ANNUAL MEETING ON WOMENS' CANCER®

BUILDING BRIDGES // BREAKING BARRIERS

SGO // PHOENIX, ARIZONA // MARCH 19 – 22, 2022

LIO-1: Initial Phase 2 Experience of Lucitanib + Nivolumab in Patients With Metastatic or Recurrent Cervical Cancer (NCT04042116; ENGOT-GYN3/AGO/LIO)

Ana Oaknin,[1] Floor J. Backes,[2] Els Van Nieuwenhuysen,[3] Ramez N. Eskander,[4] Antonio González-Martín,[5] Vicky Makker,[6] Christian Marth,[7] Manish Patel,[8] Richard T. Penson,[9] Andrés Redondo,[10] Maria Jesús Rubio Pérez,[11] Erika Hamilton,[12] Nicole Concin,[7,13] Alex McNees,[14] Kenton Wride,[14] Denise Lepley,[14] Rachel Dusek,[14] Terri Cameron,[15] Sandro Pignata[16]

[1]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [2]Ohio State University Wexner Medical Center and James Cancer Hospital, Columbus, OH, USA; [3]Campus Gasthuisberg, University Hospitals Leuven, Leuven, Belgium; [4]UC San Diego Moores Cancer Center, La Jolla, CA, USA; [5]GEICO and Clínica Universidad de Navarra, Madrid, Spain; [6]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical Center, New York, NY, USA; [7]Medical University of Innsbruck, Innsbruck, Austria; [8]Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL, USA; [9]Massachusetts General Hospital, Boston, MA, USA; [10]GEICO and Hospital Universitario La Paz, Madrid, Spain; [11]GEICO and University Hospital Universitario Reina Sofia, Cordoba, Spain; [12]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [13]Evang. Kliniken Essen-Mitte, Essen, Germany; [14]Clovis Oncology, Inc., Boulder, CO, USA; [15]Clovis Oncology UK Ltd., Cambridge, UK; [16]Istituto Nazionale Tumori - Fondazione "G. Pascale" - Napoli, Naples, Italy

ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 19 – 22, 2022

SGO Society of Gynecologic Oncology

Presenting Author Disclosures

- Advisory boards: Clovis Oncology, Agenus, AstraZeneca, Corcept Therapeutics, Deciphera Pharmaceuticals, Eisai Europe Limited, EMD Serono, F. Hoffmann-La Roche, GlaxoSmithKline, ImmunoGen, KL Logistics, Medison Pharma, Merck Sharp & Dohme de España, Mersana Therapeutics, Novocure GmbH, PharmaMar, prIME Oncology, Roche Farma, Sattucklabs, and Sutro Biopharma
- Support for travel or accommodation: Clovis Oncology, AstraZeneca, PharmaMar, and Roche
- Institutional research grant support: Clovis Oncology, AbbVie Deutschland Gmbh & Co Hg, Ability Pharmaceuticals, Advaxis, Agenus, Aprea Therapeutics AB, AstraZeneca AB, BeiGene USA, Belgian Gynaecological Oncology Group (BGOG), Bristol-Myers Squibb International Corporation (BMS), Corcept Therapeutics, Eisai, F. Hoffmann-La Roche, ImmunoGen, Iovance Biotherapeutics, Lilly, MedImmune, Merck Healthcare, Merck Sharp & Dohme, Millennium Pharmaceuticals, Mundipharma Research, Novartis Farmacéutica, Regeneron Pharmaceuticals, Seagen, Seattle Genetics, Sutro Biopharma, Tesaro, and Verastem

Unlabeled/Investigational Uses

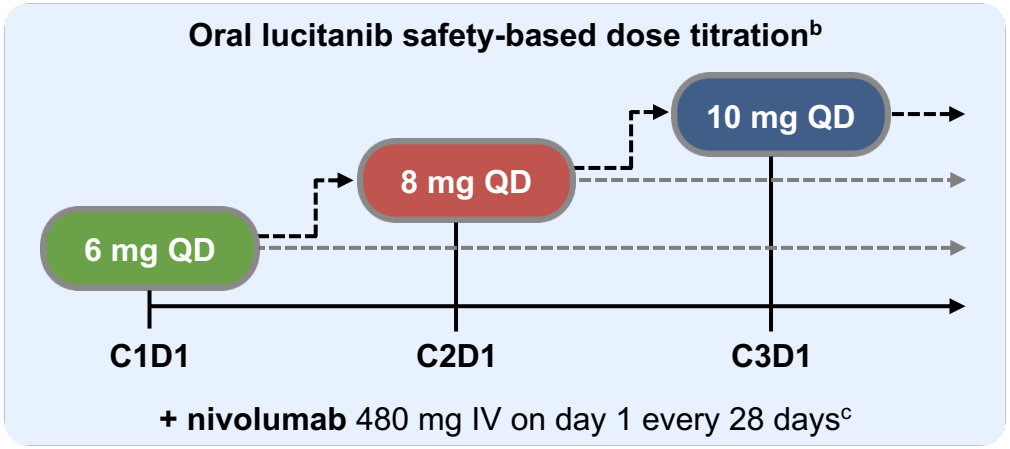
- I will be discussing unlabeled or investigational uses of lucitanib + nivolumab in patients with cervical cancer

Introduction

- Lucitanib is a potent, selective inhibitor of tyrosine kinases including VEGFR1–3, PDGFRα/β, and FGFR1–3[1]
- Tumor-secreted proangiogenic growth factors promote generation of new blood vessels and mediate immunosuppression, which may dampen the effect of immune checkpoint inhibitors. Therefore, inhibiting angiogenesis with a TKI may relieve immunosuppression and enhance PD-(L)1 inhibitor efficacy[2,3]
- **LIO-1 is a phase 1/2 study investigating lucitanib + the PD-1 inhibitor nivolumab. Here, we present data from stage 1 of the phase 2 cervical cancer cohort**

Phase 2: Advanced, recurrent, or metastatic gynecological tumors – Simon 2-stage design

- Endometrial cancer[a] N up to 22–41
- **Cervical cancer N up to 22–40**
- Ovarian cancer[a] N up to 22–40
- Clear-cell ovarian/ endometrial cancer N up to 22–40



Primary endpoint
Investigator-assessed confirmed best ORR by RECIST

[a]Excluding clear-cell histology. [b]Lucitanib treatment until PD, unacceptable toxicity or other reason for discontinuation. [c]Nivolumab treatment for up to 24 months or until PD, unacceptable toxicity or other reason for discontinuation. C, cycle; D, day; FGFR1–3, fibroblast growth factor receptors 1–3; IV, intravenous; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death receptor 1; PDGFR, platelet-derived growth factor receptors; PD-L1, programmed cell death ligand 1; QD, once daily; RECIST, Response Evaluation Criteria In Solid Tumors version 1.1; TKI, tyrosine kinase inhibitor; VEGFR1–3, vascular endothelial growth factor receptors 1–3.

1. Bello et al. *Cancer Res*. 2011;71:1396-405. 2. Fukumura et al. *Nat Rev Clin Oncol*. 2018;15:325-40. 3. Khan et al. *Nat Rev Clin Oncol*. 2018;15:310-24.

ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 19 - 22, 2022
SGO Society of Gynecologic Oncology

Key Eligibility Criteria and Baseline Characteristics: LIO-1 Cervical Cancer Cohort

- Key eligibility criteria for cervical cancer cohort:
  - Metastatic or recurrent cervical cancer
  - ≥1 prior regimen of platinum-based chemotherapy, with or without bevacizumab, for metastatic or recurrent disease
  - No prior VEGFR-TKI, or PD-(L)1 inhibitor allowed
  - Measurable disease
  - ECOG PS 0 or 1
  - Fresh biopsy or sufficient archival tumor tissue

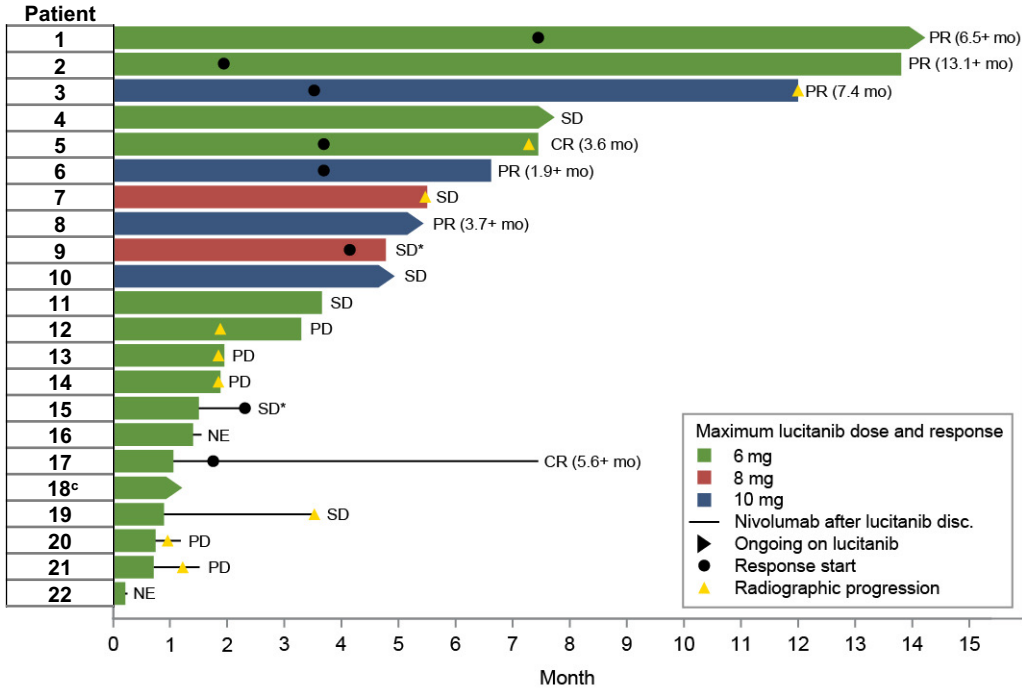
Characteristic	N=22
Age, median years (range)	54.0 (36.0–77.0)
ECOG PS 0, n (%)	10 (45.5)
Histology, n (%)	
Squamous	10 (45.5)
Adenocarcinoma (including mucinous)	10 (45.5)
Adenosquamous	2 (9.1)
Number of prior anticancer regimens, n (%)	
1	9 (40.9)
2	10 (45.5)
3	3 (13.6)
Prior bevacizumab, n (%)	10 (45.5)

- **Primary endpoint:** investigator-assessed confirmed best ORR by RECIST

Data cutoff: January 10, 2022. ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, objective response rate; PD-1, programmed cell death receptor 1; PD-L1, programmed cell death ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors, version 1.1; TKI, tyrosine kinase inhibitor; VEGFR, vascular endothelial growth factor receptor.

Lucitanib + Nivolumab: Investigator-Assessed Tumor Response and Time on Treatment

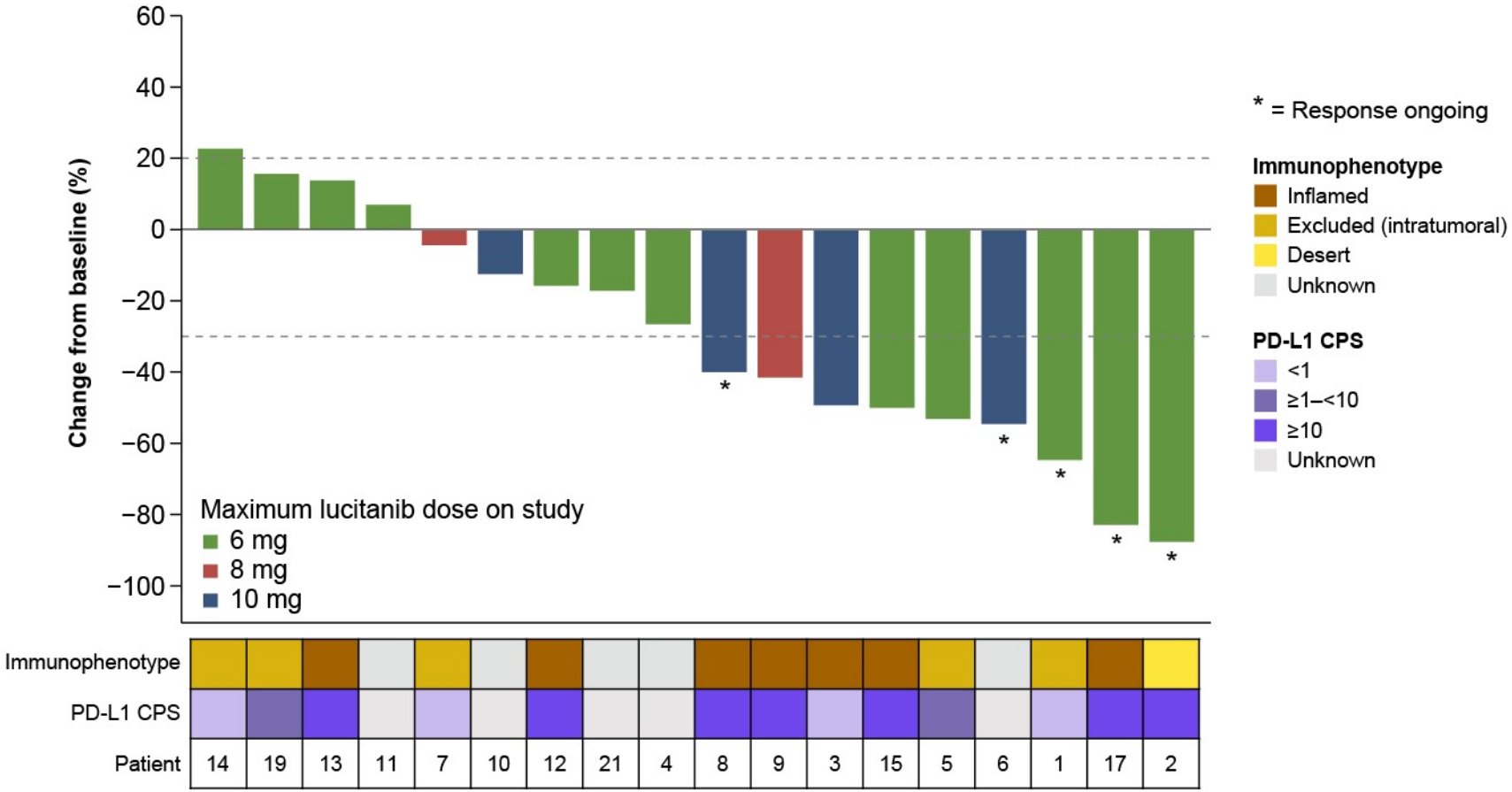
	N=22
Confirmed RECIST ORR, n (%) [95% CI]	**7 (31.8) [13.9–54.9]**
CR[a]	2 (9.1)
PR[b]	5 (22.7)
SD	7 (31.8)
PD	5 (22.7)
NE[c]	2 (9.1)



- Median (range) treatment duration was 4.2 (0.3–13.9) months
- Response duration ranged from 1.9+ to 13.1+ months
  - 6/7 responders had duration of response ≥3 months; 4/7 responders had received prior bevacizumab
- 3/22 responses were required to proceed to stage 2

Data cutoff: January 10, 2022. [a]Both patients received a maximum dose of lucitanib 6 mg. [b]2 received a maximum dose of lucitanib 6 mg and 3 received lucitanib 10 mg. [c]1 additional patient was ongoing but had no post-baseline scans at the time of data cutoff. *Unconfirmed PR. Values shown represent duration of confirmed response; ongoing responses are indicated with a +. A gap between lucitanib dosing and PD occurs when lucitanib was discontinued prior to PD. Patients may have stayed on nivolumab until PD occurred. Two patients who achieved a CR each had 2 target lesions in lymph nodes with measurements <10 mm (ie, nonpathological per RECIST). CR, confirmed complete response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors version 1.1; SD, stable disease.

Best Change in Sum of Target Lesions from Baseline Following Lucitanib + Nivolumab Treatment



Data cutoff: January 10, 2022. CPS, combined positive score; PD-L1, programmed cell death ligand 1; RECIST, Response Evaluation Criteria In Solid Tumors version 1.1.

Summary of TEAEs in Patients Treated With Lucitanib + Nivolumab

- The only grade ≥3 TEAE considered related to study treatment and reported in ≥2 patients was hypertension[a] (n=5 [22.7%])
- 2 (9.1%) patients reported a TEAE leading to lucitanib dose reduction:
  - Hypertension and proteinuria
- 5 (22.7%) patients and 4 (18.2%) patients reported a TEAE leading to discontinuation of lucitanib or nivolumab, respectively:
  - Lucitanib: hypertension[a], myocarditis, proteinuria, and urogenital fistula
  - Nivolumab: hypertension[a], intestinal obstruction, myocarditis, and thyroiditis
- 5 (22.7%) patients reported a serious TEAE considered related to study treatment:
  - Colonic fistula, hyponatremia, pancreatitis, pelvic infection, and thyroiditis

	N=22	
Most common TEAEs (≥25%), n (%)	**Any-grade**	**Grade ≥3**
Any TEAE	**21 (95.5)**	**17 (77.3)**
Hypertension[a]	16 (72.7)	5 (22.7)
Fatigue[b]	13 (59.1)	0
Decreased appetite	11 (50.0)	0
Nausea	10 (45.5)	0
Diarrhea	9 (40.9)	0
Proteinuria	9 (40.9)	1 (4.5)
Hypothyroidism[c]	8 (36.4)	0
Vomiting	8 (36.4)	1 (4.5)
Abdominal pain	6 (27.3)	1 (4.5)
Anemia	6 (27.3)	2 (9.1)

Data cutoff: January 10, 2022. [a]Hypertension and hypertensive crisis. [b]Asthenia and fatigue. [c]Increased blood thyroid-stimulating hormone and hypothyroidism.
TEAE, treatment-emergent adverse event.

Conclusions

- Encouraging signs of antitumor activity were observed in patients with metastatic or recurrent cervical cancer treated with lucitanib + nivolumab
- Adverse events have been manageable and consistent with those previously reported for lucitanib and nivolumab, and other agents of both classes
- Target lesion reductions were observed in patients without classical biomarkers of response to checkpoint inhibitor therapy (ie, tumors that are PD-L1 negative)
- Stage 2 has completed enrollment; follow-up and additional biomarker analysis continue

PD-L1, programmed cell death ligand 1.

Acknowledgements

We thank all the LIO-1 investigators, and the LIO-1 study patients and their families and caregivers

ENGOT
European Network of Gynaecological Oncological Trial groups

AGO Study Group

Nicole Concin (KEM Evangelical Huyssens-Foundation Hospital)
Christian Marth (Medical University of Innsbruck)
Pauline Wimberger (University Hospital Carl Gustav Carus)

BGOG

Jean-François Baurain (Cliniques Universitairies Saint-Luc)
Els Van Nieuwenhuysen (University Hospitals Leuven)

GEICO
Grupo Español de Investigación en Cáncer de Ovario

Antonio González-Martín (Clínica Universidad de Navarra)
Ana Oaknin (Hospital Universitari Vall d'Hebron)
Andrés Redondo (La Paz University Hospital)
Maria Jesús Rubio-Pérez (Hospital Universitario Reina Sofía)

Multicentre Italian Trials in Ovarian cancer
MITO

Domenica Lorusso (Fondazione Policlinico Universitario)
Sandro Pignata (INT IRCCS-Fondazione G. Pascale)
Claudio Zamagni (Polyclinico S.Orsola-Malpighi)

Jill Alldredge (University of Colorado Cancer Center – Anschutz Medical Campus)
Floor J. Backes (Ohio State University)
Ramez N. Eskander (University of California San Diego)
Camille Gunderson Jackson (University of Oklahoma – Stephenson Cancer Center)
Erika Hamilton (Tennessee Oncology)
Gottfried E. Konecny (University of California Los Angeles)
Vicky Makker (Memorial Sloan Kettering Cancer Center)
Fernanda B. Musa (Swedish Cancer Institute)
Alexander B. Olawaiye (University of Pittsburgh Medical Center)
Manish Patel (Florida Cancer Specialists)
Richard T. Penson (Massachusetts General Hospital)
Bhavana Pothuri (New York University)
Debra Richardson (University of Oklahoma – Stephenson Cancer Center)
Angeles Alvarez Secord (Duke University)

ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 19 - 22, 2022

We thank Jowell Go (Clovis Oncology, Inc.) for clinical operations support.
This study was funded by Clovis Oncology, Inc. Medical writing support and editorial support funded by Clovis Oncology was provided by Shelly Lim and Stephen Bublitz of Ashfield MedComms, an Ashfield Health company.

SGO
Society of Gynecologic Oncology