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Updated overall survival of patients with AL amyloidosis after CAEL-101

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INTRODUCTION

AL amyloidosis continues to carry poor prognosis, with median survival less than 1 year from diagnosis in patients with advanced cardiac involvement.[1,2] More generally, median time to organ response after treatment initiation is estimated at 10.4 months; end-organ damage drives the majority of 2-year mortality after diagnosis.[1]

CAEL-101 (11-1F4 mAb) is a monoclonal IgG1 antibody that directly binds to a conformational epitope on human κ and λ light-chain amyloid fibrils.[3] Preclinical studies found that 11-1F4 localized to human amyloid and induced a macrophage-mediated response, resulting in rapid fibril elimination.[3,4]

AIM

We have previously reported excellent activity and safety of the drug in a phase 1 clinical trial.[5] We present updated results from the CAEL-101 phase Ia/Ib study, including exploratory survival analyses with comparison to historical controls.

METHODS

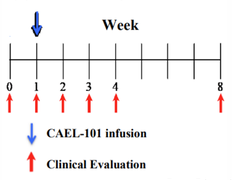
Patients with relapsed/refractory AL amyloidosis enrolled in phase Ia/Ib NCT02245867 9/2014-4/2017. Total n = 27 (8 phase Ia, 19 phase Ib). 5 patients participated in both.

- Phase Ia: single dose, stepwise dose escalation
- Phase Ib: 4 weekly doses, stepwise dose escalation
- Maximum dose 500mg/m^2

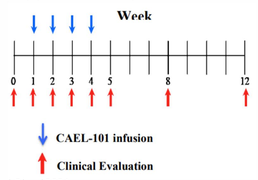
AL amyloidosis patients at our center not treated with CAEL-101 1/01/2012-12/30/19 served as clinical comparisons.

We evaluated the long-term outcomes of patients treated on the study compared to the historical control group. We assessed all patients included in either arm of the study.

(a) Phase 1a, stepwise treatment



(b) Phase 1b, stepwise treatment



From Edwards et al *Blood* 2021

RESULTS

Characteristics of patients

	CAEL-101 (N=22)	Control (N=86)	Cardiac control (N=62)
Age	66	63	62
Gender (M/F)	14/8	46/40	32/30
Cardiac involvement	54%	72%	100%
Renal involvement	45%	61%	51%
NT-proBNP	1377 (662-13131)	1040 (89-17000)	2289 (191-17000)
Creatinine	1.03 (0.8-1.3)	1.07 (0.53-5.4)	1.01 (0.59-5.4)
Light chain type (K/L)	11/11 (50%/50%)	19/67 (78%/22%)	14/48 (22%/78%)
24h urine protein (mg)	3062 (1200-7260)	2346 (600-23,000)	3700 (330-23,000)

Long-term organ-specific data were available for 19/22 patients. Median follow-up was 81.3 months (IQR 60.4-87.7).

5 patients died: 3 from progressive AL amyloidosis; 1 from organ transplantation complication; 1 from venous thromboembolism sequelae. Median OS was not reached. Median PFS was 93.3 months (38.9-NR).

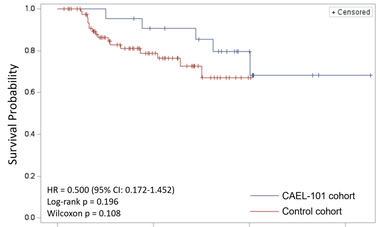
10/17 had hematologic progression and received next line therapy. 5/17 patients had organ progression of disease (PD). All patients with organ PD had previous/concomitant hematologic PD.

Comparison of phase Ib cohort with historical controls revealed trends toward improved OS.

Of 12 evaluable cardiac patients: 3/12 had organ PD; 9/12 had stable disease (SD) or better. 2/3 with organ PD died; 1/9 with at least SD died; 0/6 with cardiac response died.

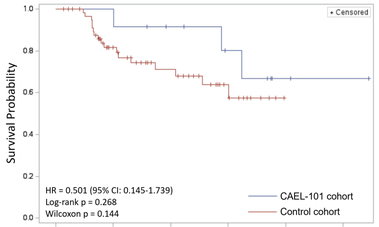
Figure 1: Overall Survival (OS) from Diagnosis

(a) OS, CAEL-101 cohort vs all-comers controls



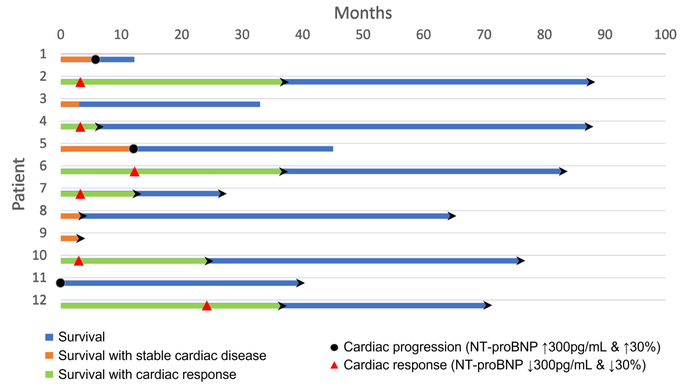
	0 months	20 months	40 months	60 months	80 months	100 months
No. at risk	104	81	60	41	25	8
CAEL-101	22	22	20	17	15	7
Control	82	59	40	24	10	1

(b) OS, CAEL-101 cohort vs cardiac controls



	0 months	20 months	40 months	60 months	80 months	100 months
No. at risk	72	53	35	26	13	2
CAEL-101	12	12	10	8	6	2
Control	60	41	25	18	7	0

Figure 2: Individual Patient Course from Enrollment, Cardiac-Specific



CONCLUSIONS

Patients with AL amyloidosis and persistent organ involvement received low cumulative doses of the novel anti-amyloid antibody CAEL-101. Some patients only received a single dose. Nevertheless, they experienced:

(1) high rates of cardiac response, confirmed by global longitudinal strain measurement in 9/10 patients;
(2) lengthy overall and progression free survival, favorable vs historical controls.

The CAEL101-301 and CAEL101-302 phase 3 trials are underway to confirm these findings.

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CONTACT INFORMATION

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