

Clinical validation of experimental radioimmunoinaging of human AL amyloid deposits

¹Jonathan Wall, ¹Steve Kennel, ¹Tina Richey, Alan Stuckey, ¹Sallie Macy, ¹David Townsend, ^{2,3}Bjoern Jakoby, ⁴Karen Wells, ⁴Gary Smith, and ¹Alan Solomon

¹Department of Medicine and ⁴Department of Radiology, University of Tennessee Graduate School of Medicine, Knoxville, TN. ²Siemens Medical Solutions, Knoxville, TN, ³The University of Surrey, Guildford, UK.

Amyloidosis is a protein-folding disorder characterized by the aggregation and deposition of proteinaceous fibrils in vital organs and tissues leading to organ dysfunction and ultimately death. Amyloid can affect any organ or tissue however, the kidneys, pancreas, liver, spleen, nervous tissue and heart constitute the major sites of deposition in patients with familial or sporadic forms of peripheral amyloid disease. The most common form of sporadic, peripheral amyloid is immunoglobulin light chain (LC) amyloidosis (AL), a monoclonal plasma cell dyscrasia that has an incidence of 5 per 100,000 persons per year in the USA. It is one fifth as common as multiple myeloma but more devastating with a median survival of only 13.2 months due partly to the rapidly progressive nature of the organ destruction, the lack of effective anti-amyloid therapeutics and the inability to successfully diagnose the disease before organ failure occurs.

We have previously described a monoclonal antibody (mAb), designated 11-1F4 that binds to a conformational epitope present on LC fibrils but not the monomeric LC precursor proteins. When administered to mice bearing either AL κ or AL λ amyloidomas the mAb 11-1F4 expedited dissolution of the amyloid material by opsonizing the fibrils and inducing cell-mediated removal. Furthermore, when radioiodinated and injected into mice with human AL κ and AL λ amyloidomas the mAb 11-1F4 co-localized with the material in an isotype-independent manner, as evidenced using microSPECT and now microPET imaging.

Under the auspices of an Investigational New Drug application we now have studied the distribution of ¹²⁴I-labeled 11-1F4 mAb in patients with AL amyloidosis. Each of the 11 patients received < 2 mCi and < 1 mg of ¹²⁴I-11-1F4 and the distribution of the reagent was visualized using PET/CT imaging. In ~40% of the patients the mAb co-localized with biopsy proven sites of AL amyloidosis, as evidenced in the PET data. As predicted by the preclinical murine imaging studies, the ¹²⁴I-11-1F4 mAb bound patient amyloid deposits of both AL κ and AL λ isotype. Furthermore, there was no evidence of mAb binding to tissues that did not contain amyloid, which was further predicted by our murine model of AL amyloidoma.

These studies provide the first clinical validation of the fibril-specific immunoreactivity of the mAb 11-1F4. The data correlate well with our preclinical imaging studies, and further support the use of this reagent as an immunotherapeutic for patients with AL amyloidosis.