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ON THE COVER
Pearson and colleagues performed a translational clinical trial in which patients with FGFR alterations were treated with the pan-FGFR inhibitor AZD4547. Responses occurred in 12.5% of patients with FGFR1-amplified breast cancer, and 33% patients with FGFR2-amplified gastroesophageal cancer. High-level, but not low-level, copy-number amplification of FGFR2 was associated with response to AZD4547, and was detectable in the plasma DNA of responding patients. FGFR1- and FGFR2-amplified cells both exhibited oncogene addiction with dependence on MAPK signaling, and high-level FGFR2-amplified cells also exhibited a unique dependence on FGFR-mediated PI3K–AKT signaling. These findings indicate that FGFR inhibitors may be more effective in tumors with high-level FGFR amplification and may guide clinical development of inhibitors targeting FGFR or other amplified receptor tyrosine kinases. For details, please see the article by Pearson and colleagues on page 838.
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