A comparison of ascertainment of Lynch syndrome in colorectal cancer patients via reflex testing vs. hereditary guideline-based testing


British Columbia Cancer Agency
Background

- Lynch Syndrome (LS) is the most common hereditary form of Colorectal Cancer (CRC)

- Referrals to Hereditary Cancer Program (HCP) are triggered by personal or family history as well as young onset age (usually < 50 years old)

- Reflex immunohistochemical (IHC) testing provides an alternative means using Mismatch Repair (MMR) status combined with BRAF V600E

- **Aim of this study**: to compare the efficacy of reflex IHC testing vs. pedigree or age directed criteria to identify patient with LS.
Methods

• From January 2012 to July 2013, reflex IHC MMR testing was performed in all cases of resected CRC across the Vancouver Coastal Health Authority.

• BRAF IHC was implemented in April 2014 and tumor samples previously collected were retrospectively analysed.

• Additional characteristics collected from chart review were:
  – Age at diagnosis
  – Personal history of cancer
  – Familial history of cancer
  – Status of referral to HCP
  – Additional genetic testing and results
Results

1500 cases

198 dMMR (13%)

1302 MMR Intact

122 < 50y old
1180 ≥ 50y old

164 dMLH1 (83%)
18 dMSH2 (9%)
9 dMSH6 alone (4.5%)
7 dPMS2 alone (3.5%)

105 BRAF m (64%)
59 BRAF wt (36%)

Figure 1: Results from MMR and BRAF IHC testing, high risk and low risk profiles.
Figure 2: Age, HCP referral status and germline testing results for high risk profiles for LS.
Key points of the results

- **Decrease of HCP Consultations:**
  - Of 135 patients < 50y: 122 were MMR intact: ↓ 92% of consultations
  - Of 164 dMLH1: with reflex BRAF: ↓ 59 cases (↓ 64% of consultations)

- **Increase Screening**
  - In dMMR with at risk profile:
    - 47 (50.5%) were not referred and 96% were ≥ 50y old
    - Of the 45/80 patients ≥ 50y old not referred: 15 (33%) had very clear indications
    - 25 (27%) had no family data documented
  - In dMLH1/BRAFwt ≥ 50y referred (18/54)
    - 3 did not meet criteria prior to BRAF testing (1 LS identified)
Conclusions

- Reflex IHC testing should be considered a standard of care

- Better use of resources
  - Not all young patients warrants an HCP referral
  - Not all dMMR warrants an HCP referral

- Better screening of Lynch Syndrome
  - Thorough family history often missing
  - Bethesda criteria not mastered by all physicians
  - Families are getting smaller
  - Surveillance colonoscopy
  - Some mutations have low penetrance

- Future directions
  - Best algorithm?
  - Universal screening? Other purposes?