PROCLAIM-CX-072:
Analysis of Patients With Advanced Solid Tumors Receiving Long-Term Treatment With CX-072, a PD-L1 PROBODY Therapeutic, as a Single Agent or in Combination With Ipilimumab

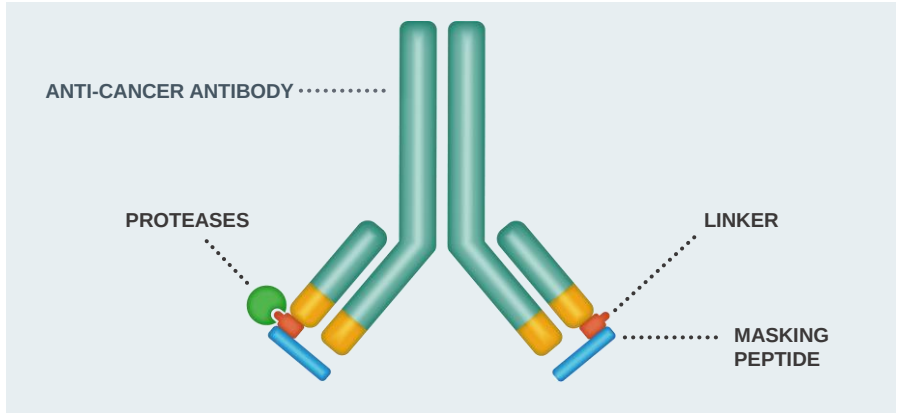
Thistlethwaite F,[1]* Naing A,[2]* Gil-Martin M,[3] LoRusso P,[4] Randhawa M,[5] Eskens F,[6] Sanborn R,[7] Uboha N,[8] Cho D,[9] Spira A,[10] Bondarenko I,[11] Plummer ER,[12] Garcia-Corbacho J,[13] Victoria I[13], Lavernia J,[14] Melero I,[15] de Vries EG,[16] Garner W,[17] Arkenau HT,[18]** Bendell J[19]**

[1]The Christie NHS Foundation Trust and the University of Manchester, Manchester, UK; [2]The University of Texas MD Anderson Cancer Center, Houston, TX; [3]Insitut Català d'Oncologia-IDIBELL, Hospital Duran I Reynals, Barcelona, Spain; [4]Yale University School of Medicine, New Haven, CT; [5]Beatson West of Scotland Cancer Centre, Glasgow, Scotland, UK; [6]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [7]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR; [8]University of Wisconsin, Carbone Cancer Center, Madison, WI; [9]NYU Clinical Cancer Center, New York, NY; [10]Virginia Cancer Specialists, Fairfax, VA; [11]Dnipropetrovsk State Medical Academy, Oblast, Ukraine; [12]Newcastle University, Newcastle, UK; [13]Hospital Clinic Barcelona, Barcelona, Spain; [14]Instituto Valenciano de Oncologia, Valencia, Spain; [15]Clinica Universidad de Navarra, Pamplona, Spain; [16]University Medical Center Groningen, Groningen, Netherlands; [17]CytomX Therapeutics, Inc, South San Francisco, CA; [18]Sarah Cannon Research Institute UK Limited, London, UK; [19]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN

*Co-Lead authors
**Co-Senior authors

CX-072: An Anti-PD-L1 Probody Therapeutic Designed to Reduce Immune-related Adverse Events

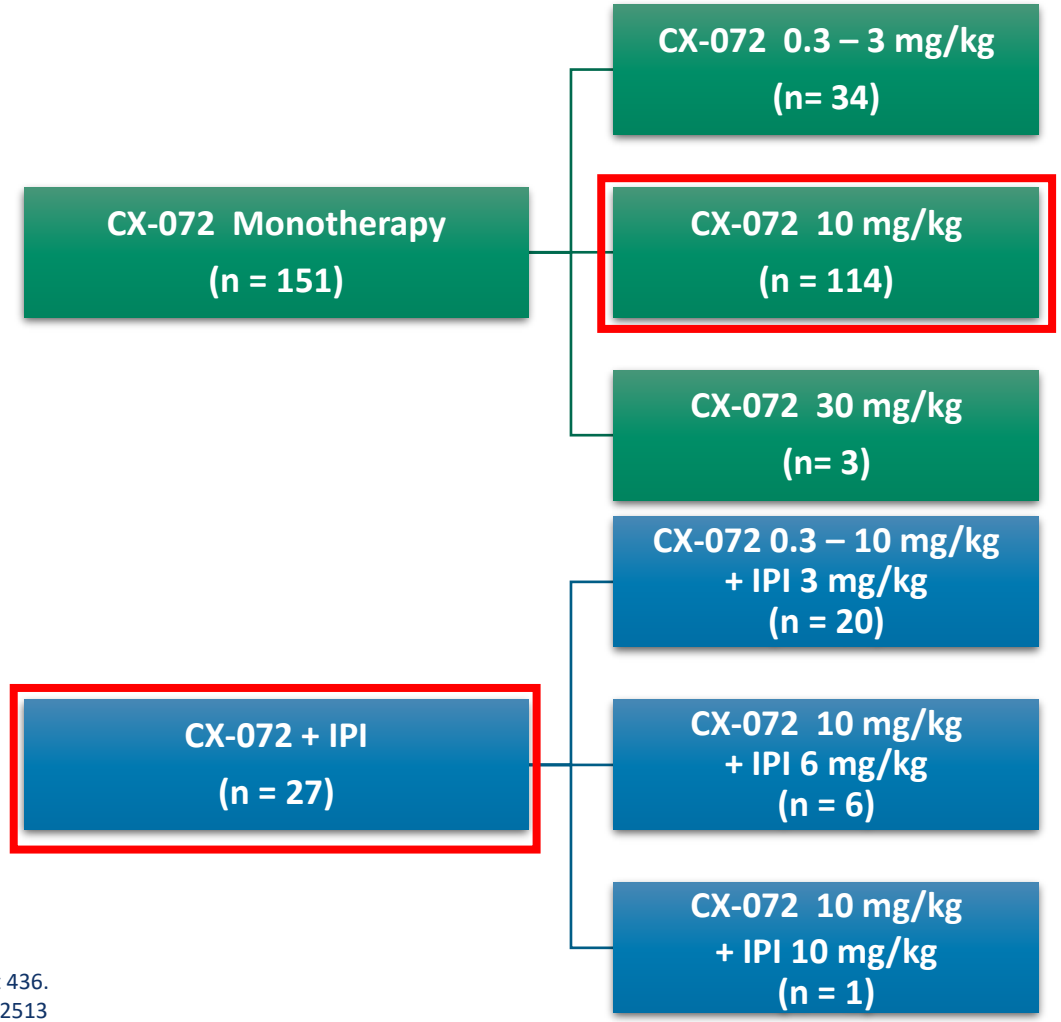
- Probody therapeutics are recombinant antibody prodrugs designed to remain inactive in healthy tissue, and activated in the tumor microenvironment by tumor-associated proteases[1]
- CX-072 is an investigational Probody therapeutic directed against PD-L1, designed to show potent anti-cancer effects with reduced immune-related adverse events
- Translational evidence of CX-072 localization and activation in solid tumors is separately presented in ASCO poster 3108



1. Desnoyers LR et al. Sci Transl Med. 2013;5:207ra144

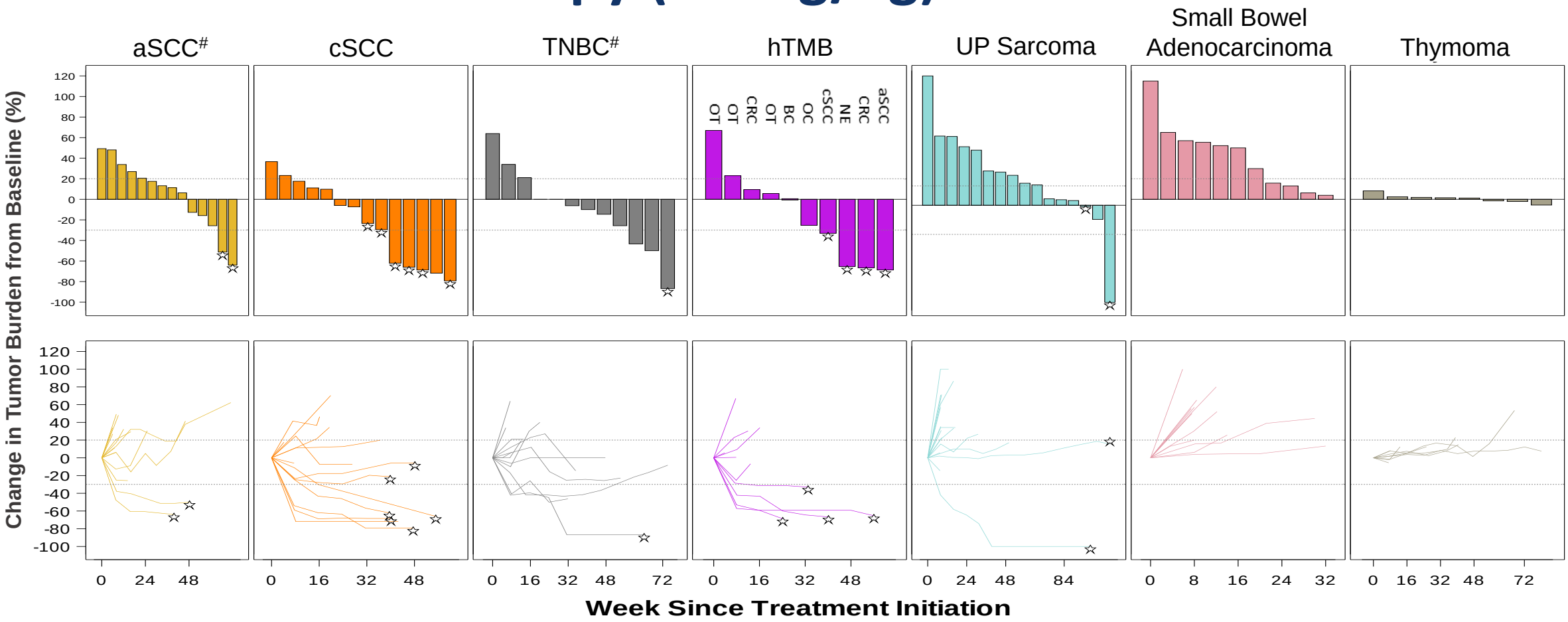
CX-072 Clinical Trial Design

- Phase 1: monotherapy q2w[1-2]
  - CX-072 0.03 – 30 mg/kg (MTD was not reached)
- Phase 1: combination with ipilimumab (IPI)[3-4]
  - MTD was CX-072 10 mg/kg + IPI 3 mg/kg
- Phase 2 (monotherapy)[5]: CX-072 10 mg/kg q2w
  - Anal squamous cell carcinoma (aSCC)
  - Cutaneous squamous cell carcinoma (cSCC)
  - Triple negative breast cancer (TNBC)
  - Small bowel adenocarcinoma (SBA)
  - Undifferentiated pleomorphic sarcoma (UPS)
  - High tumor mutational burden (hTMB)[6]
  - Thymoma or thymic cancers



1. Autio, Arkenau, O'Neil et al. ASCO 2018, Abstract 3071
2. Boni, Garcia-Corbacho, Ott et al, ESMO 2018, Abstract 435
3. Sanborn, Menke, Autio et al. ASCO 2018. Abstract 3072
4. Plummer, Sanborn, DeVries et al. ESMO 2018, Abstract 436.
5. Naing, Thistlethwaite, Spira et al. ASCO 2019, Abstract 2513
6. hTMB status as assessed locally

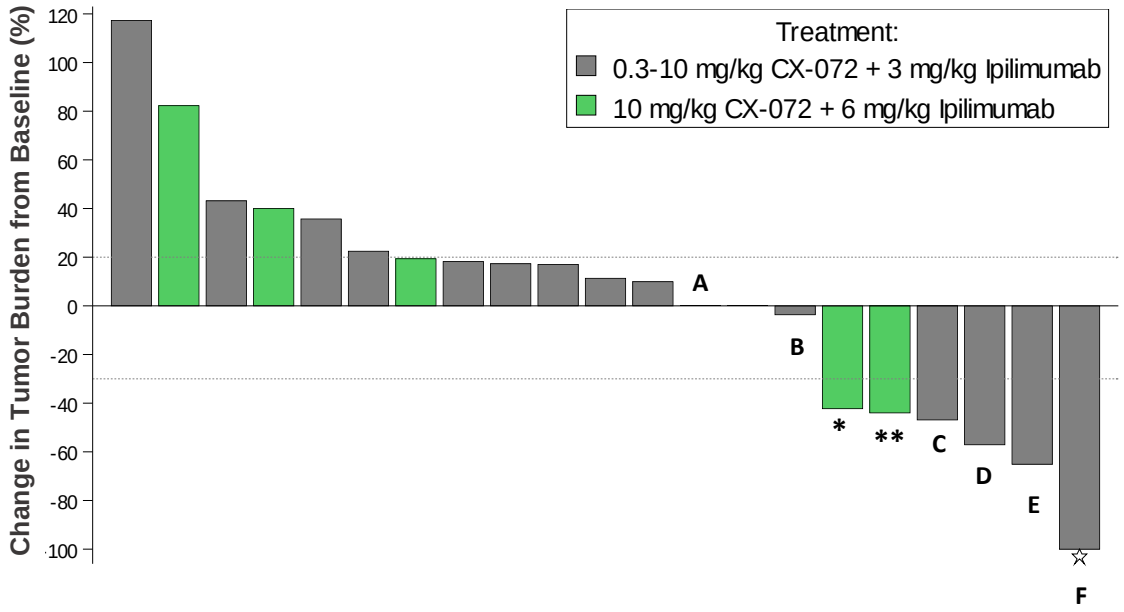
Activity Observed in IO-Responsive Tumors: CX-072 Monotherapy (10 mg/kg)

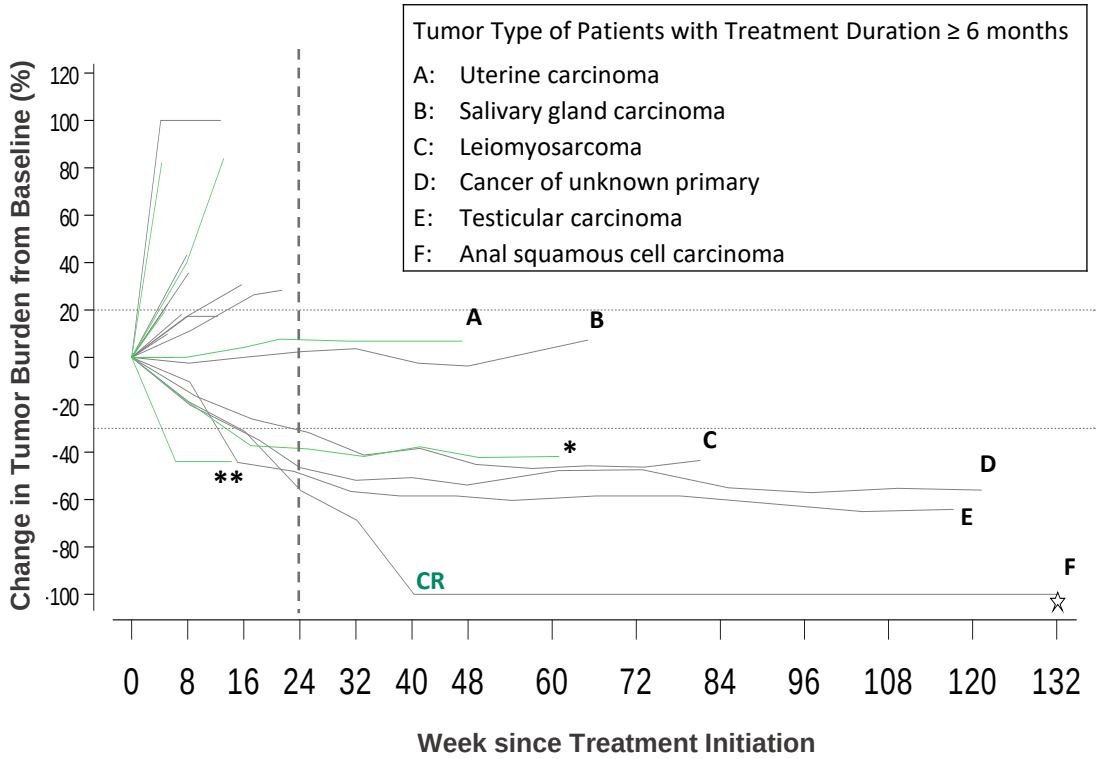


☆ Denotes patient considered to be on treatment as of data cut-off date; evaluable patients include those in the safety population with post-baseline response assessment. # Includes all evaluable patients from dose escalation at 10 mg/kg (n=2, TNBC and anal SCC) and dose expansion. aSCC: anal squamous cell carcinoma, cSCC: cutaneous squamous cell carcinoma, TNBC: triple-negative breast cancer, hTMB: high tumor mutational burden; UP: undifferentiated pleiomorphic, CRC: colorectal cancer, NE: neuroendocrine carcinoma, OC: ovarian cancer, BC: breast cancer, OT: other tumor type

Data cutoff: 20-Apr-2020

Activity Observed in Phase 1 Dose Escalation Unselected Patients Treated with CX-072 + Ipilimumab





☆Denotes patient considered to be on treatment as of data cut-off date; evaluable patients include those in the safety population with post-baseline response assessment.
* Patient with cervical cancer discontinued due to adverse event on day 43, but continued to have stable disease on follow-up tumor scans
** Patient with mesothelioma
CR: complete response

Data cutoff: 20-Apr-2020

CX-072 Chronic Administration: Tolerability

- CX-072 in the phase 1 trial performed as designed:
  - Circulating predominantly in the intact form[1]
  - Activated in tumor tissues at high levels (with >98% receptor occupancy at doses of ≥ 3 mg/kg)[1]
  - Demonstrated anticancer activity in both PD-1 sensitive and insensitive tumors[2-4]
  - Favorable toxicity profile, including in combination with ipilimumab administered at doses ≥ 3 mg/kg[3-4]

- Preliminary results from Phase 2 monotherapy were previously reported in 72 patients[5]

- This presentation will investigate toxicity observed upon chronic administration
  - 34 of 114 patients received CX-072 monotherapy (10 mg/kg) for ≥ 6 months
  - 6 of 27 patients received CX-072 (various dose levels) plus ipilimumab (3 or 6 mg/kg) for ≥ 6 months

1. Lyman et al. SITC Annual Meeting, 2018 Abstract 87
2. Boni, Garcia-Corbacho, Ott et al, ESMO 2018, Abstract 435
3. Sanborn, Menke, Autio et al. ASCO 2018. Abstract 3072
4. Plummer, Sanborn, DeVries et al. ESMO 2018, Abstract 436.
5. Naing, Thistlethwaite, Spira et al. ASCO 2019, Abstract 2513

Demographics

Majority of patients enrolled had low or no tumor expression of PD-L1

	CX-072 10 mg/kg < 6 months (n=80)	CX-072 10 mg/kg ≥ 6 months (n=34)	CX-072 + IPI < 6 months (n=21)	CX-072 + IPI ≥ 6 months (n=6)
Age – median (min, max)	59.5 (32, 83)	63.5 (32, 83)	56 (28, 70)	54.5 (39, 68)
Sex – Male / Female, %	39 / 61	41 / 59	43 / 57	33 / 67
# prior cancer treatments – median (min, max)	2.5 (0, 12)	2 (0, 5)	3 (1, 10)	4 (1, 4)
Baseline ECOG – 0 / 1, %	31 / 69	56 / 44	43 / 57	33 / 67
PD-L1 status, %				
High expression	15.0	29.4	4.8	0
Low expression	30.0	32.4	19.0	16.7
No expression	50.0	26.5	52.4	66.7
Unknown / NE	3.8 / 1.3	11.8 / 0	19.0 / 4.8	16.7 / 0
Tumor Types, n (%)				
Undifferentiated pleiomorphic sarcoma	16 (20)	4 (11.8)	0	0
TNBC	10 (12.5)	5 (14.7)	1 (4.8)	0
Anal SCC	10 (12.5)	5 (14.7)	0	1 (16.7)
Cutaneous SCC	6 (7.5)	8 (23.5)	0	0
Small bowel adenocarcinoma	13 (16.3)	1 (2.9)	0	0
Thymoma or thymic cancers	6 (7.5)	4 (11.8)	0	0
hTMB	8 (10.0)	2 (5.9)	0	0
Other	11 (13.8)	5 (14.7)	20 (95.2)	5 (95.2)

Data cutoff: 20-Apr-2020

Exposure

Long-term exposure to CX-072 was observed in both monotherapy and following combination treatment with ipilimumab

	CX-072 10 mg/kg < 6 months (n=80)	CX-072 10 mg/kg ≥ 6 months (n=34)	CX-072 + IPI < 6 months (n=21)	CX-072 + IPI ≥ 6 months (n=6)
Number of CX-072 Doses Administered, n (%)				
<=5	55 (68.8)	0	19 (90.5)	0
6-15	25 (31.3)	4 (11.8)	2 (9.5)	0
16-25	0	16 (47.1)	0	2 (33.3)
>25	0	14 (41.2)	0	4 (66.7)
Median doses of CX-072 administered (min, max)	4 (1, 13)	23 (12, 55)	2 (1, 8)	42 (21, 72)
Median duration of CX-072 exposure in months (min, max)	1.8 (0.5, 6.0*)	11.3 (6.2, 26.2)	1.2 (0.5, 4.9)	21.3 (11.3, 34.1)
Number of Ipilimumab Doses Administered, n (%)				
1	NA	NA	6 (28.6)	0
2	NA	NA	7 (33.3)	0
3	NA	NA	5 (23.8)	1 (16.7)
4	NA	NA	3 (14.3)	5 (83.3)
Median doses of ipilimumab administered (min, max)	NA	NA	2 (1, 4)	4 (3, 4)

* Two subject's treatment durations were 5.98 months

Data cutoff: 20-Apr-2020

Adverse Event (AE) Overview

Treatment related grade 3+ adverse event and immune-related adverse event rates were low

	CX-072 10 mg/kg < 6 months (n=80)	CX-072 10 mg/kg ≥ 6 months (n=34)	CX-072 + IPI < 6 months (n=21)	CX-072 + IPI ≥ 6 months (n=6)
Treatment-Emergent AE (TEAE), n (%)	78 (97.5)	33 (97.1)	20 (95.2)	6 (100.0)
Related to CX-072	36 (45.0)	30 (88.2)	17 (81.0)	6 (100.0)
TEAE Grade 3+, n (%)	45 (56.3)	16 (47.1)	13 (61.9)	5 (83.3)
Related to CX-072	8 (10.0)	2 (5.9)	7 (33.3)	2 (33.3)
TEAE Leading to CX-072 Discontinuation, n (%)	3 (3.8)	1 (2.9)	3 (14.3)	0
Related to CX-072	2 (2.5)	0	3 (14.3)	0
Serious TEAE, n (%)	24 (30.0)	17 (50.0)	10 (47.6)	3 (50.0)
Related to CX-072	4 (5.0)	2 (5.9)	7 (33.3)	1 (16.7)
Related to Ipilimumab	NA	NA	6 (28.6)	1 (16.7)
TEAE Leading to Death, n (%)	1 (1.3)	0	0	0
Related to CX-072	0	0	0	0
Immune-related Adverse Events (irAEs), n (%)	9 (11.3)	7 (20.6)	11 (52.4)	5 (83.3)
Grade 3+	2 (2.5)	0	6 (28.6)	0

Data cutoff: 20-Apr-2020

All Grade Treatment Related AE (>10% mono; >20% combo)

	CX-072 10 mg/kg < 6 months (n=80)	CX-072 10 mg/kg ≥ 6 months (n=34)	CX-072 + IPI < 6 months (n=21)	CX-072 + IPI ≥ 6 months (n=6)
Subjects with at least one Related TEAE, n (%)	**36 (45.0)**	**30 (88.2)**	**17 (81.0)**	**6 (100.0)**
Fatigue	9 (11.3)	9 (26.5)	2 (9.5)	3 (50.0)
Aspartate aminotransferase (AST) increased	8 (10.0)	7 (20.6)	5 (23.8)	1 (16.7)
Alanine aminotransferase (ALT) increased	7 (8.8)	5 (14.7)	3 (14.3)	2 (33.3)
Rash	4 (5.0)	5 (14.7)	1 (4.8)	1 (16.7)
Arthralgia	3 (3.8)	5 (14.7)	1 (4.8)	1 (16.7)
Decreased appetite	3 (3.8)	5 (14.7)	1 (4.8)	1 (16.7)
Lipase increased	1 (1.3)	4 (11.8)	0	2 (33.3)
Amylase increased	1 (1.3)	2 (5.9)	2 (9.5)	2 (33.3)
Infusion related reaction	7 (8.8)	4 (11.8)	3 (14.3)	1 (16.7)
Nausea	2 (2.5)	3 (8.8)	7 (33.3)	2 (33.3)
Pruritus	2 (2.5)	3 (8.8)	8 (38.1)	1 (16.7)
Anemia	0	4 (11.8)	1 (4.8)	0

Data cutoff: 20-Apr-2020

Treatment Related Grade 3+ AE (≥ 1 patient)

Grade 3+ events were uncommon

	CX-072 10 mg/kg < 6 months (n=80)	CX-072 10 mg/kg ≥ 6 months (n=34)	CX-072 + IPI < 6 months (n=21)	CX-072 + IPI ≥ 6 months (n=6)
Subjects with at least one Related Grade 3+ TEAE, n (%)	**8 (10.0)**	**2 (5.9)**	**7 (33.3)**	**2 (33.3)**
Colitis	0	0	2 (9.5)**	0
GGT increased	2 (2.5)	0	0	0
Aspartate transferase increased	1 (1.3)	0	1 (4.8)	0
Alanine transferase increased	0	0	1 (4.8)**	0
Transaminases increased	0	0	1 (4.8)	0
Lipase increased	1 (1.3)	1 (2.9)*	0	1 (16.7)*
Amylase increased	0	0	0	1 (16.7)*
Diarrhea	0	0	1 (4.8)	0
Pneumonitis	0	0	1 (4.8)**	0
Dyspnea	0	0	1 (4.8)**	0
Guillain Barré syndrome	0	0	1 (4.8)	0
Hyponatremia	0	0	0	1 (16.7)*
Rash Maculopapular	1 (1.3)	0	0	0
Hypoxia	0	0	1 (4.8)**	0
Infusion related reaction	0	0	1 (4.8)	0
Neutropenia	0	0	1 (4.8)	0
Enterocutaneous fistula	0	1 (2.9)*	0	0
Fatigue	1 (1.3)	0	0	0
Hypertension	1 (1.3)	0	0	0
Myocarditis	1 (1.3)	0	0	0

* Events reported during first 6 months of treatment

** One patient was treated with CX-072 0.3mg/kg + IPI 3 mg/kg

Data cutoff: 20-Apr-2020

Immune-related AE (≥ 2 patients or ≥ 1 patient for Grade 3+)

Rates were low across all groups and no Grade 3+ events were reported in long-term patients

	CX-072 10 mg/kg < 6 months (n=80)		CX-072 10 mg/kg ≥ 6 months (n=34)		CX-072 + IPI < 6 months (n=21)		CX-072 + IPI ≥ 6 months (n=6)	
	All Grade	Grade 3+	All Grade	Grade 3+	All Grade	Grade 3+	All Grade	Grade 3+
Subjects with at least one irAE, n (%)	**9 (11.3)**	**2 (2.5)**	**7 (20.6)**	**0**	**11 (52.4)**	**6 (28.6)**	**5 (83.3)**	**0**
Alanine aminotransferase increased	3 (3.8)	0	1 (2.9)	0	0	0	0	0
Aspartate aminotransferase increased	3 (3.8)	0	2 (5.9)	0	1 (4.8)	0	0	0
Transaminases increased	0	0	0	0	1 (4.8)	1 (4.8)	0	0
Hypothyroidism	2 (2.5)	0	2 (5.9)	0	1 (4.8)	0	1 (16.7)	0
Rash	2 (2.5)	0	1 (2.9)	0	0	0	3 (50.0)	0
Rash maculo-papular	2 (2.5)	1 (1.3)	0	0	3 (14.3)	0	1 (16.7)	0
Pruritus	0	0	0	0	3 (14.3)	0	1 (16.7)	0
Colitis	0	0	0	0	2 (9.5)	2 (9.5)**	0	0
Diarrhea	0	0	0	0	2 (9.5)	1 (4.8)*	0	0
Hyperthyroidism	0	0	0	0	1 (4.8)	0	1 (16.7)	0
Pneumonitis	0	0	0	0	1 (4.8)	1 (4.8)**	0	0
Myocarditis	1 (1.3)	1 (1.3)	0	0	0	0	0	0
Neutropenia	0	0	0	0	1 (4.8)	1 (4.8)*	0	0
Guillain-Barré syndrome	0	0	0	0	1 (4.8)	1 (4.8)	0	0

* Events reported in the same patient

** One patient was treated with CX-072 0.3mg/kg + IPI 3 mg/kg

Data cutoff: 20-Apr-2020

Conclusions

- Consistent with other checkpoint inhibitors, CX-072 showed highly durable objective responses
- CX-072 was well tolerated alone or in combination with ipilimumab administered at doses ≥3 mg/kg
  - irAEs including pneumonitis, hepatitis, colitis, rash, and endocrinopathies were infrequently observed
- Long term patients experienced fewer irAEs and had no grade 3+ irAEs suggesting that tolerability early on can impact duration of treatment
- The Probody platform, applied to PD-L1, appears to work as designed by limiting irAEs and potentially improving the durability of response

Acknowledgements

- We would like to extend our grateful thanks to our co-investigators, their research personnel, and colleagues at CytomX Therapeutics and MedPace.

- Our sincere thanks to all patients and their caregivers who took part in this clinical trial.

Acknowledgements

Hendrik-Tobias Arkenau	Sarah Cannon Research Institute UK Limited
Karen Autio	Memorial Sloan Kettering Cancer Center
Johanna Bendell	Sarah Cannon Research Institute
Igor Bondarenko	Dnipropetrovsk State Medical Academy
Valentina Boni	Centro Integral Oncologico Clara Campal
Daniel Cho	NYU Medical Oncology Associates
E.G.E. de Vries	Universitair Medisch Centrum Groningen
Greg Durm	Indiana University Melvin and Bren Simon Cancer Center
Anthony El-Khoueiry	University of Southern California - Norris Comprehensive Cancer Center
Ferry Albert Louis Maria Eskens	Erasmus MC Cancer Institute
Jeff Evans	Beatson, West of Scotland Cancer Centre
Jaime Feliu Batlle	Hospital Universitario La Paz
Mary Josephine Fidler	Rush University Medical Center
Javier Garcia-Corbacho	Hospital Clinic de Barcelona
Omid Hamid	The Angeles Clinic
Christopher Hoimes	University Hospitals Cleveland Medical Center
Marta Gil-Martin	Instituto Catalan de Oncologia - Hospital Duran I Reynals
Javier Lavernia	Instituto Valenciano De Oncologia
Patricia LoRusso	Yale University School of Medicine - Yale Cancer Center
Ignacio Melero	Clinica Universitaria de Navarra - Pamplona
Catharina Wilhelmina Menke-Van der Houven van Oordt	Amsterdam UMC - Locatie VUmc
Aung Naing	MD Anderson Cancer Center
Bert O'Neil	Indiana University Melvin and Bren Simon Cancer Center
Patrick Ott	Dana-Farber Cancer Institute
Ruth Plummer	Freeman Hospital/Northern Centre for Cancer Care
Manreet Randhawa	Beatson, West of Scotland Cancer Centre
Rachel Sanborn	Earle A. Chiles Research Institute, Providence Cancer Institute
Erlene Seymour	Barbara Ann Karmanos Cancer Institute
Alexander Spira	Virginia Cancer Care Specialist
James Strauss	Mary Crowley Cancer Research Centers
Fiona Thistlethwaite	Cancer Research UK, Department of Medical Oncology-The Christie NHS Foundation Trust
Nataliya Uboha	University Of Wisconsin Carbone Cancer Center
Amy Weise	Barbara Ann Karmanos Cancer Institute
Jerzy Wydmanski	NZOZ Vegamed