OP201: A Phase 1/2 Study of Melflufen and Dexamethasone in Patients With Immunoglobulin Light Chain Amyloidosis

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BACKGROUND
- Immunoglobulin light chain (AL) amyloidosis is a rare, life-threatening disease arising from a neoplasia of plasma cells resulting in excessive production of monoclonal light chains (FLC)s that are misfolded, aggregate, and form toxic deposits in vital organs, including the heart, kidneys, and liver.
- The primary goal of AL amyloidosis therapy is to reduce or eliminate the amyloidogenic light chains, halt the progression of organ damage, and improve function.
- Measures that can improve AL amyloidosis hematologic response may improve organ response and survival.
- Treatments used in other plasma cell disorders such as multiple myeloma (MM) are commonly used to treat AL amyloidosis, including autologous stem cell transplantation (ASCT).
- However, there are no approved therapies for AL amyloidosis, and effective treatment, especially for patients with advanced cardiac involvement, remains a high unmet medical need.

METHODOLOGY
- Melflufen is a novel peptide-drug conjugate that rapidly delivers a cytotoxic payload into tumor cells (Figure 1).
- Phases 1 and 2 of the study are open-label, dose escalation trials.
- Phase 1 (dose escalation) will be conducted in 3+3 design, with 3–6 patients evaluable for dose-limiting toxicity (DLT) at each melflufen dose level. The recommended phase 2 dose (RP2D) will be determined in phase 1.
- Phase 2 (dose expansion) will include 26 patients (20 from phase 2 and 6 from phase 1) treated at the RP2D.
- Proportion of patients with hematologic CR, VGPR, and PR (phase 1)
- Determination of DLT or a lower dose at the discretion of the data safety monitoring committee

PRIMARY OBJECTIVES
- Phase 1: The primary objective of phase 1 is to explore the safety and tolerability of treatment with melflufen and to identify the recommended phase 2 dose (RP2D).
- Phase 2: The primary objective of phase 2 is to evaluate the hematologic ORR after 4 cycles at the RP2D determined in phase 1.

PRIMARY ENDPOINTS
- Phase 1: The primary endpoint of phase 1 is the proportion of patients who achieve a hematologic complete response (CR), very good PR (VGPR), or PR.
- Phase 2: The primary endpoint of phase 2 is the proportion of patients who achieve a hematologic complete response (CR), very good PR (VGPR), or PR.

REFERENCES

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