

## SUPPLEMENTAL TABLES AND FIGURES

Pembrolizumab Plus Axitinib versus Sunitinib in Metastatic Renal Cell Carcinoma: Outcomes of Japanese Patients Enrolled in the Randomized, Phase 3, Open-Label KEYNOTE 426 Study

Satoshi Tamada,<sup>1</sup> Chihiro Kondoh,<sup>2</sup> Nobuaki Matsubara,<sup>3</sup> Ryuichi Mizuno,<sup>4</sup> Go Kimura,<sup>5</sup> Satoshi Anai,<sup>6</sup> Yoshihiko Tomita,<sup>7</sup> Masafumi Oyama,<sup>8</sup> Naoya Masumori,<sup>9</sup> Takahiro Kojima,<sup>10</sup> Hiroaki Matsumoto,<sup>11</sup> Mei Chen,<sup>12</sup> Mengran Li,<sup>13\*</sup> Kenji Matsuda,<sup>13</sup> Yoshinobu Tanaka,<sup>13</sup> Brian I. Rini,<sup>14</sup> Hirotsugu Uemura<sup>15</sup>

<sup>1</sup>Bell Land General Hospital, Osaka, Japan; <sup>2</sup>Toranomon Hospital, Tokyo, Japan; <sup>3</sup>National Cancer Center Hospital East, Kashiwa, Japan; <sup>4</sup>Keio University Hospital, Tokyo, Japan; <sup>5</sup>Nippon Medical School Hospital, Tokyo, Japan; <sup>6</sup>Nara Medical University Hospital, Kashihara, Japan; <sup>7</sup>Niigata University Medical & Dental Hospital, Niigata, Japan; <sup>8</sup>Saitama Medical University International Medical Center, Saitama Japan, <sup>9</sup>Sapporo Medical University, Sapporo, Japan; <sup>10</sup>University of Tsukuba, Tsukuba, Japan; <sup>11</sup>Yamaguchi University, Yamaguchi, Japan; <sup>12</sup>Merck & Co., Inc., Kenilworth, NJ, USA; <sup>13</sup>MSD K.K., Tokyo, Japan; <sup>14</sup>Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA; currently at Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; <sup>15</sup>Kindai University, Osaka, Japan

\*At the time the study was conducted

Corresponding author

Satoshi Tamada

Higashiyama 500-3, Naka-ku, Sakai City, Osaka, 599-8247, Japan

satoshitamada@osaka.med.or.jp

**Supplementary Table 1** Baseline patient characteristics of the Japanese population

	Japanese Population		Global Population	
	Pembrolizumab + Axitinib ( <i>n</i> = 44)	Sunitinib ( <i>n</i> = 50)	Pembrolizumab + Axitinib ( <i>n</i> = 432)	Sunitinib ( <i>n</i> = 429)
Male, n (%)	36 (82)	39 (78)	308 (71)	320 (75)
Age, years, median (range/IQR) <sup>a</sup>	66 (43–84)	65 (39–90)	62 (55–68)	61 (53–68)
Age, n (%)				
<65	20 (45)	25 (50)	260 (60)	278 (65)
≥65	24 (55)	25 (50)	172 (40)	151 (35)
Karnofsky Performance Status Scale score, n (%) <sup>b</sup>				
90/100	39 (89)	48 (96)	346 (80)	341 (79)
70/80	5 (11)	2 (4)	85 (20)	88 (21)
IMDC risk category, n (%)				
Favorable	19 (43)	16 (32)	138 (32)	131 (31)
Intermediate/poor	25 (57)	34 (68)	294 (68)	298 (69)
PD-L1 status, n (%)				
CPS ≥1	25 (57)	31 (62)	242 (56)	253 (59)
CPS <1	19 (43)	18 (36)	165 (38)	156 (36)
Missing	0	1 (2)	25 (6)	20 (5)
Sarcomatoid feature, n (%)	7 (16)	5 (10)	51 (12)	54 (13)

*CPS* combined positive score; *IMDC* International Metastatic Renal Cell Carcinoma Database Consortium; *IQR*

interquartile range; *PD-L1* programmed death-ligand 1

<sup>a</sup>Range in the Japanese population; IQR in the global population

<sup>b</sup>One patient had missing information in the global population (pembrolizumab-axitinib group)

**Supplementary Table 2** Subsequent therapy after study drug discontinuation in the Japanese population

n (%)	Pembrolizumab + Axitinib (n = 44)	Sunitinib (n = 50)
Discontinued study treatment	33 (75)	42 (84)
Received any subsequent systemic anticancer therapy after discontinuation <sup>a</sup>	24 (73)	39 (93)
Any VEGF/VEGFR inhibitor <sup>b</sup>	18 (55)	26 (62)
Nivolumab <sup>c</sup>	4 (12)	28 (67)
Other type <sup>d</sup>	6 (18)	4 (10)
1 subsequent line	24 (73)	39 (93)
2 subsequent lines	6 (18)	19 (45)
≥3 subsequent lines	1 (3)	6 (14)

*PD-L1* programmed death ligand 1; *VEGF* vascular endothelial growth factor; *VEGFR* vascular endothelial growth factor receptor

<sup>a</sup>Percentages are calculated with 33 discontinuations as the denominator

<sup>b</sup>Axitinib, cabozantinib, pazopanib, sorafenib, or sunitinib

<sup>c</sup>Only PD-L1 inhibitor used as subsequent therapy

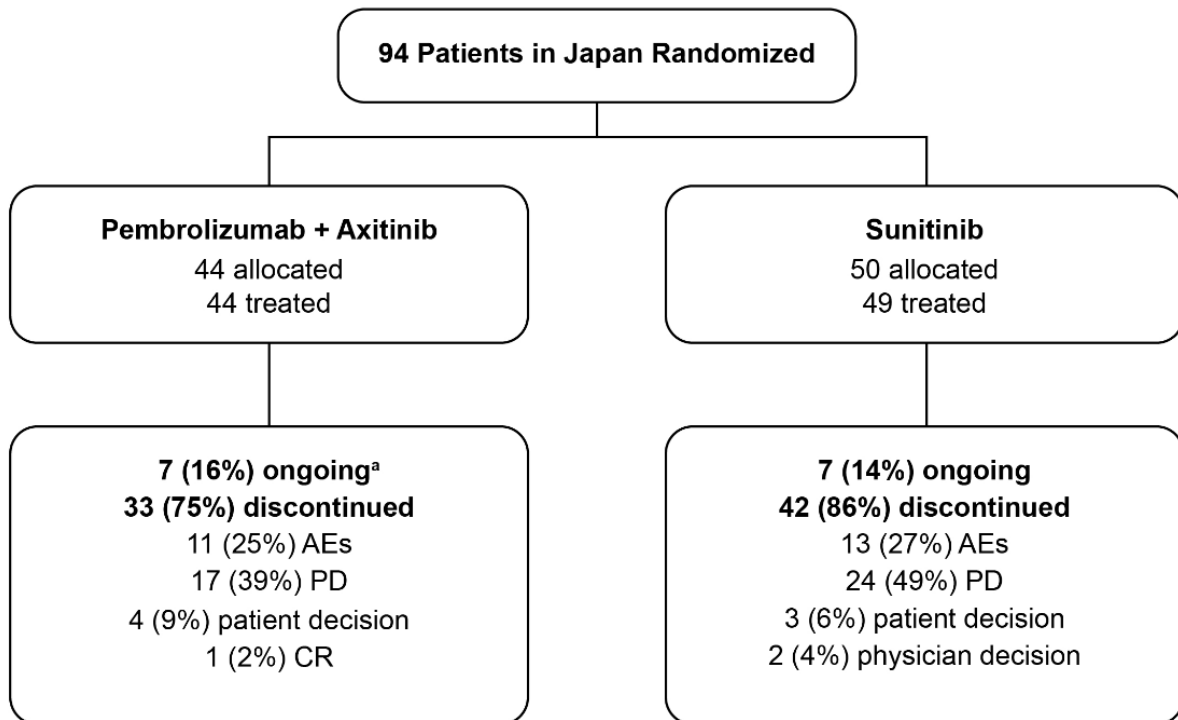
<sup>d</sup>Everolimus, interferon (unspecified), investigational drug (unspecified), ipilimumab, temsirolimus.

**Supplementary Table 3** Adverse events (AEs) of interest

AEs of interest	Pembrolizumab-axitinib ( <i>n</i> = 44)			Sunitinib ( <i>n</i> = 49)		
	Any grade	Grade 1/2	Grade 3/4	Any grade	Grade 1/2	Grade 3/4
Any	28 (63.6)	20 (45.5)	8 (18.2)	26 (53.1)	26 (53.1)	0
Hypothyroidism	15 (34.1)	15 (34.1)	0	21 (42.9)	21 (42.9)	0
Hyperthyroidism	7 (15.9)	7 (15.9)	0	2 (4.1)	2 (4.1)	0
Adrenal insufficiency	5 (11.4)	5 (11.4)	0	0	0	0
Colitis	5 (11.4)	2 (4.5)	3 (6.8)	0	0	0
Pneumonitis	3 (6.8)	2 (4.5)	1 (2.3)	1 (2.0)	1 (2.0)	0
Thyroiditis	3 (6.8)	3 (6.8)	0	2 (4.1)	2 (4.1)	0
Myasthenic syndrome	2 (4.5)	2 (4.5)	0	0	0	0
Myositis	2 (4.5)	2 (4.5)	0	0	0	0
Hepatitis	1 (2.3)	0	1 (2.3)	0	0	0
Hypophysitis	1 (2.3)	0	1 (2.3)	0	0	0
Infusion reactions	1 (2.3)	1 (2.3)	0	1 (2.0)	1 (2.0)	0
Myocarditis	1 (2.3)	0	1 (2.3)	0	0	0
Nephritis	1 (2.3)	1 (2.3)	0	1 (2.0)	1 (2.0)	0
Severe skin reactions	1 (2.3)	0	1 (2.3)	1 (2.0)	1 (2.0)	0
Uveitis	1 (2.3)	1 (2.3)	0	0	0	0

Data are *n* (%) and are from the as-treated population.

**Supplementary Figure 1.** Patient disposition of the Japanese population. *AE* adverse event; *CR* complete response; *PD* progressive disease



<sup>a</sup>Four patients completed 2 full years of pembrolizumab.