In Vitro and In Vivo Activity of Melflufen in Amyloidosis

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**Background**

- **In vivo studies:** Light chain (LC) amyloidosis is a severe disease triggered by overproduction of monoclonal LCs. Melflufen (melphalan flufenamide ethyl ester) is a peptide-drug conjugate with potent antifolate and direct cytoskeletal disrupting effects. Melflufen showed promising efficacy in patients with AA amyloidosis.
- **Cellular toxinology and apoptosis:** Melflufen demonstrated superior efficacy in amyloidosis and bone marrow plasma cell toxicity compared to melphalan.
- **Ex vivo analysis:** Amyloidogenic populations of plasma cells, including the heart and kidneys, caused organ dysfunction in a model of AA amyloidosis.

**Methods**

- **Patient derivation:** MM.1S, RPMI-8226, and ALMC-1 cell lines were derived from amyloidosis patients and will be used to analyze the effects of melflufen on amyloidogenic populations of cells.
- **In vitro assay:** The human myeloma cell line, MM.1S, and patient-derived light chain secreting ALMC-1 and ALMC-2 were treated with melflufen in vitro.
- **In vivo study:** Single cell sequencing on transplanted mouse models will be used to analyze the effects of melflufen on amyloidogenic populations of cells.

**Results**

- **Ex vivo assay:** Melflufen demonstrated superior efficacy to melphalan in inhibiting plasma cell toxicity in vivo.
- **In vivo study:** Melflufen demonstrated significant efficacy in reducing amyloidogenic populations of cells, including the heart and kidneys, causing organ dysfunction in a model of AA amyloidosis.

**Conclusions**

- **In vivo study:** Melflufen demonstrated superior efficacy in inhibiting plasma cell toxicity compared to melphalan with increased plasma cell death and decreased secretion of light chains.
- **Ex vivo assay:** Melflufen demonstrated superior efficacy in inhibiting plasma cell toxicity compared to melphalan with increased plasma cell death and decreased secretion of light chains.

**Disclosures**

- **Oncopeptides:** Employment.
- **Orion Pharma:** Employment.
- **Celgene:** Employment.
- **Varney:** Employment.
- **Lehmann:** Employment.
- **Varney:** Consultancy.
- **Lehmann:** Consultancy.
- **None:**

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**Presented at the 61st Annual Meeting of the American Society of Hematology (ASH), December 7-10, 2019, Orlando, FL, USA.**