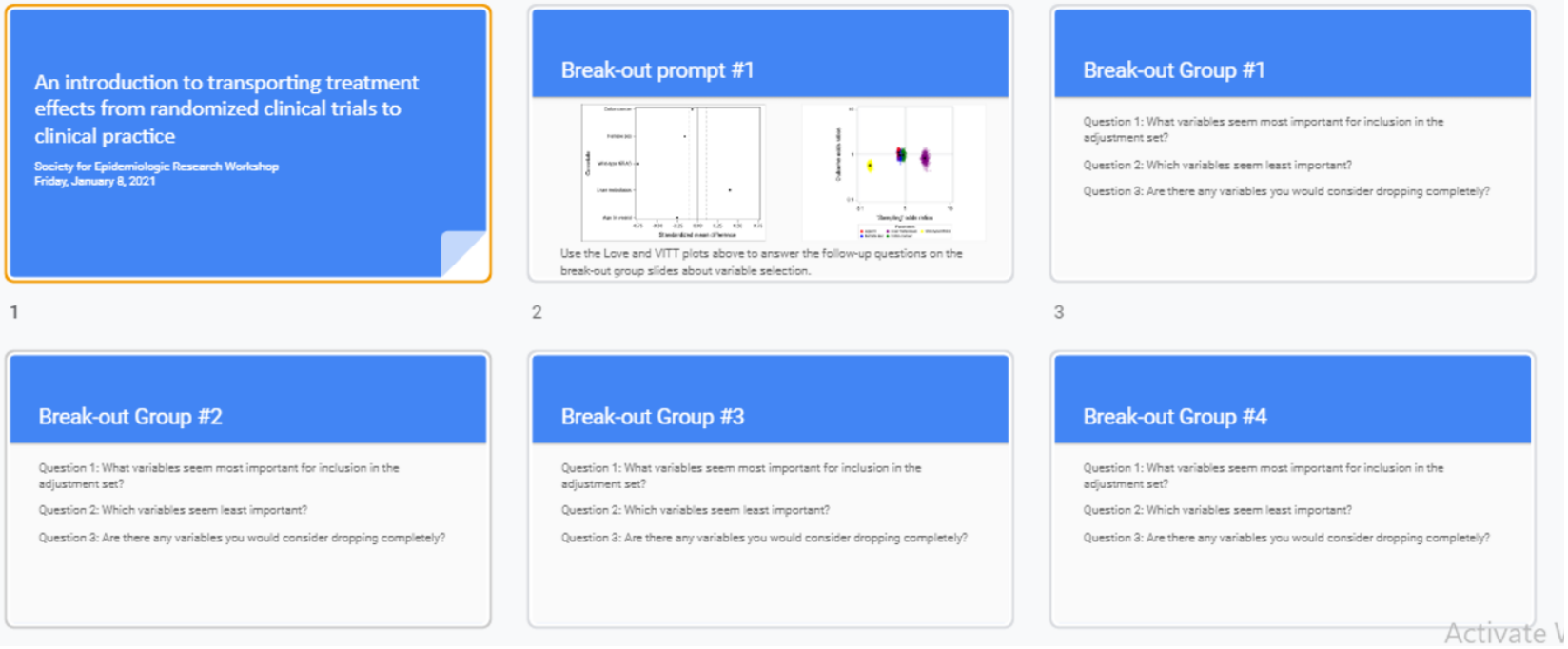
Workshop logistics

- Interactive application (60 minutes)
- Discussion and Q&A (10-15 minutes)
- Wrap-up (5-minutes)

Interactive application

- Zoom breakout rooms
  - Groups of 6-10 individuals will be randomly assigned
  - There will be two break-outs of 10-minutes each
- Google slides
  - Will be used to allow break-out groups to record responses during discussion
  - Assign a scribe to record responses/discussion
  - Link here: https://docs.google.com/presentation/d/1hTequBIiVuTIVQ14BFZ31IjZxlywDFv1Bsx1Y8jxcbQ/edit?usp=sharing

Google Slides



Programs and course content

- All materials for the workshop are available on the following GitHub site: https://github.com/tonymatthews/transportability-workshop
- Please note: we cannot store the datasets on the GitHub site, as they require approval for use (see Word doc about how to obtain trial data access, if desired)

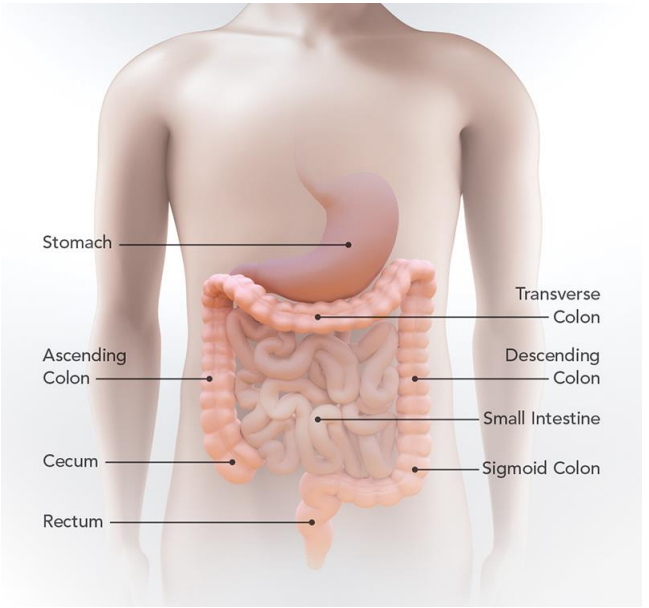
Questions?

THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

Workshop example and clinical context

Example: Metastatic Colorectal Cancer

- Colorectal cancer (CRC) is the third most common cancer in US men and women
- About 22% are diagnosed when they have already metastasized (mCRC)
- Prognosis is poor in mCRC with a 5-year survival rate of 14%



Randomized, Phase III Trial of Panitumumab With Infusional Fluorouracil, Leucovorin, and Oxaliplatin (FOLFOX4) Versus FOLFOX4 Alone As First-Line Treatment in Patients With Previously Untreated Metastatic Colorectal Cancer: The PRIME Study

VOLUME 28 · NUMBER 31 · NOVEMBER 1 2010

JOURNAL OF CLINICAL ONCOLOGY

- Open-label, phase III, multi-center trial comparing the efficacy of panitumimab + FOLFOX4 versus FOLFOX4 alone
- Panitumimab is a monoclonal antibody therapy targeting the epidermal growth factor receptor (EGFR), shown to be a clinically meaningful target for mCRC
- FOLFOX4 is an infused chemotherapy regimen including a combination of oxaliplatin and 5-fluorouracil, and was standard of care for mCRC at the time of this trial

The role of KRAS in panitumumab efficacy

- An earlier pivotal phase III study of panitumumab as monotherapy in the mCRC setting provided evidence that clinical benefit was specific to patients with wild-type (WT) KRAS tumors.
- The PRIME study was designed to compare the treatment effect in **all patients** but was amended to focus on prospective hypothesis testing in the WT KRAS stratum.
- KRAS testing was initiated after the study population was enrolled.

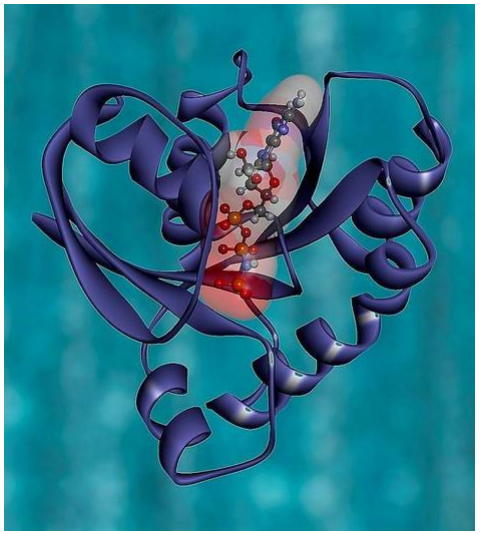
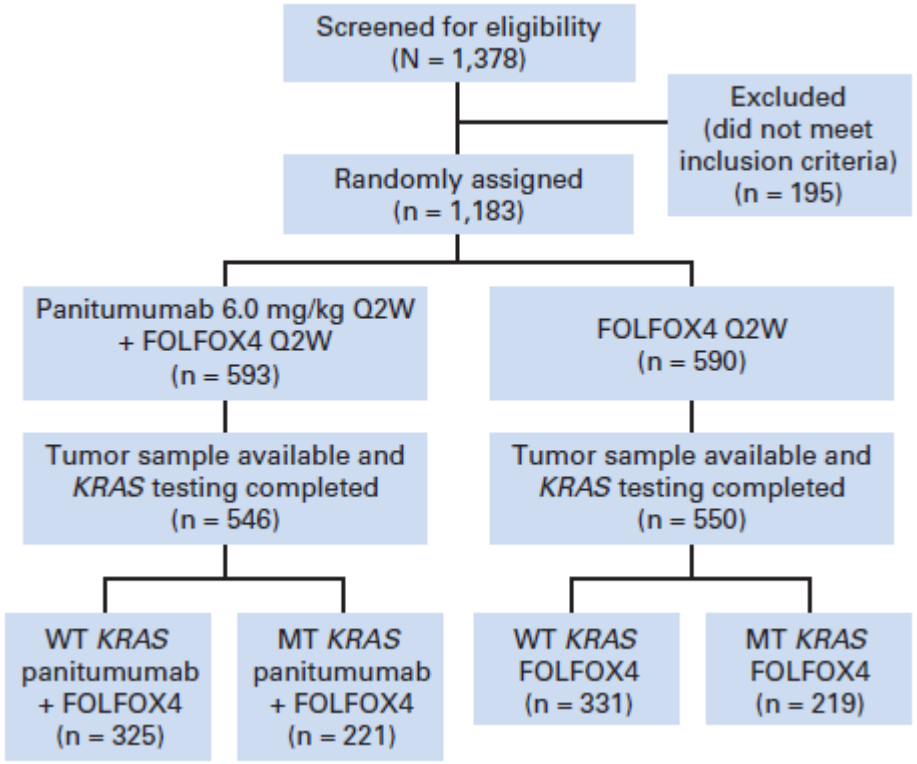


Illustration of the KRAS protein. Image credit: National Institutes of Health

PRIME Study Eligibility Criteria

- 18+ years old
- Untreated metastatic colon or rectal cancer
- ECOG performance status (physical function): 0-2
- One measurable lesion

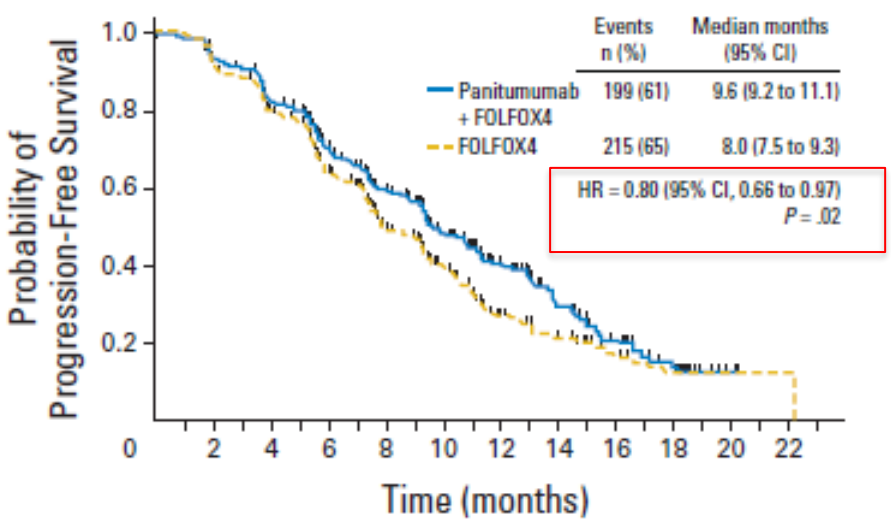


The PRIME study population

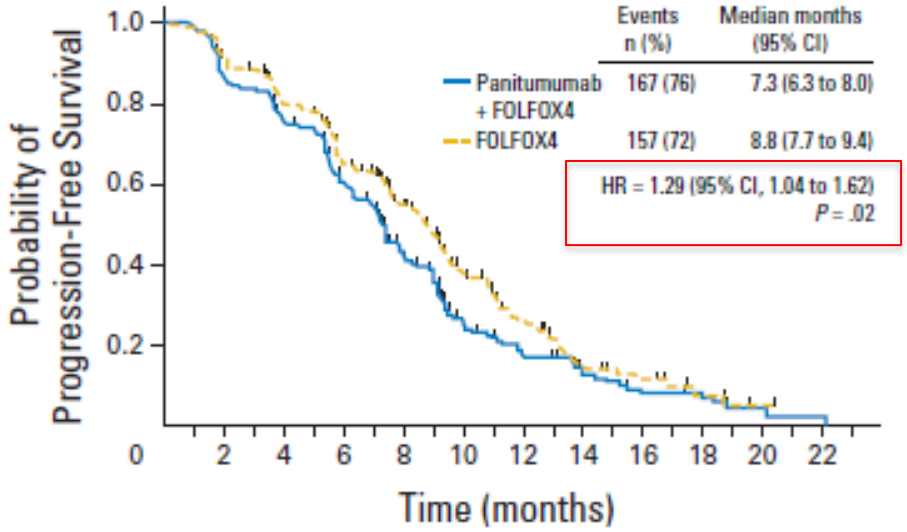
- 1183 patients were randomized from Aug 2006-Feb 2008
- See trial Table 1
  - Average age ≈ 62 years
  - 60% had WT KRAS; 40% had mutant KRAS
  - Trial conducted primarily in Western Europe, Canada, and Australia (not the US)
  - 66% had colon cancer; 34% had rectal cancer

PRIME Study Findings

Wild type-KRAS



Mutant-KRAS



In May 2014, the Food and Drug Administration approved panitumumab in combination with FOLFOX for the first-line treatment of mCRC for patients with **wild-type KRAS tumors** (assessed using the therascreen KRAS test)

Who is the target population?

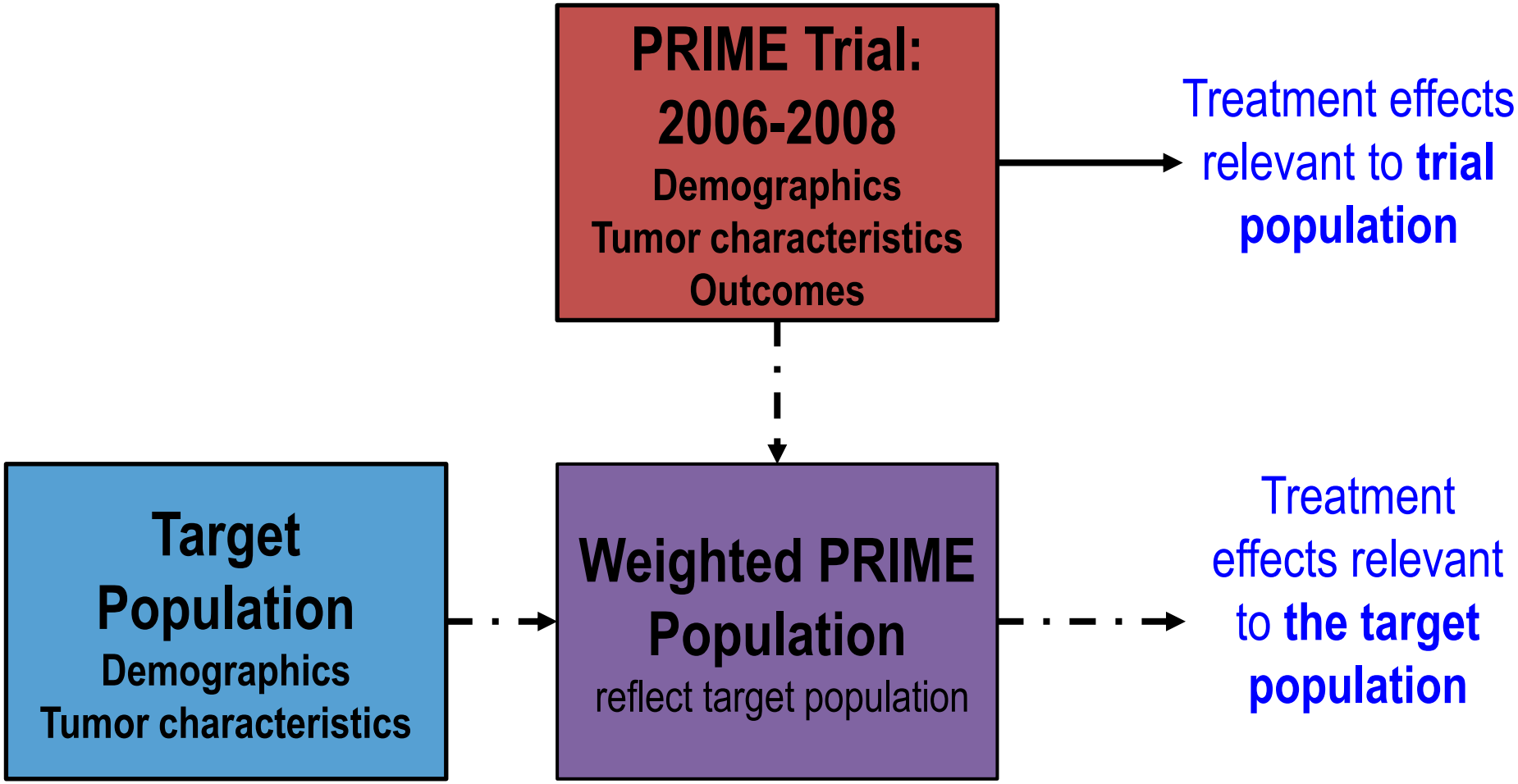
TRIAL POPULATION

- **Population:** PRIME Study Eligibility
- **Place:** Ex-US
- **Time:** 2006-2008

TARGET POPULATION

- **Population:** Meets PRIME eligibility with KRAS wild-type tumors
- **Place:** Simulated
- **Time:** Simulated

Our goal for today



Questions?

jennifer.lund@unc.edu
mawc@live.unc.edu