

# Impact of Baseline Steroids on Efficacy of Programmed Cell Death-1 and Programmed Death-Ligand 1 Blockade in Patients With Non-Small-Cell Lung Cancer

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# Impact of Baseline Steroids on Efficacy of Programmed Cell Death-1 and Programmed Death-Ligand 1 Blockade in Patients With Non–Small-Cell Lung Cancer

Kathryn C. Arbour, Laura Mezquita, Niamh Long, Hira Rizvi, Edouard Auclin, Andy Ni, Gala Martínez-Bernal, Roberto Ferrara, W. Victoria Lai, Lizza E.L. Hendriks, Joshua K. Sabari, Caroline Caramella, Andrew J. Plodkowski, Darragh Halpenny, Jamie E. Chaft, David Planchard, Gregory J. Riely, Benjamin Besse, and Matthew D. Hellmann

Author affiliations and support information (if applicable) appear at the end of this article.

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K.C.A. and L.M. contributed equally to this work.

B.B. and M.D.H. contributed equally to this work.

Corresponding author: Matthew D. Hellmann, Memorial Sloan Kettering Cancer Center, 885 2nd Ave, New York, NY, 10017; e-mail: [hellmanm@mskcc.org](mailto:hellmanm@mskcc.org).

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## A B S T R A C T

### Purpose

Treatment with programmed cell death-1 or programmed death ligand 1 (PD-(L)1) inhibitors is now standard therapy for patients with lung cancer. The immunosuppressive effect of corticosteroids may reduce efficacy of PD-(L)1 blockade. On-treatment corticosteroids for treatment of immune-related adverse events do not seem to affect efficacy, but the potential impact of baseline corticosteroids at the time of treatment initiation is unknown. Clinical trials typically excluded patients who received baseline corticosteroids, which led us to use real-world data to examine the effect of corticosteroids at treatment initiation.

### Methods

We identified patients who were PD-(L)1-naïve with advanced non–small-cell lung cancer from two institutions—Memorial Sloan Kettering Cancer Center and Gustave Roussy Cancer Center—who were treated with single-agent PD-(L)1 blockade. Clinical and pharmacy records were reviewed to identify corticosteroid use at the time of beginning anti-PD-(L)1 therapy. We performed multivariable analyses using Cox proportional hazards regression model and logistic regression.

### Results

Ninety (14%) of 640 patients treated with single-agent PD-(L)1 blockade received corticosteroids of  $\geq 10$  mg of prednisone equivalent daily at the start of the PD-(L)1 blockade. Common indications for corticosteroids were dyspnea (33%), fatigue (21%), and brain metastases (19%). In both independent cohorts, Memorial Sloan Kettering Cancer Center ( $n = 455$ ) and Gustave Roussy Cancer Center ( $n = 185$ ), baseline corticosteroids were associated with decreased overall response rate, progression-free survival, and overall survival with PD-(L)1 blockade. In a multivariable analysis of the pooled population, adjusting for smoking history, performance status, and history of brain metastases, baseline corticosteroids remained significantly associated with decreased progression-free survival (hazard ratio, 1.3;  $P = .03$ ), and overall survival (hazard ratio, 1.7;  $P < .001$ ).

### Conclusion

Baseline corticosteroid use of  $\geq 10$  mg of prednisone equivalent was associated with poorer outcome in patients with non–small-cell lung cancer who were treated with PD-(L)1 blockade. Prudent use of corticosteroids at the time of initiating PD-(L)1 blockade is recommended.

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## ASSOCIATED CONTENT

Listen to the podcast by Dr Rangachari at [ascopubs.org/jco/podcasts](http://ascopubs.org/jco/podcasts)

Appendix  
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## INTRODUCTION

The development of immune checkpoint blockade (ICB) therapy has dramatically changed the treatment landscape for patients with cancer.<sup>1</sup> For patients with advanced non–small-cell lung cancer (NSCLC), treatment with anti-programmed cell death 1 (PD-1) or programmed

death-ligand 1 (PD-L1) therapy (PD-(L)1 blockade) is now a standard of care.<sup>2-4</sup> As real-world clinical experience with ICB agents continues to grow, new questions have emerged regarding the treatment of patients that could not be answered in the initial groundbreaking clinical trials.

Corticosteroids are commonly used in patients with NSCLC to treat a variety of indications,

including fatigue, dyspnea, decreased appetite, and symptomatic brain metastases.<sup>5-9</sup> Given the immunosuppressive properties of corticosteroids and the potential effect on T-cell function,<sup>10</sup> there is understandable concern that the use of these agents could decrease the efficacy of ICB. As a result, use of corticosteroids before the start of therapy has been a uniform exclusion criterion in clinical trials of ICB. It is perhaps surprising, but reassuring, to see emerging data that on-treatment corticosteroids used for the management of immune-related adverse events<sup>11</sup> do not seem to negatively affect efficacy.<sup>12-15</sup> Yet there are no data to date that evaluate whether corticosteroids at baseline affect the efficacy of ICB. We therefore evaluated the potential impact of systemic corticosteroids at the start of ICB on the efficacy of PD-(L)1 blockade in more than 600 patients who were treated at two independent cancer centers.

## METHODS

### Patients

Patients with advanced NSCLC who were treated with single-agent PD-(L)1 inhibitor (pembrolizumab, nivolumab, atezolizumab, or durvalumab) with treatment initiation between April 2011 to September 2017 were identified at Memorial Sloan Kettering Cancer (MSKCC; n = 455) and Gustave Roussy Cancer Center (GRCC; n = 185). Patients' records, including pharmacy records, were reviewed to determine if patients were documented as having received any oral or intravenous corticosteroids on the day PD-(L)1 blockade was started. Use of corticosteroids within 30 days of the start of PD-(L)1 blockade was also collected for the MSKCC cohort. Information about the type of corticosteroid, indication, and route of administration were collected. Dose of corticosteroids was expressed as total daily milligrams of prednisone equivalents. Clinicopathologic characteristics, including age, gender, histology, Eastern Cooperative Oncology Group performance status, and smoking history, were collected for all patients. Efficacy of PD-(L)1 blockade was determined by local specialized radiologists (C.C. at GRCC and N.L., A.P., and D.H. at MSKCC) using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. All patients were observed until death or data lock—March 2017 for MSKCC and December 2017 for GRCC.

### Statistical Analysis

Patient characteristics were described according to the status of corticosteroid use at baseline and compared with Fisher's exact test or  $\chi^2$  test for categorical data. Progression-free survival (PFS) was defined as the time from ICB initiation to the first event (tumor progression or death from any cause); overall survival (OS) was defined as the time from ICB initiation to death from any cause. Patients with no event were censored at the date of last follow-up. Best overall response differences were analyzed using Fisher's exact test or  $\chi^2$  test. Patients who died before radiologic assessment were categorized as nonresponders. Other patients who were not evaluable for response (n = 4 in MSKCC cohort, none in GRCC cohort), were not included in objective response assessment but were included for PFS and OS. Survival curves were estimated using the Kaplan-Meier method and compared with the log-rank test (univariable analysis). Univariable hazard ratios (HRs) were calculated using the log-rank method. We used multivariable Cox proportional hazards regression model to determine HRs and 95% CIs for PFS and OS and odds ratios for best overall response. The pooled cohort (N = 640) was used in subgroup and multivariable analysis to increase power. Statistical tests were two sided, and P values < .05 were considered statistically significant. Statistical analyses were carried out using R statistical software.

## RESULTS

We identified 640 patients treated with PD-(L)1 blockade at MSKCC (n = 455) and GRCC (n = 185). At the time of ICB initiation, 90 (14%) of the 640 patients received  $\geq 10$  mg of prednisone equivalent—53 (12%) of 455 patients in the MSKCC cohort and 37 (20%) of 185 patients in the GRCC cohort. A small fraction of additional patients (n = 17; 3%) received < 10 mg of prednisone equivalent at the initiation of ICB and were included in the noncorticosteroid group, as this low dose was considered to be in the range of physiologic adrenal replacement and is not typically excluded in clinical trials. The most common indications for corticosteroids were dyspnea or other respiratory symptoms (33%), fatigue (21%), and brain metastases (19%; Appendix Table A1, online only). In each group, clinicopathologic characteristics were typical of patients with advanced NSCLC and were generally well balanced between those who did or did not receive corticosteroids, with the two expected exceptions; poor performance status and history of brain metastases were more common in those who received corticosteroids (Table 1).

In the MSKCC cohort, use of baseline corticosteroids of  $\geq 10$  mg was associated with decreased overall response rate (ORR; 6% v 19%;  $P = .02$ ; Fig 1A), shorter PFS (median, 1.9 months v 2.6 months; HR, 1.7;  $P = .001$ ; Fig 1B), and shorter OS (median, 5.4 months v 12.1 months; HR, 2.1;  $P < .001$ ; Fig 1C). In the GRCC cohort, ORR was decreased but not significantly different in those who received baseline corticosteroids  $\geq 10$  mg (8% v 18%;  $P = .2$ ; Fig 1D), whereas PFS and OS were significantly shorter (PFS: median, 1.7 months v 1.8 months; HR, 1.5;  $P < .001$ ; Fig 1E; and OS: median, 3.3 months v 9.4 months; HR, 2.0;  $P < .001$ ; Fig 1F).

In the pooled cohort of patients from both centers (N = 640), baseline corticosteroids had a consistently negative effect on efficacy of PD-(L)1 blockade (Appendix Fig A1, online only), with diminished PFS and OS observed in nearly every subgroup examined (Fig 2).

Cognizant of the potential confounding effects of prognostic variables associated with corticosteroid use and other predictive features associated with response to PD(L)-1 blockade, we performed a multivariable analysis in the pooled cohort (N = 640), incorporating smoking history, performance status, and history of brain metastases. Corticosteroid use ( $\geq 10$  mg v < 10 mg) at the time of the initiation of PD-(L)1 blockade remained associated with decreased ORR (odds ratio, 0.42;  $P = .053$ ) and significantly shorter PFS (HR, 1.31;  $P = .03$ ) and OS (HR, 1.66;  $P < .001$ ; Table 2).

We also examined the effect of corticosteroid dose and timing on efficacy. In the pooled cohort from both centers, there was a similar detriment in efficacy when examining > 20 mg of prednisone or 10 mg to 19 mg compared with patients who received < 10 mg of corticosteroids (Appendix Fig A2, online only). In the MSKCC cohort (data not available from GRCC cohort), patients who received and discontinued corticosteroids days 1 to 30 before to the initiation of PD-(L)1 (66 of 455 patients) had intermediate PFS and OS compared with those who received corticosteroids on the day of ICB initiation (53 of 455 patients) and those who received no corticosteroids within 30 days of the start of therapy (Appendix Fig A3, online only).

**Table 1.** Baseline Patient Characteristics of the Memorial Sloan Kettering Cancer Center and Gustave Roussy Cancer Center Cohorts

Baseline Characteristic	MSKCC			GRCC		
	Prednisone ≥ 10 mg (n = 53)	Prednisone < 10 mg (n = 402)	<i>P</i>	Prednisone ≥ 10 mg (n = 37)	Prednisone < 10 mg (n = 148)	<i>P</i>
Age, years						
≥ 65	60 (32)	55 (221)	.55	35 (13)	39 (57)	.9
< 65	40 (21)	45 (181)		65 (24)	61 (91)	
Sex						
Male	49 (26)	48 (194)	1.0	70 (26)	65 (96)	.6
Female	51 (27)	52 (208)		30 (11)	35 (52)	
ECOG performance status						
0-1	70 (37)	92 (369)	< .01	57 (21)	83 (123)	< .01
≥ 2	30 (16)	8 (33)		43 (16)	17 (25)	
Smoking status						
Ever	77 (41)	83 (335)	.3	92 (34)	87 (129)	.8
Never	22 (12)	17 (67)		8 (3)	11 (16)	
Histology						
Squamous	15 (8)	18 (72)	.7	24 (9)	28 (40)	.8
Nonsquamous	85 (45)	82 (330)		76 (28)	73 (108)	
EGFR mutation status						
EGFR mutant	11 (6)	8 (32)	.4	5 (2)	5 (7)	.7
EGFR wild type	77 (41)	83 (333)		62 (23)	70 (104)	
EGFR unknown	11 (6)	9 (37)		32(12)	25 (37)	
Line of therapy						
First or second line	56 (30)	67 (268)	.2	38 (14)	52 (78)	.1
Third line or later	46 (23)	33 (134)		62 (23)	47 (70)	
History of brain metastases						
Yes	42 (22)	23 (94)	< .01	51 (19)	13 (19)	< .01
No	58 (31)	77 (308)		49 (18)	87 (129)	

NOTE. Data are given as No. (%).

Abbreviations: ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; GRCC, Gustave Roussy Cancer Center; MSKCC, Memorial Sloan Kettering Cancer Center.

Six patients (MSKCC [n = 3], GRCC [n = 3]) experienced a partial response to PD-(L)1 blockade despite the use of corticosteroids at the time of treatment initiation (Appendix Table A2, online only). These patients received 10 mg to 20 mg of corticosteroids for palliative indications, such as fatigue, respiratory symptoms, and pain. There were no evident differences in the clinical features of patients who experienced responses; all responders had an Eastern Cooperative Oncology Group performance status of 1. Four of six patients had continued response to therapy for more than 15 months, although the responses of two patients were more limited, including one patient whose response lasted for only 2.4 months and was followed by rapid clinical deterioration and death as a result of progressive disease.

## DISCUSSION

We report that the use of corticosteroids at the start of PD-(L)1 blockade is associated with inferior outcomes in two independent cohorts. This analysis of 640 patients from two institutions evaluated a patient population that was largely excluded from clinical trials that evaluated PD-(L)1 blockade such that this can only be addressed with real-world data.

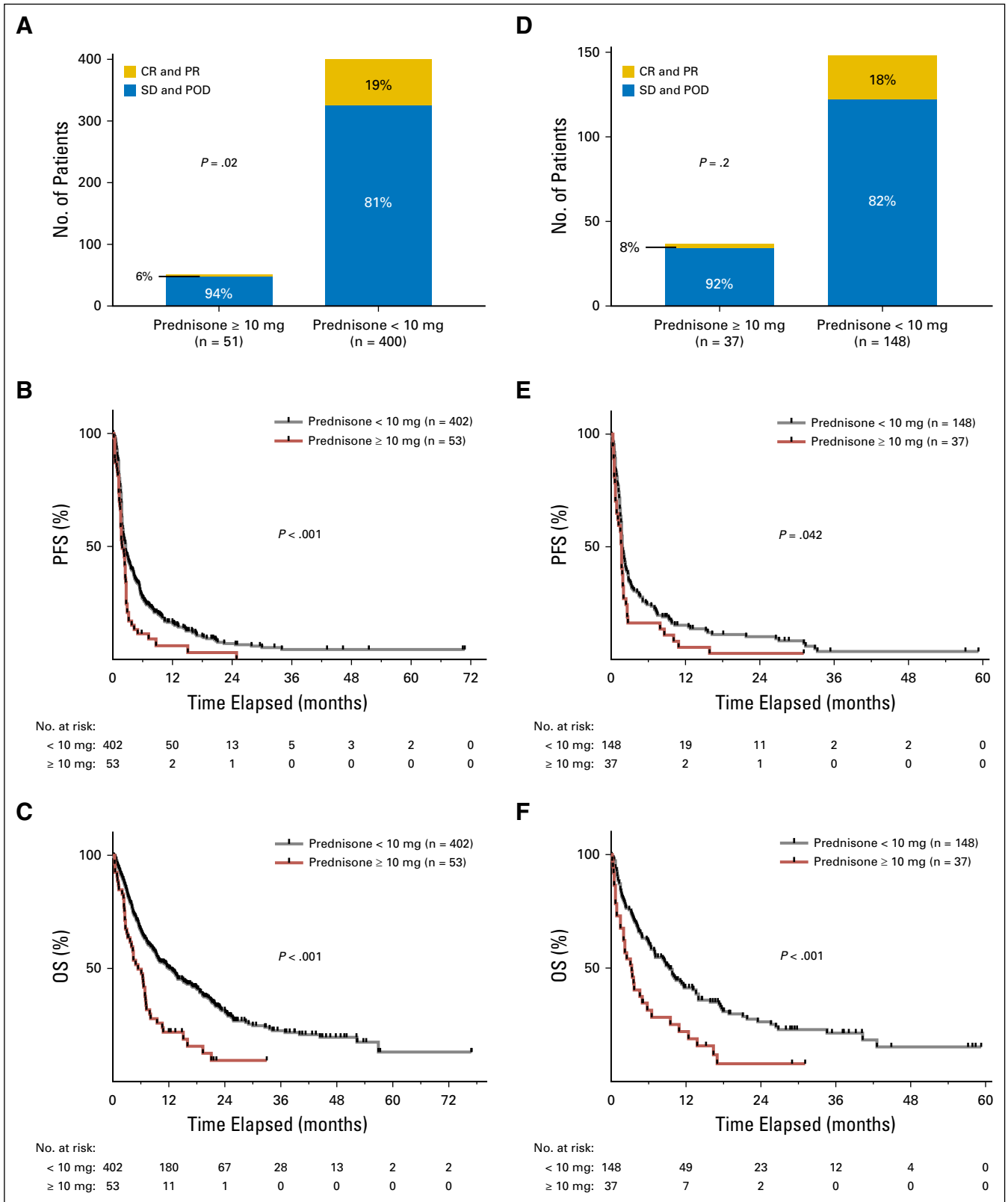
Corticosteroids, specifically systemic adrenal glucocorticoids, play a critical physiologic role in feedback inhibition of inflammatory responses and immune system homeostasis and have long been used for their immunosuppressive properties. These effects can offer significant benefit in the treatment of autoimmune

diseases, but may have unintended consequences in patients with cancer. Exogenous dexamethasone has been demonstrated to suppress IL-2–mediated activation of effector T cells<sup>16</sup> and increase immunosuppressive regulatory T cells.<sup>17,18</sup>

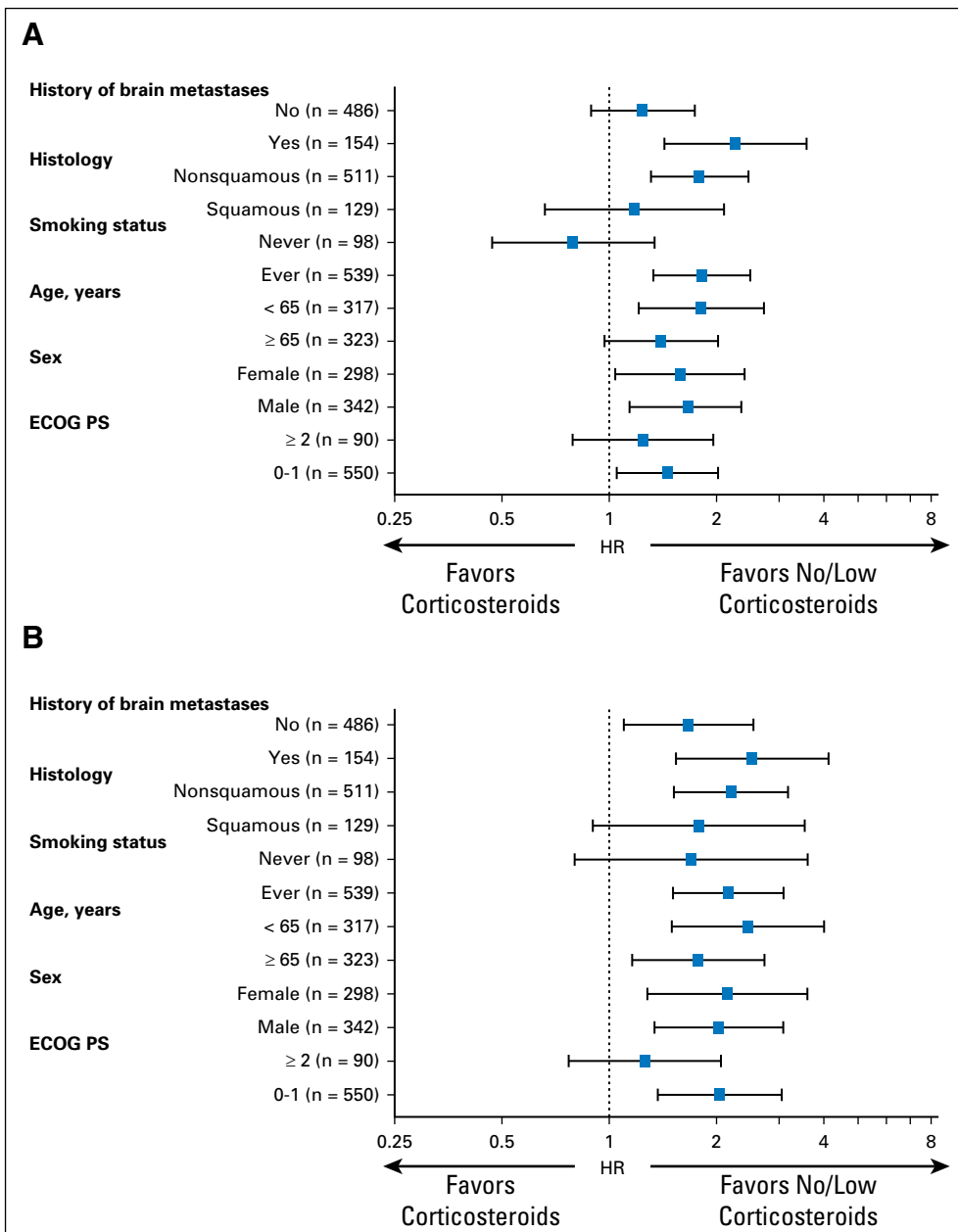
Corticosteroids are the mainstay for the treatment of immune-related adverse events in patients who receive ICB therapy, and fortunately the use of corticosteroids in patients with melanoma<sup>13,14</sup> and NSCLC<sup>12</sup> (and other immune modulating medications, such as infliximab) in this context has not been associated with decreased efficacy of ICB. Still, it is possible that treatment with corticosteroids immediately before the initiation of PD-(L)1 blockade could distinctly affect efficacy, perhaps by blunting a proliferative burst of CD8-positive T cells needed in response to PD-(L)1 blockade.<sup>19</sup>

Corticosteroids are an important and common treatment of a variety of symptoms in patients with cancer, particularly NSCLC. Corticosteroids may be required for the control of brain metastasis and can improve symptoms of fatigue, dyspnea,<sup>9</sup> and anorexia. On the basis of these data, in patients for whom treatment with PD-(L)1 blockade is planned, it may be prudent to attempt to manage these symptoms with other pharmacologic<sup>9,20,21</sup> and/or nonpharmacologic<sup>8,22</sup> methods. These strategies could enable patients to be tapered off corticosteroids before the start of PD-(L)1 blockade to potentially achieve maximum benefit from these agents; however, of importance, medically necessary corticosteroids (eg, management of brain metastases) should not be avoided.

This work has focused on patients who were treated with single-agent PD-(L)1 inhibitor. Of note, regimens that combine



**Fig 1.** Response rates (A and D), progression-free survival (PFS; B and E), and overall survival (OS; C and F) of patients treated with programmed death-ligand 1 blockade on the basis of reported corticosteroid usage at Memorial Sloan Kettering Cancer Center (MSKCC; A-C) and Gustave Roussy Cancer Center (GRCC; D-F). Four hundred fifty-one of 455 patients were evaluable for response in the MSKCC cohort (A) and 185 of 185 patients were evaluable for response in the GRCC cohort (D). CR, complete response; POD, progression of disease; PR, partial response; SD, stable disease.



**Fig 2.** Forest plot of subgroup analyses of independent prognostic factors for (A) progression-free survival and (B) overall survival in the pooled cohort (Memorial Sloan Kettering Cancer Center and Gustave Roussy Cancer Center combined). ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; PS, performance status.

chemotherapy and PD-(L)1 blockade<sup>23</sup> are emerging with promising efficacy, despite the routine use of corticosteroids as a supportive medication for the prevention of rash, nausea, and potential hypersensitivity reactions. It is possible that transient corticosteroids given along with chemotherapy and PD-(L)1 blockade are not deleterious in the same way as more chronically administered corticosteroids leading up to PD-(L)1 blockade. Alternatively, the efficacy of these regimens despite corticosteroid administration could be a signal of synergy between chemotherapy and ICB, overcoming the otherwise deleterious effects of concurrent steroids. It will be interesting to examine the outcomes of chemotherapy plus PD(L)-1 combinations that minimize corticosteroid use—for example, use of abraxane in the IMpower130 (ClinicalTrials.gov identifier: NCT 02367794)<sup>24</sup> and KEYNOTE-407 (ClinicalTrials.gov identifier: NCT 02775435)<sup>25</sup> studies.

Although data on the effects of baseline corticosteroids is only possible through such real-world studies as this, there are important limitations. Although outcomes were assessed retrospectively, objective response was determined by direct review of scans by radiologists and quantified by RECIST. The overall sample size is large (N = 640), but only a modest number of patients received corticosteroids of any dose at the time of ICB initiation (n = 107), which may reflect the caution of clinical providers in administering corticosteroids to patients being treated with ICB. A pooled analysis of both independent cohorts was used in subgroup and multivariable analyses to increase power; however, this sample size limited the comprehensive exploration of varying cut points of dose or timing of corticosteroids associated with distinctly inferior outcomes. The prednisone threshold of 10 mg was chosen here as it is typically applied as an exclusion in clinical trials, and we found

**Table 2.** Multivariable Analysis of Best Overall Response Rate, Progression-Free Survival, and Overall Survival in a Pooled Cohort of Patients: Memorial Sloan Kettering Cancer Center and Gustave Roussy Cancer Center Combined

Patient Characteristic	Best Overall Response		Progression-Free Survival		Overall Survival	
	Odds Ratio (95% CI)	<i>P</i>	Hazard Ratio (95% CI)	<i>P</i>	Hazard Ratio (95% CI)	<i>P</i>
Smoking status (never v ever)	0.33 (0.15 to 0.74)	.007	1.64 (1.30 to 2.04)	< .001	1.03 (0.81 to 1.33)	.78
ECOG performance status ( $\geq 2$ v 0-1)	0.29 (0.11 to 0.75)	.11	1.97 (1.55 to 2.50)	< .001	2.29 (1.75 to 2.98)	< .001
History of brain metastases (yes v no)	0.88 (0.52 to 1.49)	.6	1.16 (0.96 to 1.41)	.1	1.37 (1.11 to 1.7)	.003
Corticosteroid use ( $\geq 10$ mg v < 10 mg)	0.42 (0.17 to 1.01)	.053	1.31 (1.03 to 1.67)	.03	1.66 (1.28 to 2.16)	< .001

Abbreviation: ECOG, Eastern Cooperative Oncology Group.

similar detrimental effects in patients who received 10 mg to 19 mg daily versus  $\geq 20$  mg of prednisone.

An additional limitation of this work is distinguishing between the prognostic and predictive effects of corticosteroids in patients who receive ICB. Use of corticosteroids may simply identify patients with aggressive disease and greater symptom burden necessitating their use. Given the persistent deleterious effect of corticosteroids in both the subgroup and multivariable analyses, we propose that baseline corticosteroids have a predictive effect, but we do not have functional or mechanistic data to prove this with certainty. In addition, data on the known predictive biomarkers, such as PD-L1 staining and tumor mutational burden, were not available in the majority of patients in this analysis and so could not be included here. We propose that baseline corticosteroid use should be incorporated in future data analyses to further optimize predictive models of PD-(L)1 efficacy. Ultimately, whether baseline corticosteroids represent correlation or causation, it is clinically relevant for both patients and providers to recognize the effect of corticosteroids on ICB efficacy in patients with NSCLC.

Treatment with PD-(L)1 blockade has been a significant advance for patients with NSCLC and other malignancies. As these agents have become a standard of care, it is imperative that we recognize and inform common practices that may affect the efficacy of these agents. The administration of corticosteroids for a variety of indications, from decreased appetite and fatigue to symptomatic brain metastases, is one such common practice. We have demonstrated that the use of corticosteroids at the time of the

initiation of PD-(L)1 blockade is associated with diminished efficacy of ICB. Prudent use of corticosteroids at the time of initiating PD-(L)1 blockade is warranted.

#### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at [jco.org](http://jco.org).

#### AUTHOR CONTRIBUTIONS

**Conception and design:** Kathryn C. Arbour, Laura Mezquita, Hira Rizvi, Gregory J. Riely, Benjamin Besse, Matthew D. Hellmann

**Financial support:** Matthew D. Hellmann

**Provision of study materials or patients:** Benjamin Besse, Matthew D. Hellmann

**Collection and assembly of data:** Kathryn C. Arbour, Laura Mezquita, Niamh Long, Hira Rizvi, Edouard Auclin, Gala Martínez-Bernal, Roberto Ferrara, W. Victoria Lai, Lizza E.L. Hendriks, Caroline Caramella, Andrew J. Plodkowski, Darragh Halpenny, Benjamin Besse, Matthew D. Hellmann

**Data analysis and interpretation:** Kathryn C. Arbour, Laura Mezquita, Niamh Long, Andy Ni, Lizza E.L. Hendriks, Joshua K. Sabari, Jamie E. Chaff, David Planchard, Gregory J. Riely, Benjamin Besse, Matthew D. Hellmann

**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

**Accountable for all aspects of the work:** All authors

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### Affiliations

Matthew D. Hellmann, Parker Institute for Cancer Immunotherapy; Kathryn C. Arbour, Niamh Long, Hira Rizvi, Andy Ni, W. Victoria Lai, Joshua K. Sabari, Andrew J. Plodkowski, Darragh Halpenny, Jamie E. Chaft, Gregory J. Riely, and Matthew D. Hellmann, Memorial Sloan Kettering Cancer Center; Kathryn C. Arbour, W. Victoria Lai, Joshua K. Sabari, Jamie E. Chaft, Gregory J. Riely, and Matthew D. Hellmann, Weill Cornell Medical College, New York, NY; Laura Mezquita, Roberto Ferrara, Lizza E.L. Hendriks, Caroline Caramella, Benjamin Besse, and David Planchard, Gustave Roussy Cancer Center, Villejuif; Edouard Auclin, Hôpital Européen Georges Pompidou; Benjamin Besse, Paris-Sud University, Le Kremlin Bicêtre, Paris, France; Gala Martínez-Bernal, Virgen del Rocío Hospital, Seville, Spain; Lizza E.L. Hendriks, Maastricht University Medical Center, Maastricht, the Netherlands.





## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

**Impact of Baseline Steroids on Efficacy of Programmed Cell Death-1 and Programmed Death-Ligand 1 Blockade in Patients With Non–Small-Cell Lung Cancer**

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**Kathryn C. Arbour**

No relationship to disclose

**Laura Mezquita**

No relationship to disclose

**Niamh Long**

No relationship to disclose

**Hira Rizvi**

No relationship to disclose

**Edouard Auclin**

No relationship to disclose

**Andy Ni**

No relationship to disclose

**Gala Martínez-Bernal**

**Employment:** Amgen, Janssen Pharmaceuticals

**Honoraria:** Amgen, Janssen Pharmaceuticals

**Speakers' Bureau:** Amgen, Janssen Pharmaceuticals

**Roberto Ferrara**

No relationship to disclose

**W. Victoria Lai**

No relationship to disclose

**Lizza E.L. Hendriks**

**Consulting or Advisory Role:** Bristol-Myers Squibb, Bristol-Myers Squibb (Inst), Boehringer Ingelheim (Inst)

**Research Funding:** Roche (Inst), Boehringer Ingelheim (Inst)

**Travel, Accommodations, Expenses:** Amgen, Roche, Bristol-Myers Squibb

**Joshua K. Sabari**

No relationship to disclose

**Caroline Caramella**

**Consulting or Advisory Role:** Bristol-Myers Squibb, Pfizer

**Andrew J. Plodkowski**

No relationship to disclose

**Darragh Halpenny**

No relationship to disclose

**Jamie E. Chaft**

**Consulting or Advisory Role:** Genentech, AstraZeneca, MedImmune, Merck, Bristol-Myers Squibb

**Research Funding:** Genentech (Inst), Bristol-Myers Squibb (Inst), AstraZeneca (Inst), MedImmune (Inst)

**David Planchard**

**Consulting or Advisory Role:** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Novartis, Roche, Pfizer, MSD Oncology, Celgene

**Gregory J. Riely**

**Research Funding:** Novartis (Inst), Genentech (Inst), Millennium Pharmaceuticals (Inst), GlaxoSmithKline (Inst), Pfizer (Inst), Infinity Pharmaceuticals (Inst), Ariad Pharmaceuticals (Inst)

**Patents, Royalties, Other Intellectual Property:** Patent application submitted covering pulsatile use of erlotinib to treat or prevent brain metastases (Inst)

**Travel, Accommodations, Expenses:** Merck Sharp & Dohme

**Benjamin Besse**

**Research Funding:** AstraZeneca (Inst), Genentech (Inst), Pfizer (Inst), Boehringer Ingelheim (Inst), Eli Lilly (Inst), Servier (Inst), Onxeo (Inst), Bristol-Myers Squibb (Inst), Ose Pharma (Inst), Inivata (Inst), Novartis (Inst), OncoMed (Inst), Loxo (Inst)

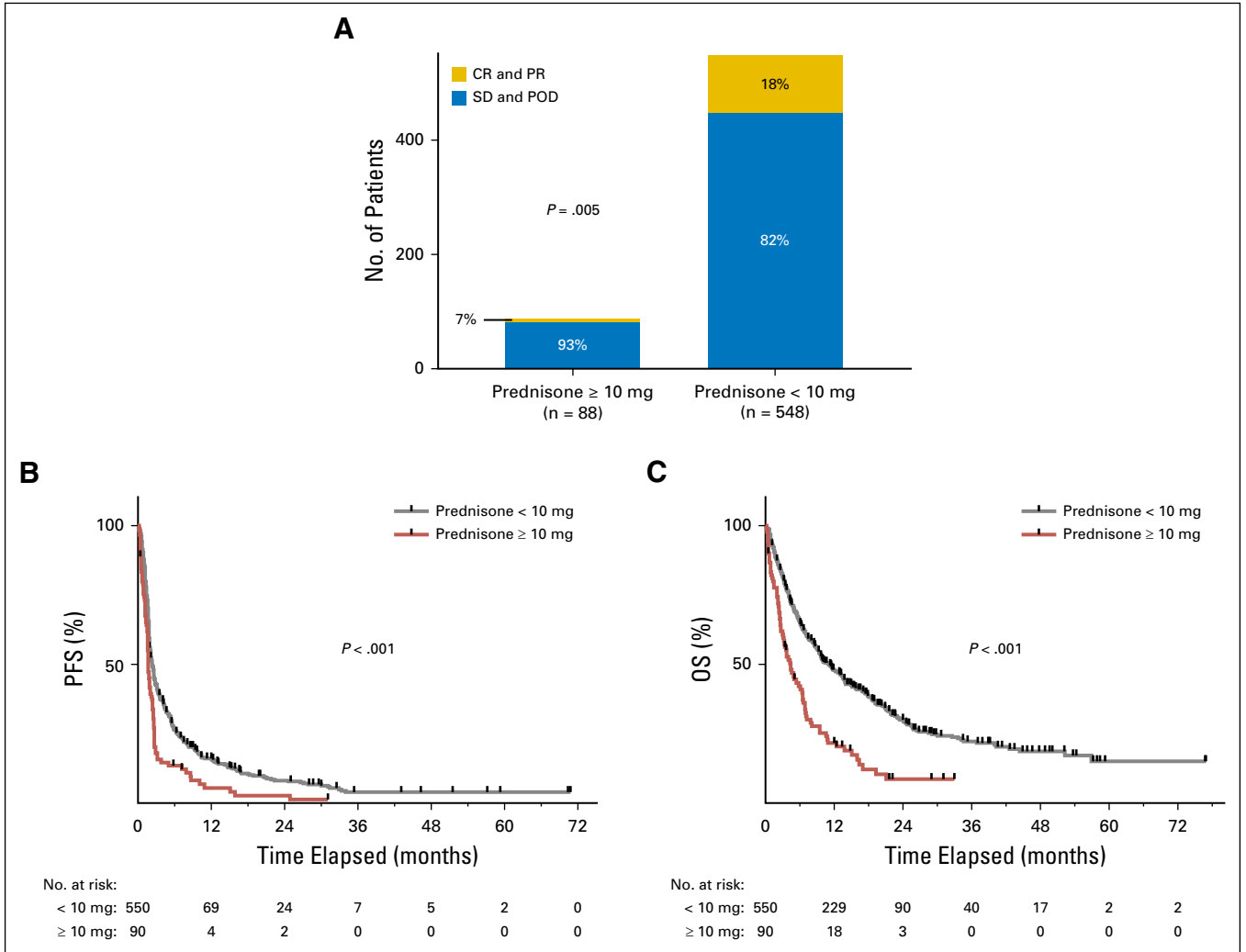
**Travel, Accommodations, Expenses:** Roche, Pfizer, Bristol-Myers Squibb, Medarex, Novartis, Pierre Fabre

**Matthew D. Hellmann**

**Consulting or Advisory Role:** Bristol-Myers Squibb, Merck, Genentech, AstraZeneca, MedImmune, Janssen Pharmaceuticals, Mirati Therapeutics, Syndax, Shattuck Labs

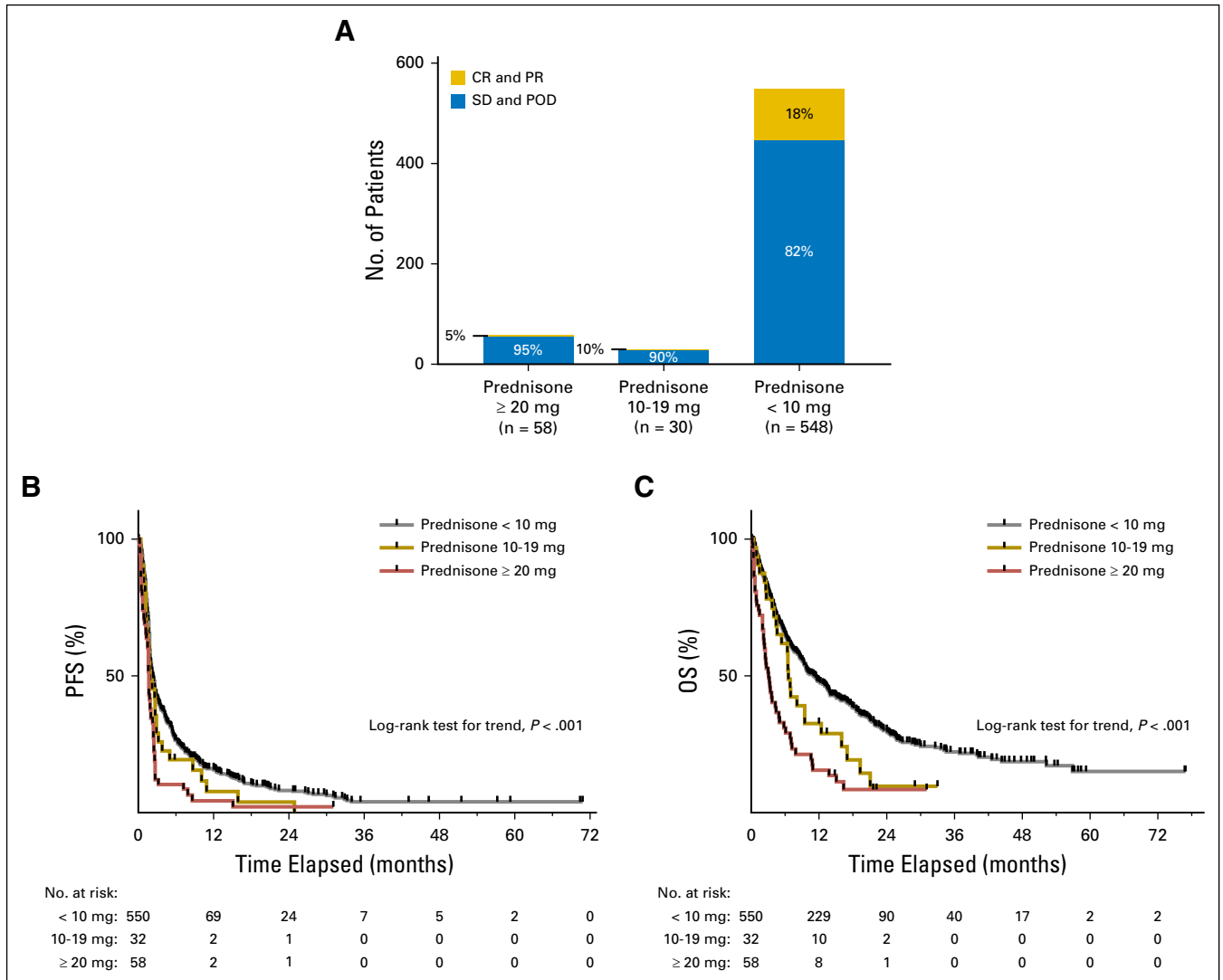
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Appendix

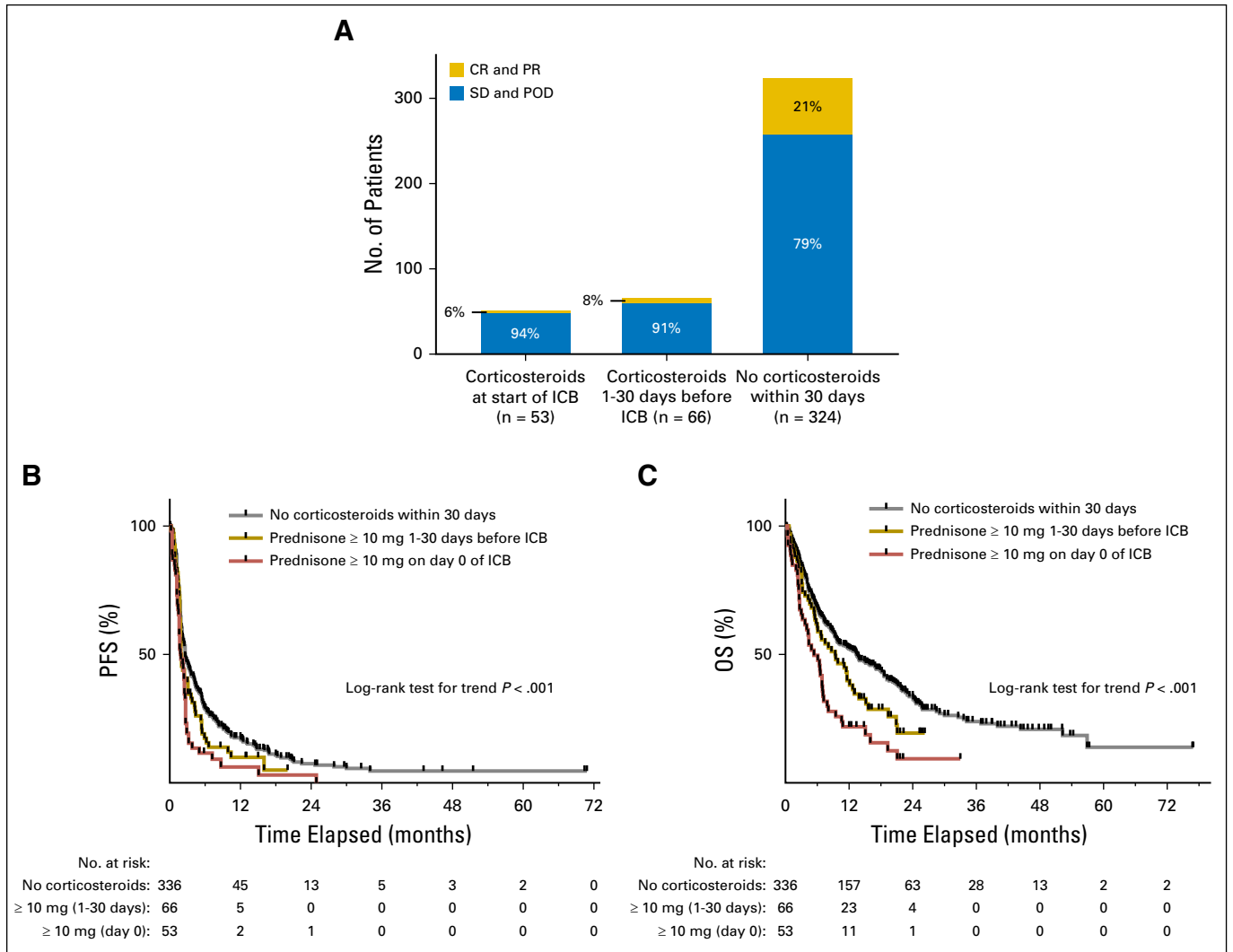


**Fig A1.** (A) Response rates of patients treated with programmed cell death-1 and programmed death-ligand 1 blockade according to different doses of corticosteroids in the pooled cohort of patients from Memorial Sloan Kettering Cancer Center (MSKCC) and Gustave Roussy Cancer Center (GRCC; n = 636; four patients from MSKCC were not evaluable for response). (B) Progression-free survival (PFS) and (C) overall survival (OS) of patients treated with PD-(L)1 blockade according to different doses of corticosteroids in the pooled cohort of patients from MSKCC and GRCC cohorts (N = 640). CR, complete response; POD, progression of disease; PR, partial response; SD, stable disease.

Efficacy of PD-(L)1 Blockade in Patients on Baseline Steroids



**Fig A2.** (A) Response rates of patients treated with programmed cell death-1 and programmed death-ligand 1 blockade according to different doses of corticosteroids in the pooled cohort of patients from Memorial Sloan Kettering Cancer Center (MSKCC) and Gustave Roussy Cancer Center (GRCC;  $n = 636$ ; four patients from MSKCC were not evaluable for response). (B) Progression-free survival (PFS) and (C) overall survival (OS) of patients treated with PD-(L)1 blockade according to different doses of corticosteroids in the pooled cohort of patients from MSKCC and GRCC cohorts ( $N = 640$ ). CR, complete response; POD, progression of disease; PR, partial response; SD, stable disease.



**Fig A3.** (A) Response rates (n = 451), (B) progression-free survival (PFS), and (C) overall survival (OS) of patients treated programmed cell death-1 and programmed death-ligand 1 blockade according to time at which corticosteroids were administered in the 30 days before immune checkpoint blockade (ICB) initiation (Memorial Sloan Kettering Cancer Center). CR, complete response; POD, progression of disease; PR, partial response; SD, stable disease.

Efficacy of PD-(L)1 Blockade in Patients on Baseline Steroids

**Table A1.** Patient Characteristics and Corticosteroid Indications of Patients in the Memorial Sloan Kettering Cancer Center and Gustave Roussy Cancer Center Cohorts

Baseline Characteristic	MSKCC (n = 455)	GRCC (n = 185)
Age, years, median (range)	66 (31-93)	61 (29-84)
Sex		
Male	48 (220)	66 (122)
Female	52 (235)	44 (63)
ECOG performance status		
0	19 (86)	12 (22)
1	70 (320)	66 (122)
≥ 2	11 (49)	22 (41)
Smoking status		
Ever	376	87 (161)
Never	79	10 (19)
Pack-years, median (range)	30 (1-190)	37 (3-100)
Histology		
Adenocarcinoma	76 (347)	63 (116)
Squamous	18 (80)	26 (49)
NSCLC-other	6 (28)	11 (20)
EGFR mutation status		
EGFR mutant	8 (38)	5 (9)
EGFR wild type	82 (374)	69 (127)
EGFR status unknown	9 (43)	26 (49)
Daily dose of corticosteroids (prednisone or equivalent), mg		
≥ 20	6 (29)	16 (29)
10-19	5 (24)	4 (8)
1-9	2 (10)	4 (7)
0	86 (392)	76 (141)
Median daily dose of corticosteroids (prednisone or equivalent), mg (range)	13 (3-80)	20 (3-325)
Indication for corticosteroid use ≥ 10 mg	(n = 53)	(n = 37)
Dyspnea	30 (15)	41 (15)
Fatigue	33 (18)	3 (1)
Brain metastases	13 (7)	27 (10)
Pain	9 (5)	11 (6)
Other	15 (8)	14 (5)

NOTE. Data are given as No. (%), unless otherwise indicated. Abbreviations: ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; GRCC, Gustave Roussy Cancer Center; MSKCC, Memorial Sloan Kettering Cancer Center; NSCLC, non-small-cell lung cancer.

**Table A2.** Clinical Features of Patients on Baseline Corticosteroids With Response to Programmed Death-Ligand 1 Blockade

Patient	Age, Years	Sex	ECOG PS	Smoking History (pack-years)	Indication for Corticosteroid Use	Corticosteroid Dose (prednisone equivalent), mg	Duration of Corticosteroids Before ICB, Weeks	Duration of Response, Months
MSKCC 1	54.0	M	1	Former (29.0)	Fatigue	10.0	8.0	18.0 (ongoing)
MSKCC 2	47.0	F	1	Never	Fatigue	20.0	3.0	6.0
MSKCC 3	76.0	M	1	Never	Fatigue	10.0	10.0	25.0
GRCC 1	74.0	M	1	Former (15.0)	Dyspnea	10.0	Unknown	12.0
GRCC 2	73.0	M	1	Former (10.0)	Dyspnea and pain	20.0	Unknown	31.0 (ongoing)
GRCC 3	62.0	F	1	Former (50.0)	Dyspnea and pain	20.0	Unknown	2.4

Abbreviations: ECOG, Eastern Cooperative Oncology Group; F, female; GRCC, Gustave Roussy Cancer Center; ICB, immune checkpoint blockade; M, male; MSKCC, Memorial Sloan Kettering Cancer Center; PS, performance status.