Small Bowel Adenocarcinoma

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KEYWORDS

• Rare tumor • Small intestine adenocarcinoma • Carcinogenesis • Lynch syndrome • Prognostic factor • Chemotherapy

KEY POINTS

- The most frequent location of small bowel adenocarcinoma is duodenum.
- Small bowel adenocarcinoma occurs in around 20% in a context of predisposing disease.
- Small bowel adenocarcinoma molecular phenotype is close to that of colorectal adenocarcinoma.
- After an R0 resection, lymph node invasion is the main prognostic factor.
- The benefit of adjuvant chemotherapy should be demonstrated by a prospective clinical trial.

INTRODUCTION

Small bowel adenocarcinoma (SBA) is a rare cancer, but there is a growing impetus to perform multicenter or collaborative studies to answer key questions in patient management.[1] Large biological studies are now possible to potentially exploit the molecular and cellular basis of SBA development and progression to develop novel therapies. Collaboration through the International Rare Cancer Initiative has led to

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an adjuvant therapy trial, which is ongoing. Other important information will be obtained from large prospective cohorts.

EPIDEMIOLOGY

Small Intestine Cancer

Despite the fact that the small intestine makes up 75% of the length of the digestive tract and 90% of its mucosal surface area, small bowel cancer is rare, accounting for less than 5% of gastrointestinal cancers.[2] According to the National Cancer Data Base (NCDB, 1985-2005) and the Surveillance Epidemiology and End Results (SEER, 1973-2004) database, the incidence of all small bowel cancers in the United States increased from 11.8 cases/million persons in 1973 to 22.7 cases/million persons in 2004.[3] Four histologic types of cancer predominate in the small bowel: adenocarcinomas, neuroendocrine tumors, gastrointestinal stromal tumors and lymphomas.

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SBA accounts for around 30% to 40% of all cancers of the small intestine.[3–5] The incidence of SBA varies according to geographic location, with higher rates in North America and Western Europe, and lower rates in Asian countries. In the United States, the estimated annual incidence of SBA is about 5300 new cases, with 1100 deaths per year.[6] The median age at diagnosis is in the sixth decade of life, with a sex ratio close to 1. In Europe, the annual incidence is about 5.7 cases per million inhabitants resulting from an estimated number of annual new cases of SBA of 3600 according to the EUROCARE database.[7]

Duodenum Adenocarcinoma

Duodenum adenocarcinoma is the most common tumor site, as it is seen in more than half of SBA cases, followed by the jejunum and ileum.[3,5,8–11] The increasing incidence of SBA is mainly owing to the increase in duodenum tumors.[12]

TUMOR PHENOTYPING

Many of the main molecular aberrations that are implicated in the pathogenesis of colorectal cancer have been investigated in SBA (**Table 1**).

Wnt/Adenomatous polyposis coli /β-Catenin Signaling Pathway

Adenomatous polyposis coli

The adenomatous polyposis coli (*APC*) gene causes a loss of the regulation of β-catenin, which accumulates in the cytoplasm and then in the nucleus and acts as a transcription factor that stimulates the expression of genes involved in cellular proliferation. This mutation is considered one of the main trigger events in colorectal carcinogenesis. The prevalence of the *APC* gene mutation in SBA is about 10% to 18%[13–16] contrasting to the prevalence of 80% of *APC* gene mutation observed in colorectal cancer.

Nuclear accumulation of β-catenin

Nuclear accumulation of β-catenin, probably caused by a gain-of-function mutation in the *β-CATENIN* gene, is observed in 20% to 50% of cases.[16–18] Moreover, aberrant activation of the Wnt/β-catenin pathway has been correlated with poor prognosis.[19] Thus, Wnt/β-catenin pathway, even if less common than in colorectal cancer, remains an important pathway for SBA pathogenesis.