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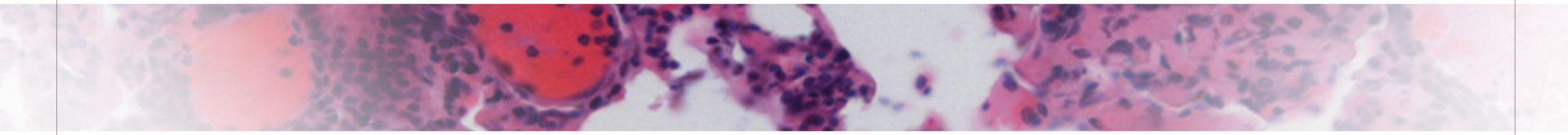

Safety, Tolerability and Efficacy of CAEL-101 in AL Amyloidosis Patients Treated on a Phase 2, Open-Label, Dose Selection Study to Evaluate the Safety and Tolerability of CAEL-101 in Patients with AL Amyloidosis (Abstract 729)

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Introduction

- CAEL-101 is an investigational IgG1 monoclonal antibody that targets the mis-folded light chains of AL amyloid fibrils, a hallmark of AL amyloidosis
- CAEL-101 specifically binds to a conformational epitope present on both human kappa and lambda light-chain amyloid fibrils
- Phase 1 study established safety and tolerability of monotherapy CAEL-101 as a weekly treatment for 4 weeks up to an MTD of 500 mg/m2 in relapse/refractory patients
  - No dose limiting toxicity or drug related deaths were seen.
- Cardiac response was seen in 67% (8/12) and renal responses were seen in 33% (4/12) of evaluable patients (Edwards CV et al Blood (2016) 128 (22): 643)

Accelerating Organ Response through Amyloid Clearance from Organs

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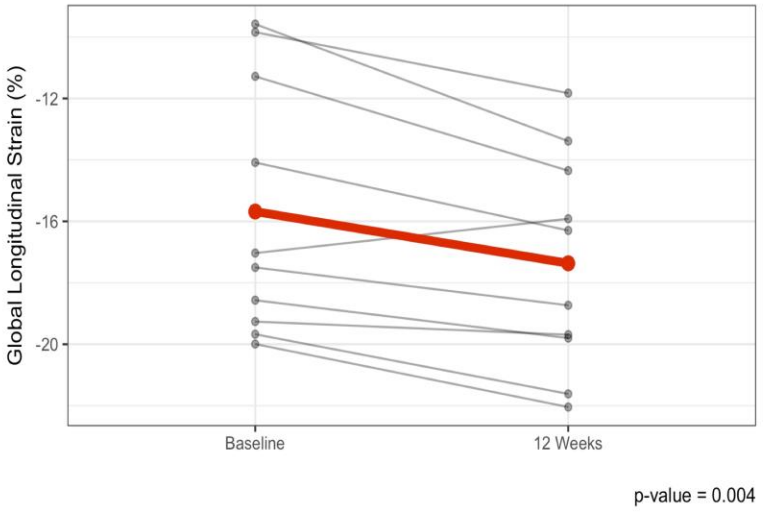
- **Novel anti-plasma cell therapies continue to emerge with improvements in hematologic responses**
- **Organ response even after hematologic response is established is still unpredictable**
- **Persistent organ dysfunction irrespective of hematologic response remains an issue**
- **There remains a need for therapies that target amyloid fibril removal to prevent and reverse organ damage**

Phase 1 CAEL-101 results: Improvement in GLS in Cardiac Patients at 12 weeks – irrespective of hematologic response



Ongoing CAEL-101-203 Phase 2 Trial Design

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Part A: Open-label, sequential cohort dose-selection phase (3+3)

- Cohort 1 (n=4), 2 (n=3), and 3 (n=6) received CAEL-101 IV over 2 hours at 500 mg/m2, 750 mg/m2 and 1000 mg/m2 respectively, all weekly for 4 weeks then every other week for the remainder of the study
- Dosed with CyBorD regimen
- DLT observation period: IV weekly for 4 weeks

Part B: Daratumumab Expansion

- Up to 10 patients treated with Dara-CyBorD and CAEL-101 1000 mg/m2
- DLT observation period: IV weekly for 4 weeks
- Post DLT period – IV biweekly

Primary objectives:

- Evaluate the safety and tolerability of CAEL-101 in combination with CyBorD
- Determine MTD or recommended dose for Phase 3 studies of CAEL-101

Secondary objectives:

- Evaluate the serum PK of CAEL-101 (abstract 2277)

IV, intravenous; MTD, maximum tolerated dose; PK, pharmacokinetics; CyBorD: cyclophosphamide, bortezomib, dexamethasone

Study Methodology: Dosing

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- Bortezomib 1.3 mg/m2 subcutaneous, cyclophosphamide 300 mg/m2 (dose capped at 500 mg) IV and dexamethasone 20 mg IV (CyBorD) were given weekly, day 1, 8, 15 of a 35 day cycle in the first cycle to align treatments with CAEL-101 and then weekly day 1, 8, 15 of a 28 day cycle for up to 6 total cycles
- CAEL-101 was continued every other week after the conclusion of CyBorD
- No dose adjustments of CAEL-101 could be made during the dose escalation phase
- Dose adjustments in CyBorD due to toxicity were made at the discretion of the treating physician
- If the recommended phase 3 dose was proven to be 1000 mg/m2, patients at lower dose levels were permitted to increase their dose to 1000 mg/m2

Key inclusion and exclusion criteria

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- Newly diagnosed and relapsed disease permitted
- Patients with multiple myeloma and AL amyloidosis excluded
- Mayo stage IIIb excluded

Patient and Disease Characteristics

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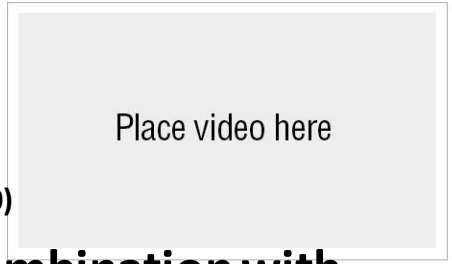
	CAEL-101 500 mg/m^2 + CyBorD N=4	CAEL-101 750 mg/m^2 + CyBorD N=3	CAEL-101 1000 mg/m^2 + CyBorD N=6	CAEL-101 1000 mg/m^2 + CyBorD + Dara (interim data) N=2	All Patients N=15
Median age, years (range)	55 (49 to 62)	70 (48 to 70)	75 (62 to 80)	63 (63 to 64)	64 (48 to 80)
Sex, n (% male)	4 (100%)	2 (66.7%)	4 (66.7%)	2 (100%)	12 (80%)
Number Previous PCD treatments range	3-4	0-4	0-4	Not yet available	0-4
Time since Diagnosis (months), median (range)	46 (19 to 163)	13 (3 to 23)	12 (3 to 23)	3 (2 to 3)	13 (2 to 163)
Mayo Stage n (%)					
I	1 (25.0)	0	0	0	1 (6.7)
II	2 (50.0)	2 (66.7)	5 (83.3)	2 (100.0)	11 (73.3)
IIIA	1 (25.0)	1 (33.3)	1 (16.7)	0	3 (20.0)
AL amyloidosis in Heart n (NTproBNP>650 pg/mL, %)	2 (50.0)	3 (100.0)	3 (50.0)	2 (100.0)	10 (66.7)
NT-ProBNP (pg/mL) median (range)	928 (50 to 3712)	752 (612 to 1002)	2926 (545 to 18696)	1799 (823 to 2774)	1002 (50 to 18696)
cTnT (ng/mL) median (range)	0.034 (0.010 to 0.041)	0.018 (0.010 to 0.047)	0.012 (0.010 to 0.106)	0.019 (0.013 to 0.024)	0.016 (0.010 to 0.106)
Baseline eGFR, median (range),	45 (34 to 54)	60 (44 to 60)	33 (22 to 60)	101 (84 to 118)	47 (22 to 118)

Safety and dosing summary



- CAEL-101 treatment duration 40 to 276 days (data cut 11/1/20)
- CAEL-101 was shown to be safe and well tolerated in combination with CyBorD with 1000 mg/m2 established as recommended Phase 3 dose for Caelum CARES ongoing trials
  - No dose limiting toxicity or treatment related discontinuation
  - 2 patients escalated to 1000 mg/m2 were dose reduced to 750 mg/m2 due to diarrhea and vomiting respectively
  - Treatment is ongoing with 40% of patients having at least 15 infusions of CAEL-101
  - No infusion reactions were seen – premedication with 1 gram oral acetaminophen and 25 mg oral diphenhydramine

Most Common TEAEs: At least Possibly Related to Study Treatment

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CTCAE Preferred Term	CAEL-101 500 mg/m2 + CyBorD N=4	CAEL-101 750 mg/m2 + CyBorD N=3	CAEL-101 1000 mg/m2 + CyBorD N=6	CAEL-101 1000 mg/m2 + CyBorD + Dara N=2	All Patients N=15
At Least One At Least Possibly Related TEAE	2 (50.0)	1 (33.3)	2 (33.3)	0	5 (33.3)
Rash	1 (25.0)	1 (33.3)	1 (16.7)	0	3 (20.0)
Diarrhea	1 (25.0)	0	0	0	1 (6.7)
Nausea	1 (25.0)	0	0	0	1 (6.7)
Dyspnea	1 (25.0)	0	0	0	1 (6.7)
Anemia	0	0	1 (16.7)	0	1 (6.7)
Abbreviations: TEAE=treatment-emergent adverse event, defined as an adverse event occurring during or after study drug administration. This table includes all TEAEs judged by the Investigator to be at least Possibly Related to Study Treatment.					

Most common TEAEs irrespective of relationship to CAEL-101 were diarrhea and nausea, similar to Phase 1. Two patients had dose reductions from 1000 mg/m2 to 750 mg/m2, one due to diarrhea and one due to vomiting), with the TEAEs subsequently resolving

Organ Response

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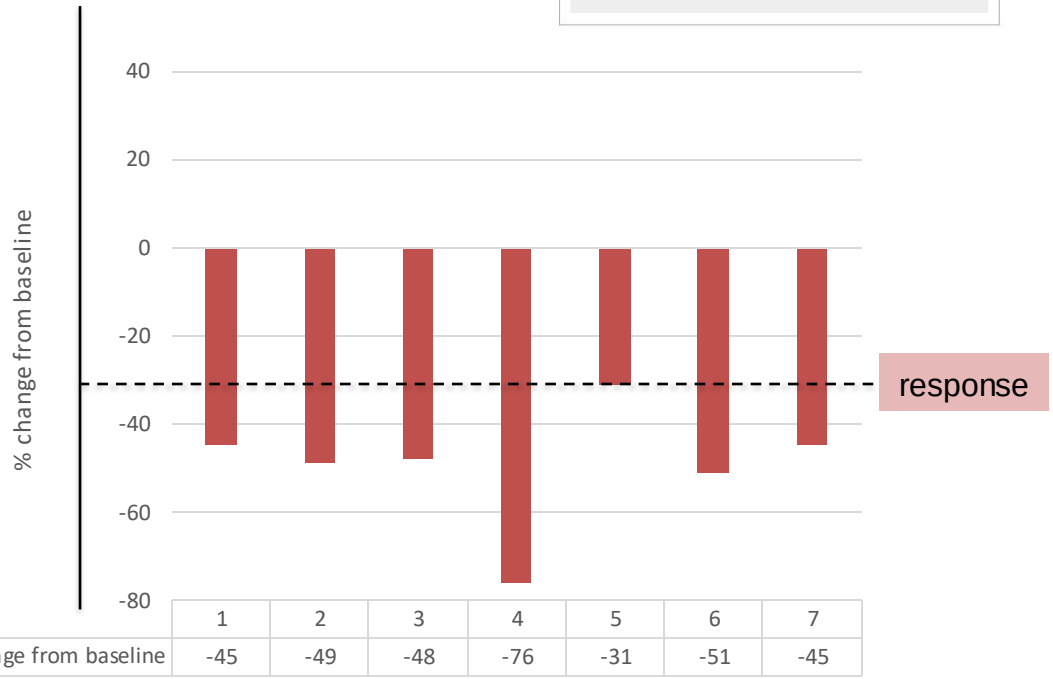
7 patients with kidney involvement: All had organ responses

(Palladini G et al Blood (2014) 124 (15): 2325–2332)

- Of MOST INTEREST was 1 patient with PR subsequently progressed back to SD
  - Despite this, the patient has an ongoing deepening renal organ response currently showing a 76% reduction in 24 hour proteinuria without change in anti-plasma cell therapy
  - Median of 56 days to organ response
- One of 8 patients achieved cardiac organ response by NT pro BNP criteria
  - (Comenzo RL et al Leukemia (2012) 26, 2317-2325)



Caelum CARES Phase 3 Program Initiated

Caelum CARES

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Mayo Stage IIIb Newly Diagnosed Treatment Naive	
CAEL-101 + CyBorD 74 Patient	Placebo + CyBorD 37 Patients
4 weekly doses followed by a maintenance dose every 2 – 4 weeks	
Primary endpoint: Overall Survival Secondary endpoints: 6MWT, QoL, NT-proBNP, GLS, Cardiac MRI, Proteinuria	

Mayo Stage IIIa Newly Diagnosed Treatment Naive	
CAEL-101 + CyBorD 178 Patient	Placebo + CyBorD 89 Patients
4 weekly doses followed by a maintenance dose every 2 – 4 weeks	
Primary endpoint: Overall Survival Secondary endpoints: 6MWT, QoL, NT-proBNP, GLS, Cardiac MRI, Proteinuria	

Summary

- CAEL-101 dosed at 1000 mg/m2 is the recommended dose in combination with CyBorD for the ongoing randomized, double blind, phase 3 trials
- Organ responses particularly in the kidney are common even in relapsed patients
- Only 1 patient is no longer on study due to need for change in anti-plasma cell therapy
- Most importantly, organ responses have been seen even without ongoing hematologic PR

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