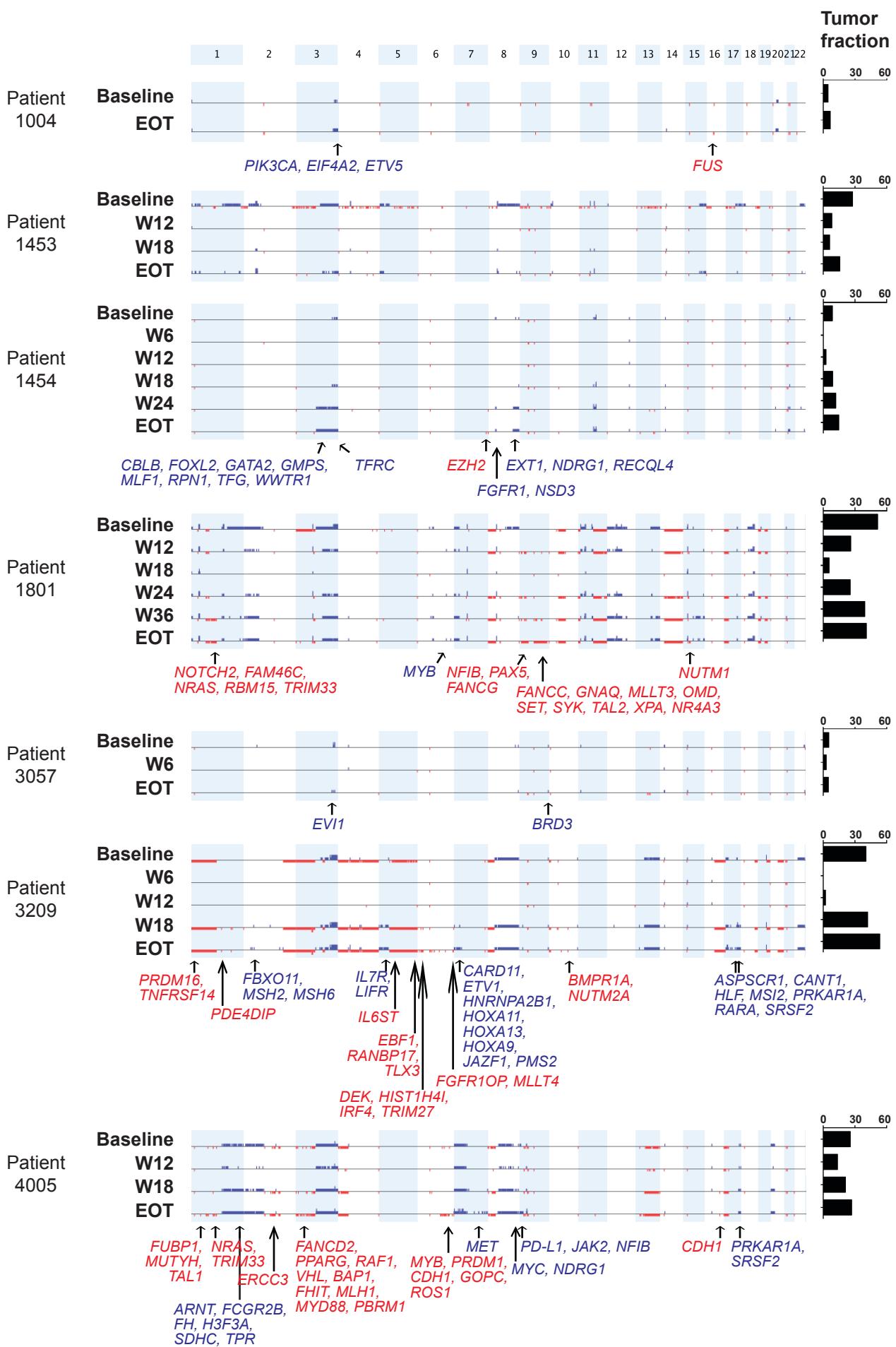
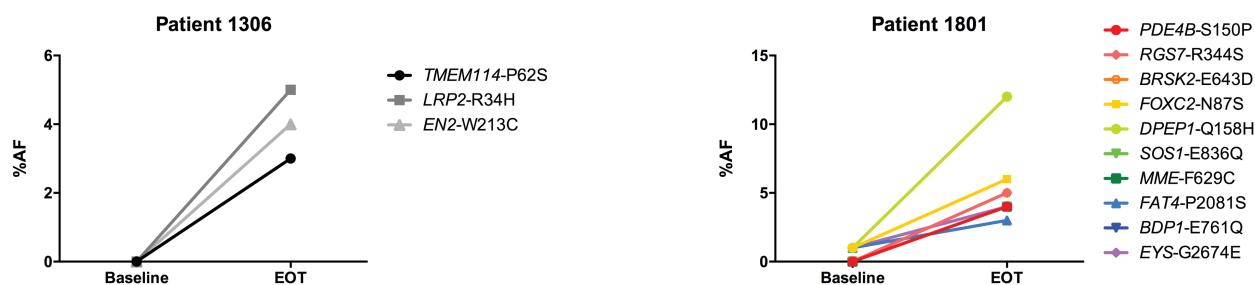


**A**

B



C

Gene	Function	Association with disease	Role in cancer	Drug resistance	Reference
<i>TMEM114</i>	Lens and eye development	Mutations associated with congenital and juvenile cataract disorders	Unknown	Unknown	1, 2
<i>LRP2</i>	Cell signaling; reuptake of ligands	Mutations cause Donnai-Barrow syndrome and facio-oculo-acoustico-renal syndrome	High expression in melanoma High expression correlates with better survival in renal clear cell carcinoma patients Overexpressed in bladder cancer	Unknown	3, 4, 5
<i>EN2</i>	Pattern formation in central nervous system development	Mutation associated with autism spectrum disorder	Downregulated in clear-cell renal cell carcinoma Downregulated in advanced prostate cancer	Unknown	6, 7, 8
<i>PDE4B</i>	Regulation of cyclic nucleotide concentration	Altered activity in schizophrenia and bipolar affective disorder	Highly expressed in CD4+ lymphoid cancer cells	Knockdown increases castration-resistant growth of prostate cancer cell line LNCaP	9, 10, 11
<i>RGS7</i>	G protein signaling	Human panic disorder	Loss-of-function promotes migration and invasion of melanoma cells	Unknown	12, 13
<i>BRSK2</i>	Polarization of neurons and axonogenesis; insulin secretion	Small-cell lung cancer-associated limbic encephalitis	Enhances survival of pancreatic ductal adenocarcinoma cells	Unknown	14, 15
<i>FOXC2</i>	Mesenchymal tissue development	Mutations cause lymphedema-distichiasis syndrome	Overexpressed in breast, stomach, cervical and ovarian cancers	Promotes resistance to cisplatin in ovarian cancer cells Knockdown confers resistance to 5-fluorouracil in colorectal cancer cells	16, 17
<i>DPEP1</i>	Leukotriene activity; renal metabolism	Unknown	Increased expression in colorectal cancer Decreased expression in pancreatic ductal adenocarcinoma	Unknown	18, 19
<i>SOS1</i>	Regulation of RAS protein activity; EGF-dependent signaling	Mutations associated with gingival fibromatosis 1 and Noonan syndrome type 4	Elevated expression in ovarian cancer and prostate cancer	Increased expression in erlotinib-resistant cell line	20, 21, 22
<i>MME</i>	B Cell Development	Alzheimer's disease, ageing, cardiac disorders	Altered expression in multiple cancers including: prostate, breast, melanoma, thyroid, stomach, colon, head and neck, colorectal, pancreatic, cervical, ovarian, and gastric cancers	Increased expression in cisplatin-resistant head and neck squamous cell carcinoma cell line	23, 24
<i>FAT4</i>	Regulation of planar cell polarity	Mutations associated with Van Maldergem Syndrome 2	Tumor suppressor role in gastric cancer and breast cancer	Unknown	25, 26
<i>BDP1</i>	Transcription from polymerase III promoters	Mutation associated with hereditary hearing loss	Decreases HER2 phosphorylation in breast cancer cells	Unknown	27, 28, 29
<i>EYS</i>	Functions of photoreceptor	Mutated in autosomal recessive retinitis pigmentosa	Unknown	Unknown	30

### Figure S8.

**A**, CNV landscapes of 7 patients treated with pictilisib and had detectable CNVs at both baseline and EOT. COSMIC genes with CNVs not found at baseline but in EOT were annotated. Blue, copy number gain; red, copy number loss. **(B-C)** Somatic variants significantly increased in EOT compared to baseline cfDNA in two patients.

**B**, Gene mutation allele frequency at baseline and EOT. **C**, Known functions of all genes enriched in EOT and their roles in disease and drug resistance.

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