



FIGURE 113-4 Survival (Kaplan-Meier plots) of patients with pancreatic neuroendocrine tumors (pNETs; $n = 1072$) (A–C) or gastrointestinal neuroendocrine tumors (GI-NETs; carcinoids) (appendix, $n = 138$; midgut, $n = 238$) (D–F) stratified according to recent proposed classification and grading systems. (Panels A–C are drawn from data in G Rindi et al: *J Natl Cancer Inst* 104:764, 2012; panels D and E are drawn from data in M Volante et al: *Am J Surg Pathol* 37:606, 2013; and panel F is drawn from data in MS Khan: *Br J Cancer* 108:1838, 2013.)

study was 95%, and with distant metastases, it was 20% (Fig. 113-4). With gastrinomas, the 5-year survival without liver metastases is 98%; with limited metastases in one hepatic lobe, it is 78%; and with diffuse metastases, 16% (Fig. 113-4). In a large study of 156 patients (67 pNETs, rest carcinoids), the overall 5-year survival rate was 77%; it was 96% without liver metastases, 73% with liver metastases, and 50% with distant disease. Another very important prognostic factor is whether the NET is well-differentiated (G1/G2) or poorly differentiated (<1% of all NETs) (G3). Well-differentiated NETs have a 5-year survival of 50–80%, whereas poorly differentiated NETs have a 5-year survival of only 0–15%.

Therefore, treatment for advanced metastatic disease is an important challenge. A number of different modalities are reported to be effective, including cytoreductive surgery (surgically or by

radiofrequency ablation [RFA]), treatment with chemotherapy, somatostatin analogues, interferon α , hepatic embolization alone or with chemotherapy (chemoembolization), molecular targeted therapy, radiotherapy with radiolabeled beads/microspheres, peptide radioreceptor therapy (PRRT), and liver transplantation.

SPECIFIC ANTITUMOR TREATMENTS

Cytoreductive surgery is considered if either all of the visible metastatic disease or at least 90% is thought resectable; however, unfortunately, this is possible in only the 9–22% of patients who present with limited hepatic metastases. Although no randomized studies have proven that it extends life, results from a number of studies suggest that it may increase survival; therefore, it is recommended, if possible. RFA can be applied to NET liver metastases if they are