

Molecular Analysis for Therapy Choice (MATCH)

MATCH Treatment Subprotocol V: Phase II Study of Sunitinib in Patients with Tumors with cKIT Mutations (Excluding GIST, Renal Cell Carcinoma or Pancreatic Neuroendocrine Tumor)

Fast Facts

Treatment: Sunitinib 50 mg po daily x 28 days with 2 weeks (14 days) rest until progression or unacceptable toxicity. *Drug is provided.*

Eligibility Criteria

1. Patients must fulfill all eligibility criteria outlined in Section 3.1 of MATCH Master Protocol.
2. Patients must have a somatic cKIT mutation in exon 9, 11, 13 or 14, excluding exon 17 or 18 mutations. See [Appendix II \(see below\)](#) for a list of inclusion and exclusion mutations, along with the corresponding Levels of Evidence (LOE).
3. Patient must have normal organ and marrow function as defined below:
 - Total bilirubin must be within normal institutional limits.
 - Creatinine must be within normal institutional limits. **OR** Creatinine clearance ≥ 60 mL/min/1.73 m² for patients with creatinine levels above institutional normal.
 - Serum Calcium must be ≤ 12.0 mg/dL.
4. Patients must have an electrocardiogram (ECG) within 8 weeks prior to treatment assignment and must have no clinically important abnormalities in rhythm, conduction or morphology of resting ECG (e.g. complete left bundle branch block, third degree heart block)
5. Patients must have an ECHO or a nuclear study (MUGA or First Pass) within 4 weeks prior to treatment assignment and must not have a left ventricular ejection fraction (LVEF) $<$ institutional lower limit of normal (LLN). If the LLN is not defined at a site, the LVEF must be $> 50\%$ for the patient to be eligible.
 - a. The following groups of patients are eligible provided they have New York Heart Association Class II cardiac function on baseline ECHO/nuclear study:
 - Patients with a history of Class II heart failure who are asymptomatic on treatment
 - Patients with prior anthracycline exposure
 - Patients who have received central thoracic radiation that included the heart in the radiotherapy port
6. Patients with any of the following conditions are excluded:
 - Serious or non-healing wound, ulcer, or bone fracture
 - History of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess within 28 days of treatment
 - Any history of cerebrovascular accident (CVA) or transient ischemic attack within 12 months prior to study entry
 - History of myocardial infarction, cardiac arrhythmia, stable/unstable angina, symptomatic congestive heart failure, or coronary/peripheral artery bypass graft or stenting within 12 months prior to study entry
 - History of pulmonary embolism within the past 12 months
7. Patients must not have known hypersensitivity or excess toxicity from sunitinib or compounds of similar chemical composition or biologic effect. This list includes, but is not limited to, patients with significant cardiac or hepatic toxicity from multikinase inhibitors with similar kinase inhibitory profiles (sorafenib, regorafenib, pazopanib). Questions regarding a significant intolerance to a prior therapy should be directed to the sub-protocol PI.

8. Patients must not have had prior therapy with sunitinib.
9. Patients must not have planned ongoing administration of STRONG and MODERATE CYP3A4 inhibitors or inducers. See Appendix V (and Appendix VI of the MATCH Master Protocol). The reference list of cytochrome p450 (CYP) isozymes and classification of strong, moderate, and weak interactions is available through the FDA website:
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionsLabeling/ucm093664.htm>
 - Strong CYP3A4 inhibitors are not permitted within 7 days before dosing and should be avoided throughout the study.
 - Strong CYP3A4 inducers are not permitted within 12 days before dosing and should be avoided throughout the study.
10. Patients must not have GIST, renal cell carcinoma, or pancreatic neuroendocrine tumor
11. Patients must not have a NCI CTCAE version 4 grade 3 hemorrhage within 4 weeks of starting study treatment
12. Patients must not have hypertension that cannot be controlled by medications (> 140/90 mmHg despite optimal medical therapy)
13. Patients must not have pre-existing thyroid abnormality with thyroid function that cannot be maintained in the normal range with medication
14. Participants may not have a major surgical procedure, open biopsy, or significant traumatic injury within 28 days prior to starting sunitinib.
15. Patients with known brain metastases should be excluded from this clinical trial because of their poor prognosis and because they often develop progressive neurologic dysfunction that would confound the evaluation of neurologic and other adverse events.
16. Patients who require therapeutic doses of coumarin derivative anticoagulants such as warfarin are excluded, although doses up to 2 mg daily are permitted for prophylaxis of thrombosis.

NOTE: Low molecular weight heparin is permitted provided that the patient's PT INR is < 1.5.

Gene Name	Variant ID	Variant Type	LOE Code	aMOI
KIT	COSM1326	Large Indel	2	p.S501_A502insAY
KIT	COSM27901	Large Indel	2	p.P551_V560delinsL
KIT	COSM1198	Large Indel	2	p.V555_V559del
KIT	COSM1230	Large Indel	2	p.W557_V560delinsF
KIT	COSM1234	Large Indel	2	p.K558_V560del
KIT	COSM1238	Large Indel	2	p.K558_N564del
KIT	COSM1235	Large Indel	2	p.K558_V559del
KIT	COSM1248	Large Indel	2	p.V559_V560del
KIT	COSM1262	Indel	2	p.V560_E561delinsG
KIT	COSM23560	Large Indel	2	p.N564_Y578del
KIT	COSM1281	Large Indel	2	p.V569_Q575del
KIT	COSM144983	Large Indel	2	p.T500_S501insSA
KIT	COSM219786	Large Indel	2	p.T500_S501insSA
KIT	COSM53306	Large Indel	2	p.S501_A502insAF
KIT	COSM1164	Large Indel	2	p.K550_V555delinsI
KIT	COSM1172	Large Indel	2	p.P559_E562del
KIT	COSM1169	Large Indel	2	p.P559_V563del
KIT	COSM1170	Large Indel	2	p.P551_Q556del
KIT	COSM1171	Indel	2	p.P551del
KIT	COSM1174	Large Indel	2	p.P551_V555delinsL
KIT	COSM1176	Indel	2	p.P551_M552delinsL
KIT	COSM36304	Large Indel	2	p.M560_D580del
KIT	COSM1177	Large Indel	2	p.M560_W565del

KIT	COSM96881	Large Indel	2	p.M560_Y561del
KIT	COSM1182	Large Indel	2	p.M552_K558del
KIT	COSM1180	Large Indel	2	p.M552_W557del
KIT	COSM18827	Large Indel	2	p.M552_V555del
KIT	COSM1179	Large Indel	2	p.M552_Y553del
KIT	COSM1181	Large Indel	2	p.M552_E554del
KIT	COSM1327	Large Indel	2	p.M552_Q556del
KIT	COSM96880	Large Indel	2	p.M552_E561delinsK
KIT	COSM36311	Large Indel	2	p.M552_E554delinsK
KIT	COSM96868	Large Indel	2	p.M552_Q556delinsK
KIT	COSM96863	Indel	2	p.M552_Y553delinsN
KIT	COSM133636	Large Indel	2	p.M552_W557delinsR
KIT	COSM1185	Large Indel	2	p.M552_V555delinsI
KIT	COSM1190	Large Indel	2	p.M552_W557del
KIT	COSM1187	Large Indel	2	p.M552_W557delinsK
KIT	COSM1189	Large Indel	2	p.M552_Q556delinsK
KIT	COSM1191	Large Indel	2	p.Y553_V559del
KIT	COSM22275	Large Indel	2	p.Y553_T574delinsS
KIT	COSM96947	Large Indel	2	p.E562_N572del
KIT	COSM36294	Large Indel	2	p.E554_D572del
KIT	COSM36310	Large Indel	2	p.E554_E562del
KIT	COSM36291	Large Indel	2	p.E554_I571del
KIT	COSM1194	Large Indel	2	p.E554_E561del
KIT	COSM1192	Large Indel	2	p.E554_K558del
KIT	COSM1203	Large Indel	2	p.E554_P573delinsG
KIT	COSM37027	Large Indel	2	p.E554_N564del
KIT	COSM1196	Large Indel	2	p.E554_I563delinsG
KIT	COSM1200	Large Indel	2	p.E554_I571delinsG
KIT	COSM1197	Large Indel	2	p.V555_Y570del
KIT	COSM1202	Large Indel	2	p.V555_V560del
KIT	COSM1199	Large Indel	2	p.V555_K558del
KIT	COSM1201	Large Indel	2	p.V555_Q556del
KIT	COSM96870	Large Indel	2	p.V555_N566delinsD
KIT	COSM1209	Large Indel	2	p.V555_T574delinsG
KIT	COSM36308	Large Indel	2	p.V555_P573delinsG
KIT	COSM1205	Large Indel	2	p.Q556_L576del
KIT	COSM36309	Large Indel	2	p.Q556_W557del
KIT	COSM1206	Large Indel	2	p.Q556_E561del
KIT	COSM1204	Large Indel	2	p.Q556_V560del
KIT	COSM36315	Large Indel	2	p.Q556_V559del
KIT	COSM23418	Large Indel	2	p.Q556_K558del
KIT	COSM1212	Large Indel	2	p.Q556_D572delinsH
KIT	COSM36312	Large Indel	2	p.W565_E570del
KIT	COSM1330	Large Indel	2	p.W565_E569del
KIT	COSM1210	Large Indel	2	p.W565_K566del
KIT	COSM133642	Indel	2	p.Q556_W557delinsR
KIT	COSM1365	Large Indel	2	p.Q556_I571delinsP
KIT	COSM1221	SNV	2	p.W557G
KIT	COSM1220	Indel	2	p.Q556_W557delinsP
KIT	COSM1213	Large Indel	2	p.Q556_V560delinsP
KIT	COSM133641	Large Indel	2	p.Q556_V559delinsP
KIT	COSM1214	Large Indel	2	p.Q556_V559delinsHT
KIT	COSM133639	Large Indel	2	p.W557_Q575del
KIT	COSM1223	Large Indel	2	p.W557_V560del
KIT	COSM1218	Large Indel	2	p.W557_V559del
KIT	COSM24748	Indel	2	p.W557_K558delinsE
KIT	COSM1229	Large Indel	2	p.W557_P573delinsS

KIT	COSM1226	Large Indel	2	p.W557_V559delinsF
KIT	COSM1239	Large Indel	2	p.W557_E562delinsL
KIT	COSM1232	Large Indel	2	p.W557_V560delinsF
KIT	COSM1233	Large Indel	2	p.W557_V559delinsF
KIT	COSM36303	Large Indel	2	p.K558_Q575del
KIT	COSM1236	Large Indel	2	p.K558_G565del
KIT	COSM1237	Large Indel	2	p.K558_D572del
KIT	COSM28991	Large Indel	2	p.K558_Y570delinsN
KIT	COSM1250	Large Indel	2	p.V567_E569del
KIT	COSM1240	Large Indel	2	p.K558_G565delinsR
KIT	COSM1241	Large Indel	2	p.K558_V560delinsI
KIT	COSM27069	Large Indel	2	p.K558_V560delinsN
KIT	COSM21976	Indel	2	p.K558delinsNP
KIT	COSM1244	Indel	2	p.K558_V559delinsN
KIT	COSM1245	Indel	2	p.K558delinsNP
KIT	COSM36300	Large Indel	2	p.V559_L576del
KIT	COSM1249	Large Indel	2	p.V559_G565del
KIT	COSM36301	Large Indel	2	p.V559_I571del
KIT	COSM1247	Indel	2	p.V559del
KIT	COSM1252	SNV	2	p.V559D
KIT	COSM36293	Large Indel	2	p.V568_L584del
KIT	COSM1257	SNV	2	p.V560D
KIT	COSM1260	SNV	2	p.V560G
KIT	COSM30545	Large Indel	2	p.V559_P573delinsA
KIT	COSM18897	Large Indel	2	p.V568_I571del
KIT	COSM133640	Large Indel	2	p.V560_I571del
KIT	COSM29442	Large Indel	2	p.I563_L576del
KIT	COSM1268	Large Indel	2	p.I563_D572del
KIT	COSM24839	Large Indel	2	p.I563_T574delinsK
KIT	COSM1270	Large Indel	2	p.N564_L576del
KIT	COSM1269	Large Indel	2	p.N564_P577del
KIT	COSM36299	Large Indel	2	p.N564_P573delinsT
KIT	COSM133635	Large Indel	2	p.Y568_L576delinsF
KIT	COSM1282	Large Indel	2	p.V569_D572del
KIT	COSM1285	Large Indel	2	p.Y578_L584del
KIT	COSM29016	Large Indel	2	p.I579_N595del
KIT	COSM29857	Large Indel	2	p.Y570_I571insIDPTQLPYDCHKWEFSPD
KIT	COSM41198	Large Indel	2	p.Y570_I571insIDPTQLPYDH
KIT	COSM133754	Large Indel	2	p.I571_L576del
KIT	COSM23417	Large Indel	2	p.Y570_I571insIDPTQLPYD
KIT	COSM308544	Large Indel	2	p.I571_D572insDPTQLPYD
KIT	COSM18751	Large Indel	2	p.I571_D572insDPTQLPYDCHKWEF
KIT	COSM30595	Large Indel	2	p.I571_D572insDPTQLPYDCHKWEFP
KIT	COSM34126	Large Indel	2	p.D572_P573insPTQLPYDH
KIT	COSM36322	Large Indel	2	p.D572_P573insPTQLPYDCHKWEFP
KIT	COSM18668	Large Indel	2	p.D572_P573insPTQLPYD
KIT	COSM33906	Large Indel	2	p.D572_P573insPTQLPYDCHKWEF
KIT	COSM1289	Indel	2	p.L576del
KIT	COSM1300	Large Indel	2	p.Q575_L576insLPYDCHKWEFP
KIT	COSM1298	Large Indel	2	p.Q575_L576insLPYDCHKWEF
KIT	COSM41632	Large Indel	2	p.L576_P577insPYDCHKWEF
KIT	COSM1290	SNV	2	p.L576P
KIT	COSM98379	Large Indel	2	p.L576_D579delinsP
KIT	COSM1296	Large Indel	2	p.L576_P577insPYDH
KIT	COSM1291	Large Indel	2	p.L576_Y578delinsP
KIT	COSM1684822	Indel	2	p.L576del
KIT	COSM18666	Large Indel	2	p.L576_P577insPYDH

KIT	COSM96866	Large Indel	2	p.P577_Y578insYDS
KIT	COSM28995	Large Indel	2	p.P577_Y578insYDH
KIT	COSM1294	Indel	2	p.D587del
KIT	COSM1295	Indel	2	p.H588del
KIT	COSM36323	Large Indel	2	p.F584_P585insIDPTQLPYDCHKWEFR
KIT	COSM1304	SNV	2	p.K642E
KIT	COSM12706	SNV	2	p.V654A
KIT	COSM12708	SNV	2	p.T670I

List of Exclusion Variants

Gene Name	Variant ID	Variant Type	LOE Code	aMOI
KIT	COSM1311	SNV	2	p.D816H
KIT	COSM1310	SNV	2	p.D816Y
KIT	COSM24675	SNV	2	p.D816A
KIT	COSM12711	SNV	3	p.D816G
KIT	COSM1314	SNV	2	p.D816V
KIT	COSM19285	SNV	3	p.D816E
KIT	COSM12710	SNV	2	p.D820Y
KIT	COSM133670	SNV	2	p.D820A
KIT	COSM1316	SNV	2	p.D820G
KIT	COSM12709	SNV	2	p.D820E
KIT	COSM19280	SNV	2	p.D820E
KIT	COSM1318	SNV	2	p.N822H
KIT	COSM1321	SNV	2	p.N822K
KIT	COSM1322	SNV	2	p.N822K
KIT	COSM18681	SNV	2	p.Y823D
KIT	COSM13172	SNV	2	p.A829P

Pre-Study Parameters:

1. History/Physical, Weight, Vitals, Performance Status
2. CBC/diff/platelets, CMP
3. Radiologic Evaluation
4. Pregnancy Test
5. Echocardiogram or Nuclear study
6. Urinalysis for proteinuria
7. Thyroid function tests