BLOOD-BASED BIOMARKERS IN POSSIBLE TRIAGE OF FIT POSITIVE SUBJECTS

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CONFLICTS OF INTERESTS

• Volition RX, Namur, Belgium
• Abbott Laboratories Inc, Chicago, USA
• Applied Proteomics Inc, San Diego, USA
CRC SCREENING IN DENMARK

- out-reach FIT test – cut-off: 100 ng/ml
- invited 391,000 – (50-74 years of age)
- compliance 64%
- 16,806 FIT positives
- 89% colonoscopy acceptance
- 913 CRC
- 4,418 HRA / MRA
FIT SCREENING IN DENMARK

- additional colonoscopies due to screening
- 1\textsuperscript{st} – 2\textsuperscript{nd} round: 4 years – 18,000 colonoscopies/year
- 2\textsuperscript{nd} – 3\textsuperscript{rd} round: 2 years – 34,500 colonoscopies/year
- plus re-colonoscopies – HRA (1\text{y}) and MRA (3\text{y}s)
- colonoscopy capacity...???

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FIT SCREENING IN DENMARK

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  • 2\textsuperscript{nd} – 3\textsuperscript{rd} round: 2 years – 34,500 colonoscopies/year
  • plus re-colonoscopies – HRA (1y) and MRA (3ys)
• colonoscopy capacity...???
• reduce numbers of colonoscopies...???
REDUCTION OF COLONOSCOPIES?

- The Netherlands 250 ng/ml
- Sweden 200 ng/ml – women
- Sweden 400 ng/ml – men
- Scotland similar to Sweden???
REDUCTION OF COLONOSCOPY?

- The Netherlands
  - 250 ng/ml
- Sweden
  - 200 ng/ml – women
- Sweden
  - 400 ng/ml – men
- Scotland
  - similar to Sweden???
- other options…??
ENDOSCOPY III, PART 1

- 01.05.14 – 31.08.16
- 8,415 FIT positive
- 5,118 FIT negative – terminated by 30.03.16
- 01.04.16 – part 2 – 30,000 FIT negative
ENDO III, PART 1 - BIOMARKERS

- proteins
- proteomics
- ctDNA: mutations – methylations
- epigenetics: nucleosomes, histone modifications
- cDNA (concentrations)
- metabolomics
- transcriptomics
- immune components – complement activity
- coagulation factors
ENDO III, PART 1 - BIOMARKERS

- proteins
- proteomics
- ctDNA: mutations – methylations
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ENDOSCOPY III, PART 1

• first 1,919 FIT positives
  - $100 \leq \text{FIT} \leq 200$ ng/ml
    - 631 subjects
    - 350 no findings
    - 11 CRC
    - 47 HRA
    - 89 MRA
    - 134 LRA
ENDO III, PART 1 - NUCLEOSOMES

- first 1,919 FIT positives
  - 100 ≤ FIT ≤ 200 ng/ml
    - 631 subjects
    - 350 no findings
    - 11 CRC - identify 6 (56%)
    - 47 HRA - identify 31 (66%)
    - 89 MRA - identify 42 (47%)
    - 134 LRA - identify 54 (40%)

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first 1,919 FIT positives  - 100 ≤ FIT ≤ 200 ng/ml

model:
predictor
logistic regression including:
ANA58, EZH2, HZAK119ub, H2AZ, H3K36ME3, H3K9AC, H3K9NE3, H3S10PH, H4K20NE3, 5MC, H4PANAC, HMBG1, MH2A1.1, PH2AX, PH2AX.A, adjusted for age and gender
sensitivity: 80%
• first 1,919 FIT positives
  - 100 ≤ FIT ≤ 200 ng/ml
    - 631 subjects
    - 350 no findings
    - 11 CRC
    - 47 HRA
    - 89 MRA
    - 134 LRA
  - 33% reduction..??
• first 1,919 FIT positives
  - 100 ≤ FIT ≤ 200 ng/ml
    - 631 subjects
    - 350 no findings
    - 11 CRC
    - 47 HRA
    - 89 MRA - real reduction: 25%
    - 134 LRA
REDUCTION OF COLONOSCOPIES?

- Netherlands (250) – 27 CRC – 69 HRA – 127 MRA
- Sweden (200) - 11 CRC – 47 HRA – 89 MRA
- Sweden (400) - 43 CRC – 97 HRA – 184 MRA
REDUCTION OF COLONOSCOPY?

- Netherlands (250)  • 27 CRC – 69 HRA – 127 MRA
- Sweden (200)   – 11 CRC – 47 HRA – 89 MRA
- Sweden (400)   – 43 CRC – 97 HRA – 184 MRA

CONCLUSION:
The triage must be advantageous compared to increased, fixed cut-offs.
TRIAGING – NEXT STEPS

- determinations of all > 13,500 Endo III samples
- CEA inclusion?
- additional proteins?
- logistics study
- report at WEO, Chicago – May 2017