



COLUMBIA UNIVERSITY
MEDICAL CENTER

“Phase 1a/1b Study of Chimeric Fibril-Reactive Monoclonal Antibody 11-1F4 in Patients With AL Amyloidosis”

CUMC IRB #AAAM5108

Protocol (v.3 / 5Mar14)

IND #117316

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mAb 11-1F4

- murine mAb 11-1F4
 - Recognizes human light-chain related fibrils via amyloid-associated conformational epitope
 - Speculate that 11-1F4 interferes with lag/hyperbolic growth phase of fibril formation
- Activity:
 - Binds/opsonizes to fibrils
 - Attracts and activates neutrophils
 - Proteolysis by neutrophil-derived endopeptidases

Primary Objectives

- Establish the maximum tolerated dose (up to 500 mg/m²) of 11-1F4

Secondary Objectives

- Demonstrate reduction in amyloid burden, as evidenced by a decrease in affected organomegaly and/or improved organ function
- Determine the pharmacokinetics of 11-1F4 when given as a single IV infusion (phase 1a) or as a series of weekly IV infusions (phase 1b)
- Obtain additional safety data of 11-1F4 when given as a single IV infusion or as a series of weekly IV infusions

Major Inclusion Criteria

- Confirmed diagnosis of AL amyloidosis based on accepted clinical/laboratory criteria
- > 21 years old
- Life expectancy > 3 months
- ECOG-specified performance status ≤ 3
- Have measurable, localized amyloid deposits (larynx, subcutaneous tissue, muscle, lung, lymph nodes) or clinically evident systemic disease (liver, kidney, heart, etc).
- Relapsed/refractory, unless they have declined or are not eligible for high-dose melphalan and autologous HSCT or any other standard therapy that has been known to be life-prolonging or life-saving

Major Inclusion Criteria (cont.)

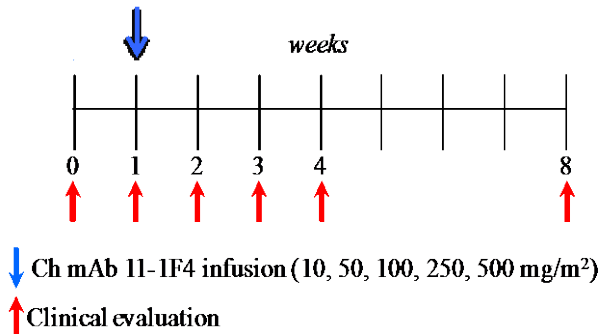
- Organ function:
 - Heart:
 - Ventricular ejection fraction $\geq 40\%$
 - Intraventricular septal (IVS) thickness ≤ 25 mm (as determined by 2D echocardiography)
 - No history of sustained ventricular tachycardia (lasting longer than 30 sec) or cardiac arrest
 - Kidney:
 - 24-hr creatinine clearance ≥ 30 cc/min
 - Liver:
 - Alkaline phosphatase ≤ 3 x ULN
 - Bilirubin, ≤ 3.0 mg/dL

Major Exclusion Criteria

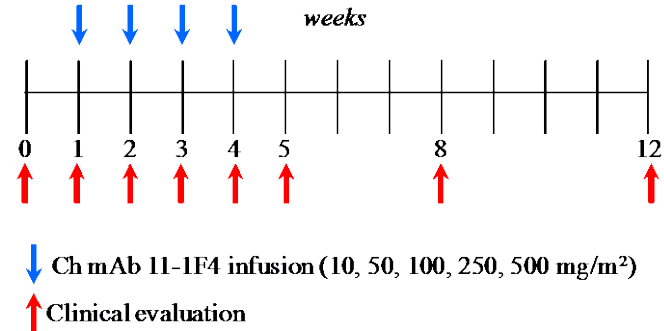
- Non-AL amyloidosis
- Renal failure (on dialysis)
- Involvement in an AL therapeutic trial within 6 mo.
- Females of child-bearing potential who are pregnant or breast-feeding
- ECOG > 3
- Seriously limited cardiac, renal, or hepatic function
- Uncontrolled infection or significant co-morbidity (*e.g.*, uncontrolled diabetes, severe diarrhea that requires TPN)
- Prior exposure to a humanized anti-amyloid mAb

Treatment overview

- Phase 1a
 - Infusion x 1



- Phase 1b
 - Infusion x 4



- 2 week interval after 4th infusion to ensure that no untoward reaction has occurred before administering drug to next patient
- Subjects from Phase 1a can be accrued to Phase 1b after completion of Week 8 assessment

*Amendment: include dose levels 0.125, 0.25, 0.5, 5 mg/m²