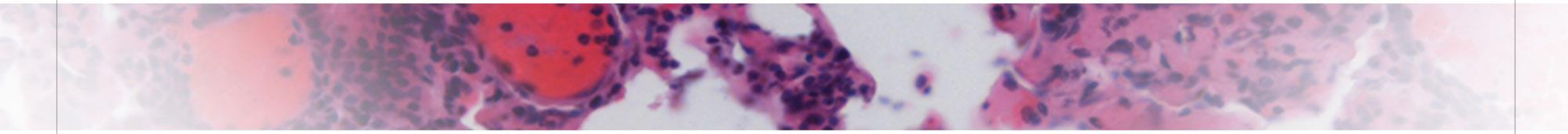
American Society of Hematology
Helping hematologists conquer blood diseases worldwide



CAEL-101 Is Well-Tolerated in AL Amyloidosis Patients Receiving Concomitant Cyclophosphamide-Bortezomib-Dexamethasone (CyborD): A Phase 2 Dose-Finding Study (NCT04304144)

Jason Valent, MD[1], John Silowsky, RN BSN[2], Michael R. Kurman, MD[3], Eileen Daniel[2], Janet Jobes[2], Mark Harnett, MS[2], Margaret Ziola, MD[2], Jessica Raviwong[2], Sherry Fada[1], Michael Spector, BS[2], Susan B. Sobolov, PhD[2], Alanna McEneny-King PhD[4], Xiaofeng Wang PhD[4], Wei-Jain Pan PhD[4]

[1]Department of Hematology and Medical Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, Ohio; [2]Caelum Biosciences, Bordentown, NJ; [3]Michael Kurman Consulting, LLC, Upper Saddle River, NJ

[4] Alexion Pharmaceutical, Boston, MA

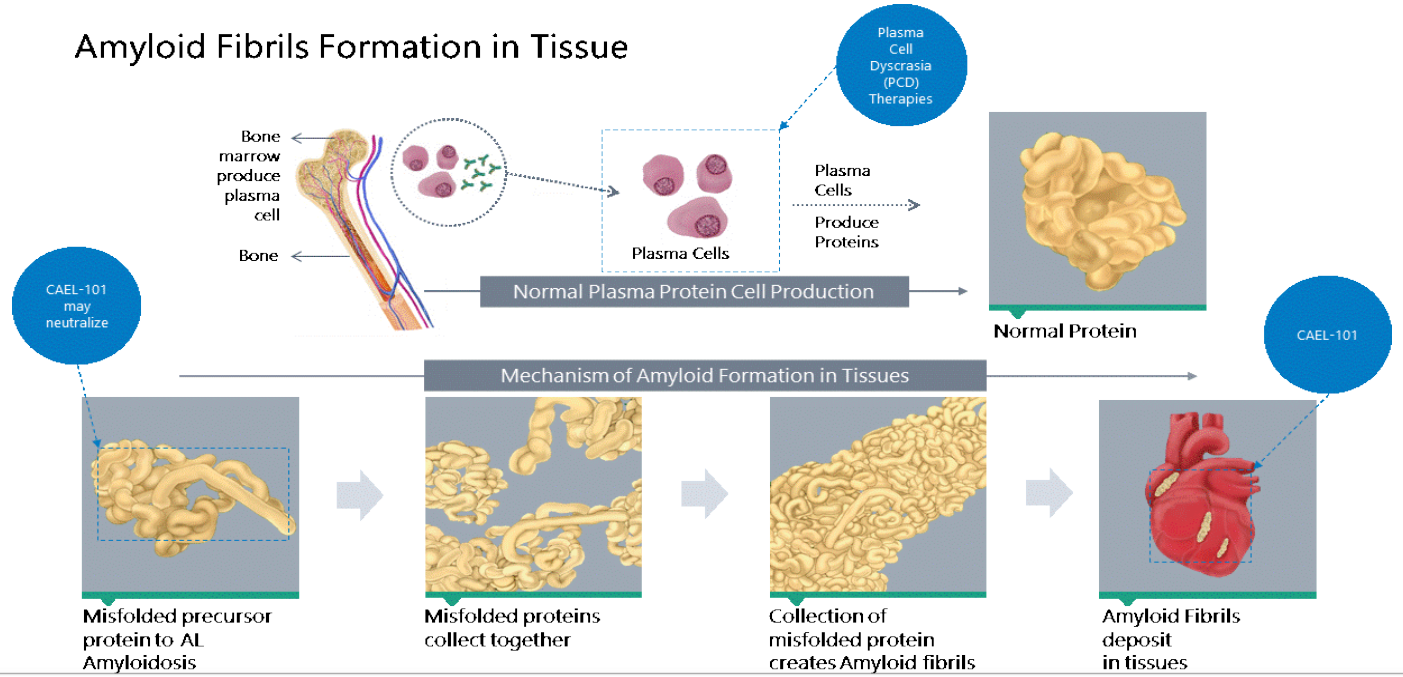
Disclosures: Dr Valent

Teaching and Speaking:

- **Celgene corporation**
- **Takeda pharmaceuticals**
- **Amgen corporation**

AL Amyloidosis Background

- AL Amyloidosis is a form of systemic amyloidosis caused by the deposition of immunoglobulin light chain fibrils in tissues and organs. The resulting amyloid deposits in the major organ systems of heart, liver and kidneys leading to severe organ damage. The amyloid can also damage the nerves, soft tissue, and gastrointestinal tract. It is a rare, progressive, and often times fatal disease.
- Novel anti-plasma cell therapies continue to emerge with improvements in hematologic responses but no amyloid targeting therapies are currently available.
- Persistent organ dysfunction irrespective of hematologic response remains an issue.



CAEL-101 Introduction

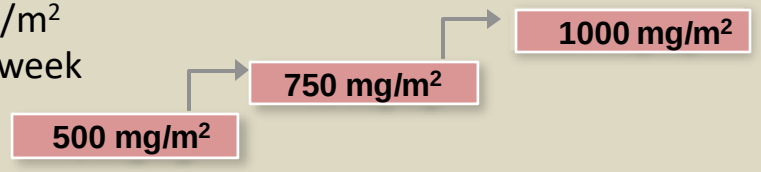
- CAEL-101 is an investigational IgG1 monoclonal antibody that targets the mis-folded light chains of amyloid fibrils, a hallmark of AL amyloidosis.
- CAEL-101 specifically binds to an N-terminus conformational epitope present on both human kappa and lambda light-chain amyloid fibrils.
- Phase 1 established safety and tolerability of monotherapy CAEL-101 as a weekly treatment for 4 weeks in doses up to 500 mg/m^2 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*.
  - Improvement in left ventricular Global Longitudinal Strain (GLS) in cardiac evaluable patients of 1.69 points**

*Edwards CV et al Blood (2016) 128 (22): 643
**Edwards CV et al ISA (2018)

Ongoing CAEL101-203 Phase 2 Trial Design

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/m^2, 750 mg/m^2 and 1000 mg/m^2 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
- Post DLT period: IV biweekly



Part B: Daratumumab Expansion

- Up to 10 patients treated with Dara-CyBorD and CAEL-101 1000 mg/m^2
- DLT observation period: IV weekly for 4 weeks
- Post DLT period – IV biweekly

Primary objective:

- Determine safety and tolerability of CAEL-101 and recommended dose for Phase 3 studies (RP3D) of CAEL-101

Secondary objectives:

- Evaluate the safety and tolerability of CAEL-101 in combination with CyBorD
- Evaluate the safety and tolerability of CAEL-101 in combination with CyBorD and daratumumab
- Evaluate the serum PK of CAEL-101

IV, intravenous; DLT dose limiting toxicity; PK, pharmacokinetics; RP3D, recommended phase 3 dose.

Patient and Disease Baseline Characteristics

	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 (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)

Summary of Adverse Events

	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
Number of patients with at least one TEAE considered to be at least possibly related[2]	2 (50.0)	1 (33.3)	2 (33.3)	0	5 (33.3)
Number of patients with at least one Grade 3 or higher TEAE	0	0	1 (16.7)	0	1 (6.7)
Number of patients with at least one treatment-emergent SAE	0	0	2 (33.3)	0	2 (13.3)
Number of patient with TEAEs leading to study discontinuation	0	0	0	0	0
Number of TEAEs leading to death	0	0	0	0	0
Number of patients with at least one DLT TEAE	0	0	0	0	0

- 2 serious adverse events (SAEs) and one grade 3 TEAE were seen to date
- No treatment related discontinuations or deaths.

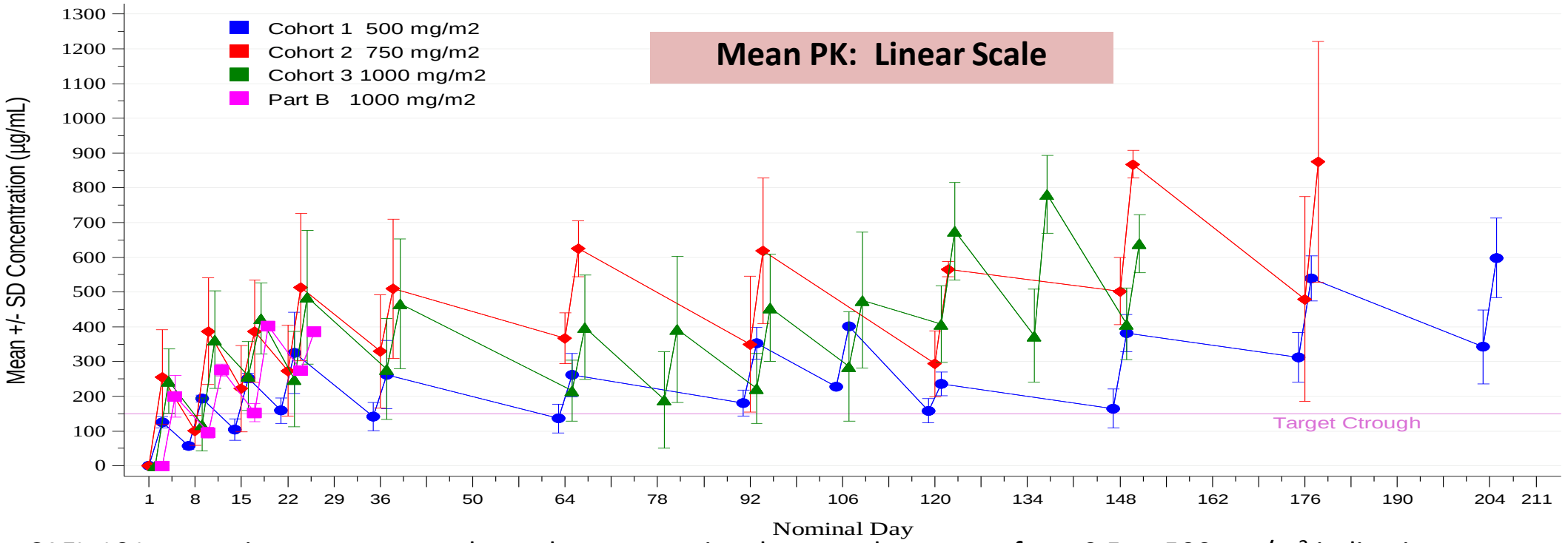
[1] A TEAE is defined as an AE occurring during or after study drug administration.
[2] Related TEAEs are defined as TEAEs with relationship of possibly related or related.

Most Common TEAEs: At least Possibly Related to Study Treatment

MedDRA 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)
Dyspnoea	1 (25.0)	0	0	0	1 (6.7)
Anaemia	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 TEAE irrespective of CAEL-101 association was diarrhea and nausea similar to Phase 1
- Two patients had dose reduction (1 diarrhea and 1 vomiting) and AEs were resolved

Study CAEL101-203: Pharmacokinetic Summary



- CAEL-101 systemic exposure was above dose proportional across dose range from 0.5 to 500 mg/m^2 indicating target mediated drug disposition (TMDD)
- CAEL-101 exposures dose proportional from 500 to 1000 mg/m^2, indicating saturation of TMDD at 500 mg/m^2
- Targeted Ctrough is 150 ug/mL based on Phase 1 exposures at NTproBNP response, Michaelis-Menton EC90 and *in vitro* binding highest EC90
- Recommended Phase 3 dose: 1000 mg/m^2- 4 weekly loading dose followed by biweekly maintenance regimen- achieve and maintain C_{trough} throughout dosing period.

Safety Summary and Conclusions

- This study demonstrated that CAEL-101 at doses up to 1000 mg/m^2, given with CyBorD, was safe and well tolerated in the AL amyloidosis population.
  - No dose-limiting toxicities nor treatment-related discontinuations
  - 2 Patients escalated to the recommended Phase 3 dose of 1000 mg/m2 CAEL-101 were dose reduced to 750 mg/m2 due to gastrointestinal tolerability
  - Treatment duration with CAEL-101 ranges from 40 days to over 200 days and over 40% of patients have had at least 15 infusions with CAEL-101
    - Treatment remains ongoing with infusions every other week
- Expansion cohort – Part B is currently enrolling AL amyloidosis patients to study safety of CAEL-101 1000 mg/m^2 in combination with Daratumumab- CyBorD.
- 1000 mg/m^2 CAEL-101 was established as the recommended Phase 3 dose for Caelum CARES ongoing trials based on safety and PK profile
- Caelum CARES are two Phase 3 studies in newly diagnosed Mayo Stage IIIa and IIIb treatment naïve patients with cardiac amyloidosis

Our thanks to the patients and their caregivers

Caelum CARES Phase 3 Program has Initiated

Caelum CARES

Mayo Stage IIIb Newly Diagnosed Treatment Naïve NCT# 04504825	
CAEL-101 + CyBorD 74 Patient	Placebo + CyBorD 37 Patients
4 weekly doses followed by a maintenance dose every 2 weeks	
Primary endpoint: Overall Survival through 12 months Secondary endpoints: 6MWT, KCCQ QoL, NT-proBNP, GLS, Cardiac MRI, Proteinuria	

Mayo Stage IIIa Newly Diagnosed Treatment Naive NCT# 04512235	
CAEL-101 + CyBorD 178 Patient	Placebo + CyBorD 89 Patients
4 weekly doses followed by a maintenance dose every 2 weeks	
Primary endpoint: Overall Survival through 12 months Secondary endpoints: 6MWT, KCCQ QoL, NT-proBNP, GLS, Cardiac MRI, Proteinuria	