THE THERAPEUTIC POTENTIAL OF AMV564, A NOVEL BISPECIFIC BIVALENT (2×2) T-CELL ENGAGER, FOR THE TREATMENT OF CD33 EXPRESSED PATIENTS

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ABSTRACT

AMV564 is a novel bispecific (2×2) MoAb that simultaneously targets CD123 and CD33, both early markers of hematologic malignancies, as well as CD3 and CD8, to potently and selectively engage T cells. In vivo efficacy and ADCC activity directed against CD33-expressing leukemic blasts were demonstrated in a murine xenograft model. In vitro ADCC activity using PBMCs from CD33+ acute myeloid leukemia (AML) patients was demonstrated.

CD33 (Signal 1) is a cellularly-ubiquitous antigen that is broadly expressed on the surface of malignantly transformed cells in both hematologic and solid malignancies, as well as on cells that potentially support tumor growth. T-cell engraftment, as well as peptide-specific effector cells (T-PSECs), such as myeloid derived suppressor cells (MDSCs), promote in vivo efficacy.

AMV564 has been shown to eliminate MDSCs and restore hematopoiesis, reduce patient cytokine levels of patients in acute leukemia and multiple myeloma, and produce robust antitumor activity in preclinical studies.

In vivo studies, including cytokinetic assay with MoAb patient samples, human T-cell activation assays, and cytokine release assays, as well as animal toxicity studies, were performed to characterize the antitumor activity of AMV564 in non-human primates (NHP). AMV564 demonstrated potent in vitro antitumor activity and serum half-lives of approximately 6 - 7 days in NHP studies. In animals, a bi-antigenic bispecific antibody was used to target CD123 and CD33, and in vitro studies demonstrated that bi-specifics are more potent than T-cell engagers against CD33-AML than a simpler bi-antigenic monoclonal antibody (mAb) of the same 1:1 ratio.

In animal safety studies, AMV564 was tolerated at exposures that were up to five times higher than the human exposure. 55% of animals treated with AMV564 showed marked splenic enlargement. 20.5% of animal’s animal had severe splenic and large lymph node enlargement. These findings are consistent with splenic enlargement and increased monocyte counts with rapid erythropoiesis.

Results from a pharmacokinetic/pharmacodynamic (PK/PD) model integrating the preclinical data support the potential for a wide therapeutic index for patients with AML.

CONCLUSION

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REFERENCES

Based on the in vitro experiments and in vivo preclinical data, AMV564 is expected to be used to generate a complete therapeutic index, within antitumor activity in AML and MDSC as dose down-scaling, the therapeutic window, and the ability to eliminate tumor cells by recruitment of cytotoxic T cells.