

CSF1R inhibition for advanced cancers

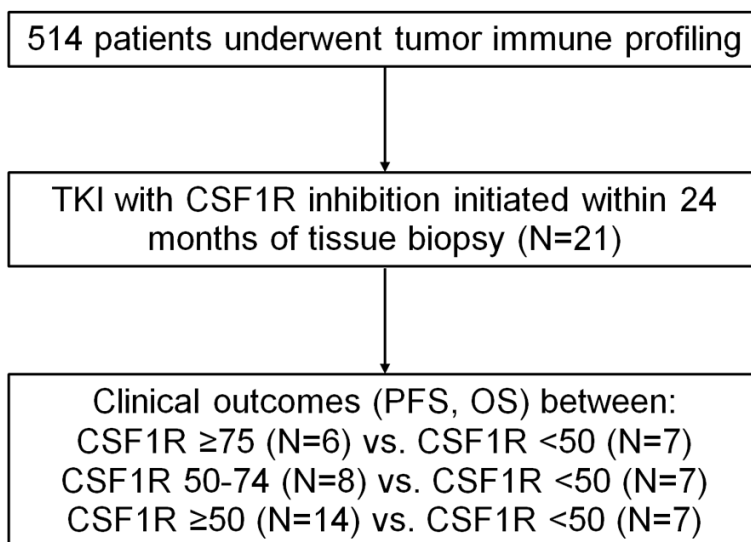


Figure S1. Consort diagram of the study. 514 patients underwent immune profiling with Omiseq assay. Twenty-one patients were initiated on tyrosine kinase inhibitors (TKI) with CSF1R inhibitor activity. Clinical outcomes of progression-free survival (PFS) and overall survival (OS) were assessed based on CSF1R RNA expression rank, using cutoffs of 50 and 75 percentile rank.

Table S1. CSF1R half-maximal inhibitory concentrations (IC50) of tyrosine kinase inhibitors with CSF1R inhibition administered to patients during the study

CSF1R inhibitor	IC50 for CSF1R	References
Pazopanib (GW786034)	146 nM	https://www.selleckchem.com/products/pazopanib.html
Regorafenib (BAY73-4506)	Kd 10 nM	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/203085Orig1s007.pdf
Sorafenib (BAY43-9006)	107 nM/L enzyme assay	Guo J, Marcotte PA, McCall JO, Dai Y, Pease LJ, Michaelides MR, Davidsen SK, Glaser KB. Inhibition of phosphorylation of the colony-stimulating factor-1 receptor (c-Fms) tyrosine kinase in transfected cells by ABT-869 and other tyrosine kinase inhibitors. <i>Mol Cancer Ther.</i> 2006 Apr;5(4):1007-13.
Sunitinib (SU11248)	20 nM/L cellular assay 7 nM/L enzyme assay	https://mct.aacrjournals.org/content/5/4/1007.long Guo J, Marcotte PA, McCall JO, Dai Y, Pease LJ, Michaelides MR, Davidsen SK, Glaser KB. Inhibition of phosphorylation of the colony-stimulating factor-1 receptor (c-Fms) tyrosine kinase in transfected cells by ABT-869 and other tyrosine kinase inhibitors. <i>Mol Cancer Ther.</i> 2006 Apr;5(4):1007-13.
Crizotinib (PF-02341066)	61 nM/L cellular assay Kd 6.68 ¹	https://mct.aacrjournals.org/content/5/4/1007.long http://ruben.ucsd.edu/dnet/tar_html/CSF1R.html
Entrectinib (RXDX-101)	Ki 7.40 ²	http://ruben.ucsd.edu/dnet/tar_html/CSF1R.html
Pexidartinib	17 nM	Benner B, Good L, Quiroga D, Schultz TE, Kassem M, Carson WE, Cherian MA, Sardesai S, Wesolowski R. Pexidartinib, a novel small molecule CSF-1R inhibitor in use for tenosynovial giant cell tumor: a systematic review of pre-clinical and clinical development. <i>Drug Des Devel Ther.</i> 2020 May 4;14:1693-1704. (Note: not used during study since it was not yet available)

¹Kd denotes dissociation constant. ²Ki denotes inhibition constant. Ki refers to inhibition constant, while Kd means dissociation constant. Both terms are used to describe the binding affinity that a small molecule or macromolecule has for an enzyme or receptor. IC50 stands for inhibitory concentration 50%. That is, the concentration of inhibitor required to reduce the biological activity of interest to half of the uninhibited value. Because it does not directly measure a binding equilibrium, IC50 is less precise than Ki or Kd.