





















12. Majewski IJ, Mitterpergher L, Davidson NM, Bosma A, Willems SM, Horlings HM, et al. Identification of recurrent FGFR3 fusion genes in lung cancer through kinome-centred RNA sequencing. *J Pathol* 2013;230:270–6.
13. Wang R, Wang L, Li Y, Hu H, Shen L, Shen X, et al. FGFR1/3 tyrosine kinase fusions define a unique molecular subtype of non-small cell lung cancer. *Clin Cancer Res* 2014;14:107–14.
14. Williams SV, Hurst CD, Knowles MA. Oncogenic FGFR3 gene fusions in bladder cancer. *Hum Mol Genet* 2013;22:795–803.
15. Wu Y-M, Su F, Kalyana-Sundaram S, Khazanov N, Ateeq B, Cao X, et al. Identification of targetable FGFR gene fusions in diverse cancers. *Cancer Discov* 2013;3:636–47.
16. Cancer Genome Atlas Research Network. Comprehensive molecular characterization of urothelial bladder carcinoma. *Nature* 2014;507:315–22.
17. Arai Y, Totoki Y, Hosoda F, Shirota T, Hama N, Nakamura H, et al. Fibroblast growth factor receptor 2 tyrosine kinase fusions define a unique molecular subtype of cholangiocarcinoma. *Hepatology* 2014;59:1427–34.
18. Bahleda R, Dienstmann R, Adamo B, Gazzah A, Infante JR, Zhong B, et al. Phase 1 study of JNJ-42756493, a pan-fibroblast growth factor receptor (FGFR) inhibitor, in patients with advanced solid tumors. *J Clin Oncol* 32:5s, 2014 (suppl; abstr 2501).
19. Greenman C, Stephens P, Smith R, Dalgleish GL, Hunter C, Bignell G, et al. Patterns of somatic mutation in human cancer genomes. *Nature* 2007;446:153–8.
20. Billerey C, Chopin D, Aubriot-Lorton MH, Ricol D, Gil Diez de Medina S, Van Rhijn B, et al. Frequent FGFR3 mutations in papillary non-invasive bladder (pTa) tumors. *Am J Pathol* 2001;158:1955–9.
21. Tomlinson DC, Hurst CD, Knowles MA. Knockdown by shRNA identifies S249C mutant FGFR3 as a potential therapeutic target in bladder cancer. *Oncogene* 2007;26:5889–99.
22. Al-Ahmadie HA, Iyer G, Janakiraman M, Lin O, Heguy A, Tickoo SK, et al. Somatic mutation of fibroblast growth factor receptor-3 (FGFR3) defines a distinct morphological subtype of high-grade urothelial carcinoma. *J Pathol* 2011;224:270–9.
23. Bernard-Pierrot I, Brams A, Dunois-Lardé C, Caillaud A, Diez de Medina SG, Cappellen D, et al. Oncogenic properties of the mutated forms of fibroblast growth factor receptor 3b. *Carcinogenesis* 2006;27:740–7.
24. Kimura T, Suzuki H, Ohashi T, Asano K, Kiyota H, Eto Y. The incidence of thanatophoric dysplasia mutations in FGFR3 gene is higher in low-grade or superficial bladder carcinomas. *Cancer* 2001;92:2555–61.
25. Gozgi JM, Wong MJ, Moran L, Wardwell S, Mohemmad QK, Narasimhan NI, et al. Ponatinib (AP24534), a multitargeted pan-FGFR inhibitor with activity in multiple FGFR-amplified or mutated cancer models. *Mol Cancer Ther* 2012;11:690–9.
26. Qing J, Du X, Chen Y, Chan P, Li H, Wu P, et al. Antibody-based targeting of FGFR3 in bladder carcinoma and t(4;14)-positive multiple myeloma in mice. *J Clin Invest* 2009;119:1216–29.
27. Miyake M, Sugano K, Kawashima K, Ichikawa H, Hirabayashi K, Kodama T, et al. Sensitive detection of FGFR3 mutations in bladder cancer and urine sediments by peptide nucleic acid-mediated real-time PCR clamping. *Biochem Biophys Res Commun* 2007;362:865–71.
28. Wang J, Mikse O, Liao RG, Li Y, Tan L, Janne PA, et al. Ligand-associated ERBB2/3 activation confers acquired resistance to FGFR inhibition in FGFR3-dependent cancer cells. *Oncogene* 2015;34:2167–77.
29. Byron SA, Chen H, Wortmann A, Loch D, Gartside MG, Dehkoda F, et al. The N550K/H mutations in FGFR2 confer differential resistance to PD173074, dovitinib, and ponatinib ATP-competitive inhibitors. *Neoplasia* 2013;15:975–88.
30. Kandath C, Schultz N, Cherniack AD, Akbani R, Liu Y, Shen H, et al. Integrated genomic characterization of endometrial carcinoma. *Nature* 2013;497:67–73.
31. Pollock PM, Gartside MG, Dejeza LC, Powell MA, Mallon MA, Davies H, et al. Frequent activating FGFR2 mutations in endometrial carcinomas parallel germline mutations associated with craniosynostosis and skeletal dysplasia syndromes. *Oncogene* 2007;26:7158–62.
32. Dutt A, Salvesen HB, Chen T-H, Ramos AH, Onofrio RC, Hatton C, et al. Drug-sensitive FGFR2 mutations in endometrial carcinoma. *Proc Natl Acad Sci U S A* 2008;105:8713–7.
33. Byron SA, Gartside MG, Wellens CL, Mallon MA, Keenan JB, Powell MA, et al. Inhibition of activated fibroblast growth factor receptor 2 in endometrial cancer cells induces cell death despite PTEN abrogation. *Cancer Res* 2008;68:6902–7.
34. Konecny GE, Kolarova T, O'Brien NA, Winterhoff B, Yang G, Qi J, et al. Activity of the fibroblast growth factor receptor inhibitors dovitinib (TKI258) and NVP-BGJ398 in human endometrial cancer cells. *Mol Cancer Ther* 2013;12:632–42.
35. Shern JF, Chen L, Chmielecki J, Wei JS, Patidar R, Rosenberg M, et al. Comprehensive genomic analysis of rhabdomyosarcoma reveals a landscape of alterations affecting a common genetic axis in fusion-positive and fusion-negative tumors. *Cancer Discov* 2014;4:216–31.
36. Taylor JG, Cheuk AT, Tsang PS, Chung J-Y, Song YK, Desai K, et al. Identification of FGFR4-activating mutations in human rhabdomyosarcomas that promote metastasis in xenotransplanted models. *J Clin Invest* 2009;119:3395–407.
37. Li SQ, Cheuk AT, Shern JF, Song YK, Hurd L, Liao H, et al. Targeting wild-type and mutationally activated FGFR4 in rhabdomyosarcoma with the inhibitor ponatinib (AP24534). *PLoS ONE* 2013;8:e76551.
38. Weiss J, Sos ML, Seidel D, Peifer M, Zander T, Heuckmann JM, et al. Frequent and focal FGFR1 amplification associates with therapeutically tractable FGFR1 dependency in squamous cell lung cancer. *Sci Transl Med* 2010;2:62ra93.
39. Heist RS, Mino-Kenudson M, Sequist L V, Tammireddy S, Morrissey L, Christiani DC, et al. FGFR1 amplification in squamous cell carcinoma of the lung. *J Thorac Oncol* 2012;7:1775–80.
40. Peifer M, Fernández-Cuesta L, Sos ML, George J, Seidel D, Kasper LH, et al. Integrative genome analyses identify key somatic driver mutations of small-cell lung cancer. *Nat Genet* 2012;44:1104–10.
41. Nogova L, Sequist LV, Cassier PA, Hidalgo M, Delord J-P, Schuler MH, et al. Targeting FGFR1-amplified lung squamous cell carcinoma with the selective pan-FGFR inhibitor BGJ398. *J Clin Oncol* 32:5s, 2014 (suppl; abstr 8034).
42. Pardo OE, Latigo J, Jeffery RE, Nye E, Poulson R, Spencer-Dene B, et al. The fibroblast growth factor receptor inhibitor PD173074 blocks small cell lung cancer growth in vitro and in vivo. *Cancer Res* 2009;69:8645–51.
43. Courjal F, Cuny M, Simony-Lafontaine J, Louason G, Speiser P, Zeillinger R, et al. Mapping of DNA amplifications at 15 chromosomal localizations in 1875 breast tumors: definition of phenotypic groups. *Cancer Res* 1997;57:4360–7.
44. Reis-Filho JS, Simpson PT, Turner NC, Lambros MB, Jones C, Mackay A, et al. FGFR1 emerges as a potential therapeutic target for lobular breast carcinomas. *Clin Cancer Res* 2006;12:6652–62.
45. Brunello E, Brunelli M, Bogina G, Caliò A, Manfrin E, Nottesgar A, et al. FGFR-1 amplification in metastatic lymph-nodal and haematogenous lobular breast carcinoma. *J Exp Clin Cancer Res* 2012;31:103.
46. Andre F, Bachelot T, Commo F, Campone M, Amedos M, Dieras V, et al. Comparative genomic hybridisation array and DNA sequencing to direct treatment of metastatic breast cancer: a multicentre, prospective trial (SAFIR01/UNICANCER). *Lancet Oncol* 2014;15:267–74.
47. Ferté C, Massard C, Ileana E, Hollebecque A, Lacroix L, Ammari S, et al. Molecular screening for cancer treatment optimization (MOSCATO 01): a prospective molecular triage trial; Interim analysis of 420 patients [abstract]. In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; 2014 Apr 5–9; San Diego, CA. Philadelphia (PA): AACR; 2014. Abstract nr CT240.
48. Turner N, Pearson A, Sharpe R, Lambros M, Geyer F, Lopez-Garcia MA, et al. FGFR1 amplification drives endocrine therapy resistance and is a therapeutic target in breast cancer. *Cancer Res* 2010;70:2085–94.
49. André F, Bachelot T, Campone M, Dalenc F, Perez-Garcia JM, Hurvitz SA, et al. Targeting FGFR with dovitinib (TKI258): preclinical and clinical data in breast cancer. *Clin Cancer Res* 2013;19:3693–702.
50. Kim S, Dubrovskaya A, Salamone RJ, Walker JR, Grandinetti KB, Bonamy GMC, et al. FGFR2 promotes breast tumorigenicity through maintenance of breast tumor-initiating cells. *PLoS ONE* 2013;8:e51671.
51. Deng N, Goh LK, Wang H, Das K, Tao J, Tan IB, et al. A comprehensive survey of genomic alterations in gastric cancer reveals systematic patterns of molecular exclusivity and co-occurrence among distinct therapeutic targets. *Gut* 2012;61:673–84.

52. Matsumoto K, Arai T, Hamaguchi T, Shimada Y, Kato K, Oda I, et al. FGFR2 gene amplification and clinicopathological features in gastric cancer. *Br J Cancer* 2012;106:727–32.
53. Guagnano V, Kauffmann A, Wöhrle S, Stamm C, Ito M, Barys L, et al. FGFR genetic alterations predict for sensitivity to NVP-BGJ398, a selective pan-FGFR inhibitor. *Cancer Discov* 2012;2:1118–33.
54. Wesche J, Haglund K, Haugsten E. Fibroblast growth factors and their receptors in cancer. *Biochem J* 2011;437:199–213.
55. Acevedo VD, Ittmann M, Spencer DM. Paths of FGFR-driven tumorigenesis. *Cell Cycle* 2009;8:580–8.
56. Sharpe R, Pearson A, Herrera-Abreu MT, Johnson D, Mackay A, Welti JC, et al. FGFR signaling promotes the growth of triple-negative and basal-like breast cancer cell lines both in vitro and in vivo. *Clin Cancer Res* 2011;17:5275–86.
57. Javerzat S, Auguste P, Bikfalvi A. The role of fibroblast growth factors in vascular development. *Trends Mol Med* 2002;8:483–9.
58. Lieu C, Heymach J, Overman M. Beyond VEGF: inhibition of the fibroblast growth factor pathway and antiangiogenesis. *Clin Cancer Res* 2011;17:6130–9.
59. Plantamura I, Casalini P, Dugnani E, Sasso M, D'Ippolito E, Tortoreto M, et al. PDGFR $\beta$  and FGFR2 mediate endothelial cell differentiation capability of triple negative breast carcinoma cells. *Mol Oncol* 2014;8:968–81.
60. Giavazzi R, Sennino B, Coltrini D, Garofalo A, Dossi R, Ronca R, et al. Distinct role of fibroblast growth factor-2 and vascular endothelial growth factor on tumor growth and angiogenesis. *Am J Pathol* 2003;162:1913–26.
61. Kopetz S, Hoff PM, Morris JS, Wolff RA, Eng C, Glover KY, et al. Phase II trial of infusional fluorouracil, irinotecan, and bevacizumab for metastatic colorectal cancer: efficacy and circulating angiogenic biomarkers associated with therapeutic resistance. *J Clin Oncol* 2010;28:453–9.
62. Allen E, Walters IB, Hanahan D. Brivanib, a dual FGF/VEGF inhibitor, is active both first and second line against mouse pancreatic neuroendocrine tumors developing adaptive/evasive resistance to VEGF inhibition. *Clin Cancer Res* 2011;17:5299–310.
63. Ware KE, Hinz TK, Kleczko E, Singleton KR, Marek LA, Helfrich BA, et al. A mechanism of resistance to gefitinib mediated by cellular reprogramming and the acquisition of an FGF2-FGFR1 autocrine growth loop. *Oncogenesis* 2013;2:e39.
64. Oliveras-Ferreras C, Cufi S, Queralt B, Vazquez-Martin A, Martin-Castillo B, de Llorens R, et al. Cross-suppression of EGFR ligands amphiregulin and epiregulin and de-repression of FGFR3 signalling contribute to cetuximab resistance in wild-type KRAS tumour cells. *Br J Cancer* 2012;106:1406–14.
65. Yadav V, Zhang X, Liu J, Estrem S, Li S, Gong X-Q, et al. Reactivation of mitogen-activated protein kinase (MAPK) pathway by FGF receptor 3 (FGFR3)/Ras mediates resistance to vemurafenib in human B-RAF V600E mutant melanoma. *J Biol Chem* 2012;287:28087–98.
66. Soria J-C, De Braud FG, Bahleda R, Adamo B, Cereda R, Camboni MG, et al. A phase I/IIa study evaluating the safety, efficacy, pharmacokinetics, and pharmacodynamics of lucitanib in advanced solid tumors. *J Clin Oncol* 2014;32:2500 (suppl; abstr 2500).
67. Bello E, Colella G, Scarlato V, Oliva P, Berndt A, Valbusa G, et al. E-3810 is a potent dual inhibitor of VEGFR and FGFR that exerts antitumor activity in multiple preclinical models. *Cancer Res* 2011;71:1396–405.
68. Angevin E, Lopez-Martin JA, Lin C-C, Gschwend JE, Harzstark A, Castellano D, et al. Phase I study of dovitinib (TKI258), an oral FGFR, VEGFR, and PDGFR inhibitor, in advanced or metastatic renal cell carcinoma. *Clin Cancer Res* 2013;19:1257–68.
69. Escudier B, Grünwald V, Ravaud A, Ou Y-C, Castellano D, Lin C-C, et al. Phase II results of dovitinib (TKI258) in patients with metastatic renal cell cancer. *Clin Cancer Res* 2014;20:3012–22.
70. Motzer RJ, Porta C, Vogelzang NJ, Sternberg CN, Szczylik C, Zolnierak J, et al. Dovitinib versus sorafenib for third-line targeted treatment of patients with metastatic renal cell carcinoma: an open-label, randomised phase 3 trial. *Lancet Oncol* 2014;15:286–96.
71. Andre F, Ranson M, Dean E, Varga A, Van der Noll R, Stockman PK, et al. Results of a phase I study of AZD4547, an inhibitor of fibroblast growth factor receptor (FGFR), in patients with advanced solid tumors [abstract]. In: Proceedings of the 104th Annual Meeting of the American Association for Cancer Research; 2013 Apr 6–10; Washington, DC. Philadelphia (PA): AACR; 2013. Abstract nr LB-145.
72. Arkenau H-T, Saggese M, Hollebecque A, Mathewson A, Lemech CR, Landers D, et al. A phase I expansion cohort of the fibroblast growth factor receptor (FGFR) inhibitor AZD4547 in patients (pts) with advanced gastric (GC) and gastroesophageal (GOJ) cancer. *J Clin Oncol* 2014;32:5s, 2014 (suppl; abstr 2620).
73. Paik PK, Shen R, Ferry D, Soria J-C, Mathewson A, Kilgour E, et al. A phase 1b open-label multicenter study of AZD4547 in patients with advanced squamous cell lung cancers: preliminary antitumor activity and pharmacodynamic data. *J Clin Oncol* 2014;32:5s, 2014 (suppl; abstr 8035).
74. Sequist LV, Cassier P, Varga A, Taberero J, Schellens JHM, Delord J-P, et al. Phase I study of BGJ398, a selective pan-FGFR inhibitor in genetically preselected advanced solid tumors [abstract]. In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; 2014 Apr 5–9; San Diego, CA. Philadelphia (PA): AACR; 2014. Abstract nr CT326.
75. Ochiwa H, Fujita H, Itoh K, Sootome H, Hashimoto A, Fujioka Y, et al. TAS-120, a highly potent and selective irreversible FGFR inhibitor, is effective in tumors harboring various FGFR gene abnormalities [abstract]. In: Proceedings of the AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics; 2013 Oct 19–23; Boston, MA. Philadelphia (PA): AACR; 2013. Abstract nr A270.
76. O'Donnell P, Goldman JW, Gordon MS, Shih K, Choi YJ, Lu D, et al. A phase I dose-escalation study of MFGR1877S, a human monoclonal anti-fibroblast growth factor receptor 3 (FGFR3) antibody, in patients with advanced solid tumors. *Eur J Cancer* 2012;48 Suppl 6:191–2.
77. Bellovin DI, Palencia S, Hestir K, Lee E, DeYoung MP, Brennan T, et al. Bellovin D. FP-1039/GSK3052230, an FGF ligand trap, enhances VEGF antagonist therapy in preclinical models of RCC and HCC [abstract]. In: Proceedings of the 105th Annual Meeting of the American Association for Cancer Research; 2014 Apr 5–9; San Diego, CA. Philadelphia (PA): AACR; 2014. Abstract nr 5449.
78. Rubin E, Allen JD, Nowak JA, Bates SE. Developing precision medicine in a global world. *Clin Cancer Res* 2014;20:1419–27.
79. Chell V, Balmanno K, Little AS, Wilson M, Andrews S, Blockley L, et al. Tumour cell responses to new fibroblast growth factor receptor tyrosine kinase inhibitors and identification of a gatekeeper mutation in FGFR3 as a mechanism of acquired resistance. *Oncogene* 2013;32:3059–70.
80. Herrera-Abreu MT, Pearson A, Campbell J, Shnyder SD, Knowles MA, Ashworth A, et al. Parallel RNA interference screens identify EGFR activation as an escape mechanism in FGFR3-mutant cancer. *Cancer Discov* 2013;3:1058–71.
81. Issa A, Gill JW, Heideman MR, Sahin O, Wlemann S, Dey JH, et al. Combinatorial targeting of FGF and ErbB receptors blocks growth and metastatic spread of breast cancer models. *Breast Cancer Res* 2013;15:R8.
82. Casey SC, Bellovin DI, Felsner DW. Noncanonical roles of the immune system in eliciting oncogene addiction. *Curr Opin Immunol* 2013;25:246–58.
83. Jones D, Hutter B, Jäger N, Korshunov A, Kool M, Warnatz HJ, et al. Recurrent somatic alterations of FGFR1 and NTRK2 in pilocytic astrocytoma. *Nat Genet* 2013;45:927–32.