PF-04136309 CCR2 Inhibitor

PF-04136309 (PF-6309) is an investigational small-molecule antagonist of the human chemokine (C-C motif) receptor 2 (CCR2) – a type of receptor that binds to cytokines (proteins that are involved in cell signaling).\(^1,2\)

**PF-6309 Mechanism of Action**

CCL2 is a chemoattractant that is released by tumor cells and binds to CCR2, which is expressed on the surface of monocytes (types of white blood cells) in the bone marrow. CCL2 is thought to play a role in the recruitment of monocytes from the bone marrow to the tumors, where these cells then become tumor associated macrophages (TAM). They in turn, have been observed to limit the effectiveness of anti-tumor immune responses, leading to tumor progression and chemoresistance.\(^3\)

**PF-6309** binds to CCR2 and has been observed to inhibit the binding of CCL2 to its receptor CCR2. The inhibition of CCR2 is thought to stop the recruitment of monocytes and reverse immune suppression within the tumor microenvironment.\(^3,4,5\)

**The Potential of CCR2 Inhibition**

Studies suggest that inhibition of CCR2 may have application in a variety of diseases, including cancer. Pre-clinical studies of PF-6309 show anti-tumor activity in localized pancreatic cancer. PF-6309 has also been evaluated in an investigator initiated Phase 1b dose escalation study in pancreatic cancer. More research is needed to fully understand the potential of CCR2 inhibition in cancer and identify potential immunotherapy combinations.

**Clinical Study**

PF-6309 is currently being studied in a Phase 1b/2 trial (dose escalation study followed by randomized Phase 2) for pancreatic cancer (NCT02732938).\(^6\)

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PF-6309 is an investigational compound.