Background

- CALGB 80405 is a Phase III clinical trial of mCRC patients that evaluated first line FOLFOX or FOLFIRI in combination with randomly assigned cetuximab or bevacizumab. Primary results did not show a statistically significant difference in arms.
- Sidedness has emerged as an important prognostic factor in treatment decisions for mCRC patients.
- However, side-dependent risk factors are currently not known. These factors may be important for further refining mCRC prognostics and informing treatment decisions.
- In order to examine the role of right versus left sidedness in mCRC, we built multivariate predictive models utilizing a novel, hypothesis-free machine learning approaches.

Results

Overall survival (full cohort): Key variables predictive of OS include primary side, AST concentration, ECOG performance status, treatment intent (palliative vs. curative), and local primary and abdominal site of disease indicators.

Primary side-stratified specific models (OS): In primary side-stratified-specific models, urine protein level, treatment intent (palliative as reference) and hemoglobin concentration were more associated with left-side survival, while liver and lung sites of disease were more associated with right-side survival.

Conclusions

- Primary side, AST level, ECOG PS, and site of metastases play a central role in explaining variation in OS and PFS.
- Depending on the primary tumor side, different factors appear to drive OS:
  - Left sided: liver and lung site of disease, side survival.
  - Right sided: liver and lung site of disease for right-side mCRC.
- Different factors may impact OS for men and women.
- Our findings suggest that side- and gender-specific variables may be important for predicting mCRC course and survival.
- Additional research, including prospective studies and evaluation of biologic pathways, is necessary to confirm these findings.

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