

	Drug	Strategy Target	Line	Pre-Clinical	Phase I	Phase II	Phase III	Approval	Available Off-Label	% US patients taking
A. Onco-protein Based										
1. Block KIT/PDGFRα protein										
	Imatinib	KIT/PDGFRα	1					2/1/2002		58% 10%
	Sunitinib	KIT/PDGFRα	2					1/26/2006		
	Nilotinib	KIT/PDGFRα	3				Ongoing		Tasigna	
	Nilotinib	KIT/PDGFRα	1			Recruiting			Tasigna	
	Sorafenib	KIT/PDGFRα	3			Recruiting			Nexavar	
	XL820	KIT/PDGFRα	3			Ongoing	STOP			
	Masitinib	KIT/PDGFRα	1			Ongoing				
	Dasatinib	KIT/PDGFRα	2			Recruiting			Sprycel	
	Dasatinib	KIT/PDGFRα	1			Recruiting			Sprycel	
	Vatalanib	KIT/PDGFRα	2			Completed				
2. Destroy mutant KIT/PDGFRα protein										
	IPI-504	HSP90	3				Recruiting			
	BIIB021	HSP90	3			Recruiting				
B. Oncogenic Signal Path Based										
3. Block KIT/PDGFRα downstream signal path										
	Everolimus + Imatinib	mTOR	3				Recruiting		Rapamune	
	Perifosine + Imatinib	AKT	2			Recruiting				
	Sorafenib	RAF	3			Recruiting			Nexavar	
	Dasatinib	SRC	2			Recruiting			Sprycel	
	Dasatinib	SRC	1			Recruiting			Sprycel	
4. Block Related GIST tumor signal paths										
	Oblimersen + Imatinib	Bcl-2	2			Ongoing				
	R1507	IGF-1R								
C. Tumor cell based										
5. Unblock GIST cell death genes										
	Romidepsin	HDAC	2			Ongoing				
	Vorinostat	HDAC							Zolinza	
	LBH589	HDAC								
6. Freeze the GIST cell division cycle										
	Alvocidib + Doxorubicin	CDK	2		Recruiting					
7. Stimulate the immune system to destroy GIST cells										
	Interleukin	NK Cells	1		Recruiting				Proleukin	
	Pegylated interferon Alpha 2B + Imatinib	TH1-T helper cells	1			Ongoing			PEG-Intron	
	Mixed bacteria vaccine	NY-ESO-1 Antigen	3		Recruiting					
D. Tumor based										
8. Inhibit GIST tumor blood vessel growth factors										
	Bevacizumab + Imatinib	VEGFR	1				Recruiting		Avastin	
	Cediranib	VEGFR	2			Ongoing				
9. Use radiation to reduce tumor size										
	3D and IMRT radiation		3		Recruiting					

Notes:

This chart is an attempt to show the current state of drugs approved or in trial for GIST. It combines specific trials with overall strategies, drug targets and trial status to give both an overview of the fight against GIST and to provide prospective trial participants with information about trial options

The rows are the major trials that have been conducted specifically for GIST in an effort to get drug approval. Adjuvant/neoadjuvant and registration trials are not listed here. Trials leading up to the current trial phase are not listed.

The first and second columns describe the strategy class and category:

A. Oncogenic Protein based strategies involve blocking the mutant protein (KIT/PDGFR) by attaching a therapy drug (imatinib, sunitinib...) to the active binding point of the protein. Resistance to these therapies can arise when additional KIT or PDGFR mutations change the shape of KIT and prevent binding. HSP90 targeted strategies enable the cells own enzymes to recognize and destroy mutant proteins including KIT and PDGFR.

B. Oncogenic signal path based strategies go one step further and attempt to block the signal path at the head of which is mutant KIT or PDGFR. Since there are multiple proteins in these paths there are multiple downstream target. These strategies can circumvent resistance that depends on additional KIT or PDGFR mutations.

C. Tumor cell based strategies target cancer factors that interfere with normal cell process or prevent the immune system from attacking cancer cells. In cancer cells many processes are disrupted. One is the normal process of cell death. Genes that would normally initiate cell death are blocked and inoperative. HDAC targeted strategies intend to unblock these transcription factors. Immune system based strategies stimulate the body's natural immune system to recognize and attack GIST cancer cells.

D. Tumor based strategies are intended to block infrastructure factors that contribute to tumor growth or to combine traditional chemotherapy or radiation and with newer tyrosine kinase based therapies to achieve synergistic tumor size reduction. VEGFR based strategies block the factors contributing to blood vessel growth in new tumors.

The **Drug** column provides the generic name of the primary drug being tested in the trial.

The **Strategy Target** column indicates the most appropriate target for this strategy. Some trials are listed twice since the drugs in trial have multiple targets bridging more than one strategy.

The **Line** column indicates is what line (first, second or third) the drug is being tested. Patients with no prior treatment history beyond surgery would be first line. Patients resistant to Imatinib would be second line. Patients resistant to both Imatinib and Sunitinib would be third line.

Pre-Clinical refers research activity leading up to the first use in humans.

The trial status indicators hyperlink to the clinicaltrial.gov listing for the trial. '**Ongoing**' indicates that the trial is still collecting data but no longer recruiting. '**Completed**' trials are no longer recruiting or collecting data. The arrow head indicate plans to move to the next trial phase

The last column contains the brand name of generic drug that is approved for other indications. These drugs are in trial for GIST and are also available off-label by prescription. The names are hyperlinked to the Prescribing Information.