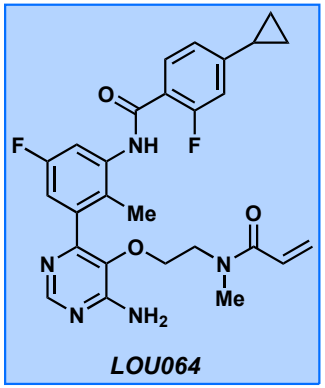
Sarlah Group

DOTW: LOU064 (Remibrutinib)

Background:



LOU064

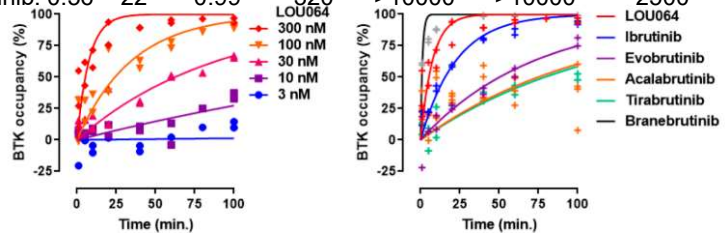
- LOU064 is a reversible, covalent Bruton's Tyrosine Kinase (BTK) inhibitor.
- BTK is a hot target for autoimmune disorders as it is a key kinase for the signalling of a variety of immune responses
- Unlike many BTK inhibitors, LOU064 demonstrates high selectivity for BTK.
- Undergoing Phase II clinical trials for chronic spontaneous urticaria and Sjoegren's syndrome
- Key residue target: Cys481
- BTK IC_{50}: 7.3μM
- For another BTK inhibitor, see *Imbrutnib*, DOTW

NOVARTIS

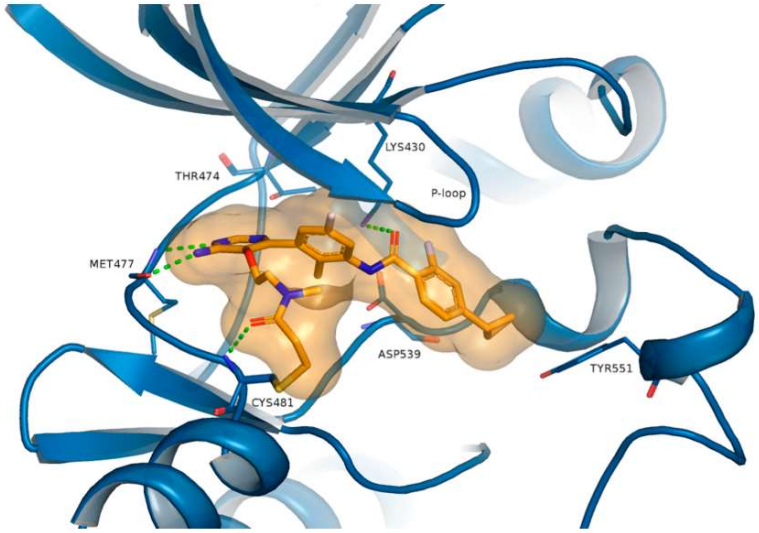
J. Med. Chem. **2020** ASAP; https://doi.org/10.1021/acs.jmedchem.9b01916
See also: *J. Med. Chem.* **2019**, *10*, 1467-72.

Specificity and binding evidence (K_d):

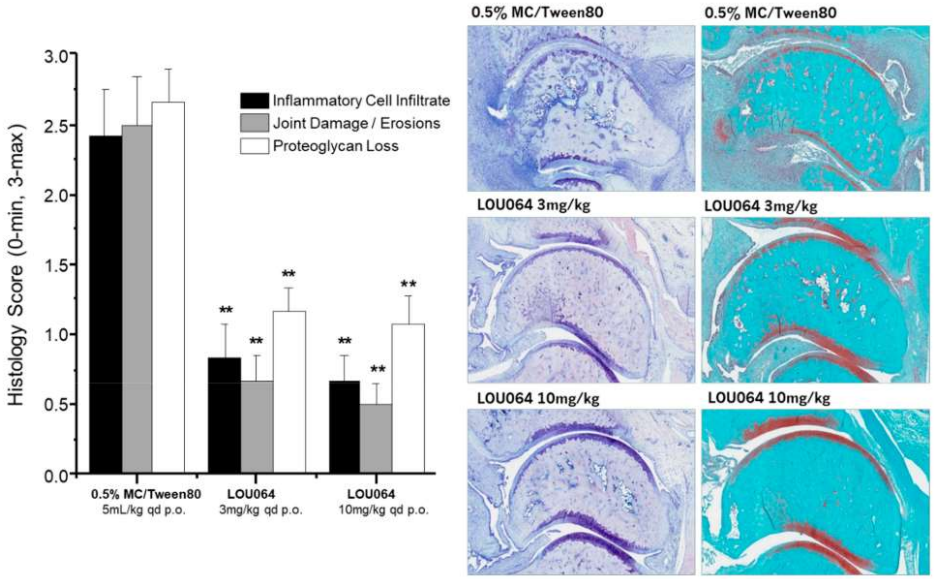
	BTK	BMX	TEC	ITK	EGFFR	ERBB2	ERBB4	JAK3
LOU064:	0.63	540	110	>10000	>10000	>10000	>10000	>10000
ibrutinib:	1.9	1.6	1.7	57	6.9	1.2	2.4	37
acalabrutinib:	21	610	14	>10000	5600	7.4	140	>10000
tirabrutinib:	14	47	6.2	>10000	>10000	610	>10000	>10000
evobrutinib:	16	31	4.5	3700	7100	>10000	5600	>10000
branebrutinib:	0.56	22	0.99	320	>10000	>10000	2500	1300



Binding Site:

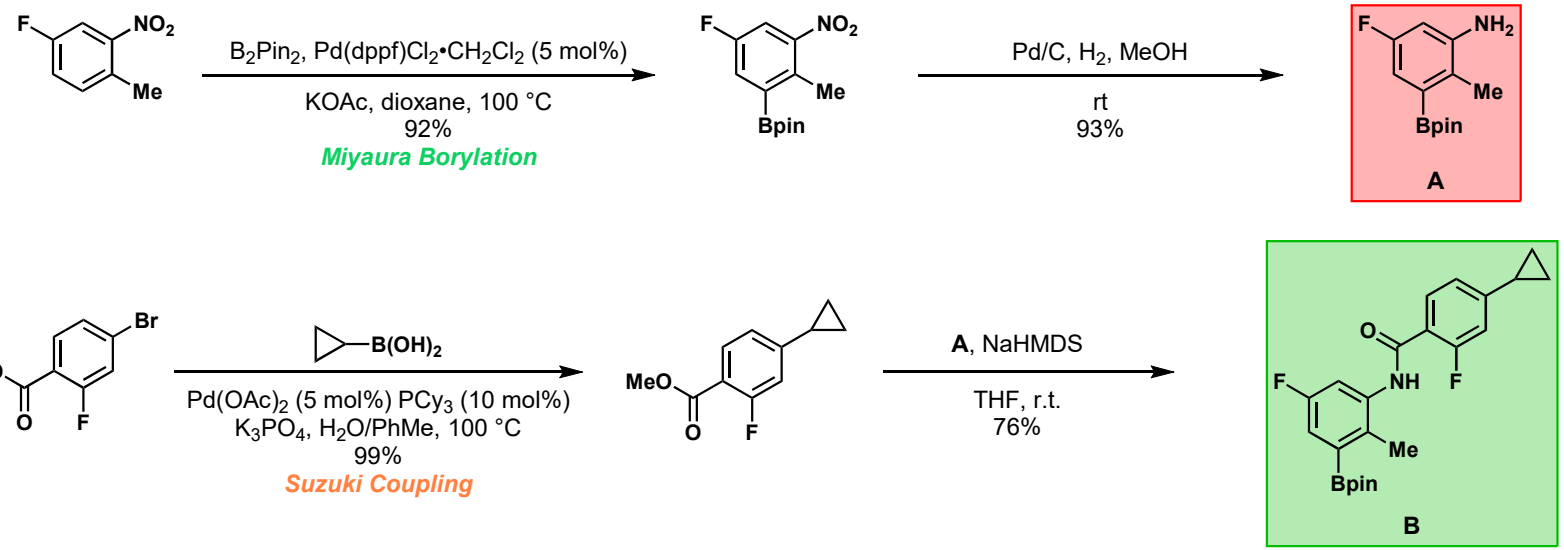


Response to collagen-induced arthritis:



DOTW: LOU064 (Remibrutinib)

Discovery Route--Fragment A and B



Discovery Route: LOU064