Supplementary Table S1. Summary of FGFR inhibitors used in the UCSD cohort (N = 16): IC_{50}

	Target IC_{50}*
Lenvatinib	VEGFR1 (4.7 nM), VEGFR2 (3 nM), KIT (85 nM), PDGFRα (29 nM), FGFR1-4 (27–61 nM)[1]
Ponatinib	VEGFR2 (1.5 nM), KIT (12.5 nM), PDGFRα (1.1 nM), FGFR1-4 (2.2–18.2 nM)[2]
Pazopanib	VEGFR2 (8 nM), KIT (2.6 nM), PDGFR β (3 nM), FGFR1-3 (84 nM)[3,4]
Infigratinib	FGFR1 (1.1 nM), FGFR2 (1.0 nM), FGFR3 (2.0 nM), FGFR4 (61 nM)[5]

∗Values listed were obtained in cell-free assays.
Abbreviations: IC_{50} = 50% inhibitory concentration

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Supplementary Table S2. Rationale for suggested therapies with FGFR inhibitor-based therapies (N = 16)

ID	Diagnosis	Molecular Characteristics (Laboratory vendor, source)	Treatment Regimen	Stable disease ≥6 months or PR/CR	Rationale for therapy	References
1	Gastroesophageal cancer	(FM, tissue) *FGFR2* amplification *CDKN2A* loss *MYC* amplification *APC* I1307K *ARID1A* P2139fs*62 *TP53* F113C	Ponatinib	No	Ponatinib is a potent FGFR inhibitor (**Supplemental Table S1**).	
2	Bladder cancer	(FM, tissue) *FGFR1* amplification *NF1* Q1218* *TP53* R267G *ERBB2* I767M *MLL2* P3668fs*5, splice site 177-1G>T *ZNF703* amplification	Pazopanib	No	Pazopanib is a potent FGFR inhibitor (**Supplemental Table S1**).	
3	Urothelial cancer	(FM, tissue) *FRS2* amplification *AKT2* amplification *BRIP1* truncation *PIK3CA* H450_V461>GS *RAF1* amplification *MDM2* amplification *MYC* amplification *RNF43* S262* *ARID2* S889* (GH, blood) *FGFR2* V516L, G131R	Lenvatinib, Olaparib	No	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・BRIP1 inactivation can lead to homologous recombination repair deficiency, which may be targetable with PARP inhibitors such as olaparib.	[1,2]
4	Biliary cancer	(FM, tissue) *FGFR2-BICC1* fusion	Infigratinib	Yes	Infigratinib is a potent selective FGFR inhibitor (**Supplemental Table S1**).	
5	Biliary cancer	(FM, tissue) *FGFR2-BICC2* fusion *POLE* R446Q (GH, blood) *PIK3CA* amplification	Lenvatinib, Everolimus	No	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*PIK3CA* amplification can activate PI3K pathway, which can be targeted with mTOR inhibitor (everolimus).	[3,4]
6	Biliary cancer	(FM, tissue) *FRS2* amplification *MDM2* amplification *CDKN2A* p16INK4a R80*, p14ARF P94L *CEBPA* G103_G104del	Lenvatinib, Palbociclib	Yes	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*CDKN2A* alteration can activate CDK4/6 which can be targeted with CDK4/6 inhibitor (palbociclib).	[5,6]
7	Osteosarcoma	(FM, tissue) *FGF23* amplification *FGF6* amplification *FRS2* amplification *CDK4* amplification *CCND2* amplification *MDM2* amplification	Lenvatinib, Palbociclib	Yes	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*CDK4* and *CCND2* amplification may be targetable with CDK4/6 inhibitor (palbociclib).	[7]
8	Gastroesophageal cancer	(FM, tissue) *FGF19* amplification *FGF3* amplification *FGF4* amplification *CCND1* amplification *CDK6* amplification *MET* amplification *ARID1A* R1276* *TERC* amplification *TP53* P278L TMB: intermediate (8Muts/Mb)	Lenvatinib, Palbociclib, Nivolumab	No	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*CDK6* and *CCND1* amplification can be targeted with CDK4/6 inhibitor (palbociclib). ・Patients with intermediate TMB could benefit from anti-PD-L1 inhibitor (nivolumab).	[7,8]
9	Glioneuronal tumor	(FM, tissue) *FGFR1* K656E	Lenvatinib	Yes	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**).	

10	Endometrial cancer	(FM, tissue) *FGFR2* N549K *PIK3CA* G1049R *PTEN* K125N *ARID1A* Q2115fs*33 *CHD4* R975H *CTCF* S282fs*21 *MLL3* S2123* *TP53* Y163C	Lenvatinib, Everolimus	No	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*PIK3CA* alteration can be targetable with mTOR inhibitor (everolimus)	[9]
11	Gastroesophageal cancer	(FM, tissue) *FGF19* amplification *FGF3* amplification *FGF4* amplification *CCND1* amplification *CDK6* amplification *CDKN2A/B* loss *PIK3CA* amplification *SOX2* amplification *PIK3CG* amplification *PRKCI* amplification *TERC* amplification *TP53* G245D TMB: intermediate (7Muts/Mb)	Lenvatinib, Palbociclib, Nivolumab	No	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*CDK6* and *CCND1* amplification can be targeted with CDK4/6 inhibitor (palbociclib). ・Patients with intermediate TMB could benefit from anti-PD-L1 inhibitor (nivolumab).	
12	Gastroesophageal cancer	(FM, tissue) *FGFR2* amplification *TP53* A159V	Lenvatinib	No	Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**).	
13	Ovarian cancer	(FM, tissue) *FGFR4* amplification *FLT4* amplification *PDGFRB* amplification *CDK6* amplification *TP53* K132R (GH, blood) *TP53* K132, K120M *PIK3CA* E545K *MET* amplification *PDGFRA* amplification *KIT* amplification	Lenvatinib, Palbociclib	Yes	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*CDK6* amplification may be targetable with CDK4/6 inhibitor (palbociclib).	
14	Gastrointestinal stromal tumor	(FM, tissue) *KIT* K558_E562del, N822K, V654A *ARID1A* truncation *NOTCH2* P6fs*27 TMB: intermediate (7Muts/Mb) (GH, blood) *FGFR1* amplification *MYC* amplification *ERBB2* amplification	Lenvatinib, Pembrolizumab	Yes	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・Patients with intermediate TMB could benefit from PD-L1 inhibitor (pembrolizumab).	[8]
15	Adenoid cystic carcinoma	(FM, tissue) *FGF19* amplification *FGF3* amplification *FGF4* amplification *CCND1* amplification *FANCA* F1263del (GH, blood) *FGFR1* amplification	Lenvatinib, Palbociclib	No	・Lenvatinib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*CCND1* amplification may be targetable with CDK4/6 inhibitor (palbociclib).	
16	Undifferentiated sarcoma	(FM, tissue) *FGFR3* amplification *AKT2* amplification *BRCA2* R1190W *CCNE1* amplification *CDK4* amplification *MDM2* amplification *AR* amplification	Pazopanib, Everolimus	No	・Pazopanib is a potent FGFR inhibitor (**Supplemental Table S1**). ・*AKT2* amplification may be targetable with mTOR inhibitor (everolimus).	[10,11]

Abbreviations: FM, Foundation Medicine; GH, Guardant Health; Muts, mutations; TMB, tumor mutation burden; PARP, Poly (ADP-ribose) polymerase; mTOR; mammalian target of rapamycin

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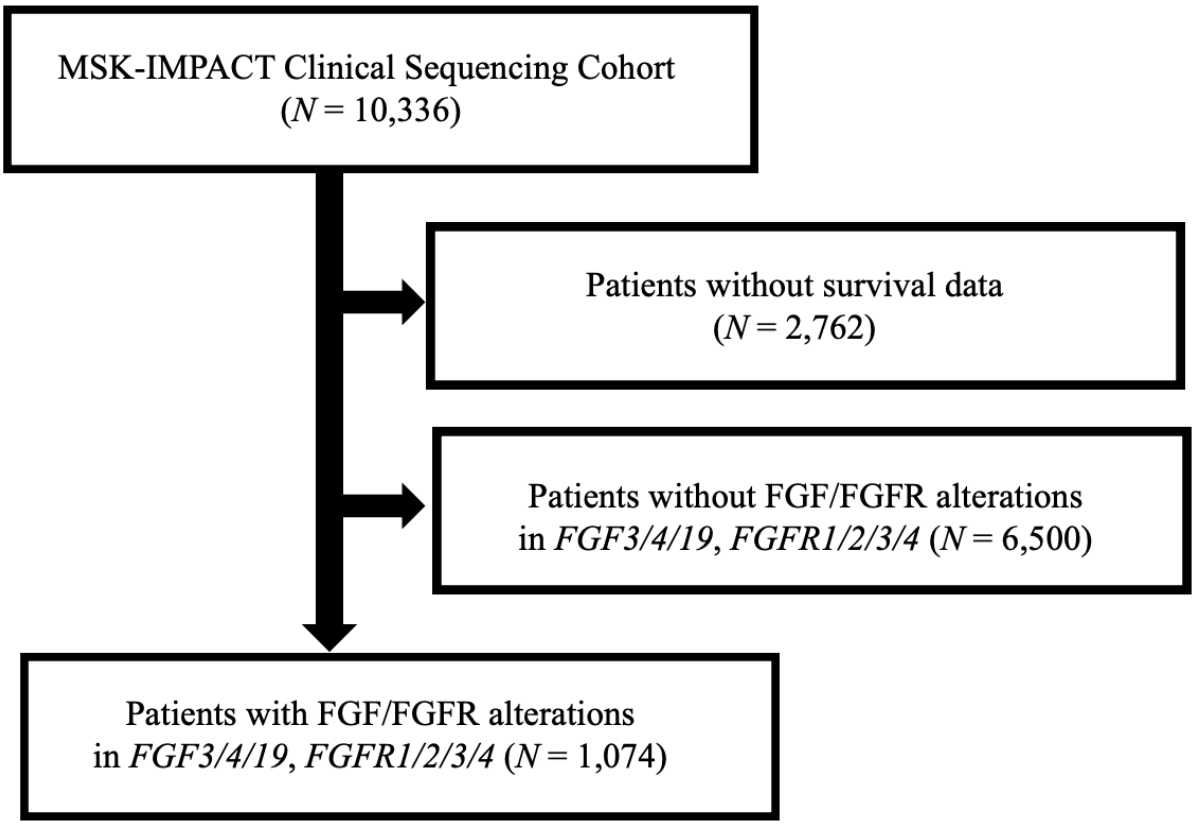
Supplementary Figure S1. STROBE diagram identifying eligible study patients from MSK-IMPACT Clinical Sequencing Cohort.



FGF6, *FGF23*, *FRS2* genes that were found in the UCSD cohort were not listed since they were not assessed in the MSK-IMPACT Clinical Sequencing Cohort.

Supplementary Figure S2. Patient flow of 858 cases discussed at UCSD Molecular Tumor Board (MTB).