CD33/IgG Chimeric Ligand Trap for Treating Myelodysplastic Syndromes (MDS)

Our technology is a chimeric antibody linking the extracellular binding domain of CD33 with an immunoglobulin (Ig) heavy chain region of human IgG1 that binds to circulating S100A9 protein. This biologic agent is for the treatment of hematologic malignancies such as MDS, with potential application to inflammatory diseases & enhancement of anti-cancer immune responses. Currently there are no therapies targeting the key pathogenetic drivers in MDS. Our biologic agent represents a first in class, novel strategy targeting a key soluble effector of the disease. This biologic agent would act similarly to Avastin or Zaltrap to neutralize the ligand in the cancer microenvironment to improve hematopoiesis.

COMMERCIAL OPPORTUNITY

- According to combined Surveillance, Epidemiology and End Results (SEER) and Medicare claims data, approximately 40-50,000 or more MDS patients are diagnosed annually in the USA, with an overall prevalence that exceeds this several fold. MDS is a stem cell malignancy that laregly afflicts individuals >60 years of age and often progresses to acute myeloid leukemia (AML).
- Aside from bone marrow transplants for severe cases, 5-azacytidine, decitabine, and lenalidomide are the three therapeutics currently approved to treat MDS, delay its progression to AML, and prolong patient survival. Annualized US sales of Celgene's 5-azacytidine (Vidaza) continue to increase (>$840M in 2013).
- MDS patients sometimes take Vidaza for up to 6 months ($9200/month) before noticing benefit. They will remain on therapy as long as their disease does not progress and side effects are tolerable. Median progression-free survival with Vidaza treatment has been reported to be close to 2 years, demonstrating the significant long-term use of therapies for MDS.
- Biologic therapeutics such as ours offer advantages over the present small molecule therapeutics because of their highly selective nature & generally high potency against key pathogenetic targets, which could result in fewer or less severe side effects & greater impact on disease.
- Our biologic is conceptually similar to the FDA approved anti-cancer therapy, Avastin, which binds to circulating Vascular Endothelial Growth Factor (VEGF) and makes it incapable of binding its cellular receptor to initiate blood vessel growth. Inhibiting new blood vessel formation starves tumors and slows their growth. Avastin has generated over $5B in global sales in 2013 as of the end of Q3.

TECHNOLOGY

Our biologic agent binds & sequesters endogenous S100A9, an inflammatory signaling molecule profoundly up-regulated in MDS. Myeloid derived suppressor cells (MDSC), which accumulate in tumor bearing cancer patients, are site specific inflammatory and T cell specific immunosuppressive effector cells that contribute to cancer progression. MDSC expansion is driven by the binding of the pro-inflammatory molecule S100A9 with its cognate receptors, TLR4 & CD33. In MDS, MDSC directly suppress hematopoiesis & S100A9 triggers apoptosis in hematopoietic progenitors. Our inhibitor is a chimeric protein with the ectodomain of CD33 that binds to S100A9 coupled to an Ig heavy chain constant region of human IgG to insure extended *in vivo* circulation. This agent neutralizes S100A9 thereby interrupting receptor engagement and alleviating ineffective hematopoiesis. Unlike a TLR4 signal antagonist, the CD33/IgG ligand trap neutralizes this key effector at its most proximal point, thereby abrogating engagement of both cognate receptors, while preserving response to bacterial endotoxin.

PATENT

Application filed on 7/5/2013 for Drs. Alan List and Sheng Wei

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LICENSING OPPORTUNITY

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