QUANTITATIVE FLUORESCENCE MOLECULAR ENDOSCOPY USING CETUXIMAB-800CW TO EVALUATE RESPONSE TO NEOADJUVANT CHEMORADIOTHERAPY IN LOCALLY ADVANCED RECTAL CANCER; LESSONS LEARNED

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Cetuximab-800CW fluorescence molecular endoscopy could not distinguish pathological complete response from residual tumor in rectal cancer patients after neoadjuvant chemoradiotherapy due to submucosal tumor localization and off-target macrophage binding.

KEY POINTS

- In a study of ten locally advanced rectal cancer patients after neoadjuvant chemoradiotherapy, five achieved pathological complete response and five had partial response.
- Quantitative fluorescence molecular endoscopy using cetuximab-800CW showed significantly higher fluorescent signal in former tumor areas compared to healthy tissue in both complete responders ($p<0.0001$) and partial responders ($p<0.0001$), but could not distinguish between the two groups.
- Fluorescence microscopy revealed specific binding of cetuximab-800CW to tumor epithelium occurred only in the submucosa, not at the luminal surface accessible to endoscopy.
- Aspecific binding to mucosal macrophages was observed in both complete and partial responders, resulting in enhanced off-target fluorescence signals that confounded interpretation.
- The authors suggest novel techniques measuring fluorescence below the superficial layer, such as ultrasound-guided needle biopsy with single fiber fluorescence spectroscopy, may overcome these limitations.

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