

# Adjuvant Pembrolizumab for Renal Cell Carcinoma Across UCLA Integrated Staging System Risk Groups and Disease Stage: Subgroup Analyses From the KEYNOTE-564 Study

T. K. Choueiri<sup>1</sup>; P. Tomczak<sup>2</sup>; S. H. Park<sup>3</sup>; B. Venugopal<sup>4</sup>; T. Ferguson<sup>5</sup>; S. N. Symeonides<sup>6</sup>; J. Hajek<sup>7</sup>; Y.-H. Chang<sup>8</sup>; J.-L. Lee<sup>9</sup>; N. Sarwar<sup>10</sup>; A. Thiery-Vuillemin<sup>11</sup>; M. Gross-Goupil<sup>12</sup>; M. Mahave<sup>13</sup>; N. B. Haas<sup>14</sup>; P. Sawrycki<sup>15</sup>; T. Zhang<sup>16</sup>; L. Xu<sup>17</sup>; K. Imai<sup>17</sup>; C. Poehlein<sup>17</sup>; T. Powles<sup>18</sup>

<sup>1</sup>Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; <sup>2</sup>Poznan University of Medical Sciences, Poznan, Poland; <sup>3</sup>Sungkyunkwan University, Samsung Medical Center, Seoul, South Korea; <sup>4</sup>Beatson West of Scotland Cancer Centre and University of Glasgow, Glasgow, United Kingdom; <sup>5</sup>Fiona Stanley Hospital, Perth, WA, Australia; <sup>6</sup>Edinburgh Cancer Centre and University of Edinburgh, Edinburgh, United Kingdom; <sup>7</sup>Fakultni Nemocnice Ostrava, Ostrava, Czech Republic; <sup>8</sup>Taipei Veterans General Hospital, Taipei, Taiwan; <sup>9</sup>Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; <sup>10</sup>Imperial College Healthcare NHS Trust, London, United Kingdom; <sup>11</sup>University Hospital Jean Minjot, Besançon, France; <sup>12</sup>University Hospital of Bordeaux-St. Andrews Hospital, Bordeaux, France; <sup>13</sup>Fundación Arturo López Pérez, Santiago, Chile; <sup>14</sup>Abramson Cancer Center, Penn Medicine, Philadelphia, PA, USA; <sup>15</sup>Provincial Hospital in Torun, Torun, Poland; <sup>16</sup>The University of Texas Southwestern Medical Center, Dallas, TX, USA; <sup>17</sup>Merck & Co., Inc., Rahway, NJ, USA; <sup>18</sup>Barts Health NHS Trust and the Royal Free NHS Foundation Trust, Barts Cancer Institute, and Queen Mary University of London, London, United Kingdom

## Background

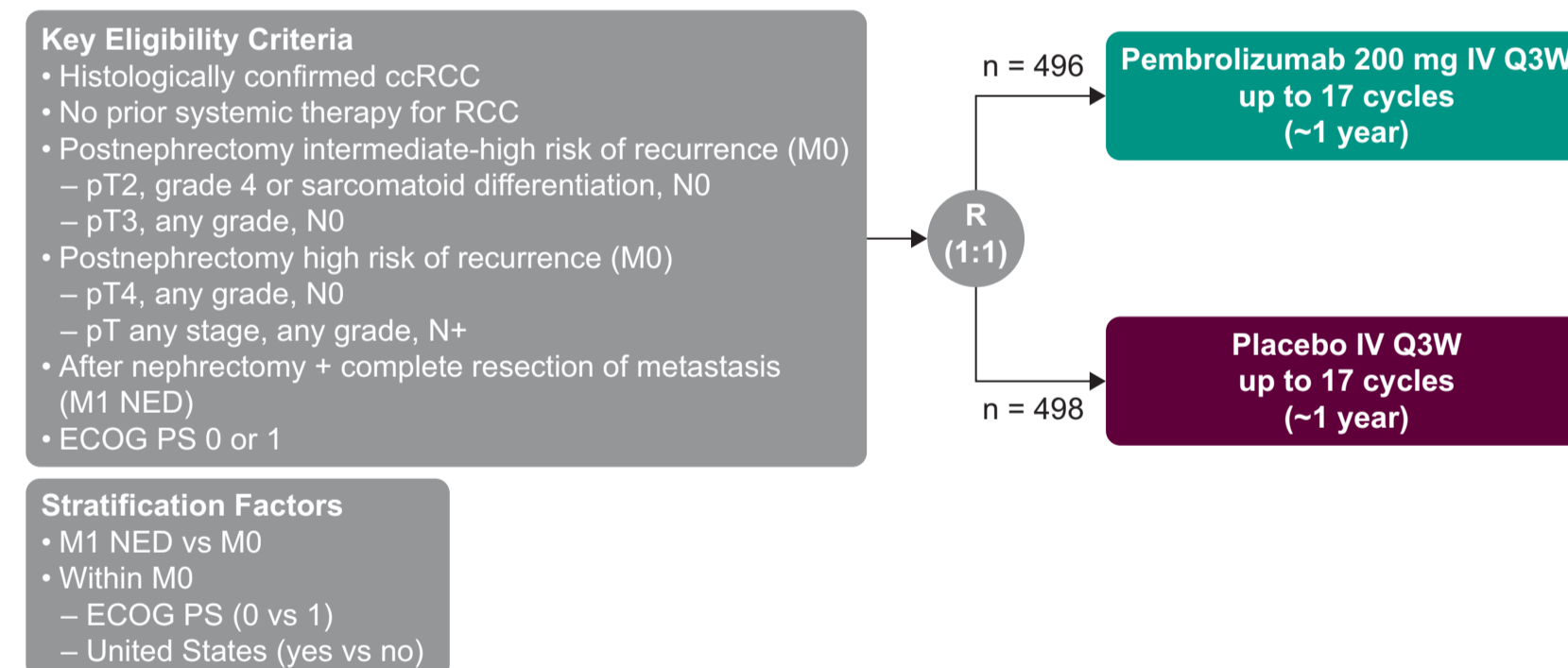
- In the randomized, placebo-controlled, double-blind phase 3 KEYNOTE-564 study (NCT03142334), adjuvant pembrolizumab was shown to significantly prolong disease-free survival (DFS) in patients with clear cell renal cell carcinoma (ccRCC) at increased risk of recurrence after nephrectomy<sup>1</sup>
  - In an updated efficacy analysis with a median study follow-up of 30.1 months, pembrolizumab continued to demonstrate a DFS benefit compared with placebo (hazard ratio [HR], 0.63; 95% CI, 0.50-0.80)<sup>2</sup>
- KEYNOTE-564 enrolled a broad population with various disease characteristics associated with increased risk of RCC recurrence, including American Joint Committee on Cancer (AJCC) primary tumor stage, Fuhrman nuclear grade, and lymph node involvement<sup>3,4</sup>
- The University of California Los Angeles Integrated Staging System (UISS) for RCC is a validated prognostic model that uses the size of the primary tumor (T), involvement of lymph nodes (N), and presence of metastases (M) (ie, TNM); Fuhrman nuclear grade; and Eastern Cooperative Oncology Group performance status (ECOG PS) to predict 5-year survival rates following nephrectomy<sup>5</sup>

## Objective

- To explore the efficacy of adjuvant pembrolizumab in subgroups of patients with ccRCC enrolled in the KEYNOTE-564 study based on UISS risk groups and disease stage

## Methods

Figure 1. Study design



IV, intravenously; NED, no evidence of disease; Q3W, every 3 weeks; R, randomization.

## Risk characterization

- UISS risk groups were derived retrospectively from TNM status, Fuhrman nuclear grade, and ECOG PS (Table 1)
- Other subgroups were evaluated based on AJCC disease stage, which classifies cancers by TNM status<sup>6</sup> and by TNM status and Fuhrman nuclear grade

## Statistical analysis

- Post hoc exploratory end points were DFS and distant metastasis-free survival (DMFS) in subgroups defined by UISS risk group and TNM disease stage
- The Kaplan-Meier method was used to estimate DFS and DMFS
  - HRs and 95% CIs were estimated using a Cox proportional hazards model with the Efron method of handling ties, with treatment group as a covariate
- As of the database cutoff date of June 14, 2021, median study follow-up, defined as time from randomization to database cutoff, was 30.1 months (range, 20.8-47.5)

Table 1. Risk group classification

UISS risk group	Disease characteristics
Intermediate risk	<ul style="list-style-type: none"> <li>pT2, G4, N0, M0</li> <li>pT3, G1, N0, M0</li> <li>pT3, G2-4, N0, M0, ECOG PS 0</li> </ul>
High risk	<ul style="list-style-type: none"> <li>pT3, G2-4, N0, M0, ECOG PS 1</li> <li>T4, any G, N0, M0</li> <li>N1, M0</li> </ul>
Metastatic disease	<ul style="list-style-type: none"> <li>M1 NED</li> </ul>
<b>AJCC disease stage</b>	
Stage 2	T2, G4, N0, M0
Stage 3	T1 or T2, N1, M0
	T3, N0 or N1, M0
Stage 4	T4, any N, M0
	M1 NED

G, Fuhrman nuclear grade.

## Results

### Patient population

Figure 2. Population distribution of (A) UISS risk category, (B) AJCC disease stage, and (C) TNM status and Fuhrman nuclear grade

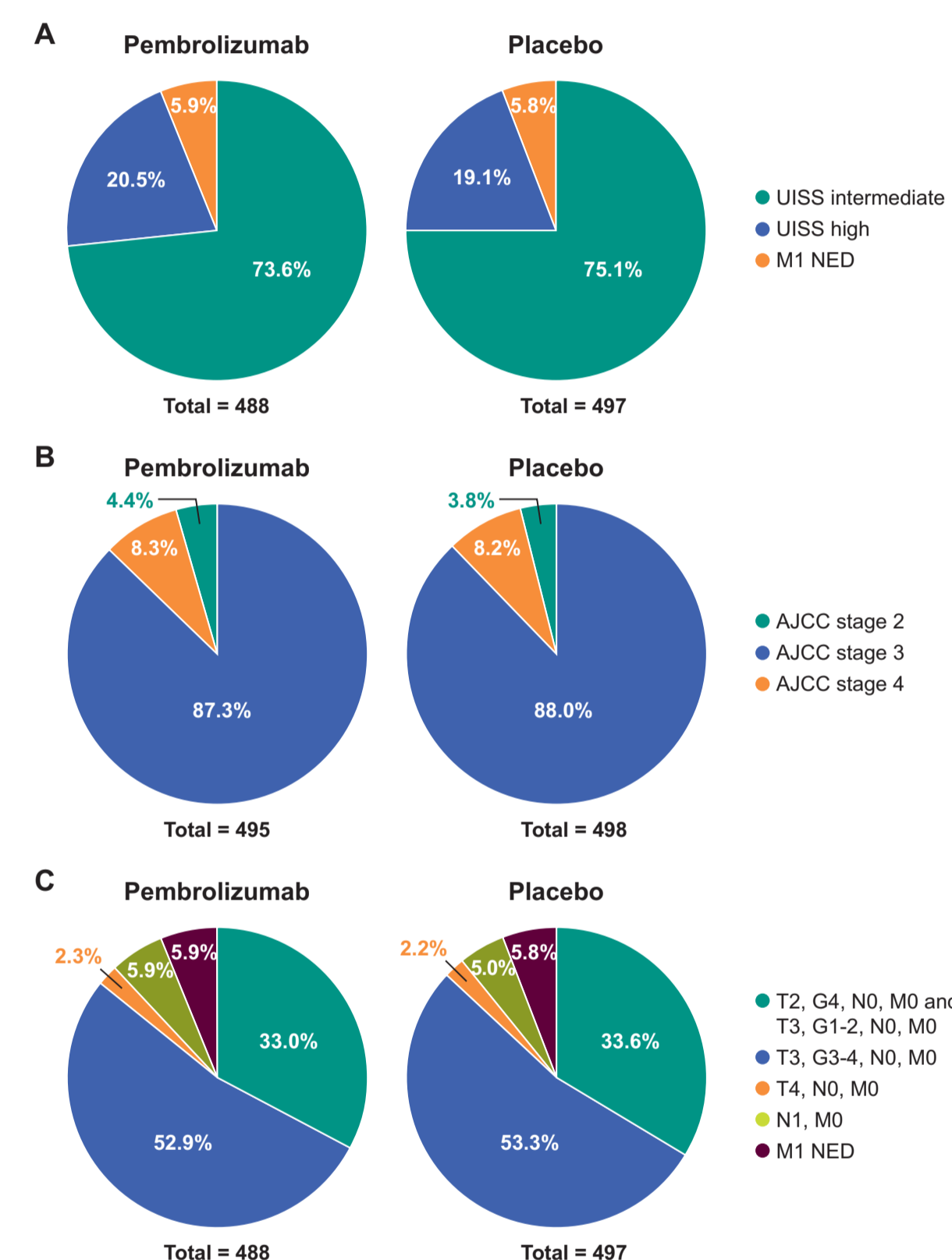


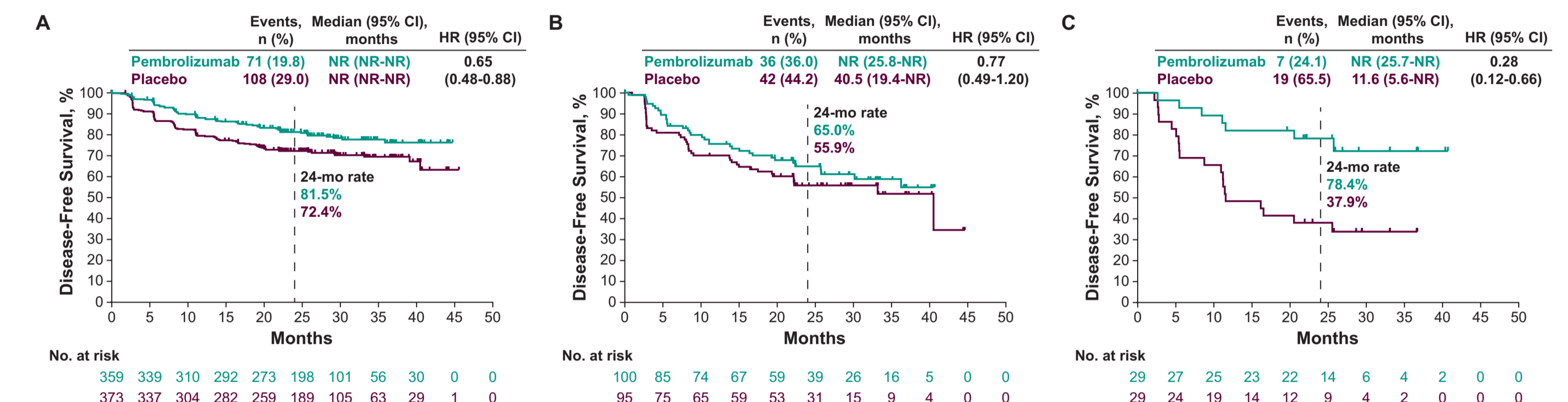
Table 2. Baseline characteristics by UISS risk category

	Pembrolizumab			Placebo		
	UISS intermediate risk n = 359	UISS high risk n = 100	M1 NED n = 29	UISS intermediate risk n = 373	UISS high risk n = 95	M1 NED n = 29
Age, median (range), years	58 (27-81)	64 (29-81)	61 (45-79)	59 (25-81)	64 (30-84)	57 (30-77)
Male	256 (71.3)	61 (61.0)	24 (82.8)	273 (73.2)	64 (67.4)	22 (75.9)
ECOG PS 0	357 (99.4)	34 (34.0)	23 (79.3)	370 (99.2)	31 (32.6)	24 (82.8)
Radical nephrectomy	329 (91.6)	96 (96.0)	27 (93.1)	340 (91.2)	92 (96.8)	27 (93.1)
<b>Primary tumor</b>						
T1	0 (0)	4 (4.0)	6 (20.7)	0 (0)	5 (5.3)	10 (34.5)
T2	16 (4.5)	4 (4.0)	1 (3.4)	18 (4.8)	3 (3.2)	11 (37.9)
T3	343 (95.5)	80 (80.0)	20 (69.0)	355 (95.2)	75 (78.9)	7 (24.1)
T4	0 (0)	12 (12.0)	2 (6.9)	0 (0)	12 (12.6)	1 (3.4)
<b>Tumor grade</b>						
Grade 1	18 (5.0)	0 (0)	1 (3.4)	16 (4.3)	0 (0)	0 (0)
Grade 2	108 (30.1)	32 (32.0)	11 (37.9)	111 (29.8)	28 (29.5)	11 (37.9)
Grade 3	159 (44.3)	45 (45.0)	11 (37.9)	157 (42.1)	40 (42.1)	15 (51.7)
Grade 4	74 (20.6)	23 (23.0)	5 (17.2)	89 (23.9)	27 (28.4)	3 (10.3)
Missing	0 (0)	0 (0)	1 (3.4)	0 (0)	0 (0)	0 (0)
<b>Lymph node stage</b>						
N0	359 (100)	71 (71.0)	27 (93.1)	373 (100)	70 (73.7)	23 (79.3)
N1	0 (0)	29 (29.0)	2 (6.9)	0 (0)	25 (26.3)	6 (20.7)

Data are n (%) unless otherwise noted.

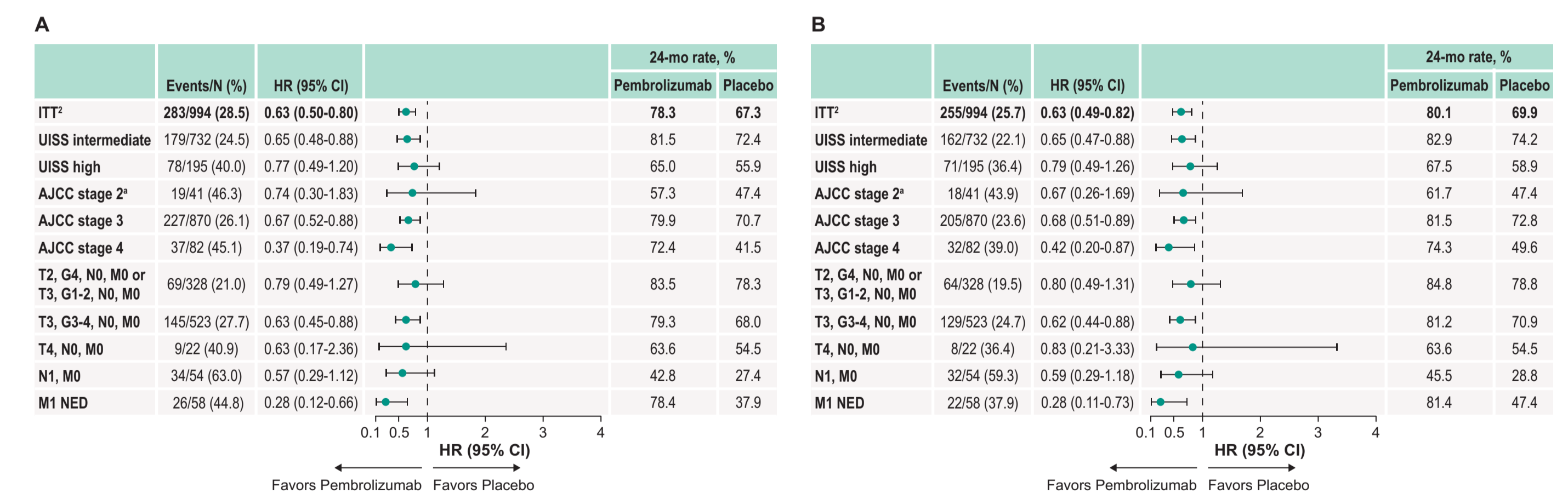
## DFS and DMFS

Figure 3. Kaplan-Meier estimates of DFS for patients with (A) UISS intermediate risk, (B) UISS high risk, and (C) M1 NED



NR, not reached.

Figure 4. Subgroup analysis of (A) DFS and (B) DMFS



ITT, intention to treat.

\*Includes only patients with grade 4 tumors.

## Conclusions

- Most patients in the pembrolizumab (73.6%) and placebo arms (75.1%) were categorized into the UISS intermediate group
- Adjuvant pembrolizumab prolonged DFS and DMFS compared with placebo across subgroups by UISS risk, AJCC stage, and TNM status and Fuhrman nuclear grade
  - The DFS and DMFS benefit across subgroups was consistent with that observed in the ITT population<sup>2</sup>
  - No formal statistical testing was conducted for this post hoc analysis, and results should be interpreted with caution due to the small sample size of some subgroups
- Results of this exploratory analysis further support the use of adjuvant pembrolizumab after nephrectomy as standard of care for patients with RCC at increased risk of recurrence

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## Contact information

Contact the author at toni\_choueiri@dfci.harvard.edu for questions or comments.

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