GOG Partners
Cervical Trials in Progress:
The Checkpoint Era

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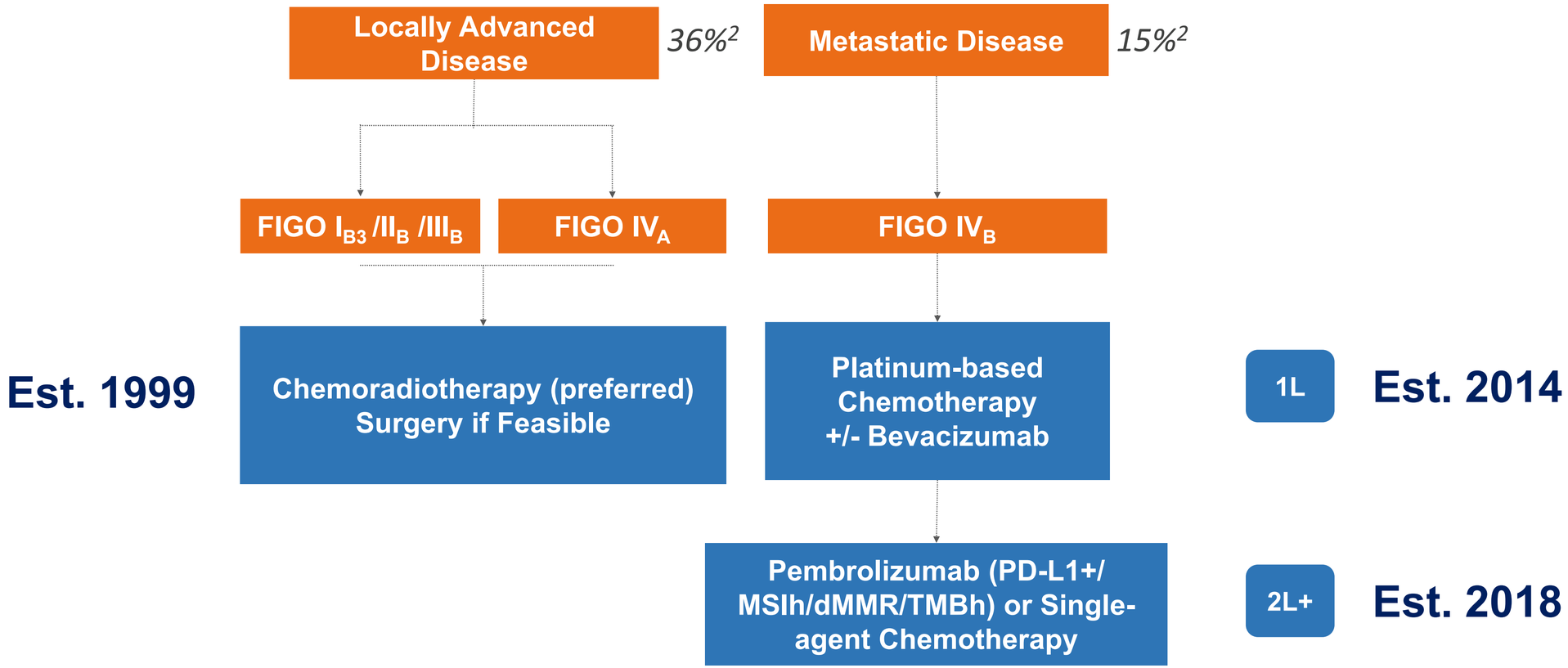
GOG Partners Cervical Cancer Trials in Progress

- **ENGOT Cx-11/GOG-3047/KEYNOTE-A18:** A Randomized, Phase 3, Double-Blind Study of Chemoradiotherapy With or Without Pembrolizumab for the Treatment of High-risk, Locally Advanced Cervical Cancer (US PI: Linda Duska, Co-PI: Ritu Salani)

- **GEICO 68-C/ENGOT Cx10/JGOG1084/GOG-3030:** Bevacizumab and Atezolizumab in Cervical Cancer (BEATcc): A Phase 3, Randomized Study of Chemotherapy and Bevacizumab with or without Atezolizumab for Metastatic, Recurrent, or Persistent Cervical Cancer (US PI: Leslie Randall, Co-PI: Katherine Moxley)

- **RaPiDS (GOG-3028):** A Randomized Phase II Study of Balstilimab (AGEN2034) as Monotherapy or in Combination with Zalifrelimab (AGEN1884) in Second-Line Cervical Cancer (US PI: Dave O'Malley, Co-PI: Camille Gunderson)

Cervical Cancer: Summary of High-Risk Disease Treatment[1]

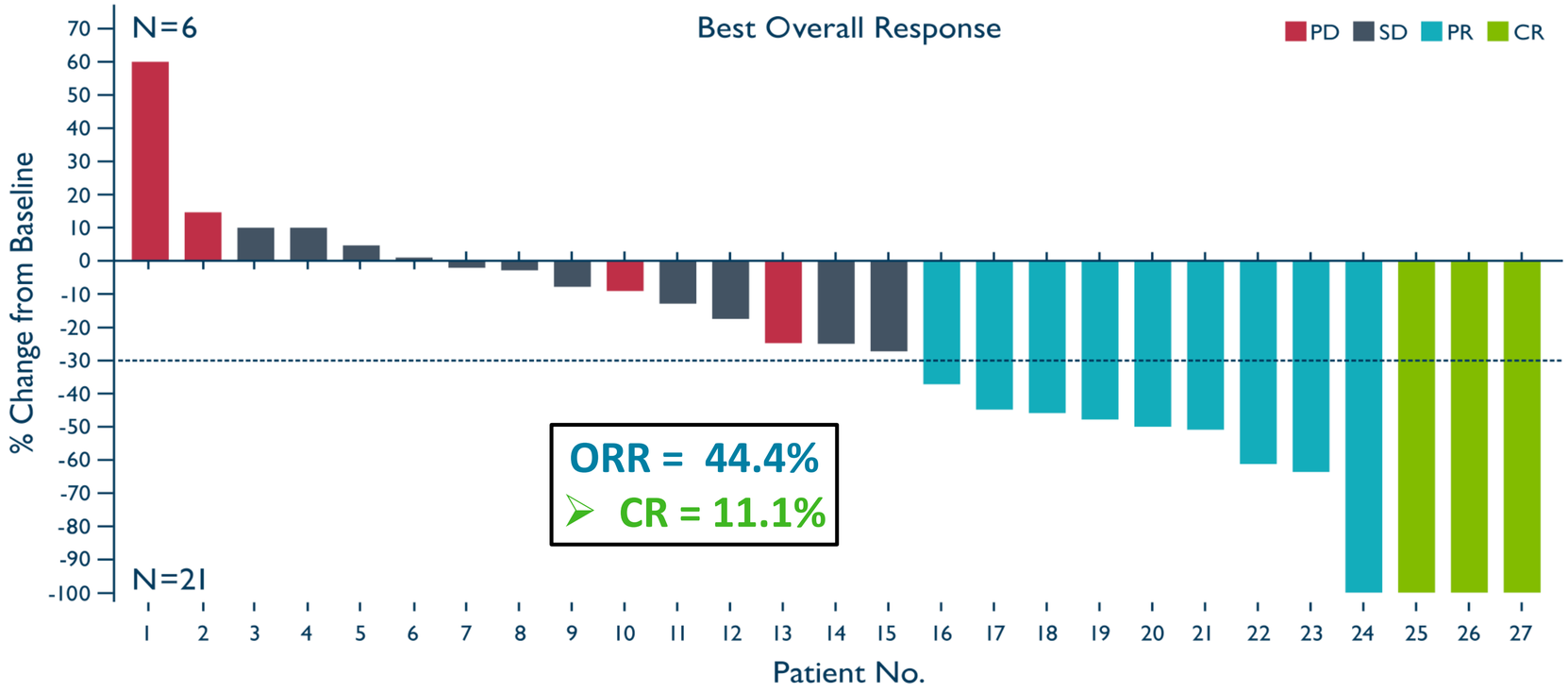


[1] NCCN Cervical Cancer Guidelines v2.2019

[2] SEER Cancer Stat Facts: Cervical Cancer. National Cancer Institute. Bethesda, MD

Autologous TILs (LN-145) 2L+
FDA Breakthrough Designation

Process time: 22 days

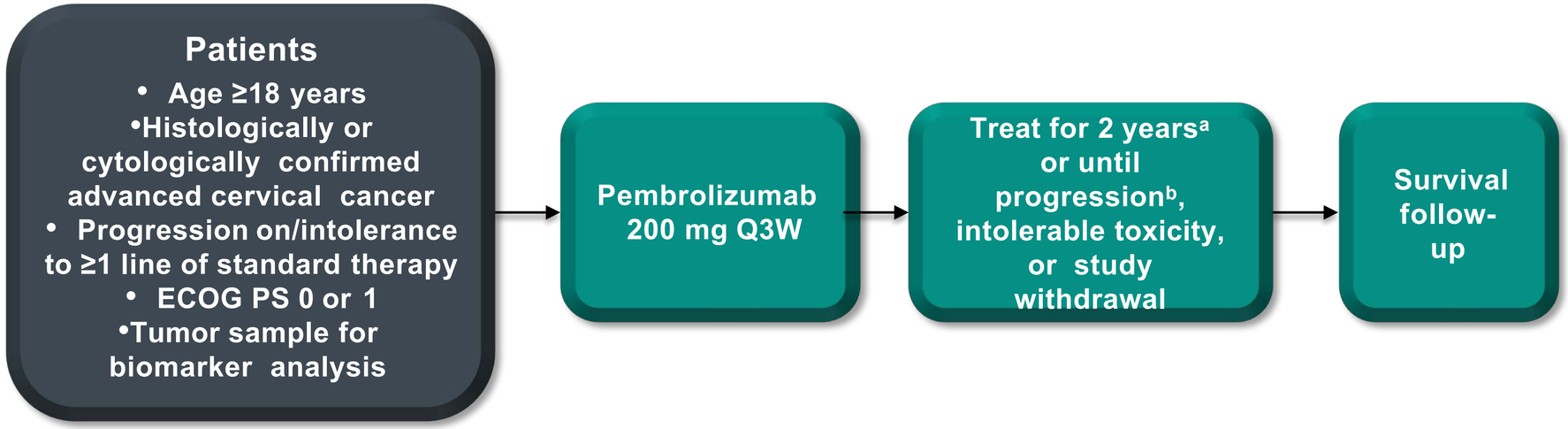


- 78% of patients had a reduction in tumor burden
- Median follow up is 7.4 months
- Mean number of TIL cells infused: 28 x 10^9
- Median number of IL-2 doses administered was 6.0

NCT03108495; Jazaeri AA et al. *J Clin Onc*. 2019;37(15)2538.

KEYNOTE-158: Study Design

- **Ongoing, international, multicohort, open-label, phase 2 study of pembrolizumab in select advanced solid tumors that have progressed on standard-of-care therapy (NCT02628067)**
- **End points**
  - **Primary: ORR (RECIST v1.1, independent central review)**
  - **Secondary: DOR, PFS, OS**



[a]Patients with stable disease or better when pembrolizumab was discontinued and subsequent progressive disease were eligible to resume pembrolizumab for up to 1 year. [b]Clinically stable patients remained on pembrolizumab until progressive disease was confirmed in a second assessment performed ≥4 weeks later. DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; OS, overall survival; ORR, objective response rate; PFS, progression-free survival; Q3W, once every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Summary of Response
(RECIST v1.1, Central Review)

	Overall[a] N = 98	PD-L1 Positive[b] n = 82	PD-L1 Negative[c] n = 15
ORR,[d] % (95% CI)	14.3 (8.0-22.8)	17.1 (9.7-27.0)	0 (0-21.8)
Best overall response, n (%)			
Complete response	5 (5.1)	5 (6.1)	0
Partial response	9 (9.2)	9 (11.0)	0
Stable disease	16 (16.3)	13 (15.9)	3 (20.0)
Progressive disease	55 (56.1)	44 (53.7)	10 (66.7)
Non-evaluable[e]	4 (4.1)	3 (3.7)	1 (6.7)
No assessment[f]	9 (9.2)	8 (9.8)	1 (6.7)

[a]Includes 1 patient with unknown PD-L1 expression level. [b]CPS ≥1. [c]CPS <1. [d]At the time of analysis, all responses were confirmed. [e]Target lesions not captured on ≥1 post-baseline imaging assessment. [f]Post-baseline tumor assessment not performed. Data cutoff date: June 27, 2019.

GOG 3016/ENGOT-cx9: Randomized Phase III Trial of Cemiplimab Versus Investigator's Choice Chemotherapy in Cervical Cancer: "EMPOWER- CERVICAL 1"

Metastatic cervical cancer resistant to platinum-based chemotherapy, ≥ Second-Line (N = 436) ECOG PS 0 or 1

Primary Endpoint is OS

Investigators' choice

Options:

- **Antifolate: Pemetrexed**
- **Nucleoside analogue: Gemcitabine**
- **Topisomerase 1 inhibitor: Topotecan or Irinotecan**
- **Vinca Alkaloid: Vinorelbine**

Cemiplimab

Cemiplimab 350 mg IV every 3 weeks

Statistical Considerations for Study Design	
Power	90%
Median Survival	7 months
Hazard Ratio	0.7
Timing of Final Analysis (Ha)	30.5 months

Accrual completed 5/29/2020

EMPOWER/GOG 3016/ENGOT cx-9
Interim analysis press release 3.15.2021

	Median OS (mos.) Cemiplimab	Median OS (mos.) MD choice chemotherapy	HR (95% CI)
Intent to treat (ITT)	12	8.5	0.69 (0.56-0.84) p<0.001
Squamous cell histology	11	8.8	0.73 (0.58-0.91) p=0.003
Adenocarcinoma histology	13.3	7	0.56 (0.36-0.85) p<0.005
Toxicity-related treatment discontinuations in 8% cemiplimab vs 5% chemotherapy patients.			

https://investor.regeneron.com/news-releases, 3.15.2021

ENGOT cx-11/GOG-3047/KEYNOTE-A18

A Randomized, Phase 3, Double-Blind Study of Chemoradiotherapy With or Without Pembrolizumab for the Treatment of High-risk, Locally Advanced Cervical Cancer

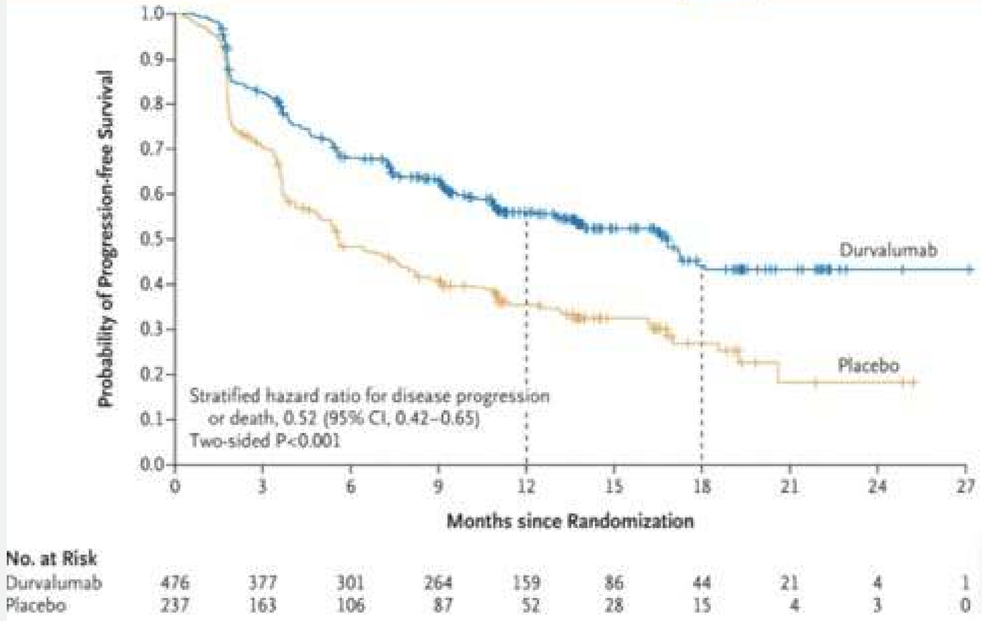
D. Lorusso[1]; Y. Xiang[2]; N. Colombo[3]; R.L. Coleman[4]; L.M. Randall[5]; L. Duska[6]; K. Hasegawa[7]; A. Nogueira Rodrigues[8]; D. Cibula[9]; M. R. Mirza[10]; B. You[11]; A. Oaknin[12]; M. Christiaens[13]; C. Taskiran[14]; J. Sehouli[15]; J. Korach[16]; C. Marth[17]; S. Keefe[18]; M. Puglisi[18]; S. Pignata[19]

ClinicalTrials.gov Identifier: NCT004221945

Sponsor: Merck Sharp & Dohme Corp.

PACIFIC: Phase III Trial of Durvalumab Post-CRT Maintenance for Locally-advanced, Unresectable NSCLC

Study Population	R	Arms	Efficacy Endpoints
• NSCLC Stage 3 Unresectable • Prior ≥2 cycles of platinum-based Tx with concurrent radiation • N= 713	2:1	→ Durvalumab 10 mg/kg IV Q2W up to 12 months Vs → Placebo	**Primary:** PFS, OS **Secondary:** 12 mo PFS, 18 mo PFS, 24 mo OS, ORR, DOR, Time to death, Time to distant metastasis



	Durvalumab	Placebo
No of Events/ No of Patients	214/476	157/237
PFS (95% CI)	16.8 (13-18.1)	5.6 (4.6-7.8)
OS (95% CI)	NR (34.7 –NR)	28.7 (22.9-NR)
12 mo PFS (95% CI)	55.9 (51-60.4)	35.3 (29-41.7)
18 mo PFS (95% CI)	44.2 (37.7-50.5)	27 (19.9-34.5)
24 mo OS (95% CI)	66.3 (61.7-70.4)	55.6 (48.9-61.8)

Antonia et al, NEJM 2017; Antonia et al, NEJM 2018

Duska, et al, SGO 2020: Randomized phase 2 translational study of pembrolizumab during and after CRT

Primary Carcinoma of the Cervix:

Squamous, adenosquamous, adenocarcinoma

Stages IB2-IVA or IB1 wpositive nodes (FIGO 2009)

PET/CT and MRI pelvis

Tissue biopsy and peripheral blood collection

Randomized 1:1

ARM1 (sequential):

CDDP 40 mg/m^2 weekly for 5-6 weeks

Concurrent XRT: EBRT plus brachytherapy

3 cycles of consolidative pembrolizumab: 200 mg every 21 days beginning week 9 for 3 cycles

ARM2 (concurrent):

CDDP 40 mg/m^2 weekly for 5-6 weeks

3 cycles of concurrent pembrolizumab: 200 mg every 21 days beginning day 1 for 3 cycles

Concurrent XRT: EBRT plus brachytherapy

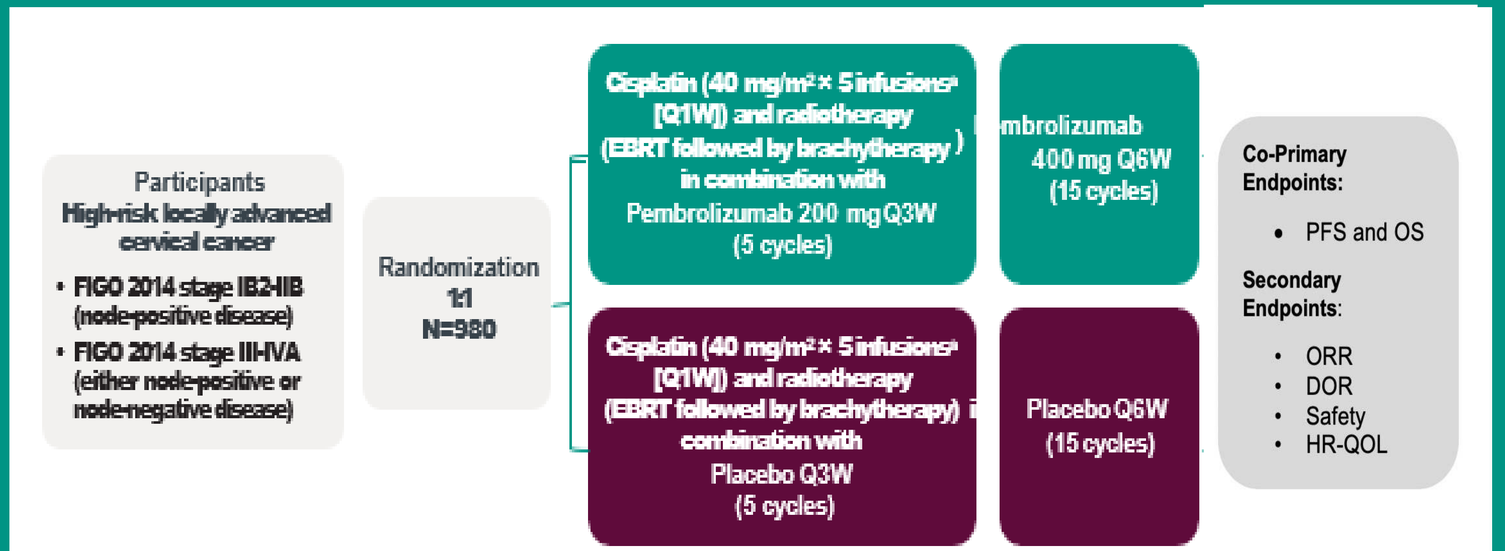
PET/CT required
MRI pelvis (optional)
Tissue biopsy and peripheral blood collection

CRT was SOC per institution, complete in 8 weeks

Duska L, et al. SGO 2020

GOG-3047/KEYNOTE-A18: Schema

Figure 2. ENGOT-cx11/GOG 3047/KEYNOTE-A18 Study Design



EBRT, external beam radiotherapy; FIGO, International Federation of Gynecology and Obstetrics; IMRT, intensity-modulated radiotherapy; OS, overall survival; QnW, every n weeks; VMAT, volumetric-modulated arc therapy. •An optional 6th dose may be administered according to local practice.

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GEICO 68-C/ENGOT Cx10/JGOG1084/GOG-3030:

Bevacizumab and Atezolizumab in Cervical Cancer (BEATcc):

A Phase 3, Randomized Study of Chemotherapy and Bevacizumab with or without Atezolizumab for Metastatic, Recurrent, or Persistent Cervical Cancer

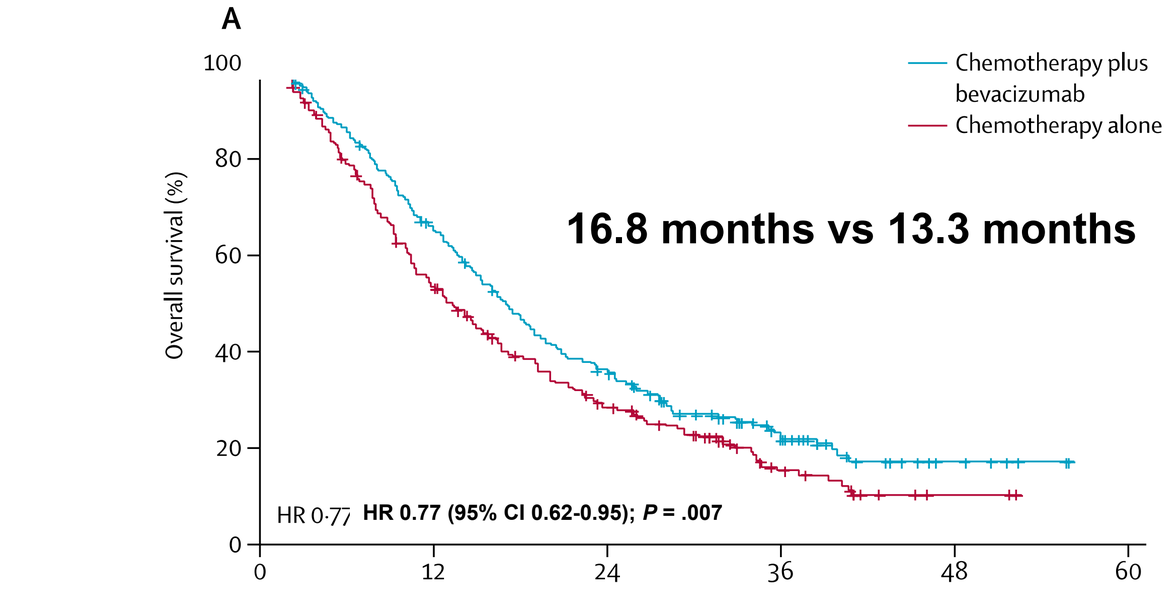
Leslie M. Randall[1], Laurance Gladieff[2], Munetaka Takekuma[3], Hanna Dahlstrand[4], Kristina Lindelmann[5], Ugo De Giorgi[6], Nicoletta Colombo[7], Linn Woelber[8], Ana Oaknin[9]

ClinicalTrials.gov Identifier: NCT03556839

Sponsor: GEICO/Roche

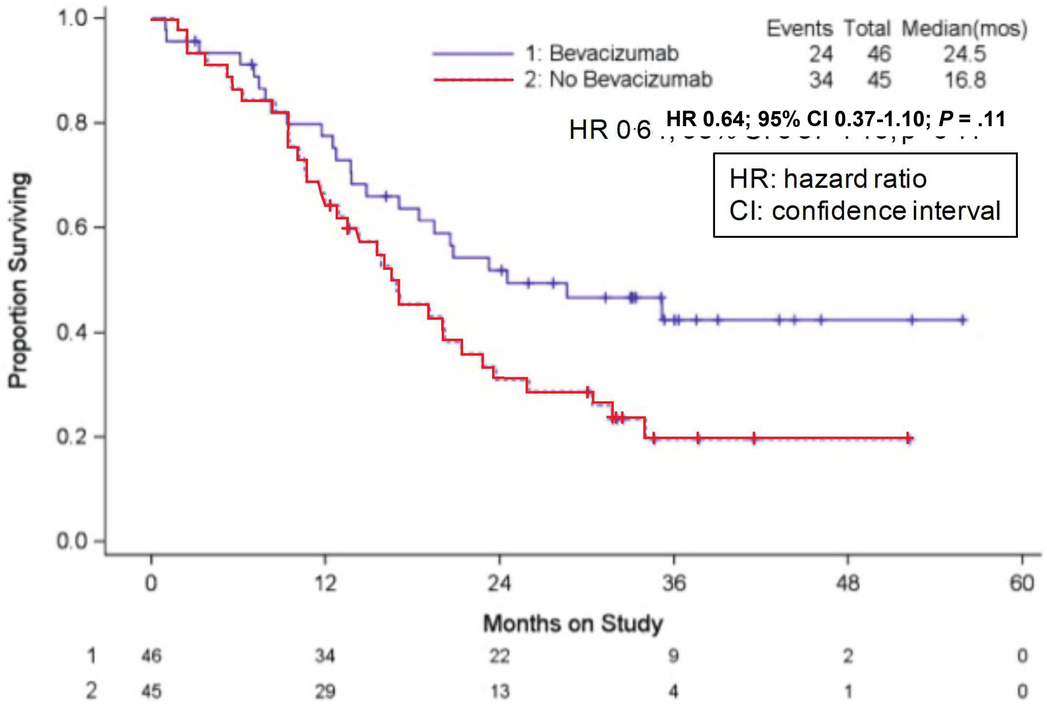
GOG 240 : Mature OS

ITT



Number at risk (number censored)						
Chemotherapy plus bevacizumab	227 (0)	142 (9)	75 (12)	30 (31)	6 (51)	0 (57)
Chemotherapy alone	225 (0)	114 (9)	54 (18)	17 (35)	2 (45)	0 (47)

Not Previously Irradiated



ITT, intent to treat

Tewari KS, et al. *Lancet*. 2017;390(10103):1654-1663.

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BEATcc: Study Design

- Primary Stage IVB, persistent or recurrent carcinoma of the cervix
- Measurable disease by RECIST v1.1
- ECOG-PS: 0-1
- No previous systemic chemotherapy for advanced or recurrent disease
- Available tissue (archival or fresh)
- N=404 pts

R: 1:1

Control Arm

Cis- or carboplatin + paclitaxel + bevacizumab (GOG 240) until disease progression, unacceptable toxicity, death or withdrawal of consent

Experimental Arm

Cis- or carboplatin + paclitaxel + bevacizumab + atezolizumab until disease progression, unacceptable toxicity, death or withdrawal of consent

Primary Endpoint:
Overall survival (OS)

Secondary Endpoints:
- PFS
- ORR
- DOR
- Safety
- HR-QOL

Stratification Factors:
- Prior ChemoRT
- Histology: SCC vs Adeno (including AdenoSquamous)
- Chemotherapy Backbone: Cisplatin vs Carboplatin

ClinicalTrials.gov Identifier: NCT03556839

US BEAT cc/GOG-3030 Participating Sites

Institution Name	PI
LSU Shreveport	Destin Black
University of Virginia	Linda Duska
Lyndon Baines Johnson Hospital	Michaela Onstad
Women & Infants Hospital of Rhode Island	Cara Mathews
University of Oklahoma Health Sciences Center	Katherine Moxley
Virginia Commonwealth University	Leslie Randall
University of California, Irvine	Krish Tewari

RaPiDS (GOG-3028): A Randomized Phase II Study of Balstilimab as Monotherapy or in Combination with Zalifrelimab in Second-Line Cervical Cancer

David M O'Malley, Leslie M. Randall, Brent A. Blumenstein, Marek Ancukiewicz, Remigiusz Kaleta, and Bradley J. Monk

ClinicalTrials.gov Identifier: NCT03894215
Sponsor: Agenus

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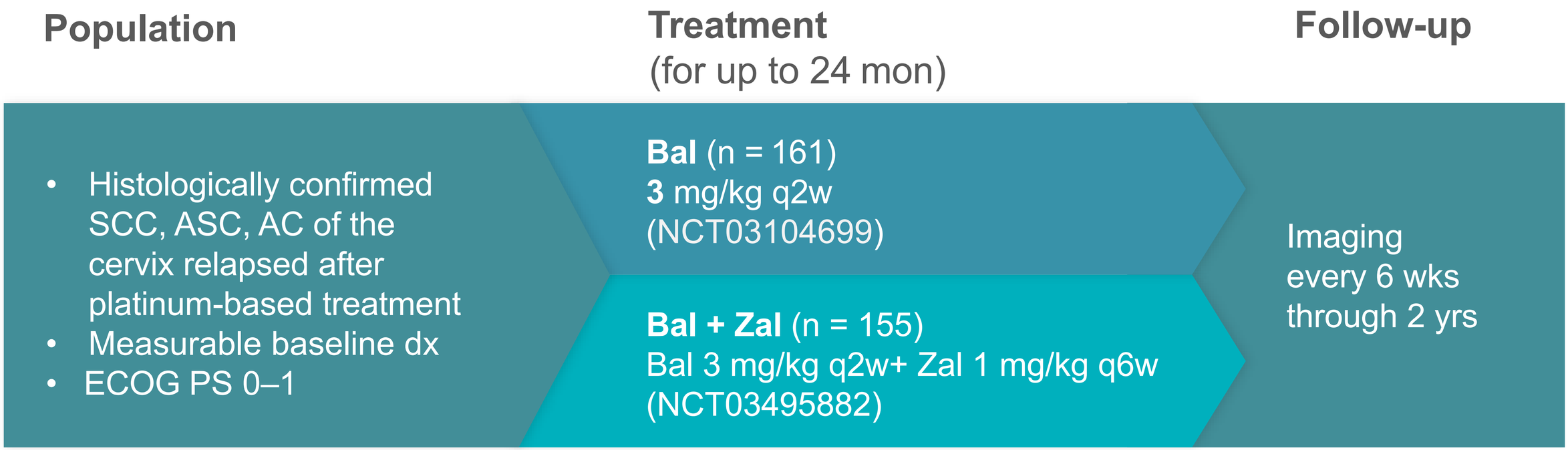
Preliminary Data, ESMO 2020

Two Parallel, Single-arm Trials Testing Balstilimab Alone and with Zalifrelimab in Recurrent/Metastatic Cervical Cancer

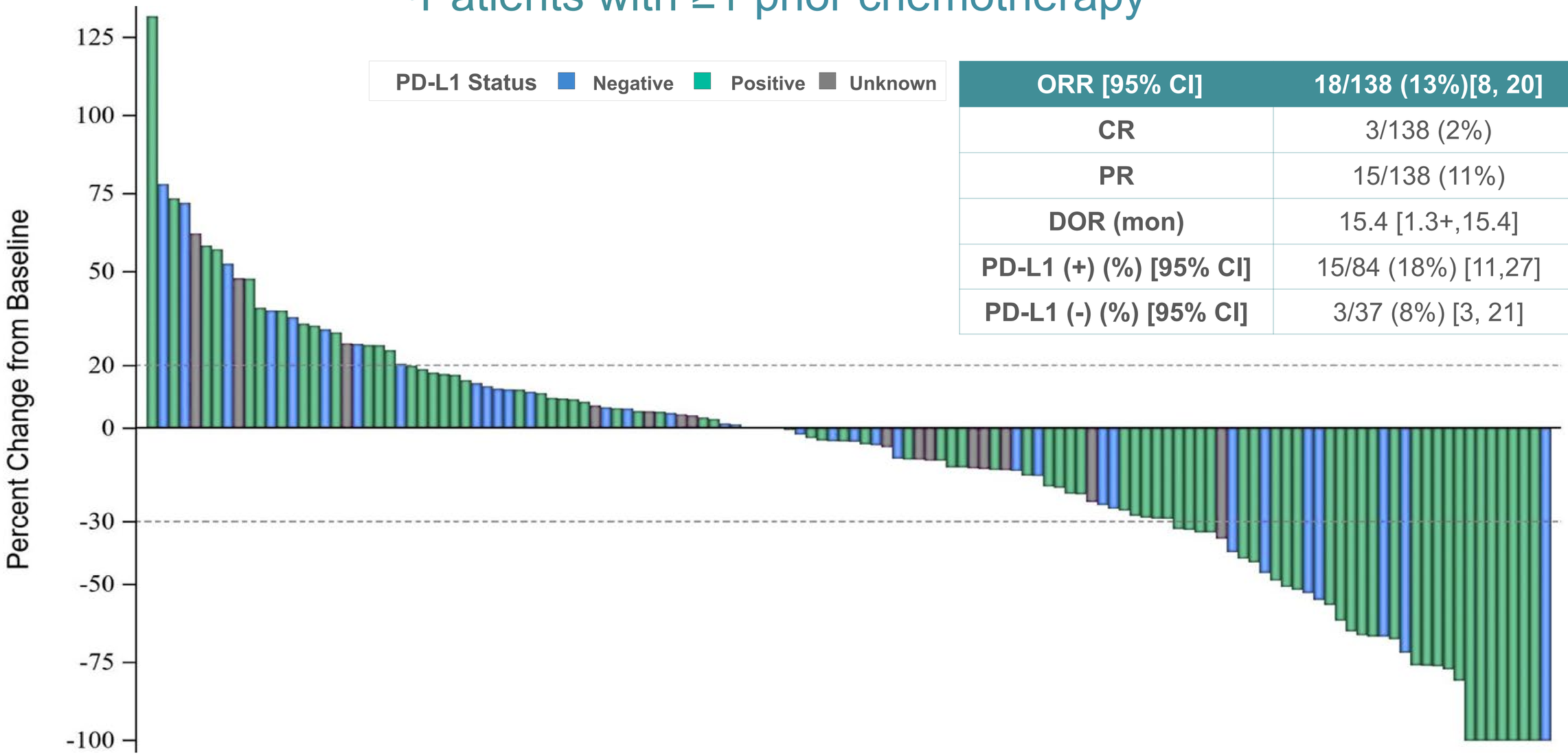


- **Primary endpoint:** Independent Review Committee (IRC) ORR by RECIST 1.1
- **Secondary endpoints:** OS, PFS, DOR

O'Malley et al, ESMO 2020

Tumor Response with Balstilimab Monotherapy

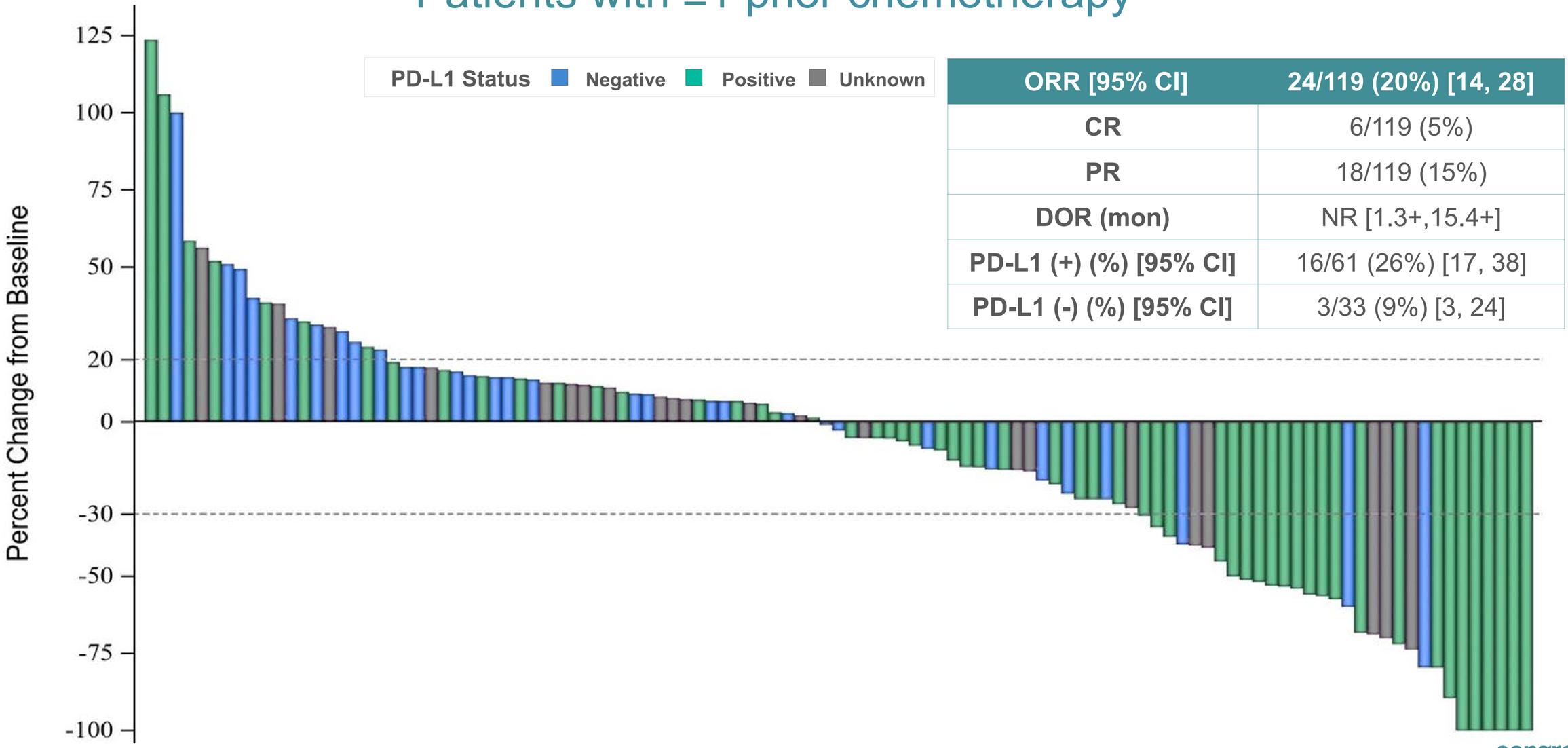
- Patients with ≥1 prior chemotherapy



ORR [95% CI]	18/138 (13%)[8, 20]
CR	3/138 (2%)
PR	15/138 (11%)
DOR (mon)	15.4 [1.3+,15.4]
PD-L1 (+) (%) [95% CI]	15/84 (18%) [11,27]
PD-L1 (-) (%) [95% CI]	3/37 (8%) [3, 21]

•Tumor Response with Balstilimab plus Zalifrelimab

•Patients with ≥1 prior chemotherapy



ORR [95% CI]	24/119 (20%) [14, 28]
CR	6/119 (5%)
PR	18/119 (15%)
DOR (mon)	NR [1.3+,15.4+]
PD-L1 (+) (%) [95% CI]	16/61 (26%) [17, 38]
PD-L1 (-) (%) [95% CI]	3/33 (9%) [3, 24]

O'Malley et al, ESMO 2020

FDA Grants Balstilimab/Zalifrelimab Dual Immunotherapy Fast Track Designation in Cervical Cancer

March 12, 2020

Jason M. Broderick

Relevant Topics

The FDA has granted a Fast Track designation to the combination of the PD-1 inhibitor balstilimab and the CTLA-inhibitor zalifrelimab for the treatment of patients with relapsed or refractory metastatic cervical cancer.

GOG-3028 - A Two Arm, Randomized, Non Comparative Blinded Phase 2 Trial of AGEN2034 (anti PD-1) as a Monotherapy or in Combination Therapy with AGEN1884 (anti-CTLA4) or with Placebo in Women with Recurrent Cervical Cancer (Second Line) – RaPiDS

Patient Eligibility

- Cervical cancer that has relapsed after a platinum-based treatment (first line) regimen for advanced (recurrent, unresectable, or metastatic) disease
- Measurable disease on imaging based on RECIST version 1.1
- ECOG PS ≤1
- sufficient and adequate formalin-fixed paraffin embedded (FFPE)

Randomization 1:1

Treatment up to 24 months

Balstilimab (300 mg) every 3 weeks
Placebo every 6 weeks

Balstilimab (300 mg) every 3 weeks
Zalifrelimab (1 mg/kg) every 6 weeks

Primary Endpoint

- ORR according to RECIST 1.1

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Thank You!!

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