



Dynamic monitoring HER2 amplification of circulating DNA in metastatic colorectal cancer patients treated with cetuximab

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Disclosure of interest

- No conflicts of interest

Background & Methods



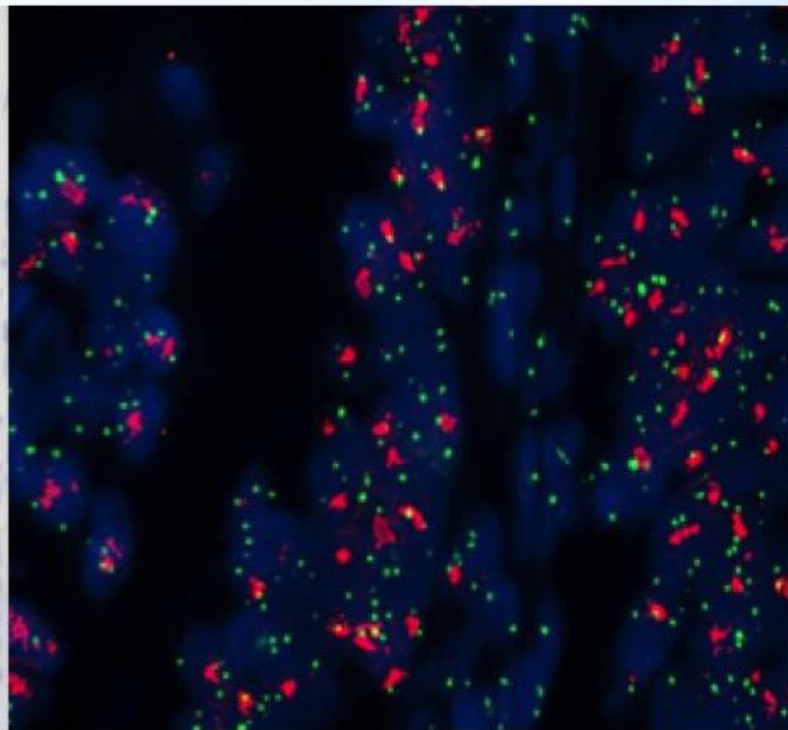
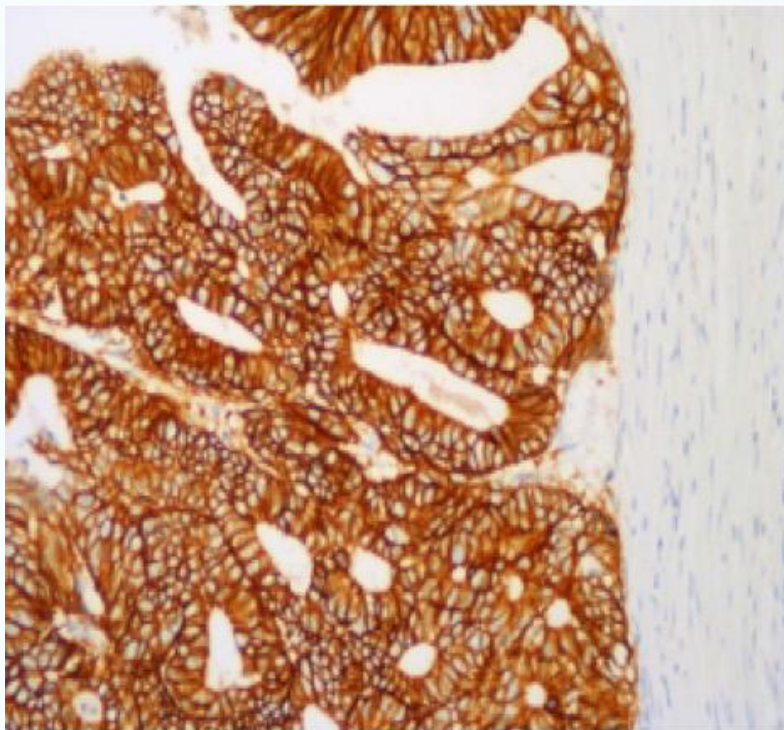
- Cetuximab & Colorectal cancer
- HER2 amplification & Cetuximab resistance
- HER2 amplification in circulating DNA
 - 8 week interval
 - droplet digital polymerase chain reaction (ddPCR)
 - 36 RAS and BRAF wt patients, who progressed after failure of cetuximab containing regimens

Results

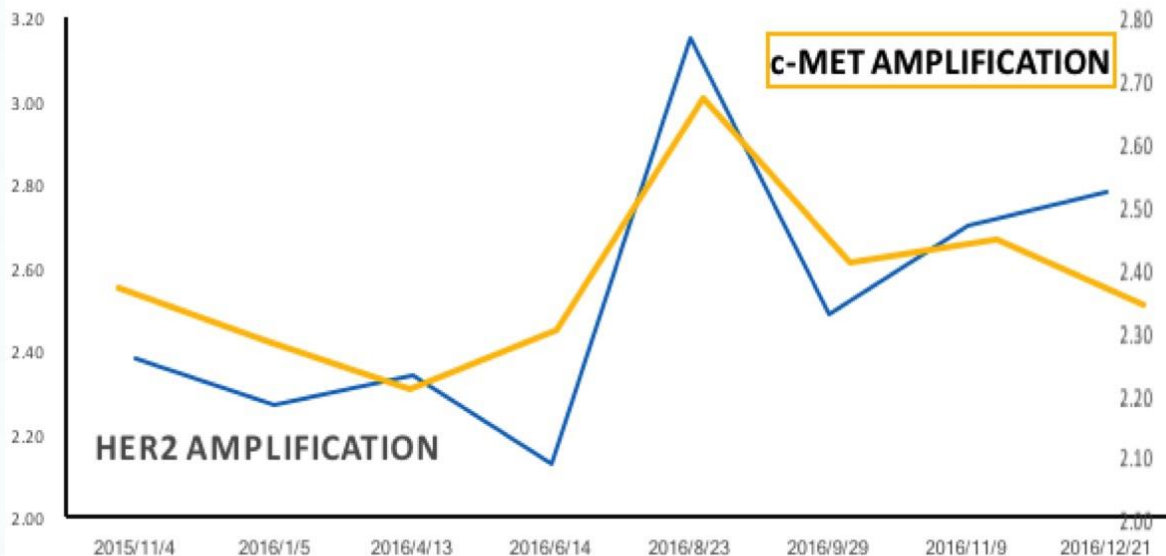


13.8% (5/36) of patients exhibited dynamic fluctuations of HER2 amplification in plasma, one of whom were found to be positive for HER2 amplification in matched tumor specimens using FISH. All 5 primary sites were left side, 4 rectums and 1 descending colon. 3 patients received cetuximab as first line therapy, whereas 2 patients in the 2nd line setting.

Results



Case 2 patient's tumor sample showed HER2 protein overexpression (A, IHC3+) and HER2 amplification (B)

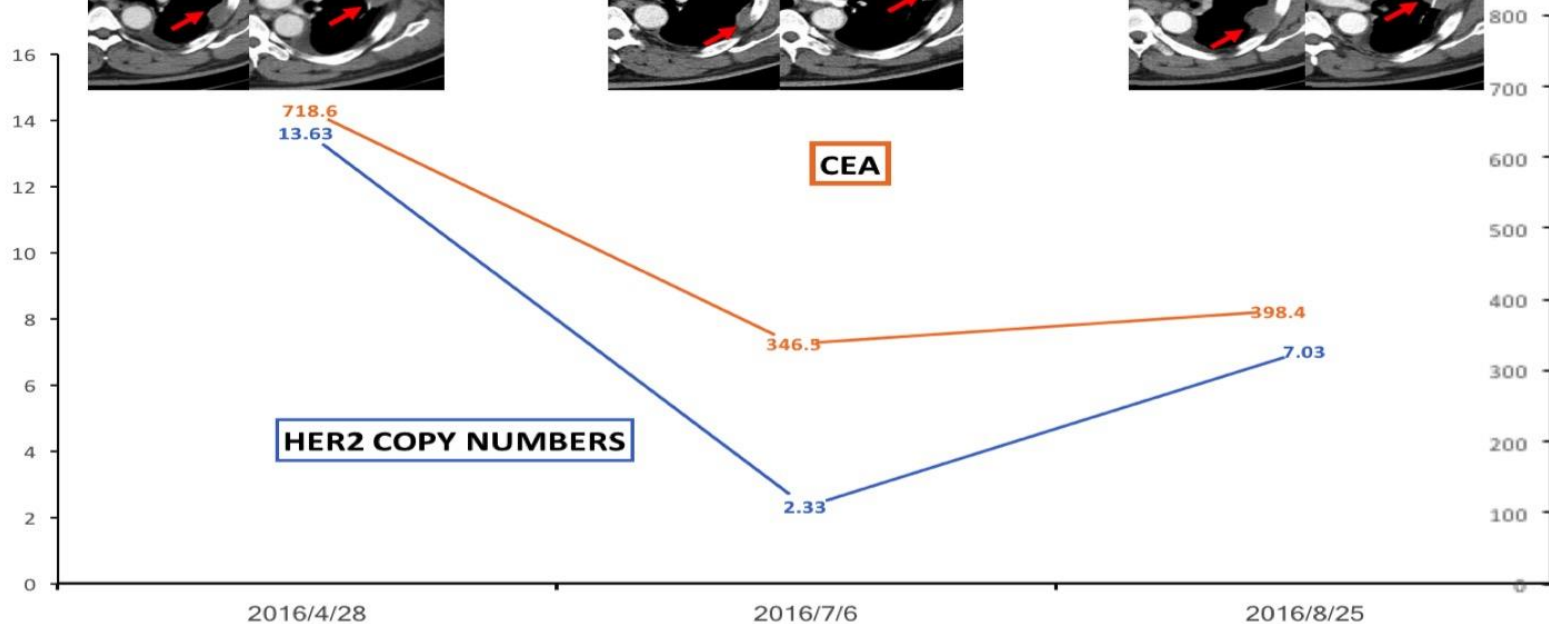
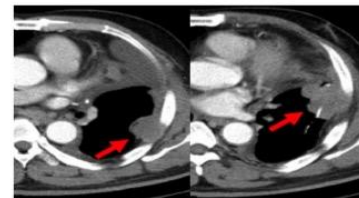
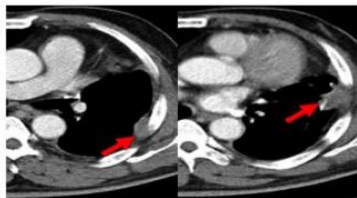
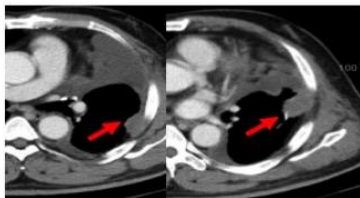


Two patients had HER2 and c-MET co-amplification. The dynamic fluctuations of copy numbers were observed with tumor response or progression over time during the treatment course.

Baseline

8 weeks- SD

16 weeks- PD



Among these 5 patients, changes in ctDNA levels showed good agreement with changes in tumor volume. Furthermore, quantifications of HER2 amplification showed obvious increase with an average lead time of 2 months compared with CT documented progress. But interestingly, there was no difference in PFS between these 5 patients and the others without *HER2* amplification (HR=0.89, 95%CI: 0.34-2.37, p=0.820).



Conclusions

Plasma HER2 amplification detected by ddPCR was showed dynamic changing over time and would predict resistance to cetuximab containing treatment. Average 2 months lead time was observed and need to validate in the further study.