Effects of IL-21, KIR Blockade, and CD137 Agonism on the Non-Clinical Activity of Elotuzumab

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Introduction
1. Elotuzumab is a humanized IgG1κ monoclonal antibody against Signaling Lymphocytic Activation Molecule (SLAMF7, also known as CD137L). Elotuzumab is currently in development.
2. Elotuzumab has demonstrated clinical activity in relapsed/refractory multiple myeloma (MM).
3. A Phase I study of elotuzumab in combination with lirilumab (anti-CD137) showed promising results.

Methods
1. Anti-CD137 studies: female severe combined immunodeficient (SCID) mice were used.
2. Anti-KIR studies: NOD.CB17-Prkdcscid mice were used.
3. CD137 expression was increased by IL-21, when compared with cells incubated with the respective antibodies.
4. Tumor growth was measured by Fowler Electronic Digital Caliper.

Results
1. IL-21 does not enhance elotuzumab activity in vivo. However, when elotuzumab was combined with lirilumab (anti-CD137), elotuzumab mediated cell-killing in vitro and synergized with lirilumab to mediate potent anti-tumor activity in a xenograft tumor model.
2. CD25% and CD54% were increased by IL-21 when compared with cells incubated with the respective antibodies.

Discussion
1. Elotuzumab mediated cell-killing in vitro and synergized with lirilumab to mediate potent anti-tumor activity in a xenograft tumor model.

Conclusions
1. IL-21 increased elotuzumab-mediated cell-killing in vitro and in vivo, but antagonized inhibitory KIR expressing NK cells.
2. CD137 agonism normally increased elotuzumab-mediated cell-killing in vitro and in vivo, but antagonized inhibitory KIR expressing NK cells.
3. Elotuzumab normal NK cell function and enhanced ADCC.
4. Blockade of platelet activating factor receptor (PAFR) in PBMC increased CD54 expression.

References

Acknowledgments
The authors acknowledge the contribution of all members of the Elotuzumab development team at Bristol-Myers Squibb and Innate Pharma.

Disclosures
The authors declare no conflicts of interest.