EC5 2014 UPDATE

Mike Vickers
The Ottawa Hospital Cancer Center

Objectives

• Review current issues in the treatment of:
  — Neuroendocrine tumors
  — LAPC and metastatic pancreatic cancer
  — mCRC and expanded RAS testing
  — Screening for CRC
Montreal Oct. 23-25, 2014

Dr. Scott Berry (EGFRIs 1st line), Dr. Benoit Samson (extended RAS), Dr. Tim Asmis (NET), Dr. Celia Marginean (NET pathology), Dr. Lucas Sideris (NET surgery), Dr. Nazik Hammad (ACRC), Dr. Malcolm Moore (Pancreas CA), Dr. Catherine Dube (Screening CRC), Dr. Scot Dowden (WCGCCC update)

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What Classification System and Diagnostic Tools Should Be Used in Reporting on NETs?

- TNM 2009 & the WHO 2010 classification
- Tumor stage and Tumor grade (#mitoses/10hpf and or Ki-67)
  - G1 = 2/10hpf or Ki-67 ≤2%; G2 = 2-20/10hpf or Ki-67 3-20%; G3 = >20/10 hpf or ki-67 ≥20%
- Chromogranin A, 24-hr Urine for 5-HIAA, CT, Octroetide imaging
- Baseline Echo for those with carcinoid syndrome
- MIBG scans in selected patients
What Is the Role of SSA in the Treatment of Metastatic or Unresectable Well-Differentiated Gastroenteropancreatic NET?

- In unresectable or metastatic, progressive, well-differentiated gastroenteropancreatic NET, regular injections of SSA should be considered to relieve symptoms and to prevent disease progression.

What Is the Role of Sunitinib and Everolimus in the Treatment of Metastatic or Unresectable NET?

- Currently, there are data to support treatment with sunitinib or everolimus in metastatic or unresectable pancreatic net PNET.
- The data are insufficient to recommend sunitinib or everolimus in the treatment of other NETS.
- The optimal sequencing of sunitinib and everolimus with respect to other treatment modalities has not been established.
What Is the Role of Chemotherapy in the Management of NET?

• Chemotherapy is a viable treatment option for well differentiated metastatic PNET.
  – Capecitabine and temozolomide or streptozocin-based combinations can be considered
  – Clinical trial if available.
• For poorly differentiated neuroendocrine carcinoma, platinum-based chemotherapy is recommended.

What Is the Role for Surgery and Locoregional Treatment in Managing NET?

• If feasible, patients should undergo primary tumour resection
• Patients with metastatic disease should be referred to a multidisciplinary team to consider primary tumour and metastases resection
• In unresectable disease (primary tumour, or liver, or both), locoregional therapy such as hepatic intra-arterial embolization, chemoembolization, or radiofrequency ablation could be an option
• Lymphadenectomy is recommended for small-bowel tumours or primaries larger than 2 cm.
• In potentially resectable disease, surgery can include lymphadenectomy, peritoneal stripping, or liver resection.
What Is the Role of Systemic Therapy in the Management of Locally advanced PCC?

• Based on expert opinion, multiple therapeutic regimens such as gemcitabine; gemcitabine and nab-paclitaxel in combination; and Folfirinox can be considered in the management of LAPC
• Patients with borderline resectable disease should be discussed at multidisciplinary rounds or referred for a clinical trial

Role of Chemoradiation the Management of LAPCC

• Recent trials failed to support the superiority of chemoradiation over chemotherapy alone in LAPCC
• Chemoradiation can be considered in selected patient populations after discussion within a multidisciplinary team or in a trial setting
Management of mPCC

• In fit patients, folfirinox or combination therapy with gemcitabine–nab-paclitaxel can be recommended as first-line therapy
• Dose modification and supportive care during folfirinox treatment are at the treating physician’s discretion
• For patients with a borderline performance status, discussion of gemcitabine or best supportive care can be appropriate
• There is evidence to support the use of second-line therapy in the management of mPCC, but the evidence at this time is insufficient to specify a regimen
• In selected patients with a genetic predisposition, consideration of individualized treatment might be appropriate. That treatment could include a platinum-based regimen or poly (ADP–ribose) polymerase 1 inhibitor, but further studies are required

What Constitutes Expanded RAS Wild-Type Analysis?

• Traditional KRAS mutation testing includes mutations in exon 2, codons 12 and 13, and accounts for 40% of the population.
• Expanded RAS mutations account for approximately 20% (15%–28%) of the additional mutations.
• Expanded RAS mutation testing is defined to include testing of KRAS and NRAS exons 2, 3, and 4
• The issue of BRAF mutation as a predictive or prognosticbiomarker was not formally reviewed
Who Should Receive Expanded RAS Testing?

• Extended RAS wild-type (wt) status correlates with significant improvements in pfs and os when patients with metastatic crc (mcrc) are treated with epidermal growth factor receptor (egfr) inhibitors in the firstline, second-line, and third-line settings.

• For initial treatment planning purposes, all patients should, upon diagnosis of mcrc, be tested in a timely manner for extended RAS mutations.

How Does the Result of Expanded RAS Testing Affect Choice of Therapy?

• Patients without extended RAS mutations might experience pfs and os benefits with the use of egfr inhibitors.

• Patients with RAS mutations show no benefit with egfr inhibitors (alone or in combination with chemotherapy); in fact, treatment with egfr inhibitor might have a deleterious effect on cancer outcomes.
What Is the Role of EGFR Inhibitor in the Treatment of mCRC in the First-Line Setting?

- Chemotherapy plus bevacizumab remains a standard palliative treatment in the first line for mCRC.
- Chemotherapy plus egfr inhibitor is an option for unresectable mCRC in the first line setting in patients with known RAS wt status.
- If considering doublet therapy (chemotherapy plus biologic therapy), then, based on the largest randomized controlled trial to date, chemotherapy plus bevacizumab remains the preferred regimen.

What Is the Recommendation for CRC Screening in the General Population?

- We recommend population-based crc screening with the fecal occult blood test (fobt), the fecal immunochemical test (fit), or flexible sigmoidoscopy for asymptomatic patients 50–74 years of age.
- Colonoscopy-based screening has no level i evidence for mortality benefit; furthermore, it is associated with issues of test access and quality.
- Colonoscopy remains the preferred follow-up test after a positive screen and should be completed within 8 weeks.
What Is the Recommendation for Screening Individuals at Increased Risk of CRC?

• To elucidate possible hereditary cancer syndromes or a genetic predisposition to CRC, we recommend that a full and appropriate family history be recorded for all patients. Patients with a positive family history should be referred for genetic evaluation.

• We endorse the guideline created by the U.S. Multi-Society Task Force on Colorectal Cancer for the screening and management of hereditary nonpolyposis CRC (HNPCC)

Vickers is dead to me!
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