of HER2/ERBB2.[6] Other agents, directed against targets genomically activated in subsets of gastric cancer, also are being evaluated. Genomic profiling ultimately may provide guidance regarding the use of emerging immunotherapies, as MSI status was shown to be a new candidate predictor of response to PD-1 inhibitor therapy in colorectal cancer.[7]

Risk Assessment Models

The AJCC recently established guidelines that will be used to evaluate published statistical prediction models for the purpose of granting endorsement for clinical use.[8] Although this is a monumental step toward the goal of precision medicine, this work was published only very recently. Therefore, the existing models that have been published or may be in clinical use have not yet been evaluated for this cancer site by the Precision Medicine Core of the AJCC. In the future, the statistical prediction models for this cancer site will be evaluated, and those that meet all AJCC criteria will be endorsed.

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Recommendations for Clinical Trial Stratification

AJCC prognostic stage group (8th Edition)
Tumor location
Histologic classification
Histologic grade
Nodal involvement and number of nodes
Invasion of tissue/lymphatics/nerve tissues
Extent of nodal dissection (D1 vs. D2)
Margin status
Number of metastatic sites
Performance status of the patient at trial entry

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