THERE’S A NATURAL KILLER INSIDE EVERYONE WITH THE POTENTIAL TO TAKE ON MULTIPLE MYELOMA
Natural Killer Cells, part of the body’s first line of defense against cancer, are initially capable of recognizing and eliminating myeloma cells while sparing normal cells. However, as a consequence of multiple myeloma, immune function declines significantly over time and mechanisms of immune evasion and immunosuppression impair Natural Killer Cell activity.

Directly enhancing Natural Killer Cell activity is a fundamentally different approach under investigation for multiple myeloma. SLAMF7, along with KIR and CD137, are among cell surface proteins that have been implicated in regulating Natural Killer Cell activity.

SLAMF7, or Signaling Lymphocytic Activation Molecule Family member 7, is a cell surface protein that is highly expressed on the surface of myeloma cells across disease stages and cytogenetic subtypes. SLAMF7 is also expressed on Natural Killer Cells, plasma cells, and other immune cells.

KIRs, or Killer Cell Immunoglobulin-like Receptors, are expressed on the surface of various immune cells, including Natural Killer Cells, and are key regulators of their activation. Myeloma cells are able to evade Natural Killer Cell-mediated recognition and cytotoxicity by upregulating the ligand for inhibitory KIRs.

CD137 is a cell surface protein that can be upregulated on the surface of Natural Killer Cells, T cells and other immune cells, and its ligand is highly expressed on myeloma cells.

**RETHINKING ENDPOINTS:**
**COMPREHENSIVE MEASURES TO ASSESS ADVANCES IN RESEARCH**

Overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) are clinical endpoints used to evaluate advances in research in multiple myeloma.

Multiple measures of PFS and OS can be visualized using a Kaplan-Meier survival curve, including hazard ratio/relative risk reduction, median duration, and time point analyses, and each provides a unique perspective on differences in the investigational arm relative to the control arm.

Measure of PFS/OS Across the Entirety of the Study Duration:
- **HAZARD RATIO/RELATIVE RISK REDUCTION** measures the magnitude of the difference between the two curves of a Kaplan-Meier plot.

Measure of PFS/OS at a Specific Point in Time:
- **MEDIAN DURATION** is the time at which 50% of patients have either progressed or died.
- **TIME POINT ANALYSES** estimate the presence or absence of sustained benefit at time points of interest (e.g., 24 months).

Measure of Response:
- **OBJECTIVE RESPONSE RATE** is based mainly on M protein levels in serum and urine, percentage of plasma cells in bone marrow, and changes in bone lesions and soft tissue plasmacytomas. Measures of ORR are evolving as continued advances necessitate the ability to detect residual disease.

*A log-rank test is conducted to determine statistical significance between arms (represented by a P-value).*
Immuno-oncology is a fundamentally different modality under investigation for multiple myeloma and Bristol-Myers Squibb is researching the potential of the SLAMF7, KIR, and CD137 pathways to activate the body’s own Natural Killer Cells to target myeloma cells.

Rethink Multiple Myeloma

Bristol-Myers Squibb is deeply committed to furthering the science behind immuno-oncology by rethinking research and emphasizing the importance of a comprehensive approach to endpoint evaluation in multiple myeloma.

www.RethinkMultipleMyeloma.com