How soon will colorectal cancer patient management be driven by molecular factors?

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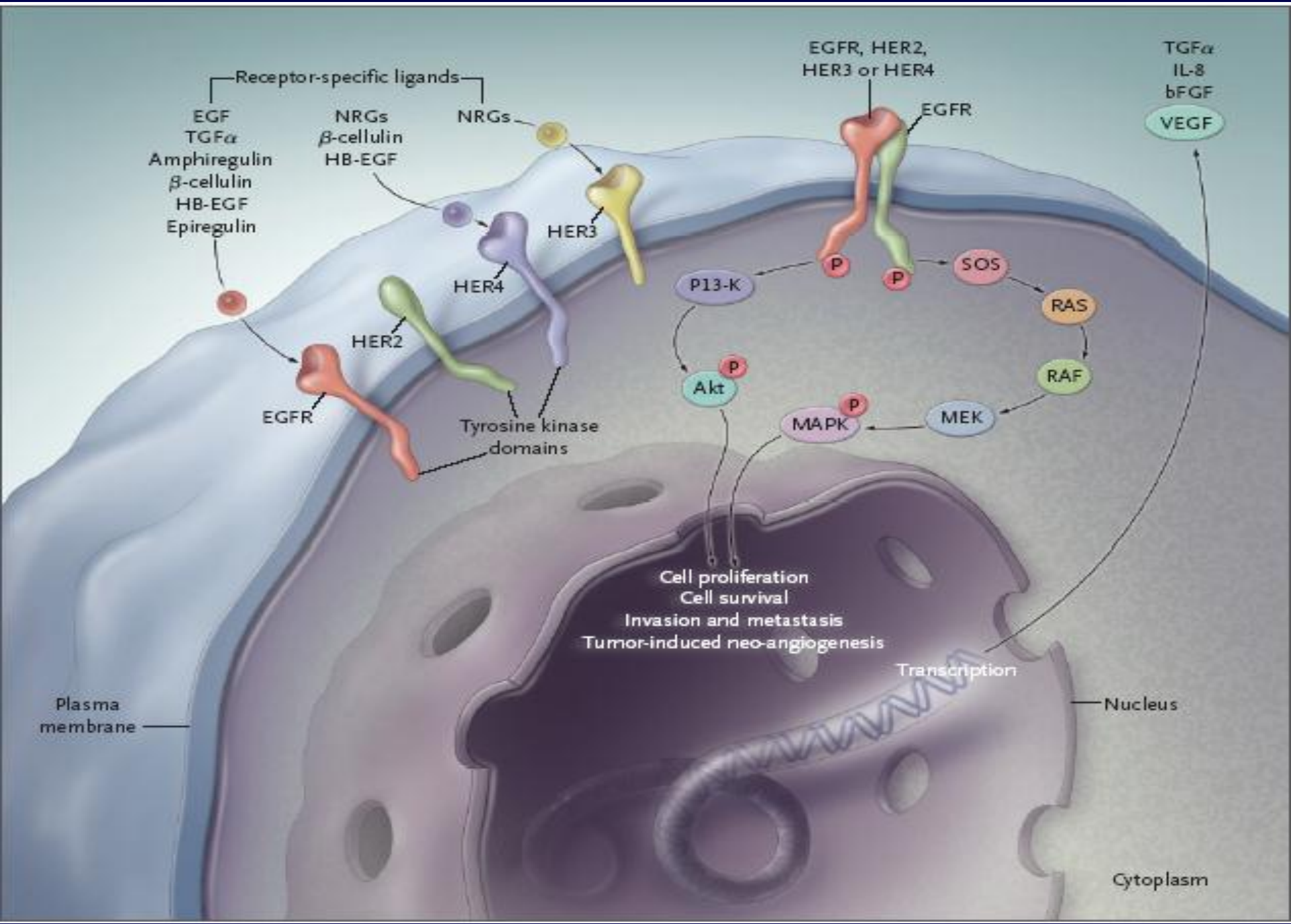
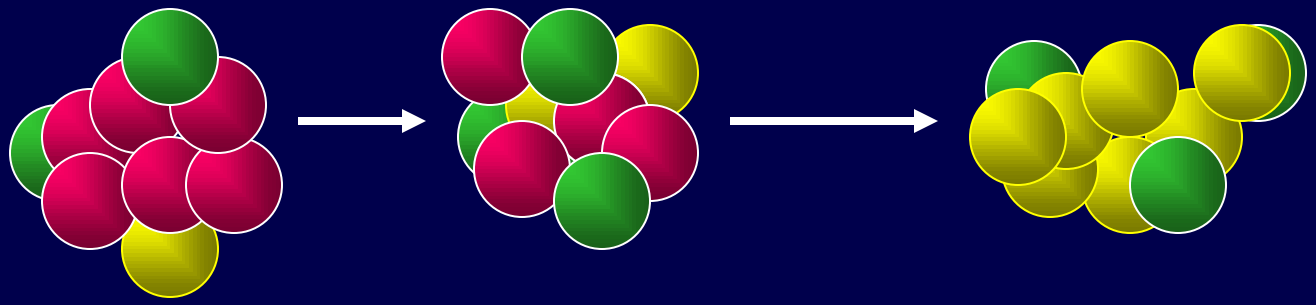
Why do we need to study molecular prognostic and predictive factors in colorectal cancer and why do we need to translate this knowledge to clinical practice?

- Colorectal cancer is not a single disease, but it is a very heterogenous disease.
- The approach of developing drugs that could be effective in all colorectal cancer patients has reached a plateau in efficacy.
- Although we use cytotoxic drugs and anti-angiogenic drugs in unselected colorectal cancer patients, these drugs are effective only in a subgroup of patients.
- KRAS gene testing is a first step in the identification of colorectal cancer patients responsive to anti-EGFR drugs, but KRAS wild type status does not identify all responders.
- Novel molecular targeted drugs will be effective only in selected subgroups of colorectal cancer patients and molecular markers should guide the identification of such patients.

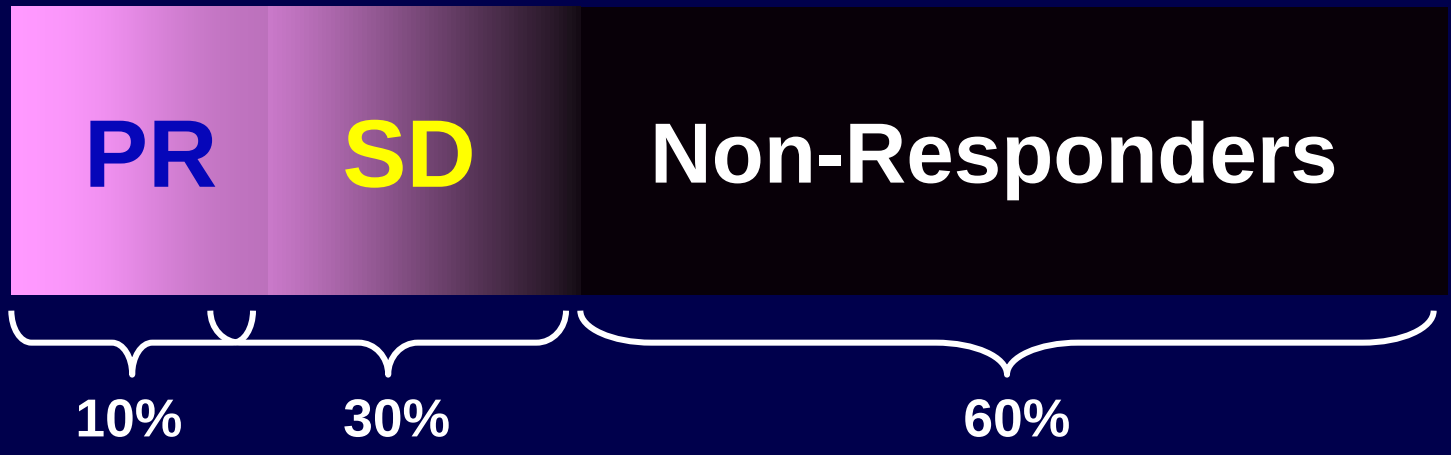


Ciardiello F and Tortora G. New Engl J Med 2008;358:1160–74.

Anti-EGFR drugs as monotherapy in unselected chemorefractory metastatic CRC : clinical results



EGFR-dependent Growth Non-EGFR-dependent Growth



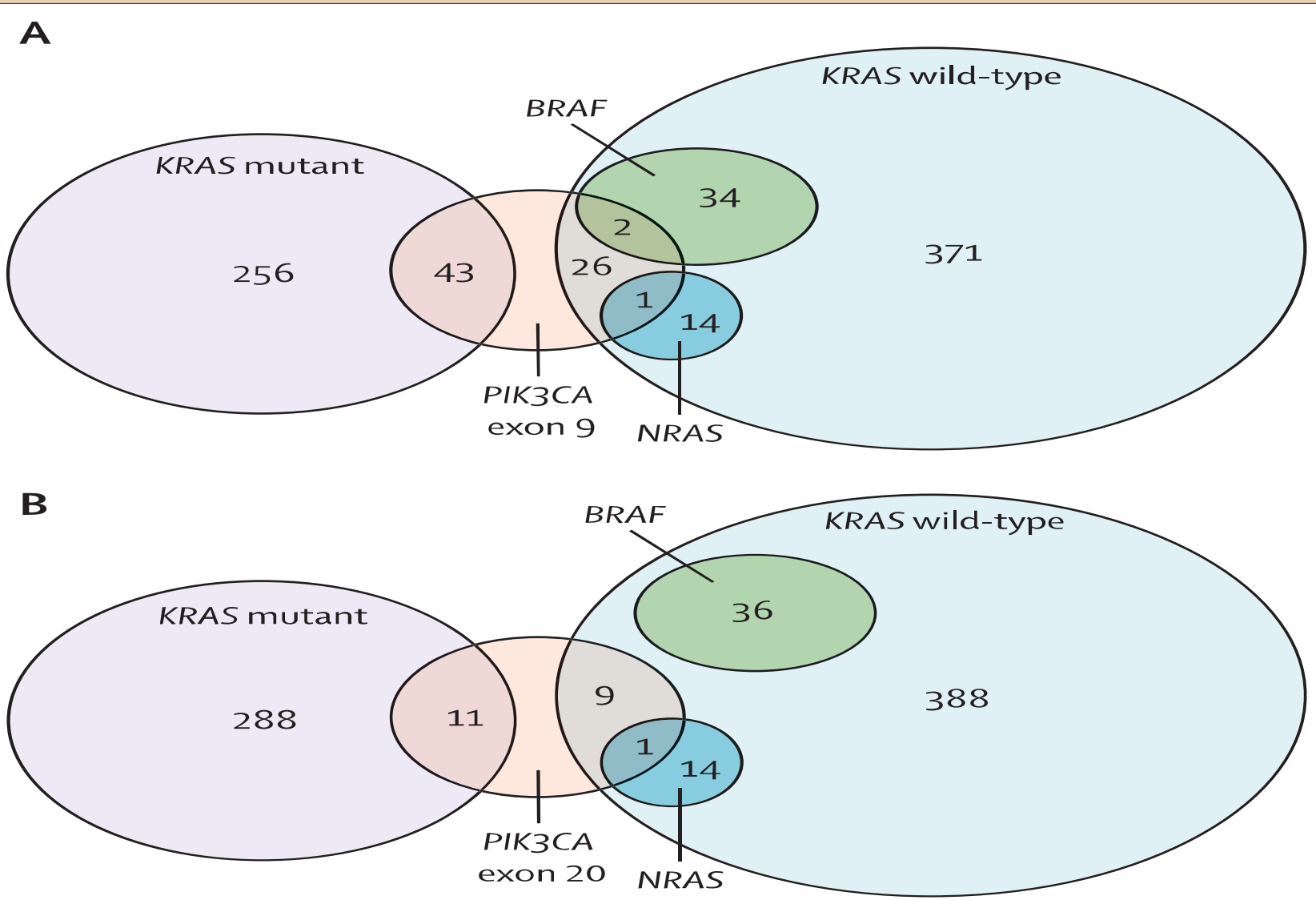
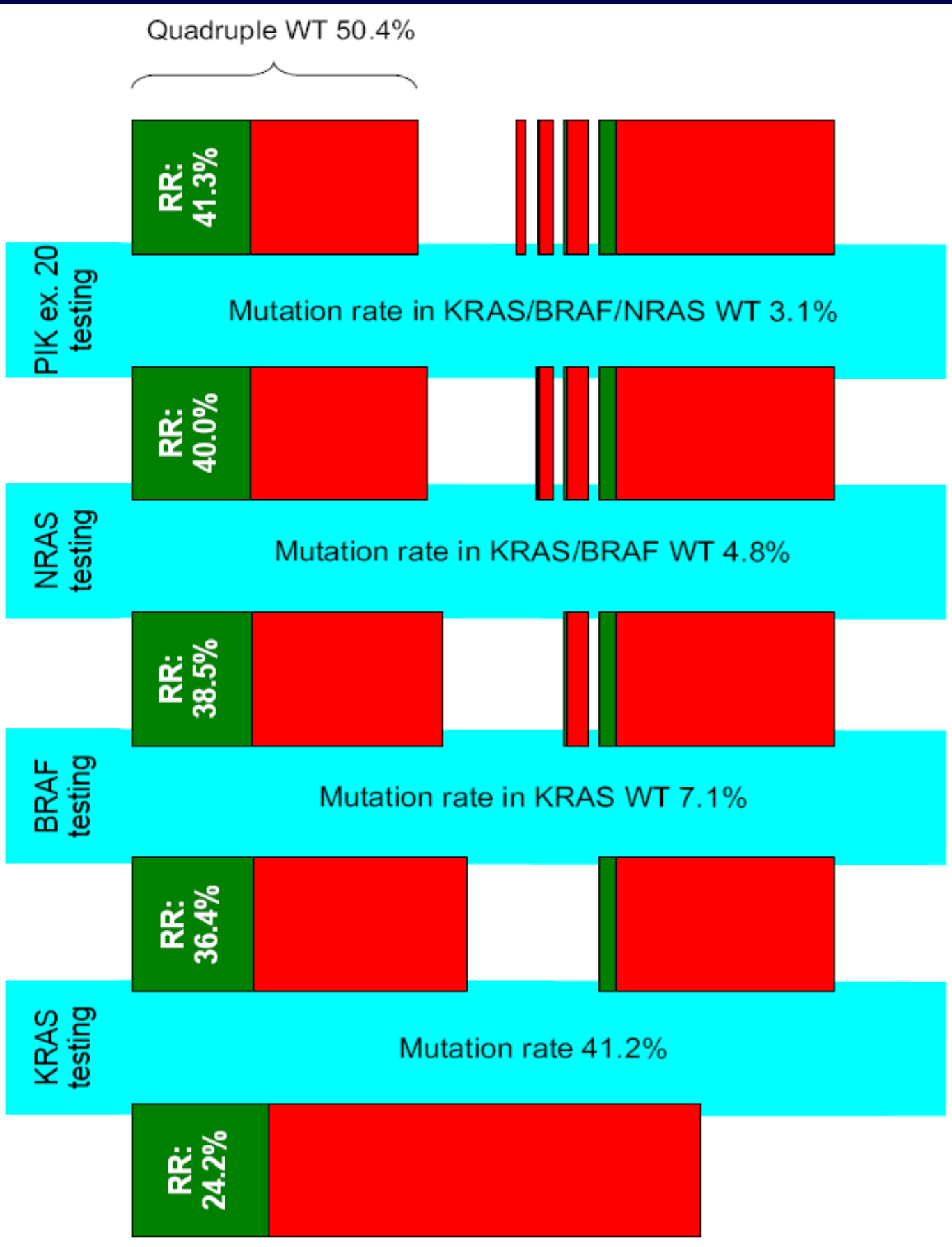


Figure 1: **Associations between mutations**
Absolute numbers of *KRAS* wild type, *KRAS* mutant, *BRAF* mutant, *NRAS* mutant, *PIK3CA* exon 9 mutant samples (A), and *PIK3CA* exon 20 mutant (B) samples are shown.


Quadruple WT 50.4%
RR: 41.3%
PIK ex. 20 testing
Mutation rate in KRAS/BRAF/NRAS WT 3.1%
RR: 40.0%
NRAS testing
Mutation rate in KRAS/BRAF WT 4.8%
RR: 38.5%
BRAF testing
Mutation rate in KRAS WT 7.1%
RR: 36.4%
KRAS testing
Mutation rate 41.2%
RR: 24.2%

How do we select an EGFR-dependent mCRC?

- KRAS wild type mCRC is an heterogeneous disease.
- Only a subset of KRAS wild type mCRC (approximately 50 to 60%) is dependent on the EGFR pathway.
- Potential markers of high dependence on the EGFR pathway:
- Quadruple negative mutations (KRAS, NRAS, BRAF, PI3KCA exon 20 wild type genes);
- High amphiregulin and/or high epiregulin;
- Early tumor shrinkage in response to treatment.

Is it currently possible to improve the efficacy of medical treatments for colorectal cancer patients without molecular selection ?

1. Yes
2. No
3. Don’t know

Do you use any molecular biomarker(s) for treatment choices in adjuvant therapy in your practice?

1. Yes
2. No
3. Don’t know

Do you use any molecular biomarker(s) for treatment choices in the management of metastatic colorectal cancer in your practice?

1. Yes
2. No
3. Don’t know