

Long term follow-up of patients with AL Amyloidosis treated on a phase 1 study of Anti-Amyloid Monoclonal Antibody CAEL-101

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BACKGROUND

- AL amyloidosis with cardiac involvement continues to carry a very poor prognosis with median survival of less than a year from diagnosis and a median survival of only 3 months in patients with cardiac stage 3b disease .

- CAEL-101 (11-1F4 mAb) is a monoclonal IgG1 antibody that directly binds to a conformational epitope present on both human kappa and lambda light-chain amyloid fibrils. In preclinical studies the antibody was able to localize to the amyloid tissue and induce a humoral immune response which led to rapid decrease in size as well as elimination of the amyloid

- We report long term survival of patients with relapsed/refractory AL Amyloidosis treated in a phase 1a/1b prospective clinical trial of CAEL-101.

METHODS

- Patients with relapsed/refractory systemic AL amyloidosis were enrolled and treated in a phase 1a (N=8) 1b study (N=19) using the anti-amyloid mAb CAEL-101, five patients enrolled on phase 1a also received treatment on phase 1b. Five patients were enrolled in both phase 1a and 1b.

- In the phase 1a part patients received a single dose of CAEL-101. First patient was treated with a dose of 0.5 mg/m² and the dose was escalated in each subsequent patient in a step-wise fashion to 5, 10, 50, 100, 250 and 500 mg/m²

- In the phase 1b part patients received 4 weekly doses of CAEL-101. Similar to the phase 1a the first patient was treated at 0.5mg/m² and then the dose was escalated as above in phase 1a.

- The primary objectives were to determine the MTD and evaluate safety of the intravenous mAb CAEL-101. Secondary objectives included determining pharmacokinetics (PK) and assessing organ responses

RESULTS

Table 1: Patient Demographic and Clinical Characteristics (N=22)[†]

Characteristic	Median	No. (%)
Age (N = 27)	66 yrs (Range: 34-79)	
Gender		Male N = 14 (64%) Female N = 8 (36%)
Race		White N = 17 (77%) Black N = 1 (5%) Other N = 2 (9%) Unknown N = 2 (9%)
Light Chain type		λ N = 11 (50%) κ N = 11 (50%)
Organ Involvement* (No.)		Heart N = 13 (59%) Kidney N = 12 (55%) Skin/Soft tissue N = 9 (41%) GI N = 6 (27%) Nervous System N = 5 (23%) Liver N = 4 (18%) Other N = 4 (18%)
Best Hematologic Response To Prior Plasma Cell Directed Therapy [#]		Complete Response N = 9 Very Good Partial Response N = 0 Partial Response N = 2 No Response N = 2
Previous Plasma cell Directed Therapy (No.)	2 (Range: 1 – 10)	1 Regimen 18% (N=4) 2 Regimen 36% (N=8) 3 Regimen 18% (N=4) >3 Regimen 27% (N=6)
Baseline NT-proBNP (ng/L) ^a	1377 (Range: 662-13131)	
Baseline 24 hr Urine Protein (mg/24hr) ^b	3062 (Range: 1200-7260)	
Time Since last Exposure to Chemotherapy (mos)	6 (Range: 0-48)	

[†]5 patients participated in both phase 1a and 1b of this study. Their data is entered separately in this table for the following parameters: age, baseline NT-proBNP and baseline 24 hr urine protein

^avalues exceeded 100% because some patients had more than one organ involved

- Cardiac response was seen in 67% (8/12) and renal responses were seen in 33% (4/12) of evaluable patients.
- At the last data cut-off on 7/30/2019, long-term survival data is available for 19/22 patients.
- With a median follow-up of 37 months (range 30-45), the median survival has not been reached and 78% (15/19) of patients are alive and 4 patients have died from progressive AL Amyloidosis.
- Among the evaluable patients 7/12 have experienced hematological progression and only 2/12 patients have experienced organ progression.

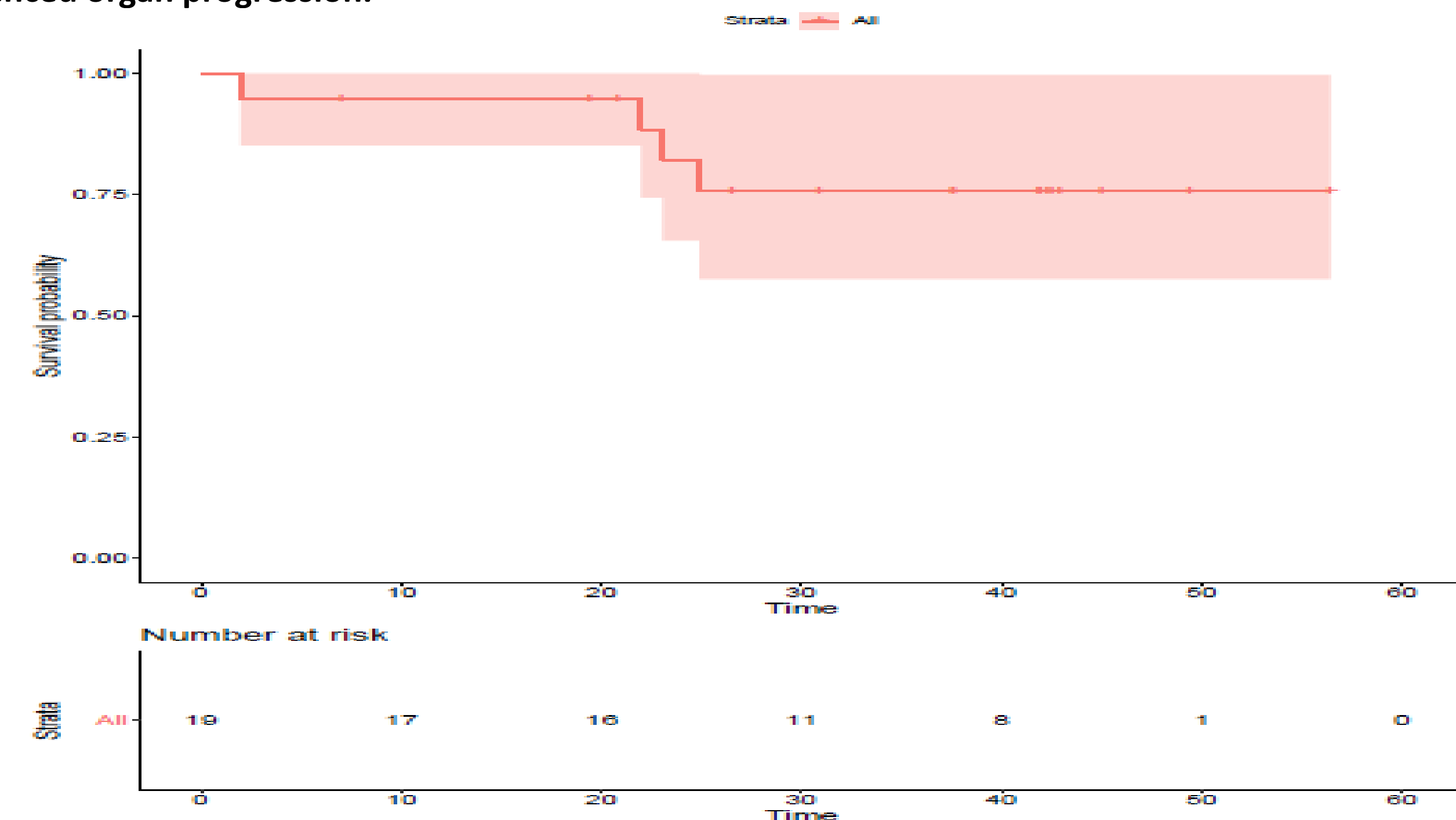


Figure 1: Overall Survival for all patients

CONCLUSIONS

- Therapy with CAEL-101 can lead to durable long-term organ responses as well as excellent overall survival in patients with systemic AL Amyloidosis.
- Further Prospective studies are currently planned to evaluate efficacy of CAEL-101 in AL Amyloidosis.

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