no preoperative treatment, there was a trend to increasing R0 resection but this was not significant nor was postoperative morbidity.
Conclusion: Liver resection for metastatic NET shows a favourable outcome for this contemporaneous group of patients. There was no clear advantage to multimodality therapy but this concept needs further research.

Expert Panel Consensus Statements on the Medical Treatment of Unresectable Pancreatic Neuroendocrine Tumors

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Background: Neuroendocrine tumors (NETs) of the pancreas (PNETs), a major subtype of gastrointestinal NETs, are rare neoplasms that lack some specificity in current treatment guidelines. We describe a physician expert panel consensus on medical treatment of well-differentiated (grade 1–2) unresectable PNETs.
Methods: PNET treatment appropriateness ratings were collected using the RAND/UCLA Delphi process: recruited physician experts (e.g., by specialty, geography, practice), reviewed treatment literature, and collected 2 rounds of ratings (before and after a face-to-face meeting) from the experts. Experts and the moderator were blinded to the funding source. Patient scenarios (rated on a 1–9 scale indicating appropriateness of interventions for a given scenario) were labeled as appropriate, inappropriate, or uncertain. No appropriateness rating was assigned to a scenario in presence of disagreement: >2 ratings from 1–3 and >2 from 7–9 range.
Results: Ten panelists (mean age: 50.4 years) from the northeast, midwest, south, and west census regions convened for a 1 day meeting. Specialties represented were medical and surgical oncology, interventional radiology, and gastroenterology. Panelists had practiced for a mean of 15.5 years (range: 6-33). Among 202 rated scenarios, disagreement decreased from 13.2% (26 scenarios) before the meeting to 1% (2) after. In the 2ndround, 46.5% (94 scenarios) were rated inappropriate, 21.8% (44) were uncertain, and 30.7% (62) were appropriate. Consensus statements from the scenarios included: 1) it is appropriate to use somatostatin analogs (SA) as 1stline therapy in patients with hormonally functional tumors, 2) it is appropriate to use everolimus, sunitinib, or cytotoxic chemotherapy therapy as 1stline therapy in patients with symptomatic or progressive tumors, and 3) beyond 1stline, these same agents can be used as can octreotide LAR (in patients with uncontrolled secretory symptoms) in doses up to 60 mg every 4 weeks or up to 40 mg every 3 or 4 weeks.
Conclusion: We systematically obtained appropriateness ratings for a variety of medical therapies in PNETs from a group of physician experts. The Delphi process allowed the experts to reliably quantify complex qualitative data in order to arrive at consensus on the appropriateness of medical therapies for the treatment of PNETs.

KI-67 Heterogeneity in Gastro-Entero-Pancreatic Neuroendocrine Tumors

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Background: The neuroendocrine tumor (NET) proliferation-based grading system (ENETs) has proved reliable for prognostic stratification, however concerns exist on Ki67 heterogeneity. Our aim was to evaluate intratumor Ki67 index heterogeneity in primary and metastatic sites.
Methods: A total of 170 GEP-NETs (between 1993–2011) were identified, 50 of them with clinical follow-up (mean follow up was 59 months, range 2–168 months). Twenty-five cases had multiple paraffin blocks on which Ki67 immunohistochemistry was performed.
Results: Thirteen out of 21 (62%) primary sites presented exactly the same Ki67 percentage and therefore the same grade in each paraffin block. Six (29%) tumors presented different Ki67 indices between paraffin blocks, but with no change in grade. Two (10%) tumors showed Ki67 index discrepancy (7% vs 2% and 4% vs 2%) which was enough to change grade (G1 to G2). Out of 14 patients with primary NET and synchronous metastases, 9 (64%) presented exactly the same Ki67 index between sites while 2 (14%) showed variability in their Ki67 index, but not in grade. Three (21%) cases showed discrepancy between primary tumor and metastases. In particular two cases showed an increase in proliferation index in nodal metastases (1% vs 5% and 17% vs 31%) and one case showed increased Ki67 index in a mesenteric localization (1% vs 5%). One case with multiple hepatic metastases showed discrepancy between each metastasis (7% vs 1%). Six patients underwent surgical excision of metachronous metastases during follow up. Three (50% - 1 nodal and 2 hepatic metastases) patients showed an increase in Ki67 rate in the metastatic site and a change in grade, from G1 to G2 (1% vs 10%; 2% vs 5%; 1% vs 7%).
Conclusion: Differences in grade between primary and synchronous/metachronous metastatic sites are important and evaluation of Ki67 at all sites may be significant for patient management.

Multi-Center Phase II Trial of Temsirolimus (TEM) and Bevacizumab (BEV) in Pancreatic Neuroendocrine Tumor (PNET): Results of a Planned Interim Efficacy Analysis

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Background: PNET has long had few effective therapies other than chemotherapy. Recent placebo-controlled phase III trials of the mTOR inhibitor everolimus and the VEGF/ PDGF receptor inhibitor sunitinib noted improved progression-free survival (PFS). However, objective response rates (RR) with these agents are still <10%. Preclinical studies suggest enhanced anti-tumor effects with combined mTOR and VEGF targeted therapy.
Methods: We conducted a phase II trial of the mTOR inhibitor TEM (25 mg IV q week) and the VEGF-A monoclonal antibody BEV (10 mg/kg IV q 2 weeks) in patients (pts) with well or moderately differentiated PNET and progressive disease by RECIST within 7 months of study entry. Co-primary endpoints were RR and 6-month PFS. Planned enrollment is 50 patients, with interim analysis for futility after the first 25 evaluable pts. Pts had no prior mTOR or VEGF targeted agents, ECOG PS 0–1, and adequate hematologic and organ function. Continued octreotide was allowed, but not required. Prior interferon, embolization, and ≤ 2 chemotherapy regimens were allowed.
Results: Confirmed PR was documented in 13 of the first 25 (52%) evaluable patients. 21 of 25 (84%) patients were progression-free at 6 months. Both endpoints exceeded the protocol-defined criteria to continue enrollment. For 36 evaluable patients, the most common grade 3–4 adverse events attributed to therapy were hypertension (14%), leukopenia (11%), lymphopenia (11%), hyperglycemia (11%), mucositis (8%), hypokalemia (8%), and fatigue (8%).
Conclusion: The combination of TEM/BEV has substantial activity in a multi-center phase II trial with RR of 52%, well in excess of single targeted