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First-in-Class Small Molecule CA-170 Targeting VISTA: A Report on Efficacy Outcomes from a Cohort of 12 Malignant Pleural Mesothelioma (MPM) Patients in Study CA-170-101

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Presenter Disclosure Information

Marjorie G. Zauderer MD

The following relationships exist during the past 12 months:

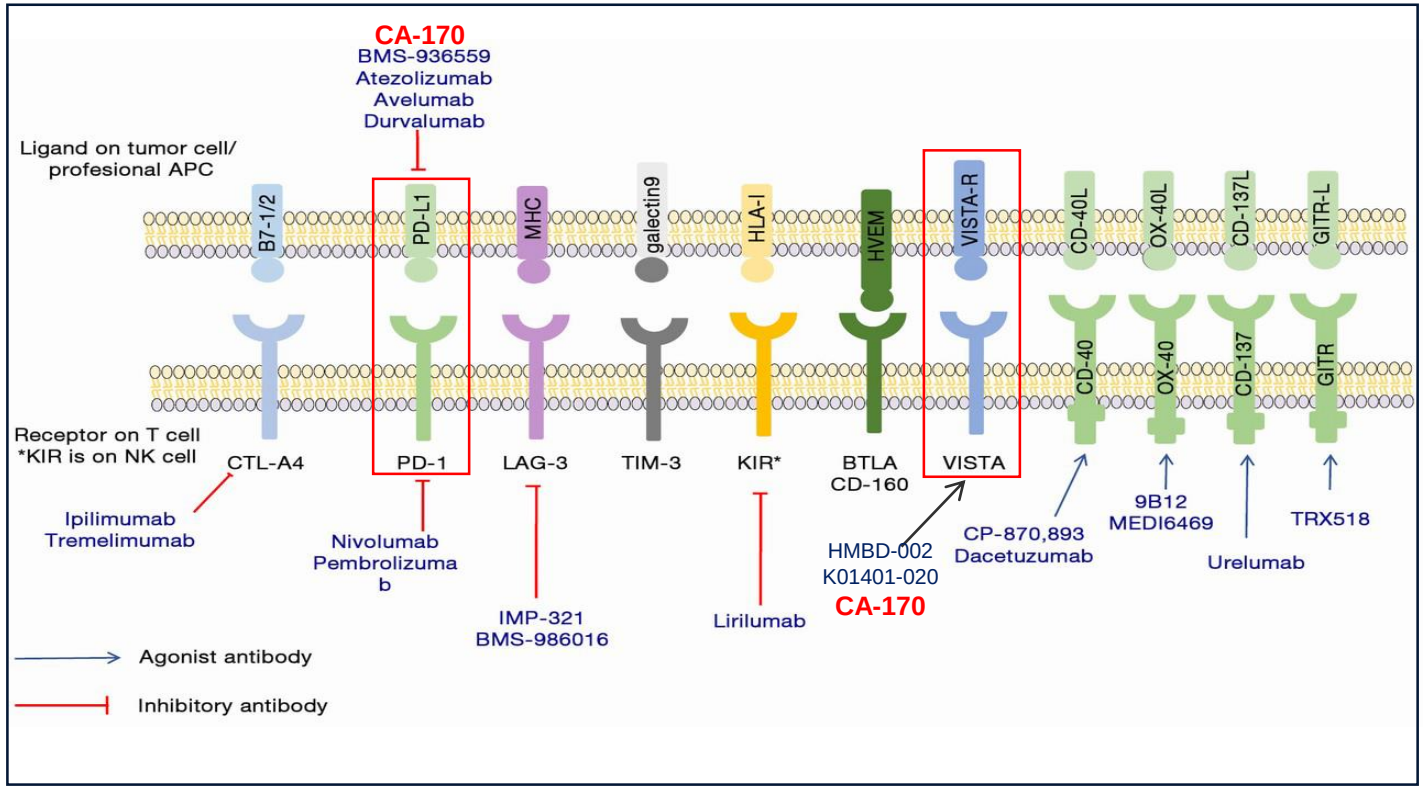
- Speaking honorarium: Medical Learning Institute, Intellisphere
- Research funding: Curis, BMS, Epizyme, Polaris, Millenium, and Roche
- Advisory boards: Novocure, Aldeyra
- Leadership position: Chair, Board of Directors, Mesothelioma Applied Research Foundation (uncompensated)

There will not be discussion about the use of products for non-FDA approved indications in this presentation.

This study was sponsored by Curis, Inc.

Background: CA-170 and MOA

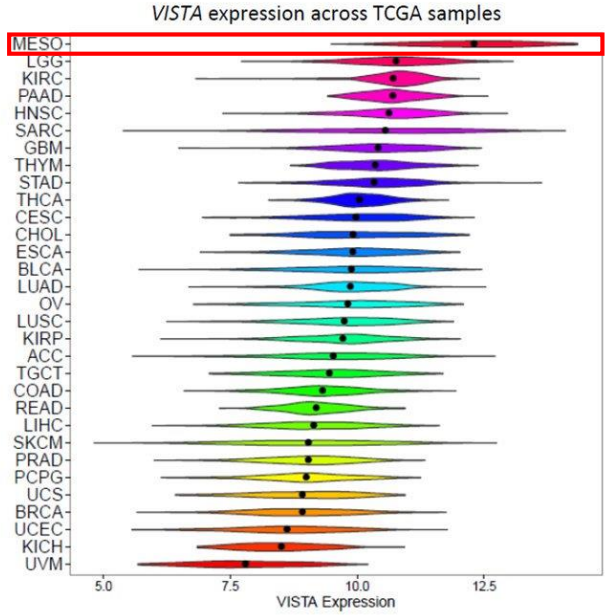
- CA-170: oral, peptidomimetic small molecule
- Designed to target B7 Ig family interaction hotspots
- Blocks activity of 2 separate and non-redundant immune checkpoint pathways:
  - PD-1/PD-L1
  - VISTA



APC = antigen presenting cell; modified from Márquez-Rodas et al. Ann Transl Med. 2015; 3(18): 1924–1932.

Background: Mesothelioma

- MPM is an aggressive disease. Only few treatment options exist, and survival is poor: mOS = ~1 year; 5 yr OS is ~10% [NCCN Guidelines]
- Standard Of Care (systemic chemo):
  - 1st line metastatic: pemetrexed +/- cisplatin (+bevacizumab in certain pts) OR clinical trial
  - 2nd line: no standard, unless 1st-line didn't include pemetrexed
- VISTA is highly expressed in metastatic pleural mesothelioma[1]
  - VISTA expression on tumor as well as normal and reactive mesothelium
  - 90% of mesothelioma cells express VISTA
  - Expression is strikingly higher in epithelioid MPM
  - Highly correlated with mesothelin expression; no correlation with PD1, PDL1 or TMB



Ladanyi, et al. Cancer Discov, 2018 Dec

PD-L1 and VISTA Tumor Expression by IHC

PD-L1	N=28 (%)
• ≥ 50%	2 (7)
• 1-50%	9 (32)
• < 1%	17 (61)
VISTA	**N=26 (%)**
• ≥50%	22 (85)
• 1-50%	3 (12)
• < 1%	1 (4)

Zauderer MG. ID 13232. WCLC 2018

[1] Muller S, Lai WV, Prasad SA, *et al*., (2019) *Modern Pathology*.

Phase 1 Study Design, CA-170-101

Relapsed/Refractory Solid Tumor or Lymphoma after failure on prior SOC

Dose-finding phase

Methods:
- ❑ Accelerated titration followed by a 3+3 design
- ❑ Selected dose levels back-filled

Objectives:
- ❑ Primary: Safety, RP2D, and MTD
- ❑ Secondary: PK, anti-cancer activity
- ❑ Exploratory: biomarkers and PD effects

Patient Population:
- ❑ Aged ≥18 years, adequate organ function
- ❑ ECOG PS 0–1
- ❑ Study sites in South Korea, US, Spain, UK

Treatment:
- ❑ Oral dosing in continuous 21-day cycles
- ❑ QD and BID dosing was tested

www.clinicaltrials.gov: NCT03328078

200mg BID OR 1200mg BID

Recurrent/progressive malignant pleural mesothelioma
***n* = 12**

- ✓ No VISTA selection
- ✓ Histology: epithelioid
- ✓ Paired tumor biopsies when medically feasible
- ✓ Measurable disease
- ✓ ECOG 0-1
- ✓ Adequate organ function

MPM baseline & disease characteristics

Characteristic	n (%)
n	12 (100)
Sex	
Male	8 (67)
Female	4 (33)
Age	
Median	68
Range	53-79
ECOG PS	
0	6 (50)
1	6 (50)

Characteristic	n (%)
n	12 (100)
Prior lines of systemic chemotherapy	
Median	2
Range	1-3
Prior immune CPI	0 (0)
Prior radiotherapy	6 (50)
Time from initial diagnosis to treatment start	
Median (yrs)	3.2
Range	1.2-10.1

Summary of Safety and Pharmacokinetics

- Overall, CA-170 has demonstrated excellent safety characteristics with low rates of drug-related, immune-related *or* serious adverse events

TEAEs in ≥10% of Patients	Total N=71 n (%)
Any Treatment-Emergent AE	**66 (93.0)**
Fatigue	19 (26.8)
Nausea	19 (26.8)
Decreased appetite	15 (21.1)
Anemia	14 (19.7)
Cough	14 (19.7)
Vomiting	12 (16.9)
Constipation	11 (15.5)
Headache	10 (14.1)
Pyrexia	9 (12.7)

Grade ≥ 3 TEAEs in >2% of Patients	Total N=71 n (%)
Any Grade 3 or Higher TE AE	**29 (40.8)**
Anemia	3 (4.2)
Dyspnea	3 (4.2)
Fatigue	2 (2.8)
Hypercalcemia	2 (2.8)
Lipase increased	2 (2.8)
Syncope	2 (2.8)
Tumor pain	2 (2.8)
Urinary tract infection	2 (2.8)

Related TEAEs in Mesothelioma (>1 Patient)	MPM (N=12) n (%)
Any Treatment-Related AE	**8 (67)**
Decreased appetite	4 (33)
Cough	3 (25)
Headache	3 (25)
Fatigue	2 (17)
Upper respiratory tract infection	2 (17)

- PK
  - Rapid oral absorption and good bioavailability
  - Dose-proportional exposures (C_{max}, C_{min}, C_{avg} and AUC) for both QD and BID schedules
  - BID dosing provides high steady-state plasma concentration

Summary of Efficacy

- 12 MPM patients treated with CA-170
- 11 patients were on treatment for at least 1 post-baseline disease assessment
- *As of the data cut-off:*
  - 11 of 12 MPM patients had discontinued study treatment
  - No PRs/CRs have been observed per RECIST criteria
  - 7 of 11 evaluable patients had a best response of Stable Disease
    - 2/3 (66%) pts @ 200 mg BID (mean duration, SD 64 days)
    - 5/8 (63%) pts assigned/escalated to 1200 mg BID (mean duration, SD 115 days)

Summary, conclusions and next steps

- The safety profile of CA-170 is distinct from immune CPI monoclonal antibodies
- CA-170 was well-tolerated and shows dose-proportional clinical PK with BID dosing
- No radiographic responses were observed among 12 mesothelioma patients treated
- VISTA's role in tumorigenesis and/or propagation is under active investigation
- Future studies are under discussion and will include translational approaches and clinical pharmacodynamics

We would like to thank the patients, their families and caregivers for their invaluable contribution and participation in this study.