Breaking Barriers in mUC 1 L Treatment: The Synergistic Potential of Nivolumab with Gemcitabine-Cisplatin

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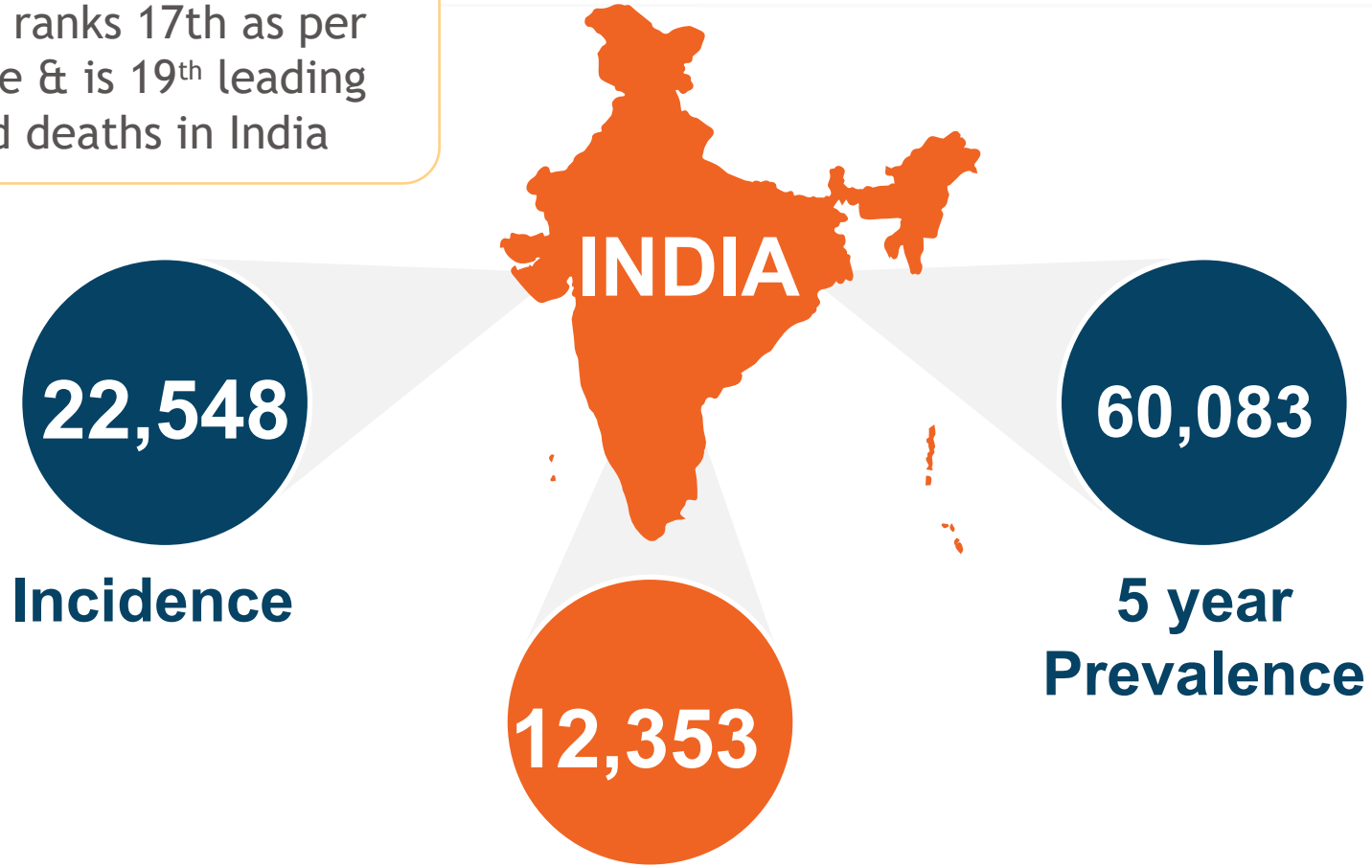
Presentation Overview

1. Epidemiology and disease burden
2. Histology and staging of Bladder cancer
3. Classification of bladder cancer
4. India retrospective study & Issues/Challenges in bladder cancer management
5. Unmet need in mUC
6. NCCN Guidelines recommendations for bladder cancer
7. Mechanism of action for treatment with Nivolumab
8. Nivolumab plus gemcitabine-cisplatin for previously untreated unresectable or metastatic urothelial carcinoma(CM 901)

Bladder cancer Indian Epidemiology: 2022

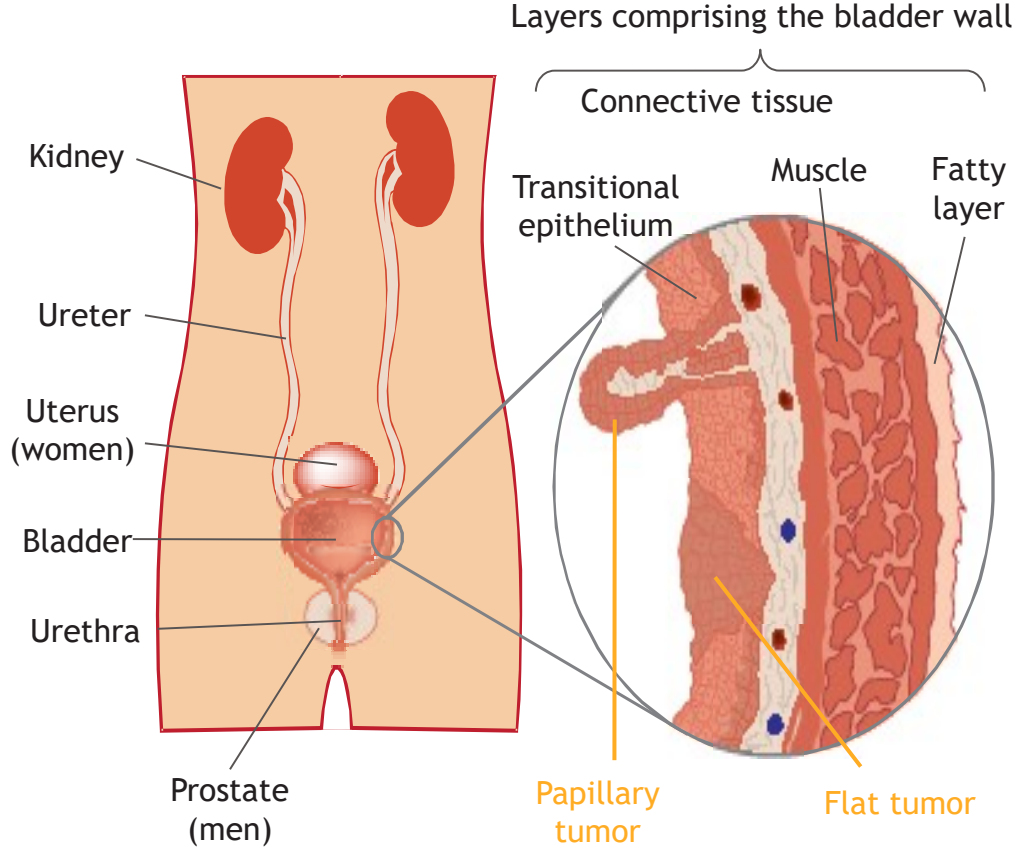
Bladder cancer in India ranks 17th as per Incidence by cancer site & is 19th leading cause of cancer-related deaths in India



World Health Organisation (2022) The global cancer observatory, source: Globocan 2022 (version 1.1) 356-india-fact-sheets.pdf. Factsheet-India. World Health Organisation. https ://gco.iarc.fr/today/data/factsheets/populations/356-india-fact-sheets.pdf. Accessed 10 June 2024

Description of bladder cancer

- A majority of all bladder cancers are UC (also known as transitional cell carcinoma [TCC])[1]
  - UC develops in the urothelial cells that line the bladder
  - Bladder cancers are often categorized by the extent to which they have invaded the bladder wall, and by subtype (papillary or flat)
- The less common types of bladder cancers include squamous cell carcinomas, adenocarcinoma, small cell carcinoma, and sarcomas[1]
- Bladder cancer is classified as a highly immunogenic tumor type[2]
  - Incidence of spontaneous tumor regression in the absence of therapy[3]
  - Evidence of tumor T-cell infiltration[4]
  - Responsiveness to intravesical immunotherapy with BCG, and newer immunotherapies[2]



Adapted from American Cancer Society[5]

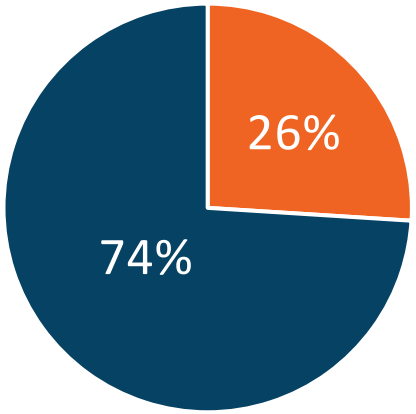
1. American Cancer Society. Bladder cancer. https://www.cancer.org/content/dam/CRC/PDF/Public/8557.00.pdf. Accessed August 28, 2017. 2. Kim J. *Investig Clin Urol* 2016;57(suppl 1):S98-S105.
3. Kucerova P, Cervinkova M. *Anticancer Drugs* 2016;27:269-277. 4. Teng MW et al. *Cancer Res* 2015;75:2139-2145. 5. Bladder anatomy image. Copyright 2017. Reprinted by the permission of the American Cancer Society, Inc. All rights reserved, www.cancer.org.

Bladder Cancer: SGPGI Lucknow (Retrospective study)

SGPGI Lucknow, urology department: **2001 to 2008 - 561 PATIENTS**

97% of the patients presented with painless hematuria.

Stage of bladder cancer patients at the time of presentation

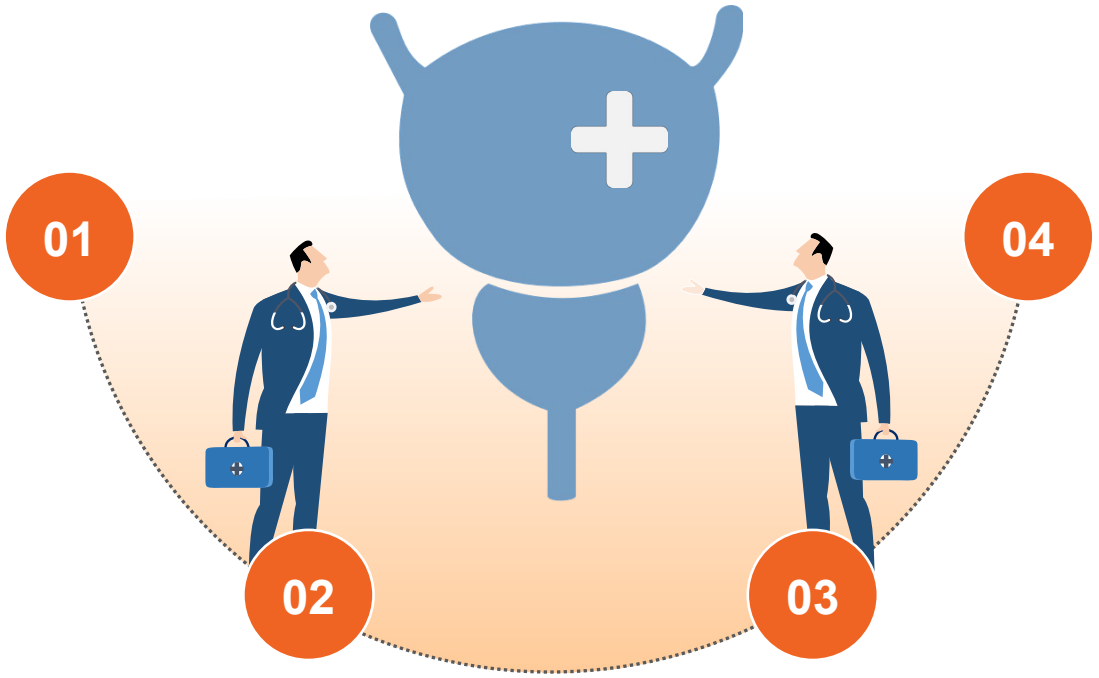


- Transitional cell carcinoma was the most common variant seen in **97.71%** of the patients
- Median age at presentation was **60 years** old
- The male to female ratio was **8.6:1** (Different from west)
- A total of **74%** of the males and **22%** of the females with bladder cancer smoked or had an intake of tobacco

Gupta P et al. Indian J Urol. 2009 Apr-Jun; 25(2): 207–210.

Bladder Cancer Management: Issues/Challenges

01 An aggressive epithelial cancer



02 **“Moderately”** chemotherapy responsive, but few CRs

03 Impacts an **“older”** patient population

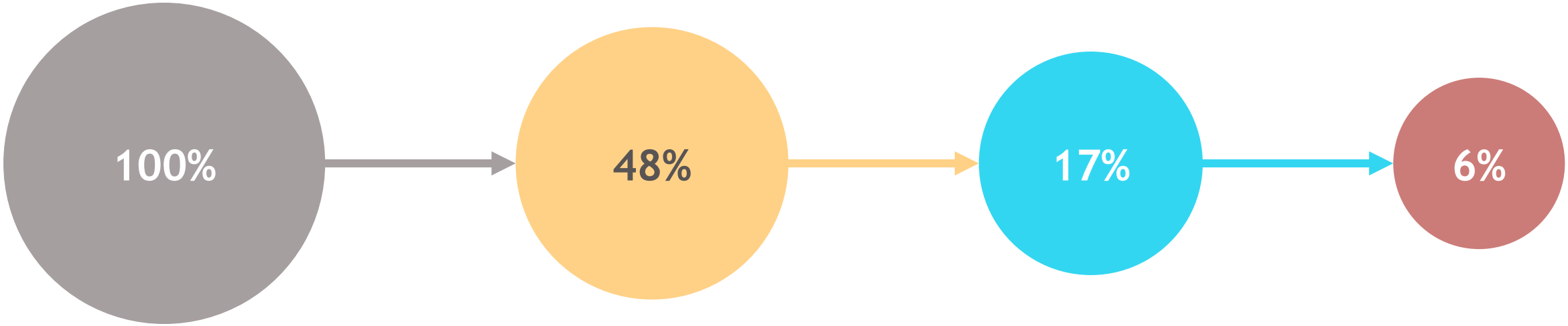
04 Relatively high rate of patients with compromised performance status and/or renal function

NCCN Guidelines Version 4.2024 Bladder Cancer

NCCN Panel designated the CM 901 regimen a category 1 recommendation as first-line therapy

Cisplatin eligible	**First-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV**
	Nivolumab, gemcitabine, and cisplatin (category 1) followed by nivolumab maintenance therapy14 (category 1)

Aggressiveness of urothelial cancer is reflected in daily practice data



Adapted with permission from *Cancer Treat Res Commun*.

Summary description of patients with advanced or metastatic bladder cancer receiving first-, second-, or third-line of therapy in real-world cohorts

Swami U et al. *Cancer Treat Res Commun*. 2021;27:100325.

Unmet Need:

- While early diagnosis and multimodality therapy have resulted in better patient outcomes, for metastatic bladder cancer, 5-year overall survival rate is dismal to the tune of 8.3%.[1]
- The standard first-line treatment for unresectable or mUC for cisplatin eligible patients population is gemcitabine and cisplatin (GC).Response rates > 40% and OS medians of ~15 months have been reported, but durable responses are rare.[2]
- Avelumab maintenance therapy, while beneficial, is only applicable after achieving a response or stable disease with first-line chemotherapy, leaving a gap in initial treatment efficacy. [3]Avelumab 1L maintenance does not offer a solution for patients who have a more aggressive disease (progressing before completing a full course of 1L platinum-based chemotherapy)
- A real-world study conducted in Germany revealed that 31% of patients with metastatic urothelial cancer experienced disease progression as a clinical outcome following their first-line treatment with Gemcitabine and Cisplatin[4]
- No novel agent has improved OS when added concurrently to platinum-based chemotherapy in the first-line treatment of unresectable or mUC.[5,6]
- There is need for new concurrent chemo-immunotherapy therapeutic options which can improve metastatic UC outcomes (e.g. Increase survival, response, and response durability with manageable toxicities) of all cisplatin eligible patients in this setting.[2]

Major unmet needs with mUC patient: Need for t/t options which may confer

1 **Survival benefit** 2 Help achieving higher response & **complete response** 3 Durability of response 4 Maintained QOL

1.National Institute of Health, National Cancer Institute, Surveillance, Epidemiology, and End Results Program. Cancer stat facts: bladder cancer. 2023. Accessed October 10, 2023. https://seer.cancer.gov/statfacts/html/ urinb.html 2. MODULE 2.5: CLINICAL OVERVIEW, CA209901: Nivolumab(BMS-936558) in Combination with Chemotherapy for Unresectable or Metastatic Urothelial Carcinoma. Bristol-Myers Squibb Company; Document Date: 26-Sep-2023 3. Powles, T., et al. (2020). Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma. New England Journal of Medicine, 383(13), 1218-1230. 4. Niegisch G et al. A Real-World Data Study to Evaluate Treatment Patterns, Clinical Characteristics and Survival Outcomes for First- and Second-Line Treatment in Locally Advanced and Metastatic Urothelial Cancer Patients in Germany. J Cancer. 2018 Mar 29;9(8):1337-1348 . 5. Galsky MD, et al. Lancet 2020;395:1547-1557. 6. Powles T, et al. Lancet Oncol 2021;22:931-945.
mUC, metastatic urothelial carcinoma; NIVO, nivolumab; OS, overall survival; SOC, standard of care.

Checkmate 901

MADRID 2023 ESMO congress

Nivolumab plus gemcitabine-cisplatin versus gemcitabine-cisplatin alone for previously untreated unresectable or metastatic urothelial carcinoma: results from the phase 3 CheckMate 901 trial

•Michiel S. van der Heijden,[1] Guru Sonpavde,[2a] Thomas Powles,[3] Andrea Necchi,[4b] Mauricio Burotto,[5] Michael Schenker,[6] Juan Pablo Sade,[7] Aristotelis Bamias,[8] Philippe Beuzeboc,[9] Jens Bedke,[10c] •Jan Oldenburg,[11] Yüksel Ürün,[12] Dingwei Ye,[13] Zhisong He,[14] Begoña P. Valderrama,[15] Yoshihiko Tomita,[16] Jeiry Filian,[17] Daniela Purcea,[18] Federico Nasroulah,[17] Matthew D. Galsky[19]

•[1]Netherlands Cancer Institute, Amsterdam, the Netherlands; [2]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [3]Barts Cancer Institute, Queen Mary University of London, London, UK; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [5]Bradford Hill Clinical Research Center, Santiago, Chile; [6]University of Medicine and Pharmacy, Craiova, Romania; [7]Alexander Fleming Institute, Buenos Aires, Argentina; [8]National and Kapodistrian University of Athens, ATTIKON University Hospital, Athens, Greece; [9]Hopital Foch, Suresnes, France; [10]Eberhard Karls University Tübingen, Tübingen, Germany; [11]Akershus University Hospital (Ahus), Lørenskog, Norway; [12]Ankara University, Ankara, Turkey; [13]Fudan University Shanghai Cancer Center, Shanghai, China; [14]Peking University First Hospital, Beijing, China; [15]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [16]Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [17]Bristol Myers Squibb, Princeton, NJ, USA; [18]Bristol Myers Squibb, Boudry, Switzerland; [19]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA

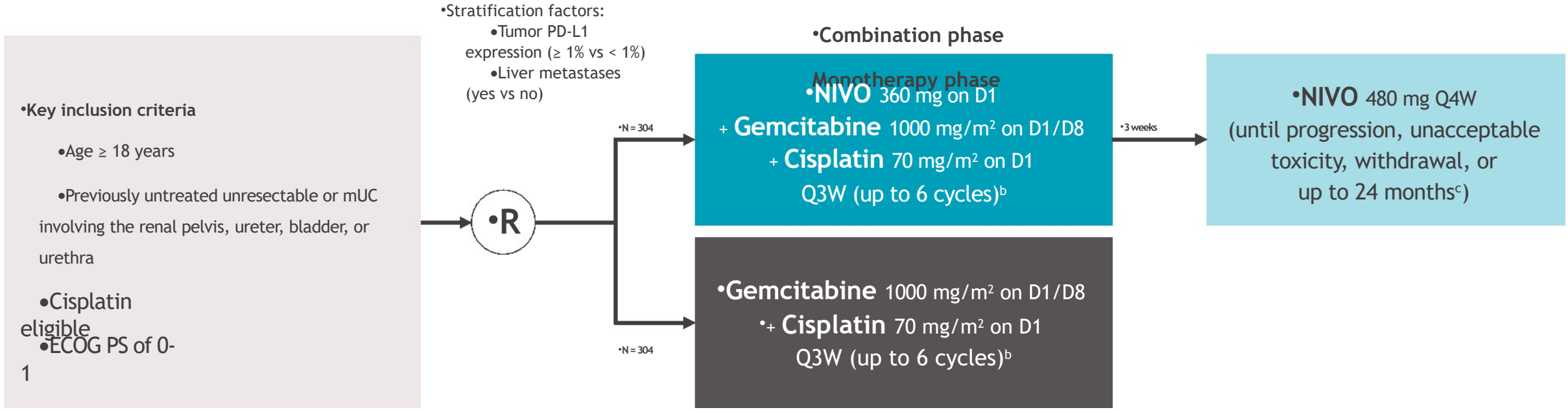
•[a]Current affiliation is AdventHealth Cancer Institute and University of Central Florida, Orlando, FL, USA. [b]Current affiliation is IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy. [c]Current affiliation is Klinikum Stuttgart, Katharinenhospital, Stuttgart, Germany.

•*Presentation number LBA7*

Checkmate 901 Study design

Phase 3, multi-center, randomized study to evaluate NIVO + gemcitabine-cisplatin vs gemcitabine-cisplatin alone in previously untreated unresectable or metastatic urothelial carcinoma

•NIVO + gemcitabine-cisplatin vs gemcitabine-cisplatin in cisplatin-eligible patients[a]



•**Median (range) study follow-up,** 33.6 (7.4-62.4) months

Primary endpoints: OS, PFS per BICR
•**Key secondary endpoints:** OS and PFS by PD-L1 ≥ 1%,[d] HRQoL
•**Key exploratory endpoints:** ORR per BICR, safety

•[a]Further CheckMate 901 trial design details are available at https://clinicaltrials.gov/ct2/show/NCT03036098. [b]Patients who discontinued cisplatin could be switched to gemcitabine-carboplatin for the remainder of the platinum doublet cycles (up to 6 in total). [c]A maximum of 24 months from first dose of NIVO administered as part of the NIVO + gemcitabine-cisplatin combination. [d]PD-L1 status was defined by the percentage of positive tumor cell membrane staining in a minimum of 100 tumor cells that could be evaluated with the use of the PD-L1 IHC 28-8 pharmDx immunohistochemical assay (Dako, Santa Clara, CA, USA).
•BICR, blinded independent central review; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; ORR, objective response rate;
•PD-L1, programmed death ligand 1; PFS, progression-free survival; Q×W, every × weeks; R, randomization.

Select baseline characteristics[a]

baseline characteristics were balanced for both arms

	NIVO+GC (N = 304)	GC (N = 304)
Median age (range), years	65 (32-86)	65 (35-85)
Male/female, n (%)	236 (78) / 68 (22)	234 (77) / 70 (23)
Geographic region, n (%)		
United States	19 (6)	21 (7)
Europe	134 (44)	142 (47)
Asia	72 (24)	61 (20)
Rest of the world	79 (26)	80 (26)
Race/ethnicity, n (%)		
White	211 (69)	225 (74)
Asian	75 (25)	63 (21)
Black or African American	0	2 (1)
Other	18 (6)	14 (5)
ECOG PS, n (%)		
0	162 (53)	162 (53)
1	140 (46)	142 (47)
> 1	2 (1)	0
Tumor type at initial diagnosis, n (%)		
Urinary bladder	235 (77)	219 (72)
Renal pelvis	33 (11)	44 (14)
Other	36 (12)	41 (13)
Tumor PD-L1 expression, n (%)[b]		
≥ 1%	111 (37)	110 (36)
< 1% or indeterminate[c]	193 (63)	194 (64)
Liver metastases, n (%)[b]	64 (21)	64 (21)

[a]In all randomized patients. [b]Per interactive response technology. [c]There were no patients with indeterminate PD-L1 status.
GC, gemcitabine-cisplatin.

Exposure and patient disposition

Median duration of study therapy (range) was 7.4 (0.0-47.9) months in the NIVO+GC arm and 3.7 (0.0-14.3) months in the GC arm[a]

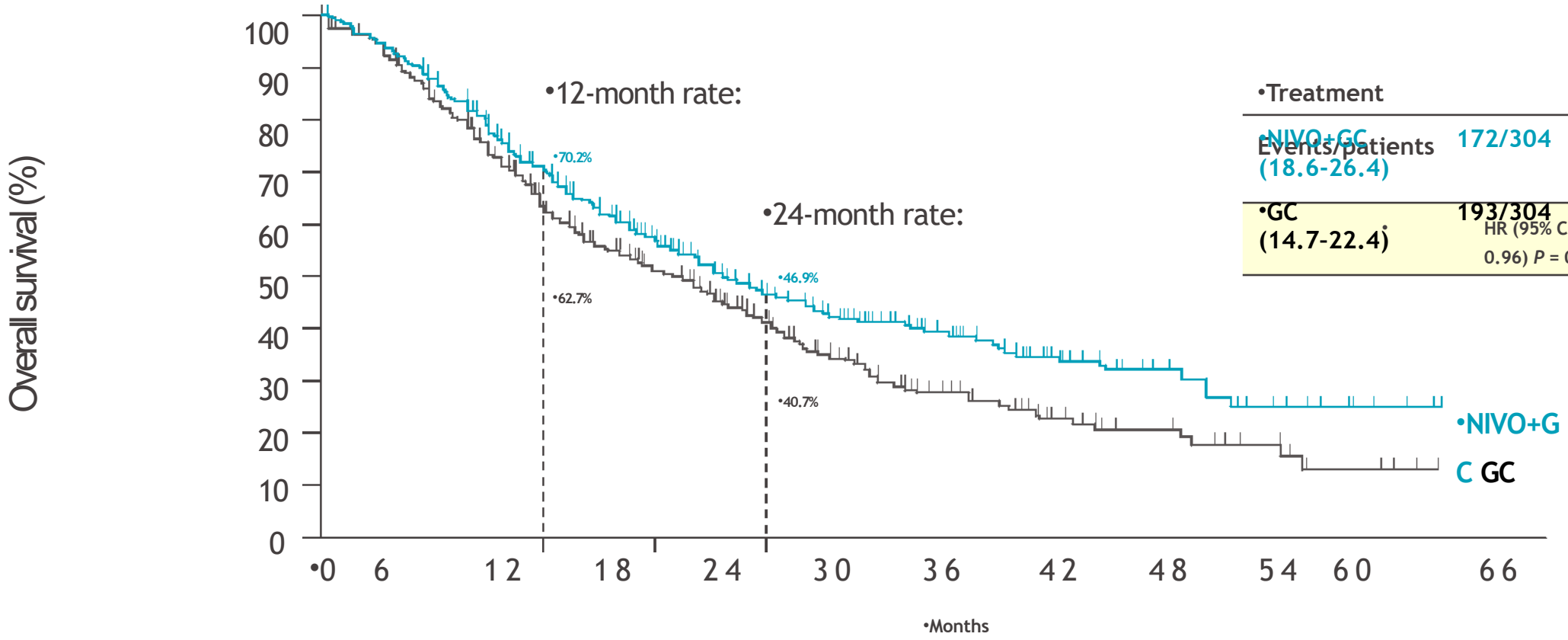
Patient disposition	NIVO+GC combination (n = 304)[b,c]	GC (n = 288)[b]
Completed 6 cycles per protocol, n (%)	225 (74)	157 (55)
Discontinued treatment, n (%)		
Any reason	79 (26)	131 (45)
Disease progression	20 (7)	50 (17)
Study drug toxicity	23 (8)	22 (8)

- In total, 244 patients randomized to the NIVO+GC arm went on to receive NIVO monotherapy — 20 patients (8%) completed monotherapy and 23 (9%) were still on therapy at database lock

[a]Represents duration of NIVO+GC combination ± NIVO monotherapy for the NIVO+GC arm and duration of GC combination for the GC arm; the protocol-defined maximum treatment duration was 24 months for the NIVO+GC arm and ~4.5 months (6 × 3-week cycles) for the GC arm.
[b]All treated patients. [c]Relates only to disposition during the NIVO+GC combination phase.

OS (primary endpoint)

NIVO+GC demonstrated statistically significant and clinically meaningful improvements in OS versus GC alone as first-line treatment for unresectable or mUC



•Treatment		• Median OS (95% CI), months
•NIVO+GC	172/304	21.7
Events/patients (18.6-26.4)		
•GC	193/304	18.9
(14.7-22.4)	HR (95% CI), 0.78 (0.63-0.96) *P* = 0.0171	

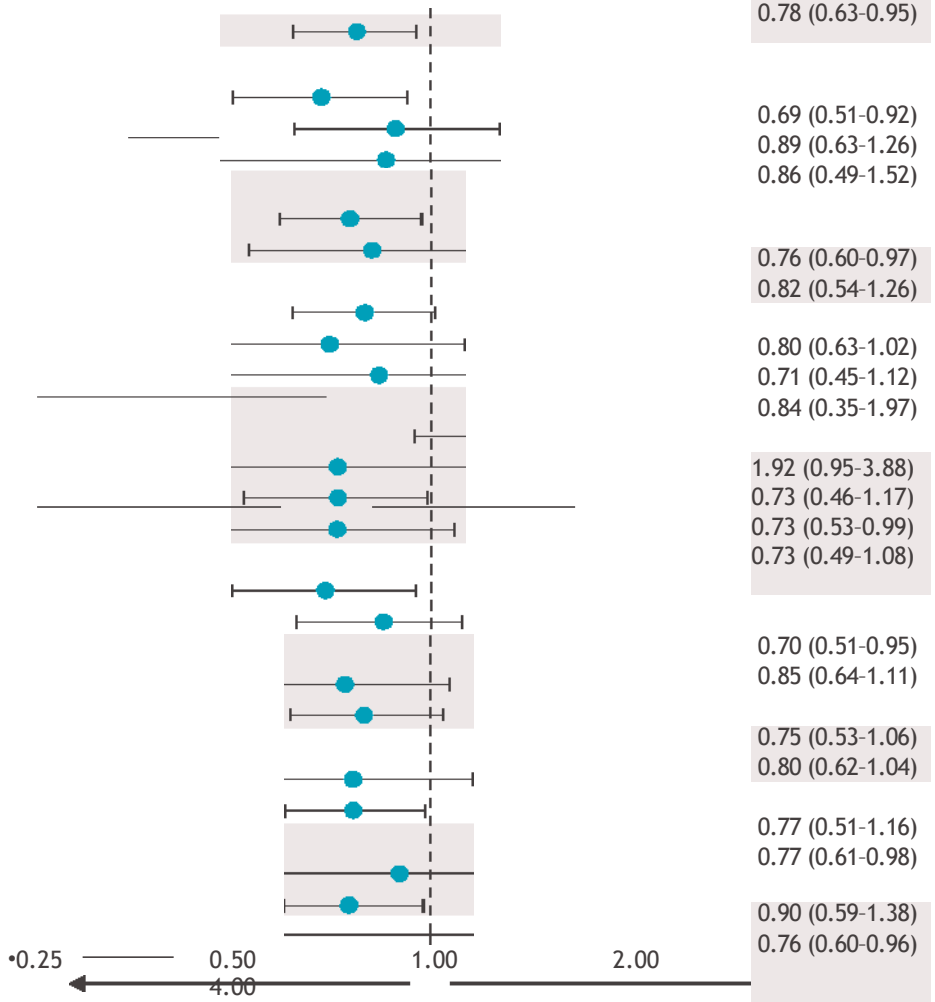
No. at risk												
NIVO+GC	304	264	196	142	97	69	48	25	15	7	2	0
GC	304	242	166	122	82	49	33	17	13	4	1	0

•Median (range) study follow-up was 33.6 (7.4-62.4) months. OS was estimated in all randomized patients and defined as time from randomization to death from any cause. For patients without documented death, OS was censored on the last date the patient was known to be alive. For randomized patients with no follow-up, OS was censored at randomization.

OS in subgroups

OS benefit was observed across the majority of key sub-groups

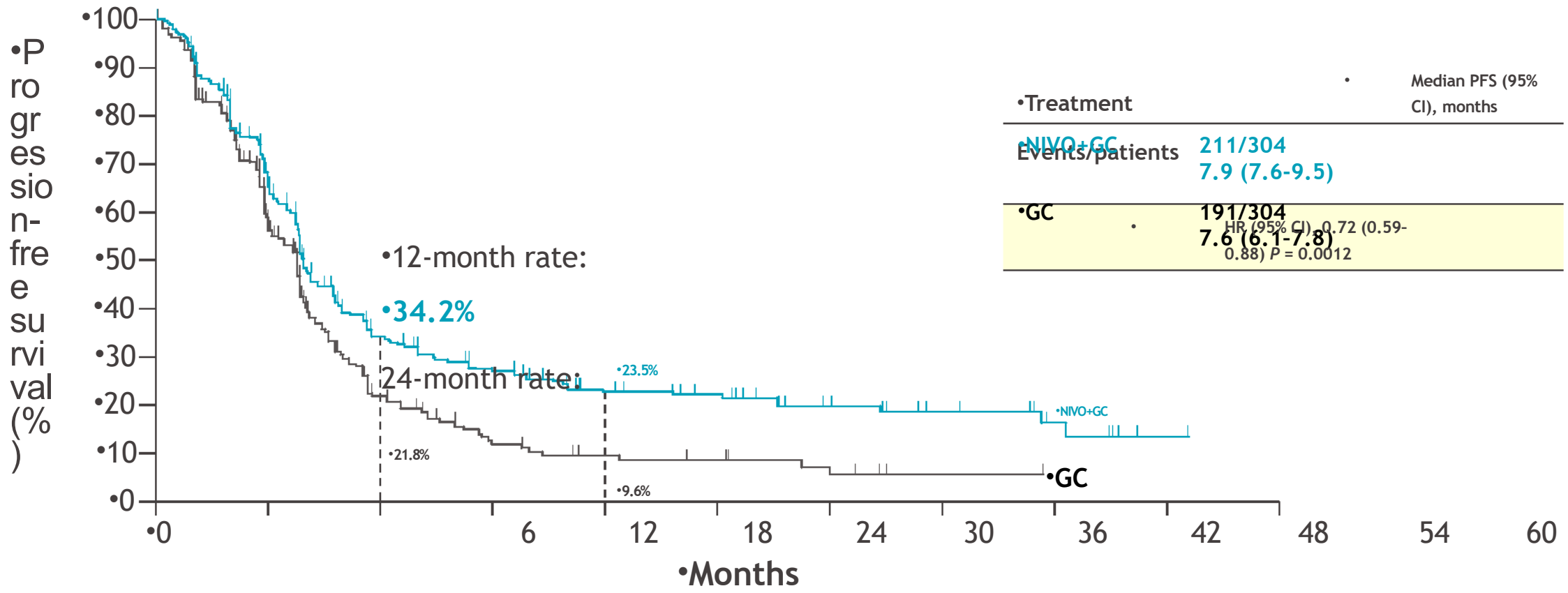
Subgroup	No. of patients	NIVO+GC *No. of events/no. of patients*	GC *No. of events/no. of patients*	Unstratified HR for death (95% CI)
Overall (N = 608)		172/304	193/304	0.78 (0.63-0.95)
Age, years				
< 65	298	85/150	100/148	0.69 (0.51-0.92)
≥ 65 and < 75	236	65/120	66/116	0.89 (0.63-1.26)
≥ 75	74	22/34	27/40	0.86 (0.49-1.52)
Sex				
Male	470	133/236	147/234	0.76 (0.60-0.97)
Female	138	39/68	46/70	0.82 (0.54-1.26)
Race				
White	436	123/211	145/225	0.80 (0.63-1.02)
Asian	138	38/75	36/63	0.71 (0.45-1.12)
Other	32	11/18	10/14	0.84 (0.35-1.97)
Region				
US	40	18/19	15/21	1.92 (0.95-3.88)
Asia	133	36/72	34/61	0.73 (0.46-1.17)
Europe	276	72/134	90/142	0.73 (0.53-0.99)
Rest of the world	159	46/79	54/80	0.73 (0.49-1.08)
ECOG PS				
0	324	74/162	87/162	0.70 (0.51-0.95)
1	282	96/140	106/142	0.85 (0.64-1.11)
PD-L1 expression				
≥ 1%	221	64/111	67/110	0.75 (0.53-1.06)
< 1% or indeterminate	387	108/193	126/194	0.80 (0.62-1.04)
Liver metastases				
Yes	128	45/64	48/64	0.77 (0.51-1.16)
No	480	127/240	145/240	0.77 (0.61-0.98)
Previous systemic anticancer therapy				
Yes	156	44/88	41/68	0.90 (0.59-1.38)
No	452	128/216	152/236	0.76 (0.60-0.96)



•All randomized patients. HRs were not computed for subgroup categories (except for age, sex, race, and region) with < 10 patients per treatment group. Categories without a meaningful estimate of the HR are not shown. PD-L1 expression and liver metastases are per interactive response technology. There were no patients with indeterminate PD-L1 status. Previous systemic anticancer therapy refers to neoadjuvant/adjuvant treatments for patients undergoing radical resection or as part of a bladder-sparing approach in muscle-invasive bladder cancer.

PFS per BICR (primary endpoint)

NIVO+GC demonstrated statistically significant improvements in PFS versus GC alone as first-line treatment for unresectable/mUC



•Treatment	• Median PFS (95% CI), months
•NIVO+GC Events/patients	211/304 7.9 (7.6-9.5)
•GC	191/304 7.6 (6.1-7.8)

• HR (95% CI), 0.72 (0.59-0.88) *P* = 0.0012

No. at risk											
NIVO+GC	304	179	82	57	41	31	19	11	6	1	0
GC	304	119	35	17	10	8	5	1	0	0	0

•Median (range) study follow-up was 33.6 (7.4-62.4) months. PFS was estimated in all randomized patients and defined as time from randomization to first documented disease progression (per BICR assessments using RECIST v1.1) or death due to any cause, whichever occurred first. Patients who did not progress or die were censored at last evaluable tumor assessment. Patients without on-study tumor assessments who did not die were censored at randomization. **Patients who started any subsequent anticancer therapy without prior reported progression were censored at last evaluable tumor assessment before initiation of subsequent therapy.**

PFS per BICR in subgroups

PFS benefit was observed across the majority of key sub-groups

Subgroup	No. of patients	NIVO+GC *No. of events/no. of patients*	GC *No. of events/no. of patients*	Unstratified HR for progression or death (95% CI)
Overall (N = 608)		211/304	191/304	0.71 (0.58-0.86)
Age, years				
< 65	298	102/150	90/148	0.72 (0.54-0.96)
≥ 65 and < 75	236	81/120	71/116	0.74 (0.54-1.02)
≥ 75	74	28/34	30/40	0.60 (0.35-1.01)
Sex				
Male	470	163/236	145/234	0.72 (0.57-0.90)
Female	138	48/68	46/70	0.68 (0.45-1.03)
Race				
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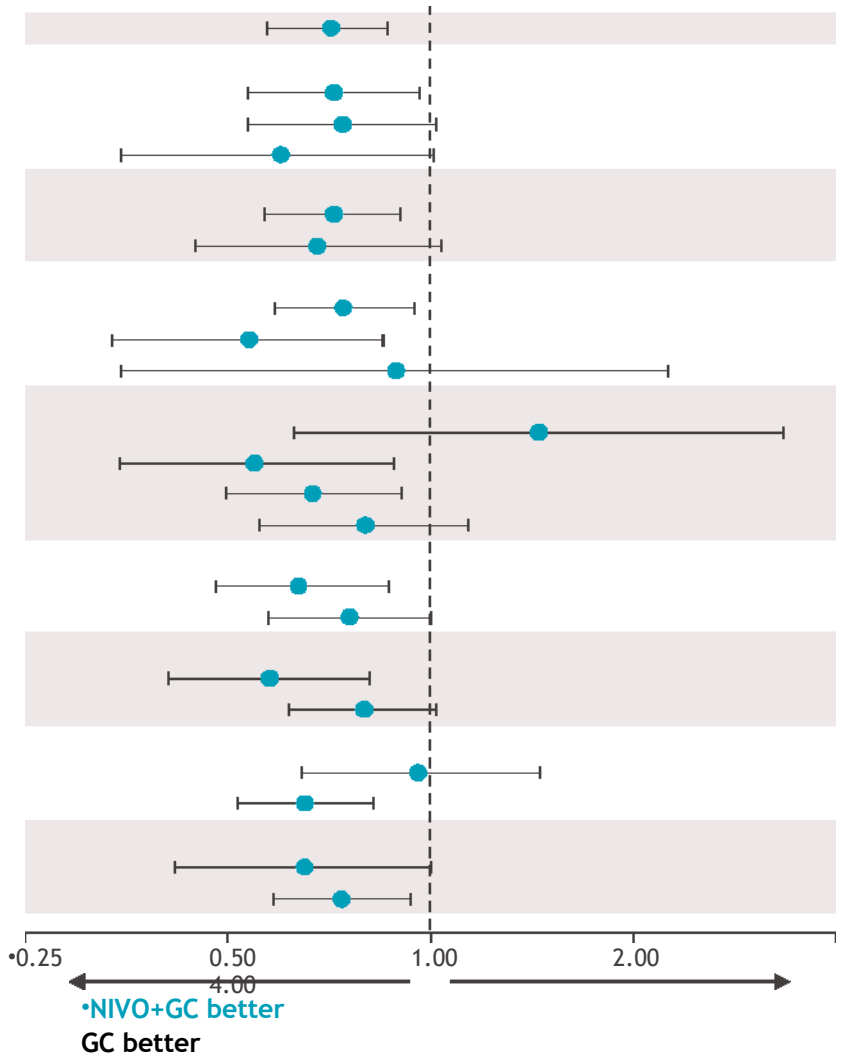
Asian	138	45/75	35/63	0.54 (0.34-0.85)
Other	32	13/18	7/14	0.89 (0.35-2.25)
Region				
US	40	14/19	10/21	1.45 (0.63-3.31)
Asia	133	43/72	33/61	0.55 (0.35-0.88)
Europe	276	94/134	84/142	0.67 (0.50-0.91)
Rest of the world	159	60/79	64/80	0.80 (0.56-1.14)
ECOG PS				
0	324	97/162	90/162	0.64 (0.48-0.86)
1	282	112/140	101/142	0.76 (0.58-1.00)
PD-L1 expression				
≥ 1%	221	71/112	70/109	0.58 (0.41-0.81)
< 1% or indeterminate	387	140/192	121/195	0.80 (0.62-1.02)
Liver metastases				
Yes	124	55/62	44/62	0.97 (0.65-1.45)
No	484	156/242	147/242	0.65 (0.52-0.82)
Previous systemic anticancer therapy				
Yes	156	55/88	38/68	0.65 (0.42-1.00)
No	452	156/216	153/236	0.74 (0.59-0.93)

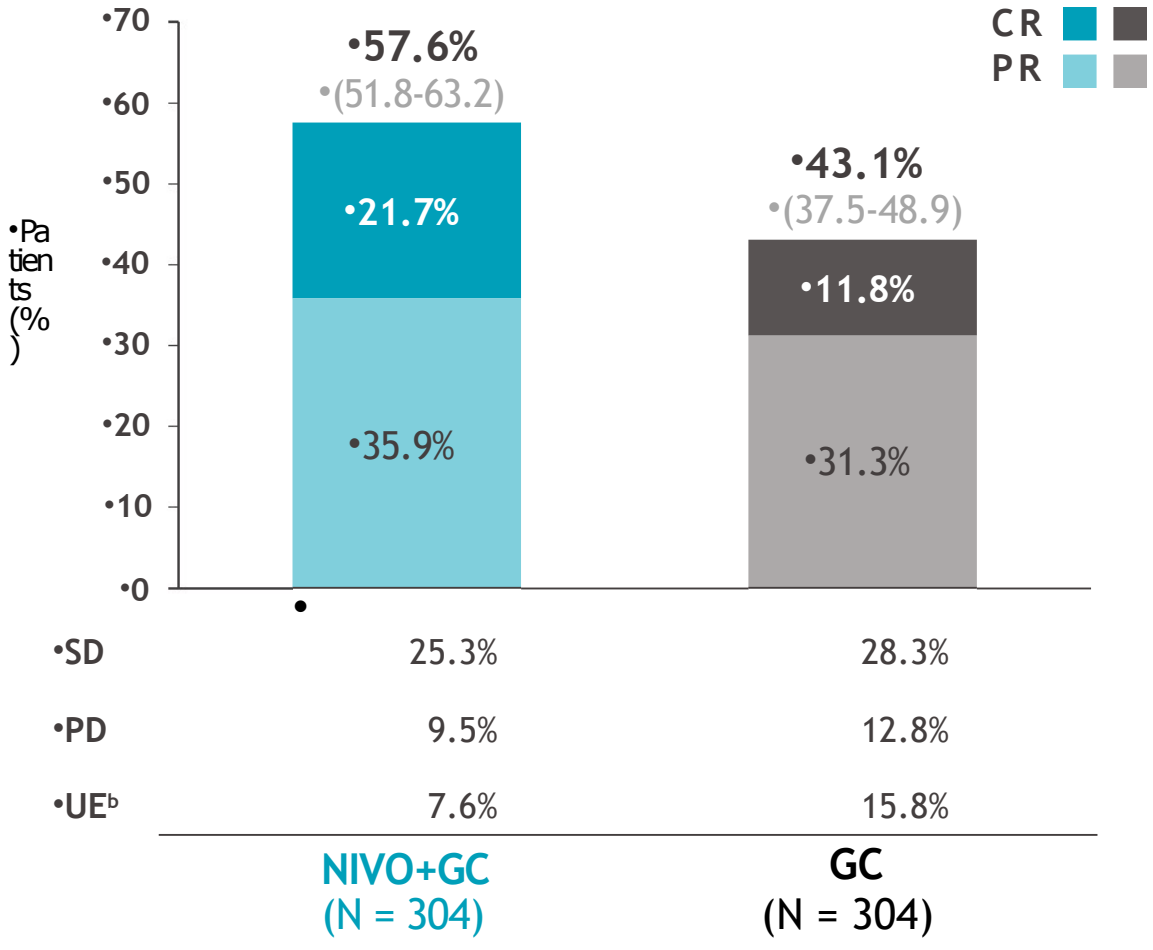


•All randomized patients. HRs were not computed for subgroup categories (except for age, sex, race, and region) with < 10 patients per treatment group. Categories without a meaningful estimate of the HR are not shown. PD-L1 expression and liver metastases are according to the clinical report. There were no patients with indeterminate PD-L1 status. Previous systemic anticancer therapy refers to neoadjuvant/adjuvant treatments for patients undergoing radical resection or as part of a bladder-sparing approach in muscle-invasive bladder cancer.

Objective response outcomes (exploratory endpoints)

ORR and CR rates were notably higher with NIVO+GC

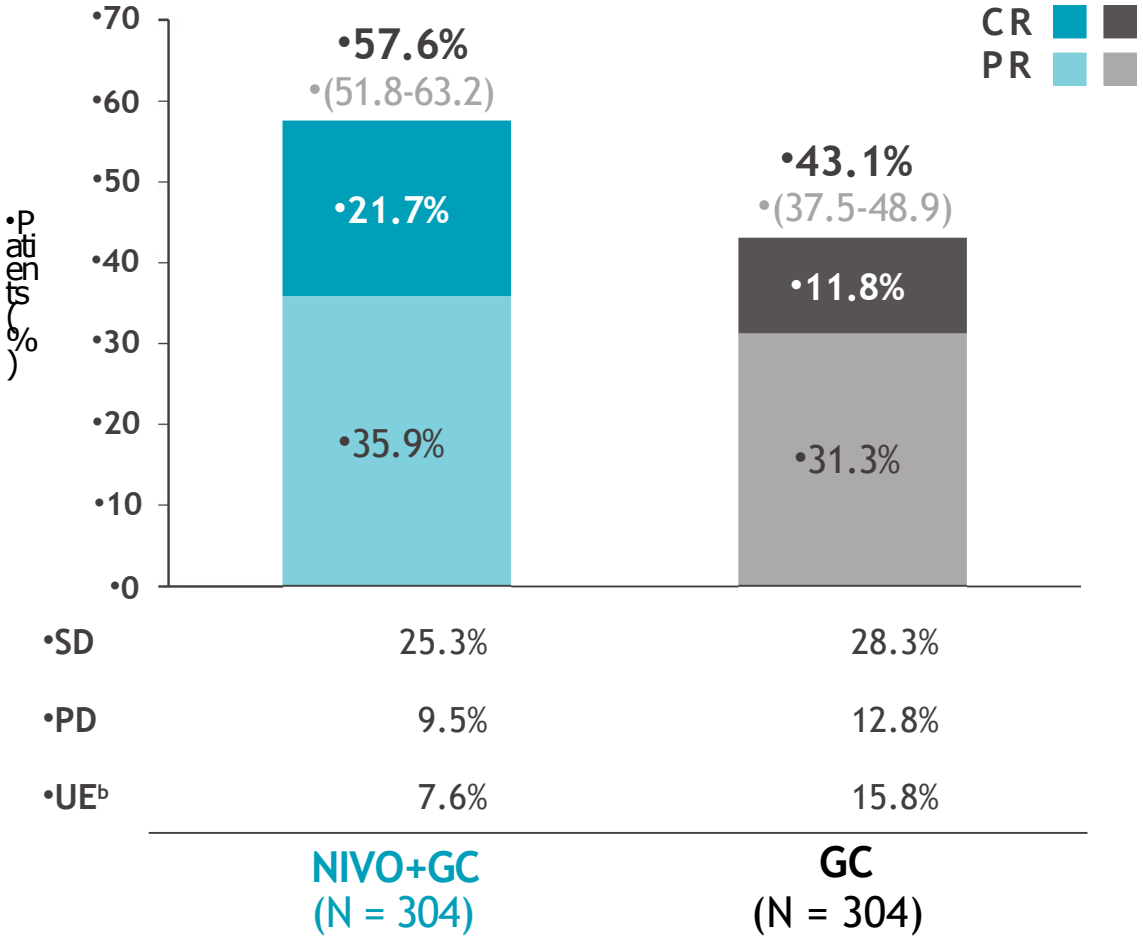
•ORR (95% CI) and BOR per BICR[a]



•[a]In all randomized patients. [b]The most common reasons for UE response included death before first tumor assessment, withdrawal of consent, treatment stopped due to toxicity, patient never treated, •and receipt of subsequent anticancer therapy before first tumor assessment. [c]Based on patients with an objective response per BICR (PR or CR as BOR). [d]Based on patients with a CR per BICR.
•BOR, best overall response; CR, complete response; DoCR, duration of complete response; DoR, duration of objective response; NE, not estimable; PD, progressive disease; PR, partial response; •Q, quartile; SD, stable disease; TTCR, time to complete response; TTR, time to objective response; UE, unevaluable.

Objective response outcomes (exploratory endpoints)

•ORR (95% CI) and BOR per BICR[a]



•Time to and duration of responses

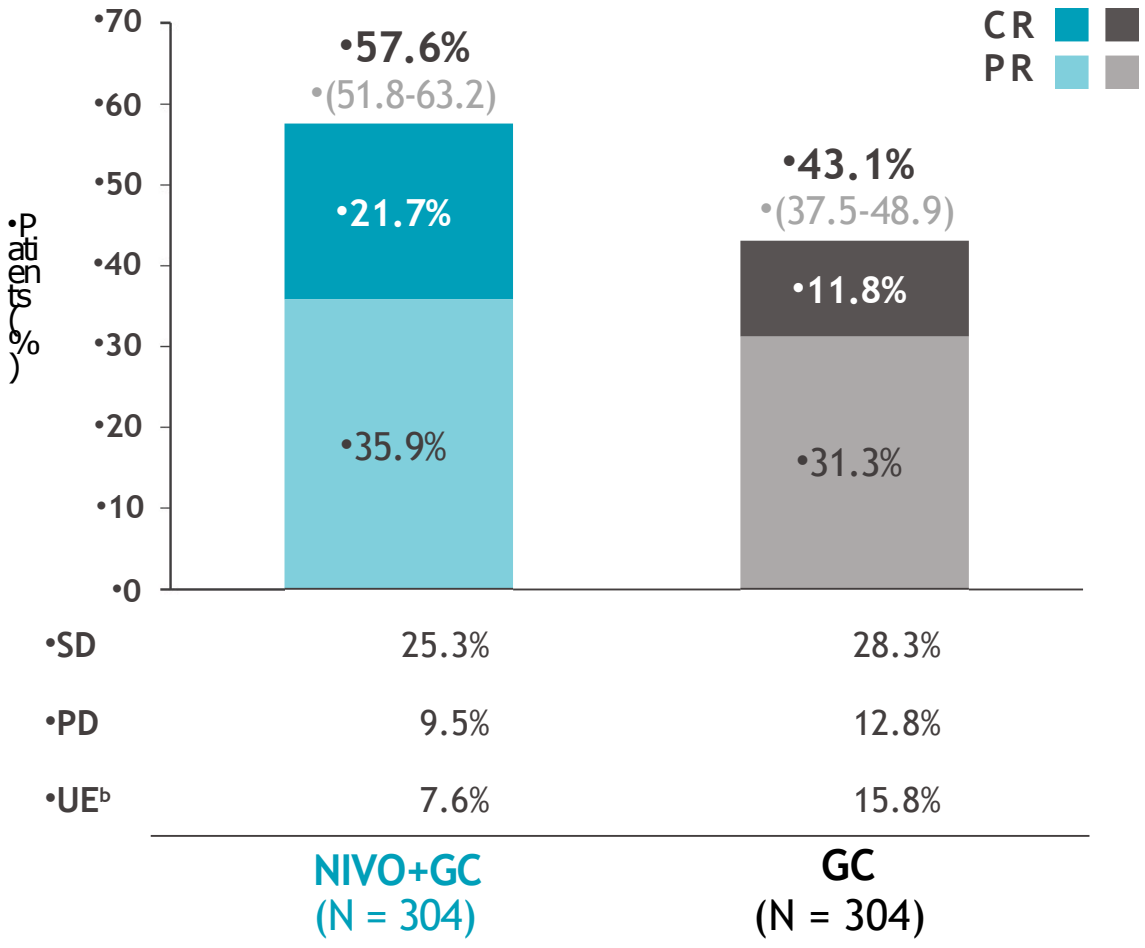
Any objective response[c]	NIVO+GC (n = 175)	GC (n = 131)
Median TTR (Q1-Q3), months	2.1 (2.0-2.3)	2.1 (2.0-2.2)
Median DoR (95% CI), months	9.5 (7.6-15.1)	7.3 (5.7-8.9)

•[a]In all randomized patients. [b]The most common reasons for UE response included death before first tumor assessment, withdrawal of consent, treatment stopped due to toxicity, patient never treated, •and receipt of subsequent anticancer therapy before first tumor assessment. [c]Based on patients with an objective response per BICR (PR or CR as BOR). [d]Based on patients with a CR per BICR.
•BOR, best overall response; CR, complete response; DoCR, duration of complete response; DoR, duration of objective response; NE, not estimable; PD, progressive disease; PR, partial response; •Q, quartile; SD, stable disease; TTCR, time to complete response; TTR, time to objective response; UE, unevaluable.

Objective response outcomes (exploratory endpoints)

The CR rate was nearly doubled (21.7% vs 11.8%) and the DoCR almost 3 times longer (37.1 vs 13.2 months) with NIVO+GC, despite a maximum of 2 years of NIVO treatment

•ORR (95% CI) and BOR per BICR[a]



•Time to and duration of responses

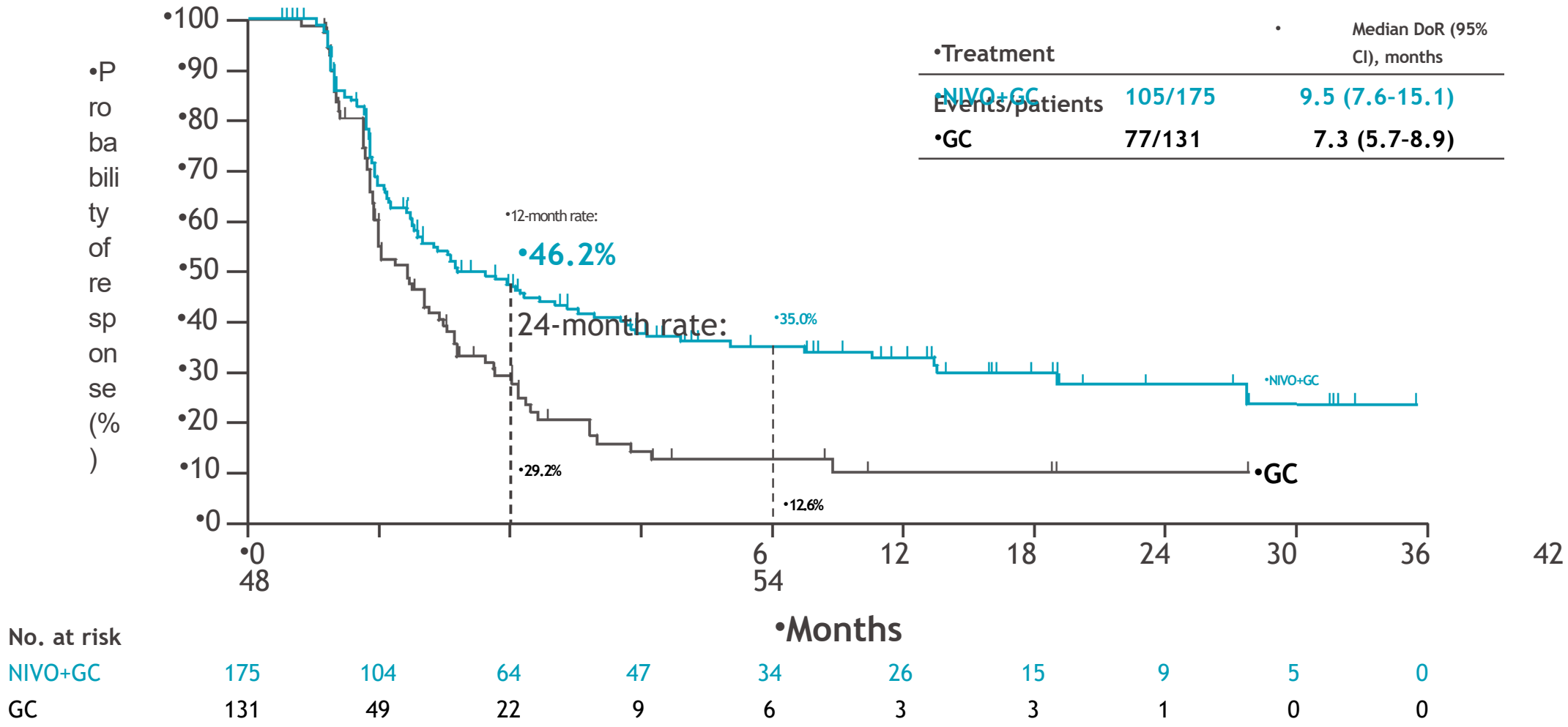
Any objective response[c]	NIVO+GC (n = 175)	GC (n = 131)
Median TTR (Q1-Q3), months	2.1 (2.0-2.3)	2.1 (2.0-2.2)
Median DoR (95% CI), months	9.5 (7.6-15.1)	7.3 (5.7-8.9)

Complete response[d]	NIVO+GC (n = 66)	GC (n = 36)
Median TTCR (Q1-Q3), months	2.1 (1.9-2.2)	2.1 (1.9-2.2)
Median DoCR (95% CI), months	37.1 (18.1-NE)	13.2 (7.3-18.4)

•[a]In all randomized patients. [b]The most common reasons for UE response included death before first tumor assessment, withdrawal of consent, treatment stopped due to toxicity, patient never treated, •and receipt of subsequent anticancer therapy before first tumor assessment. [c]Based on patients with an objective response per BICR (PR or CR as BOR). [d]Based on patients with a CR per BICR.
•BOR, best overall response; CR, complete response; DoCR, duration of complete response; DoR, duration of objective response; NE, not estimable; PD, progressive disease; PR, partial response; •Q, quartile; SD, stable disease; TTCR, time to complete response; TTR, time to objective response; UE, unevaluable.

Duration of objective response per BICR

concurrent ICI and chemotherapy combination was associated with deep and durable responses



Subsequent therapy[a]

40% patients in GC alone arm , went on to receive Immune check point inhibitors as subsequent therapy

•Subsequent immunotherapy received before PD[b] time[b]

Category, n (%)	NIVO+GC (N = 304)	GC (N = 304)
Any ICI	8 (3)	60 (20)
Anti-PD-1	6 (2)	24 (8)
Pembrolizumab	4 (1)	17 (6)
Anti-PD-L1	2 (1)	36 (12)
Avelumab	2 (1)	27 (9)
Atezolizumab	0	6 (2)

Subsequent immunotherapy received at any

Category, n (%)	NIVO+GC (N = 304)	GC (N = 304)
Any ICI[c]	25 (8)	123 (40)
Anti-PD-1	22 (7)	72 (24)
Pembrolizumab	14 (5)	54 (18)
NIVO	6 (2)	5 (2)
Toripalimab	0	6 (2)
Anti-PD-L1	3 (1)	52 (17)
Avelumab	3 (1)	32 (11)
Atezolizumab	0	13 (4)
Durvalumab	0	7 (2)

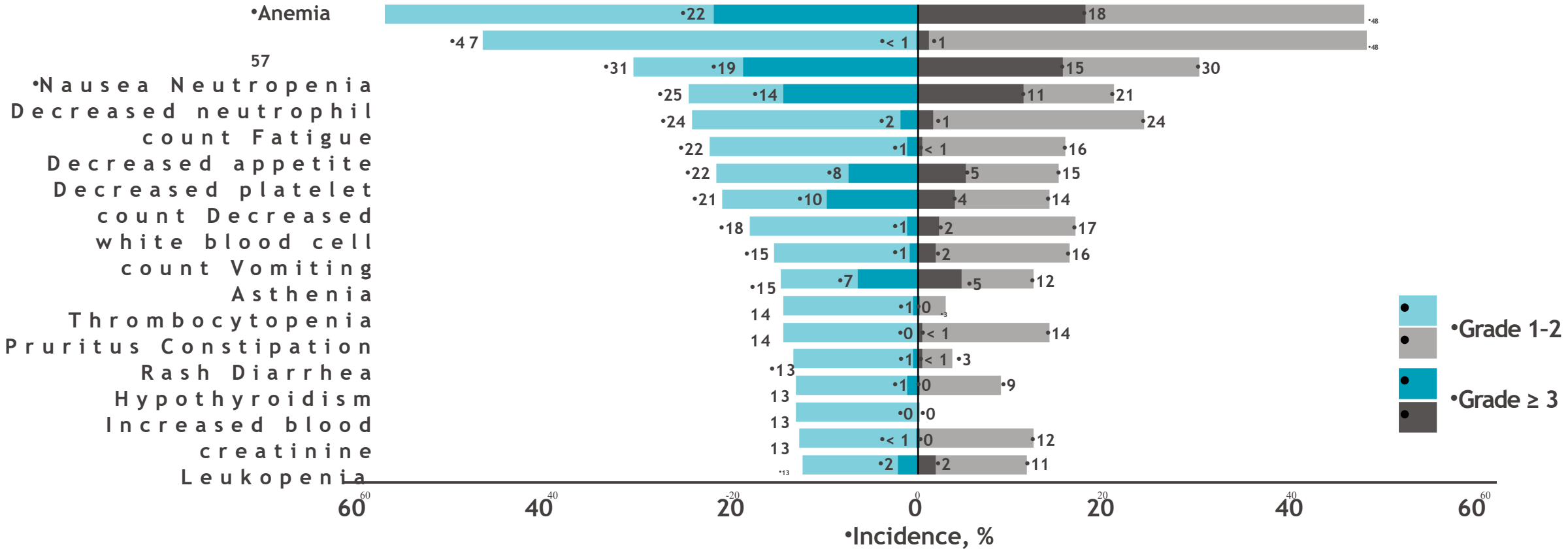
•Proportions of patients receiving subsequent surgery, radiotherapy, and/or platinum-based chemotherapy were similar in the NIVO+GC and GC arms

•[a]In all randomized patients. Subsequent therapy was defined as therapy started on or after first dosing date (randomization date if patient was never treated). Patients may have received more than 1 subsequent therapy. [b]Individual subsequent immunotherapy regimens received in > 1% of patients in either arm are listed. [c]1 patient in the NIVO+GC arm received subsequent NIVO plus ipilimumab; 3 patients in the NIVO+GC arm and 2 in the GC arm received other subsequent immunotherapy (ie, not anti-PD-1 or PD-L1).
•ICI, immune checkpoint inhibitor; PD-1, programmed death-1.

Treatment-related AEs in all treated patients

The combination of NIVO+GC resulted in no new toxicity signals, and the safety profile was consistent with the established safety of these agents in prior UC trials

Treatment-related AE, %[a]	•NIVO+GC (n = 304)		GC (n = 288)	
	Any grade	Grade ≥ 3[b]	Any grade	Grade ≥ 3[b]
Any	97	62	93	52
Leading to discontinuation	21	11	17	8

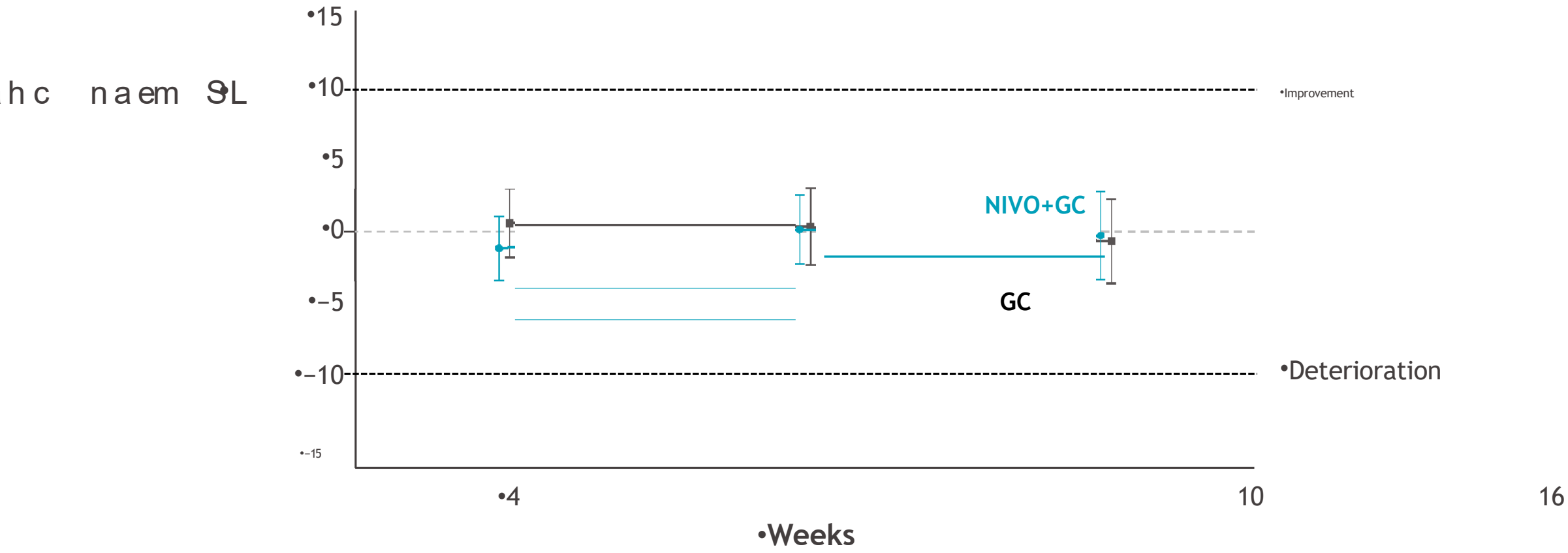


•[a]Includes events that occurred in treated patients between first dose and 30 days after last dose of study therapy. Tornado plot displays individual treatment-related AEs occurring at any •grade in ≥ 10% of treated patients in either arm. [b]One grade 5 event occurred in each arm (sepsis in the NIVO+GC arm and acute kidney injury in the GC arm).
•AE, adverse event.

HRQoL: EORTC QLQ-C30 (secondary endpoint)

Quality of life was maintained with addition of NIVO to GC

•Mean change from baseline in EORTC QLQ-C30 Global Health Status[a]



•[a]In the EORTC QLQ-C30 evaluable population. Includes patients who completed ≥ 1 of the 15 domains/scales at baseline and ≥ 1 evaluable assessment at post-baseline visits based on the EORTC QLQ-C30. Changes from baseline were used as the dependent variable. Analysis used all HRQoL data assessed during the treatment period through week 16. A mixed-effects repeated measures model was used assuming unstructured covariance and included a random intercept/slope and fixed effects by treatment group, time (ie, week, as a categorical variable), PD-L1 expression, cisplatin-eligibility (ineligible vs eligible), liver metastasis (yes vs no), baseline score, and baseline score by time interaction and treatment by time interaction.
•EORTC QLQ-C30, European Organisation for Research and Treatment of Care QLQ-C30 Global Health Status questionnaire; LS, least squares.

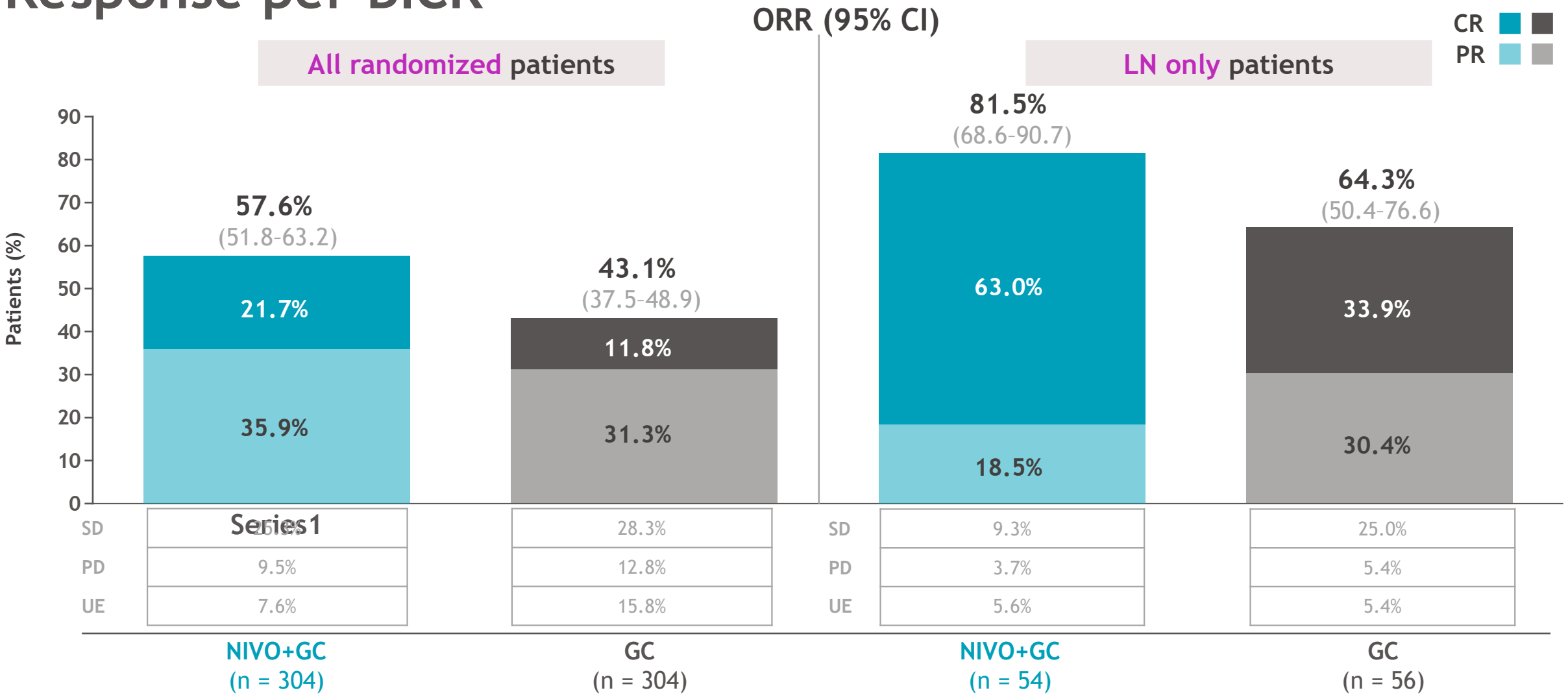
ASCO 2024: Characterization of Complete Responders to Nivolumab + Gemcitabine-Cisplatin vs Gemcitabine-Cisplatin Alone and Patients with Lymph Node–only Metastatic Urothelial Carcinoma from the CheckMate 901 Trial

Select characteristics for all patients with complete response

	All randomized patients		Patients with CR	
	NIVO+GC (N = 304)	GC (N = 304)	NIVO+GC (N = 66)	GC (N = 36)
Median age (range), years	65.0 (32-86)	65.0 (35-85)	65.0 (33-81)	63.5 (36-80)
Male sex, n (%)	236 (78)	234 (77)	53 (80)	31 (86)
Race				
White	211 (69)	225 (74)	47 (71)	27 (75)
Black or African American	0	2 (< 1)	0	0
American Indian or Alaska Native	1 (< 1)	1 (< 1)	0	1 (3)
Asian	75 (25)	63 (21)	16 (24)	6 (17)
Other	17 (6)	13 (4)	3 (5)	2 (6)
LN only disease,[a] n (%)	54 (18)	56 (18)	34 (52)	19 (53)
Disease stage at study entry, n (%)				
Stage III	37 (12)	28 (9)	9 (14)	5 (14)
Stage IV	265 (87)	274 (90)	56 (85)	31 (86)
Not reported	2 (< 1)	2 (< 1)	1 (2)	0
PD-L1 status, n (%)				
≥ 1%	112 (37)	109 (36)	28 (42)	11 (31)
< 1%	192 (63)	195 (64)	38 (58)	25 (69)
Subsequent anticancer therapy received	108 (36)	156 (51)	23 (35)	15 (42)

[a]LN only disease as defined per BICR. There may not be full concordance with investigator assessment. Galsky MD et al. Presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting. Chicago, IL. June 1–4, 2024. Abstract 4509.

Response per BICR



- CR rates for NIVO+GC-treated patients with LN only mUC were approximately twice that of GC-treated patients

Galsky MD et al. Presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting. Chicago, IL. June 1-4, 2024. Abstract 4509.

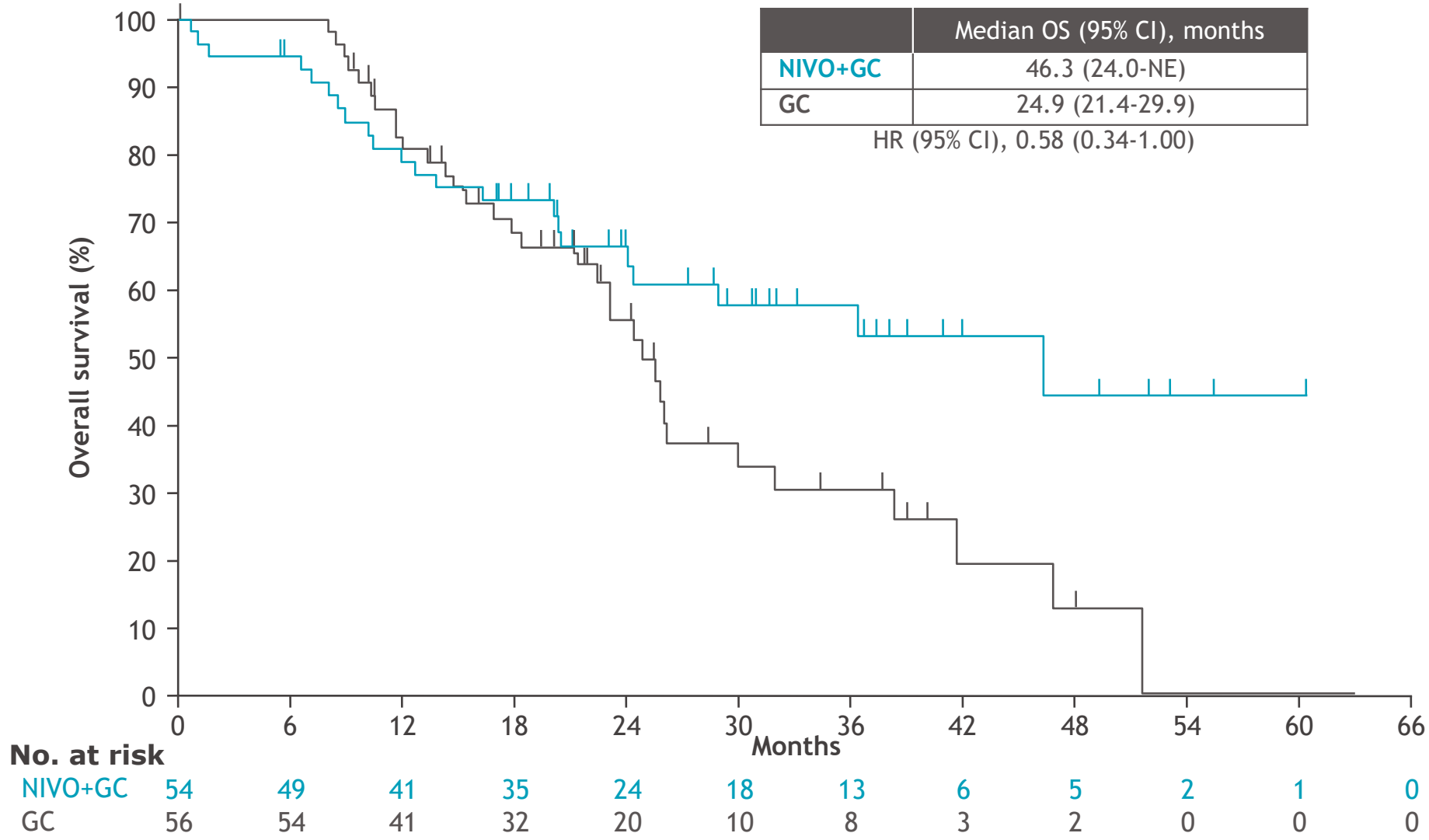
Response characteristics for LN only patients with CR

	NIVO+GC (N = 54)	GC (N = 56)
Patients with CR	n = 34	n = 19
Median time to CR (range), months	2.1 (1.8-2.2)	2.0 (1.6-3.3)
Median duration of CR (95% CI), months	NR (22.0-NE)	8.7 (6.7-15.6)
12-month CR rate (95% CI), %	70 (51-82)	32 (10-57)
24-month CR rate (95% CI), %	65 (45-79)	Not applicable (0)

- The median duration of CR was NR in the NIVO+GC group and was 8.7 months in the GC group
- The 12-month CR rate for patients treated with NIVO+GC was more than twice that of patents treated with GC

Galsky MD et al. Presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting. Chicago, IL. June 1–4, 2024. Abstract 4509.

OS: patients with LN only mUC per BICR

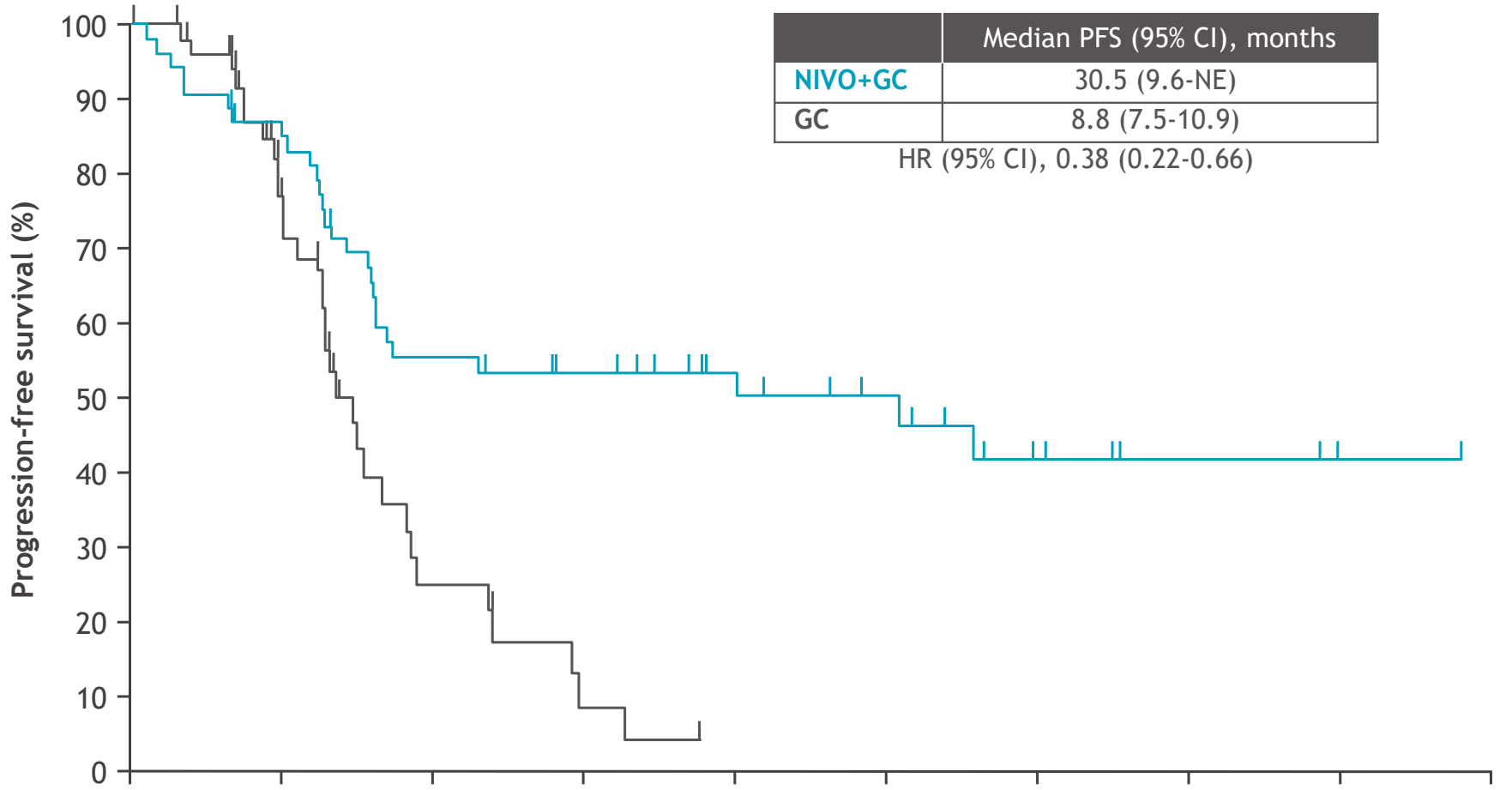


Galsky MD et al. Presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting. Chicago, IL. June 1–4, 2024. Abstract 4509.

PFS: patients with LN only mUC per BICR

	Median PFS (95% CI), months
NIVO+GC	30.5 (9.6-NE)
GC	8.8 (7.5-10.9)

HR (95% CI), 0.38 (0.22-0.66)



No. at risk

NIVO+GC	54	44	28	23	17	13	7	3	1	0
GC	56	28	7	2	0	0	0	0	0	0

Galsky MD et al. Presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting. Chicago, IL. June 1-4, 2024. Abstract 4509.

Summary: sub analysis of CM901 on LN metastases-only

- The post hoc analysis of CheckMate 901 revealed that among patients achieving complete response (CR), more than half had lymph node-only mUC.
- In patients with lymph node-only metastatic urothelial carcinoma (mUC), Nivolumab+GC demonstrated durable disease control and clinically meaningful improvements in OS and PFS compared to patients who received GC alone.
- Lymph node-only mUC represents a distinct clinical entity, and with Nivolumab+GC, we may alter the trajectory of this disease through consolidation therapy

Overall Summary

•NIVO+GC demonstrated statistically significant and clinically meaningful improvements in OS and PFS versus GC alone as first-line treatment for unresectable or mUC

•ORR and CR rates were notably higher with NIVO+GC and the concurrent ICI and chemotherapy combination was associated with deep and durable responses

- — The CR rate was nearly doubled (21.7% vs 11.8%) and the DoCR almost 3 times longer (37.1 vs 13.2 months) with NIVO+GC, despite a maximum of 2 years of NIVO treatment

•The combination of NIVO+GC resulted in no new toxicity signals, and the safety profile was consistent with the established safety of these agents in prior UC trials

•HRQoL was maintained with addition of NIVO to GC

•NIVO+GC is the first frontline concurrent ICI plus chemotherapy combination to improve OS in patients with unresectable or mUC

•These findings strengthen the rationale for Nivolumab plus cisplatin-based chemotherapy as a standard first-line treatment option for patients with mUC. Given the fixed number of cycles of CT, and the two year duration of immunotherapy, Nivolumab+GC seems more patient friendly regimen.

Thank you

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