Efficacy and Safety of Cadonilimab, An Anti-PD-1/CTLA4 Bi-specific Antibody, in Previously Treated Recurrent or Metastatic (R/M) Cervical Cancer: A Multicenter, Open-label, Single-arm, Phase II Trial

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Financial Disclosures

- I have no financial relationships with ACCME defined ineligible companies to report.

Background

- There are limited effective therapies for treating 2L+ recurrent or metastatic (R/M) cervical cancer.
- While pembrolizumab was approved in the United States under accelerated approval, only 17.1% of pts with PD-L1 positive (CPS≥1) responded with DoR NR, and mPFS was 2.1 months(mos)[1]. This represented an urgent unmet need.
- Cadonilimab is a bi-specific antibody against PD-1 and CTLA-4, designed to:
  - Retain the efficacy benefit of combination of PD-1 and CTLA-4;
  - Improve on the safety profile of the combination therapy.
- This study was designed to evaluated the efficacy and safety profile of cadonilimab in pts with R/M cervical cancer that who has progressed on or after platinum-based chemotherapy with or without bevacizumab.

1. Presented By Hyun Chung at 2021 Society of Gynecologic Oncology

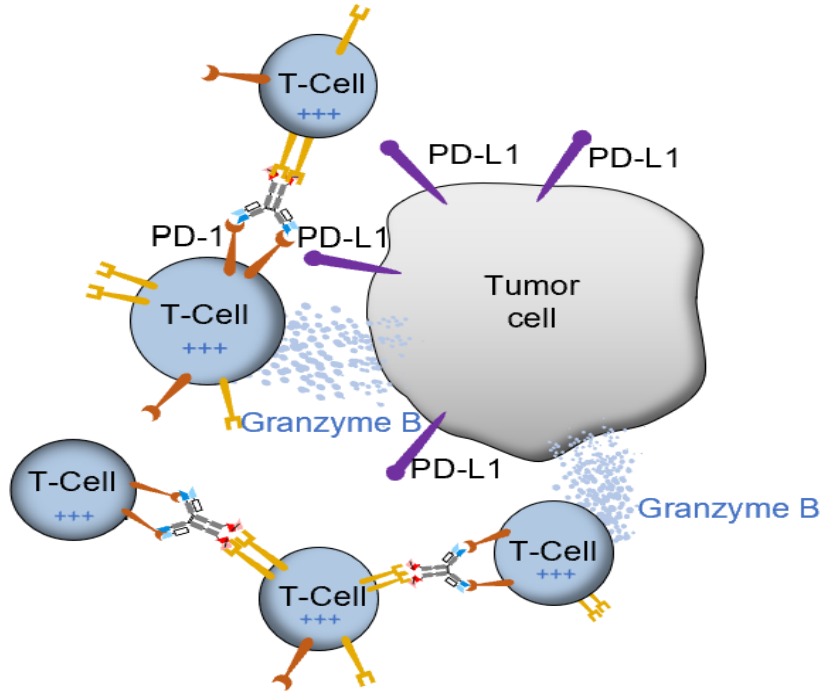
Backgroud-Cadonilimab (PD-1/CTLA-4)

PD-1 and CTLA-4 co-express in tumor infiltrating lymphocytes (TILs), but not in normal peripheral tissue lymphocytes

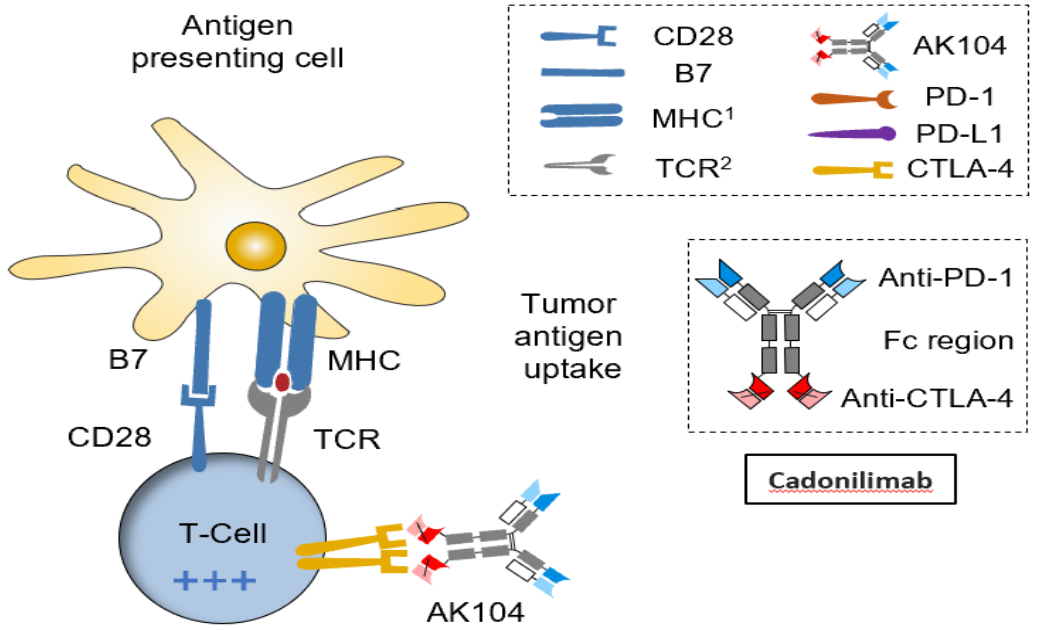
✓CTLA-4, have been found to be co-expressed with PD-1 in CD8 TILs (PD-1+ and CTLA-4+) that are found inside a wide range of tumor types

PD-1/CTLA-4 bi-specific may display higher avidity for lymphocytes in the tumor micro-environment versus peripheral sites

Tumor microenvironment (high functional affinity or avidity)

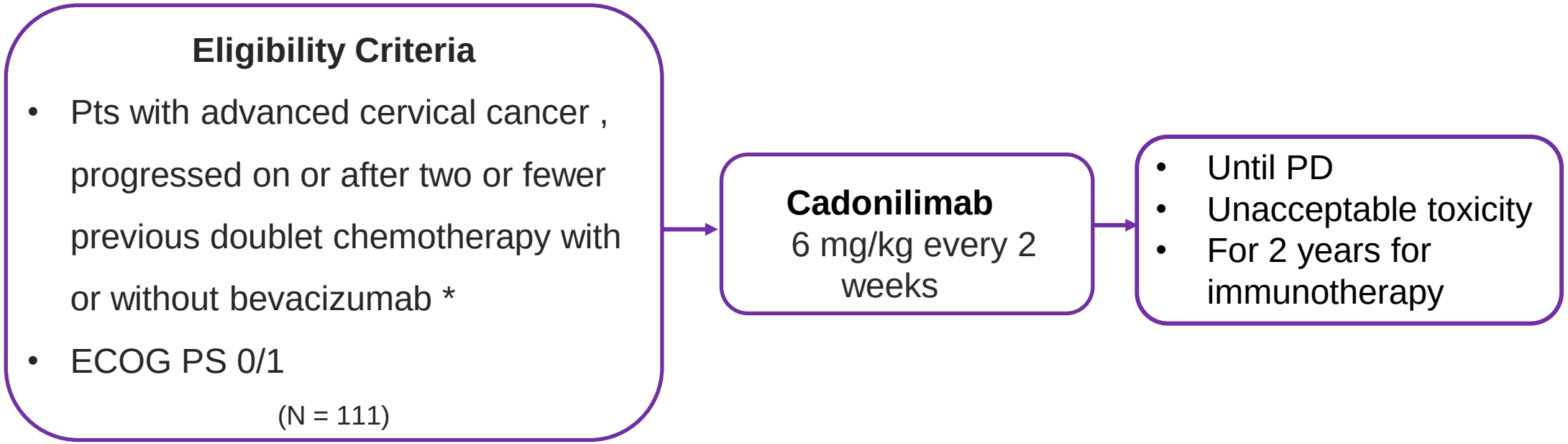


Peripheral (lower binding avidity)



Study design

- A multicenter, open-label, single-arm, phase II study(NCT03852251)



* Pts Including squamous cell carcinoma, adenocarcinoma or adenosquamous carcinoma

- Primary endpoint: **ORR** per RECIST v 1.1 by IRRC
- Secondary endpoints: **PFS, DoR, DCR, TTR** per RECIST v 1.1 by IRRC and **OS**

Baseline Characteristics

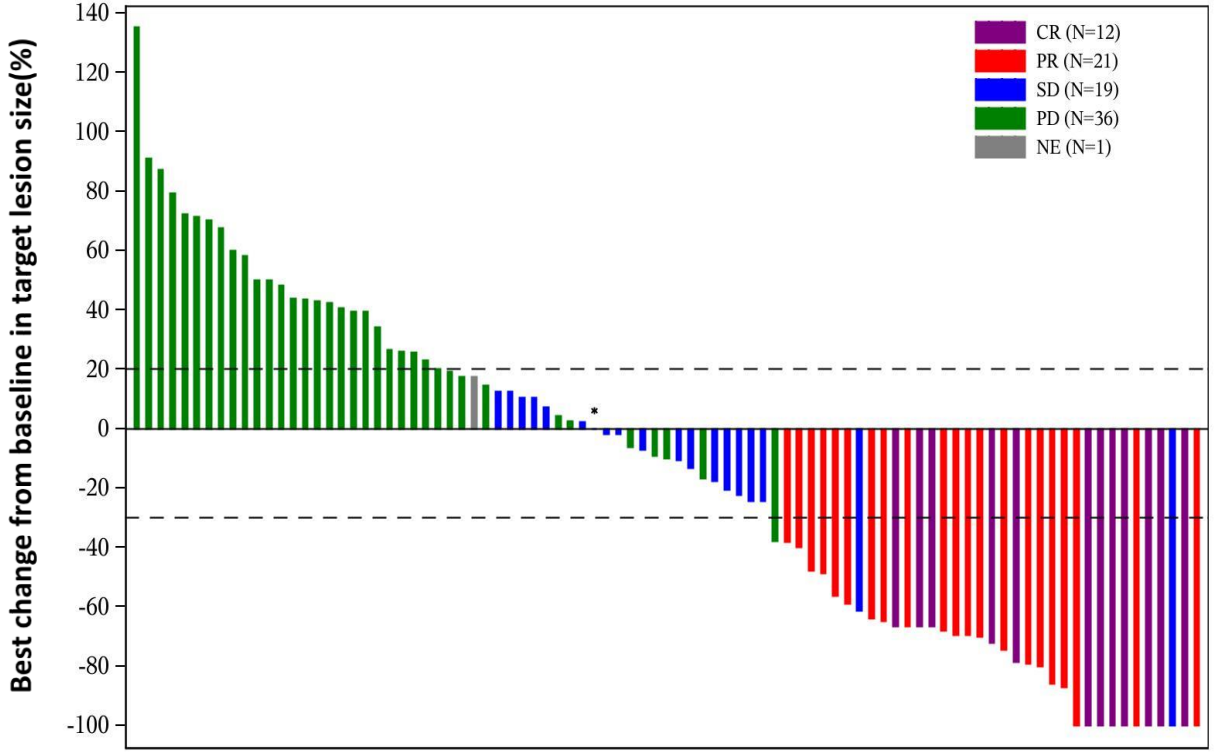
- As of Aug 5,2021, 111 pts with R/M cervical cancer had received at least one dose of cadonilimab and 100 pts were included in FAS-IRRC.
- The median follow-up of 9.63 mos (range, 0.7-21.4) .

Characteristic	FAS-IRRC[1] N=100
Median age, yrs (range)	50.1(27,73)
Histological Type, n (%)	
Squamous cell carcinoma	94(94.0)
Adenocarcinoma	3(3.0)
Adenosquamous carcinoma	3(3.0)
ECOG PS 1, n (%)	56 (56.0)
PD-L1 Status, n (%)	
CPS ≥ 1	64 (64.0)
CPS < 1	18(18.0)
Unknown	18(18.0)
No.of previous systemic therapies for R/M disease, n (%)	
1	63 (63.0)
2	37 (37.0)
Prior Bevacizumab Treatment, n (%)	25 (25.0)
Any Metastasis, n (%)	90(90.0)
Prior Cancer Radiotherapy, n (%)	84 (84.0)

1. IRRC: Independent radiological review committee

The IRRC-assessed ORR

- **ORR** in 100 eligible pts was 33.0% , with 12 pts achieved **CR** and 21 pts achieved **PR**.



Data cutoff date: Aug 5,2021

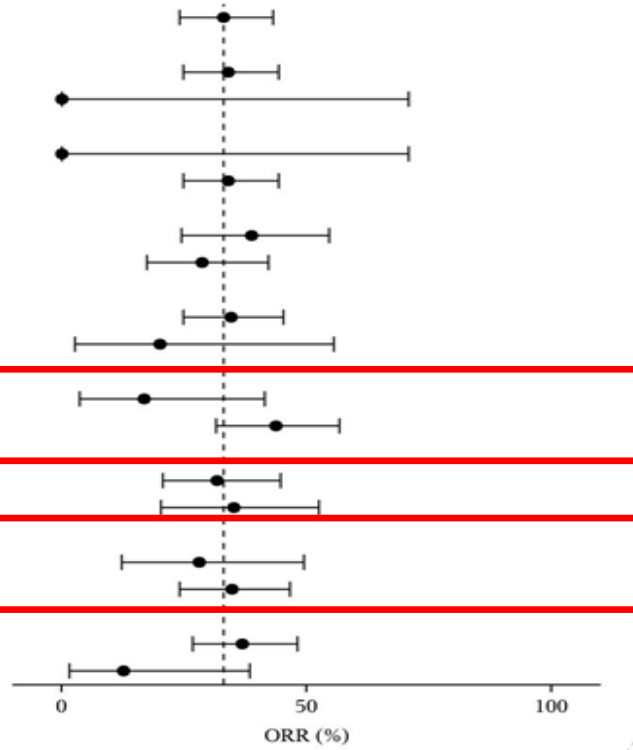
Response	FAS-IRRC [1] (N = 100)
ORR(CR+PR),n(%) (95%CI)	**33(33.0) (23.9, 43.1)**
CR,n (%)	12 (12.0)
PR,n (%)	21 (21.0)
SD,n (%)	19 (19.0)
DCR(CR+PR+SD),n(%) (95%CI)	**52(52.0) (41.8, 62.1)**
mTTR,mos (range)	**1.84 (1.68, 6.74)**
Median DoR,mos (range)	**NR[2] (0.95+, 16.43+)[3]**

1. IRRC: Independent radiological review committee
2. NR=Not Reached
3. +Represents deletion (no disease progression or death)

Subgroup Analysis

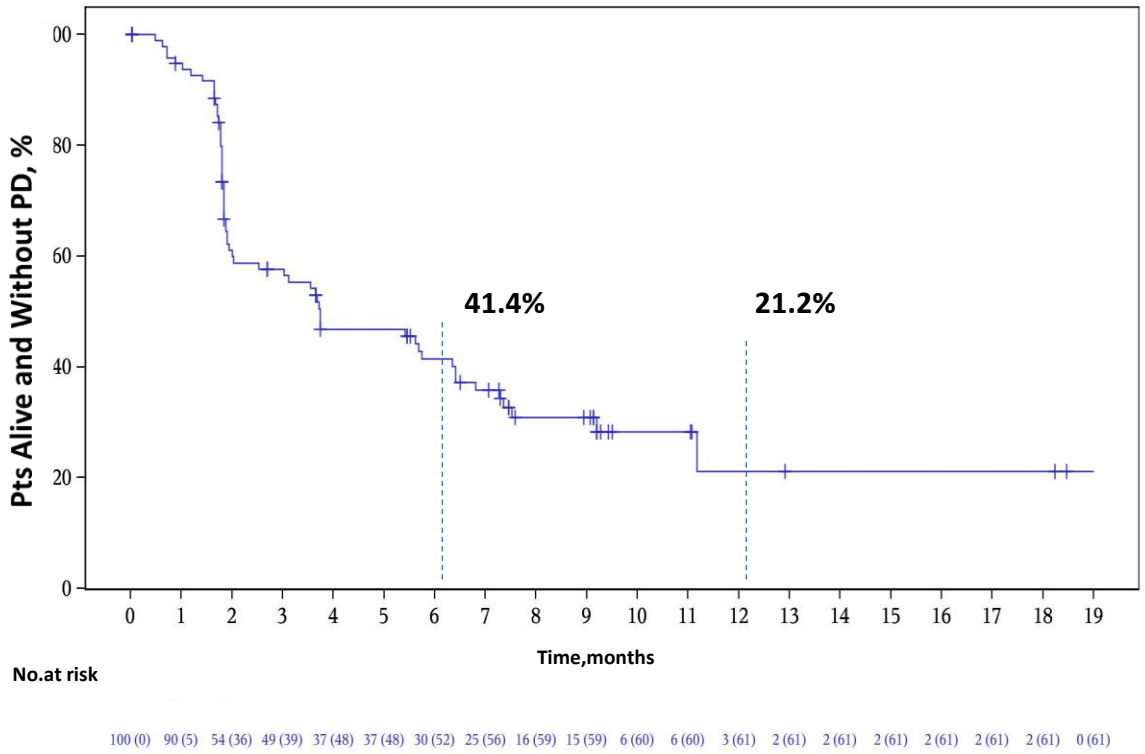
- Results from subgroup analysis of the ORR assessed by IRRC were consistent with the overall analysis.
- Pts benefited from the cadonilimab monotherapy regardless of their PD-L1 expression status, or prior bevacizumab treatment.

Subgroup	n/N	ORR(%)	95% CI
All pts(N = 100)	33/100	33.0	23.9,43.1
< 65 yrs	33/97	34.0	24.7,44.3
≥65 yrs	0/3	0.0	0.0,70.8
Adenocarcinoma	0/3	0.0	0.0,70.8
Squamous cell carcinoma Or Adenosquamous carcinoma	33/97	34.0	24.7,44.3
ECOG PS 0	17/44	38.6	24.4,54.5
ECOG PS 1	16/56	28.6	17.3,42.2
Any Metastasis	31/90	34.4	24.7,45.2
No Metastasis	2/10	20.0	2.5,55.6
PD-L1 negative(CPS < 1)	3/18	16.7	3.6,41.4
PD-L1 positive(CPS≥1)	28/64	43.8	31.4,56.7
Systemic anti-cancer Therapy 1line	20/63	31.7	20.6,44.7
Systemic anti-cancer Therapy 2lines	13/37	35.1	20.2,52.2
With bevacizumab	7/25	28.0	12.1,49.4
Without bevacizumab	26/75	34.7	24.0,46.5
With primary lesion radiotherapy	31/84	36.9	26.6,48.1
Without primary lesion radiotherapy	2/16	12.5	1.6,38.3



The IRRC-assessed PFS

- Median **PFS** was 3.75 mos
- 6- and 12-mo **PFS** rates were 41.4% and 21.2%, respectively



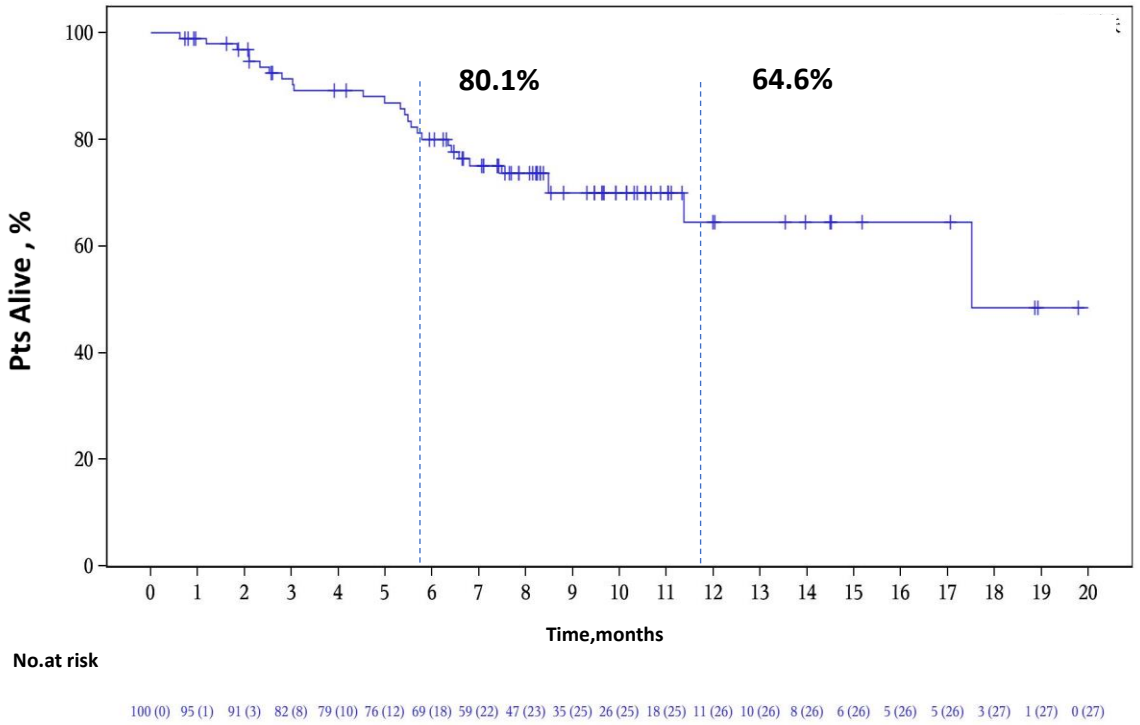
PFS	FAS-IRRC [1] (N = 100)
Median,mos (range)	3.75 (0.03+, 18.46+)[2]
6-mo rate,% (95% CI)	41.4 (30.9, 51.6)
12-mo rate,% (95% CI)	21.2 (9.0, 36.8)

Data cutoff date: Aug 5,2021

1. IRRC: Independent radiological review committee
2. +:Represents deletion (no disease progression or death)

Efficacy Results-OS

- Median **OS** was 17.51 mos
- 6- and 12-mo **OS** rates were 80.1% and 64.6%, respectively



OS	FAS-IRRC [1] (N = 100)
Median,mos (range)	17.51 (0.62, 19.78+)[2]
6-mo rate,% (95% CI)	80.1 (70.2, 87.0)
12-mo rate,% (95% CI)	64.6 (49.0, 76.5)

Data cutoff date: Aug 5,2021

1. IRRC: Independent radiological review committee
2. +Represents deletion (no disease progression or death)

Summary of TRAEs

- Treatment-related adverse events (**TRAE**s) occurred in 91.9% of 111 patients.
- ≥3 Grade **TRAE**s occurred in 27.0% of 111 patients.

	Cadonilimab N=111 n (%)
TRAE	102 (91.9)
≥3 Grade TRAE	30 (27.0)
Drug related SAE	25 (22.5)
TRAE leading to discontinuation	6 (5.4)

Data cutoff date: Aug 5,2021

Summary of TRAEs

- Most common **TRAE**s (Any Grade, incidence ≥ 10%):
  - ✓ anemia, 37(33.3%);
  - ✓ hypothyroidism, 22(19.8%);
  - ✓ alanine aminotransferase increased , 20(18.0%).

- Most common ≥3 Grade **TRAE**s (incidence ≥ 1%):
  - ✓ anemia, 6(5.4%);
  - ✓ decreases appetite, 3(2.7%);
  - ✓ dyspnea, 2(1.8%).

Preferred Term	Any Grade (incidence ≥ 10%) n (%)	≥3 Grade (incidence ≥ 1%) n (%)
Anemia	37 (33.3)	6 (5.4)
Hypothyroidism	22 (19.8)	0 (0)
Alanine aminotransferase increased	20 (18.0)	1 (0.9)
Aspartate aminotransferase increased	18 (16.2)	1 (0.9)
White blood cell count decreased	16 (14.4)	1 (0.9)
Hyperthyroidism	16 (14.4)	0 (0)
Pyrexia	14 (12.6)	0 (0)
Diarrhea	13 (11.7)	1 (0.9)
Hypoalbuminaemia	12 (10.8)	0 (0)
Decreases appetite	9 (8.1)	3 (2.7)
Dyspnea	2 (1.8)	2 (1.8)

Data cutoff date: Aug 5,2021

Summary of irAEs

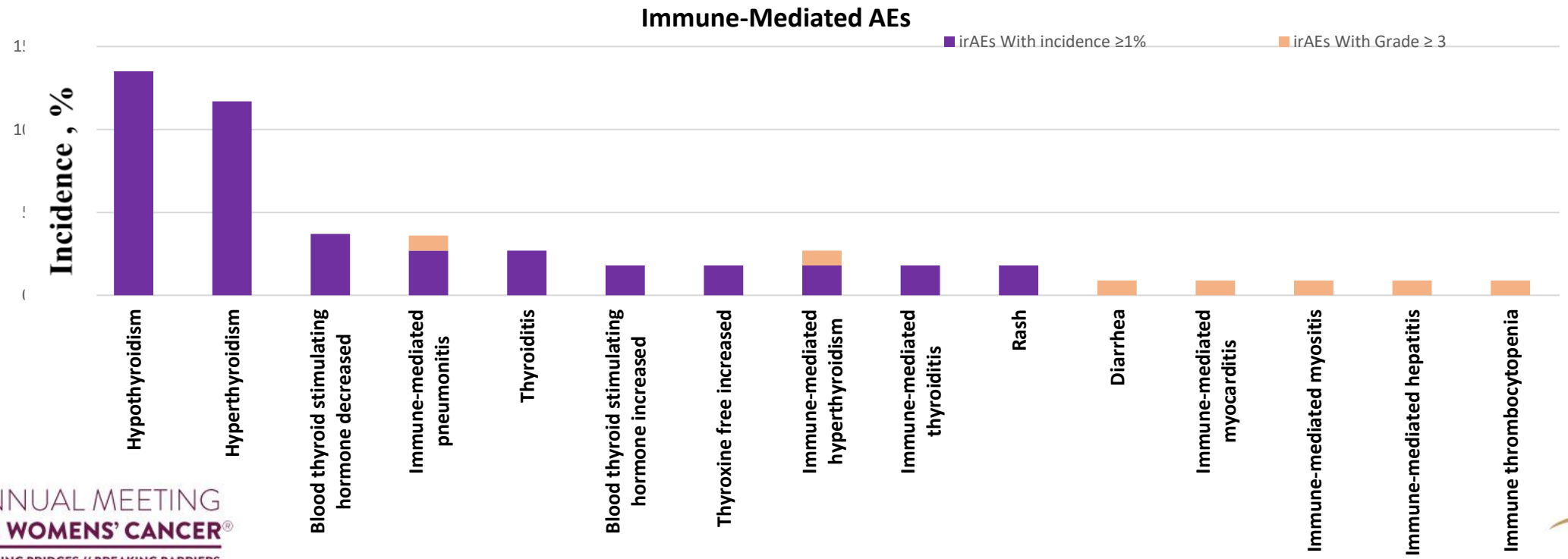
- Immune-mediated adverse events (**irAEs**) occurred in 34 (30.6%)of 111 patients.
- Grade ≥3 **irAEs** occurred in 5 (4.5%) of 111 patients.

	Cadonilimab N=111 n (%)
irAE	34 (30.6)
≥3 Grade irAE	5 (4.5)
Immune-Mediated SAE	3 (2.7)
irAE leading to discontinuation	6 (5.4)
irAE leading to death	0

Data cutoff date: Aug 5,2021

Summary of irAEs

- **Most common irAEs (Any Grade, incidence ≥ 1%):** hypothyroidism, 15(13.5%); hyperthyroidism, 13(11.7%); blood thyroid stimulating hormone decreased, 4(3.6%).
- **Most common irAEs (≥3 Grade):** immune-mediated pneumonitis, 1(0.9%); hyperthyroidism, 1(0.9%); myocarditis, 1(0.9%); myositis, 1(0.9%); hepatitis, 1(0.9%); thrombocytopenia, (0.9%); diarrhea, 1(0.9%).



Data cutoff date: Aug 5,2021

Conclusions

- Cadonilimab monotherapy is efficacious as 2L+ treatment of R/M cervical cancer pts.
  - ORR was 33.0% ,CR rate was 12%;
  - Median PFS was 3.75 mos, median OS was 17.51 mos.
- Pts benefited from the cadonilimab monotherapy regardless of their PD-L1 expression status, or prior bevacizumab treatment.
  - Pts with PD-L1 positive(CPS≥1), the ORR was 43.8%;
  - Pts with PD-L1 negative(CPS<1), the ORR was 16.7%.
- Cadonilimab monotherapy is safe and well tolerated in R/M cervical cancer pts.
- A Phase 3 confirmatory trial of cadonilimab or placebo in combination with chemotherapy plus bevacizumab as 1L treatment for R/M cervical cancer is ongoing(NCT04982237).

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