# Introduction to *BRAF* in mCRC

- BRAF is a kinase in the EGFR-mediated MAPK signaling pathway
- *BRAF*-mutated mCRC may represent its own discrete subset of mCRC, defined by:
  - Worse survival
  - Right-sided presentation
  - Mucinous histology
  - High microsatellite instability
  - Early relapse

**8.1%**

Prevalence of *BRAF* mutations in mCRC[1]

**V600E**

Mutation present in >80% of *BRAF*-mutated mCRC[2]

**10.4 MONTHS**

Median OS for *BRAF*-mutated mCRC[3,a]

[a]Compared with 34.7 months for *BRAF*-wt mCRC

1. Peeters M et al. *Eur J Cancer.* 2015;51:1704-1713. 2. Davies H et al. *Nature*. 2002;417:949-954. 3. Tran B et al. *Cancer*. 2011;117:4623-4632.

# Outcomes With Addition of EGFR Inhibitors

| Outcome | Setting | Hazard Ratio | 95% CI | P-value |
|---|---|---|---|---|
| **Overall Survival** | Any | 0.91 | 0.62-1.34 | 0.63 |
| | First-line | 0.76 | 0.54-1.08 | 0.13 |
| **Progression-free Survival** | Any | 0.88 | 0.67-1.14 | 0.33 |
| | First-line | 0.86 | 0.63-1.17 | 0.34 |
| **Overall Response Rate** | Any | 1.31 | 0.83-2.08 | 0.25 |
| | First-line | n.d.* | n.d.* | 0.31 |

*Data not reported.

**Compared with chemotherapy alone or best supportive care, cetuximab or panitumumab did not significantly improve outcomes in patients with *BRAF*-mutated mCRC.**

Pietrantonio F et al. *Eur J Cancer*. 2015;51:587-594.

# EGFR Inhibitors in *BRAF*-mut Cancer

- Cetuximab and panitumumab did not improve OS, PFS, or ORR in a clinically meaningful or statistically significant manner in patients with *BRAF*-mutated mCRC
- *BRAF* and *RAS* testing should drive treatment decisions for patients with mCRC
  - EGFR inhibitors are approved for all-*RAS*-wt advanced CRC
  - Other treatment options should be considered for *BRAF*-mutated mCRC
  - EGFR inhibitors remain viable treatment options for *BRAF*-wt mCRC, which comprises 80% to 95% of the all-*RAS*-wt mCRC population

Pietrantonio F et al. *Eur J Cancer*. 2015;51:587-594.