

Table S1: Comparison of inhibitory activity between reversible and irreversible inhibitors

Inhibitors	Synonymous	IC <sub>50</sub> (nM)	Clinical stage*	Disease	References
Irreversible inhibitors (Average IC <sub>50</sub> ≈1.28 nM)					
Ibrutinib	PCL-32765	0.5	Stage IV/Stage III	B-cell Lymphoma; Chronic Lymphocytic Leukemia, et al.	[1]
Acalabrutinib	ACP-196	3	Stage III/Stage II	Chronic Lymphocytic Leukemia; Diffuse Large B Cell Lymphoma; COVID-19; et al.	[2]
Zanubrutinib	BGB-3111		Stage III/Stage II	Chronic Lymphocytic Leukemia; B-cell Malignancies; et al.	[3]
Orelabrutinib	ICP-022		Stage II	Mantle Cell Lymphoma; Primary Central Nervous System Lymphoma; et al.	[4]
Tolebrutinib	SAR442168	0.7	Stage II	Primary Progressive Multiple Sclerosis; Relapsing Multiple Sclerosis; et al.	[5]
Spebrutinib	CC-292	0.5	Stage I	Rheumatoid Arthritis; Leukemia Lymphocytic Chronic B-cell; et al.	[6]
CGL-1746		1.9	Candidate drug	B cell-dependent Arthritis	[7]
Poseltinib		1.95	Stage I	Rheumatoid Arthritis; Healthy	[8]
Branebrutinib	BMS-986195	0.1	Stage I	Autoimmune Disorder; Rheumatoid Arthritis; Dermatitis; Atopic	[9]
LFM-A13		2.5	Candidate drug	mouse model of breast cancer	[10]
CNX-774		<1	Candidate drug	Ramos cells; fresh human and rat whole blood	[11]
Elsabrutinib	ABBV-105	0.18	Stage II	Systemic Lupus Erythematosus; Rheumatoid Arthritis	[12]
TL-895		1.5	Clinical	Acute Myeloid Leukemia; COVID-19; Cancer research	[13]
BTK inhibitor 13		1.2	Candidate drug		[14]
BTK-IN-8		0.22	Candidate drug		[15]
BTK inhibitor 19		2.7	Candidate drug		[16]
Reversible inhibitors (Average IC <sub>50</sub> ≈7.17 nM)					
ARQ531		0.85	Clinical	Arthritis	[17]
Fenbrutinib	GDC-0853	0.91(Ki)*	Stage III/Stage II	Relapsing Multiple Sclerosis; Urticaria; Systemic Lupus Erythematosus	[18]
Pirtobrutinib	LOXO-305	3.68	Stage III/Stage II	Chronic Lymphocytic Leukemia; Small Lymphocytic Lymphoma	[19]
BIIB091			Clinical	Autoimmune diseases	[20]
Tirabrutinib	ONO-4059	2.2	Stage II/Stage I	Chronic Spontaneous Urticaria; Sjogren's Syndrome; Relapsed or Refractory	[21]
Rilzabrutinib	PRN1008	1.3	Stage III/Stage II	Pemphigus; Immune Thrombocytopenia; Warm Autoimmune Hemolytic Anemia	[22]
BIIB068		1	Stage I	Systemic Lupus Erythematosus	[23]
RN486		4	Clinical	Rheumatoid Arthritis; Systemic Lupus Erythematosus	[24]
GDC-0834		5.9	Clinical	Arthritis	[25]
PCL29732		8.2 (Ki)	Clinical	Autoimmune disease; B-cell Malignancy	[26]
BMS-986142		0.5	Stage II/Stage I	Autoimmune diseases	[27]
BMS-935177		3	Clinical	Rheumatoid Arthritis	[28]
N-piperidine ibrutinib hydrochloride		51	Candidate drug		[29]
XMU-MP-3		10.7	Clinical	B-cell Malignancies	[30]

Notes: \*Ki, inhibition constant. Ki value is equivalent to IC<sub>50</sub> value to some extent, but it does not change with the change of experimental conditions. \*Clinical stage, two clinical stages are the stages in different diseases listed in disease lines

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