

Additional file 1. Baseline characteristics of patients with OS \geq 24 versus $<$ 24 months in the placebo titration arm

| Baseline Characteristics, <i>n</i> (%) | | OS \geq 24 months <i>n</i> = 30 | OS $<$ 24 months <i>n</i> = 20 ^a | <i>p</i> -value ^b |
|--|----------------|--------------------------------------|--|------------------------------|
| Age, years | <65 | 19 (63) | 15 (75) | 0.5382 |
| | \geq 65 | 11 (37) | 5 (25) | |
| Sex | Male | 25 (83) | 14 (70) | 0.3109 |
| | Female | 5 (17) | 6 (30) | |
| Race | White | 26 (87) | 18 (90) | 1.0000 |
| | Asian | 3 (10) | 2 (10) | |
| | Other | 1 (3) | 0 | |
| Weight, kg | \leq 65 | 4 (13) | 6 (30) | 0.2321 |
| | >65, \leq 76 | 6 (20) | 5 (25) | |
| | >76, \leq 89 | 12 (40) | 4 (20) | |
| | >89 | 8 (27) | 5 (25) | |
| ECOG PS | 0 | 19 (63) | 10 (50) | 0.3927 |
| | \geq 1 | 11 (37) | 10 (50) | |
| Histological classification | Clear cell | 30 (100) | 20 (100) | NA |
| | Other | 0 | 0 | |
| Prior nephrectomy | Yes | 22 (73) | 17 (85) | 0.4895 |
| | No | 8 (27) | 3 (15) | |
| No. of metastatic sites | \leq 2 | 17 (57) | 7 (35) | 0.1588 |
| | \geq 3 | 13 (43) | 13 (65) | |
| Site of metastasis | Lung only | 4 (13) | 0 | 0.1400 |
| | Lung + others | 26 (87) | 20 (100) | |
| Site of metastasis, individual | | | | |
| | Lung | 20 (67) | 14 (70) | 1.0000 |
| | Lymph node | 14 (47) | 12 (60) | 0.3991 |
| | Kidney | 10 (33) | 5 (25) | 0.7536 |
| | Liver | 5 (17) | 8 (40) | 0.1004 |
| | Adrenal | 7 (23) | 7 (35) | 0.5216 |
| | Bone | 4 (13) | 7 (35) | 0.0902 |

| | | | | |
|--|------------|---------|---------|--------|
| | Pancreas | 0 | 0 | NA |
| Time from histopathological diagnosis to treatment | | | | |
| | ≥1 year | 12 (40) | 5 (25) | 0.3654 |
| | <1 year | 18 (60) | 15 (75) | |
| Time from metastatic diagnosis to treatment | | | | |
| | ≥1 year | 2 (7) | 2 (10) | 1.0000 |
| | <1 year | 28 (93) | 18 (90) | |
| Sum of longest diameter for target lesion ^c | | | | |
| | ≤Median | 14 (48) | 7 (35) | 0.3942 |
| | >Median | 15 (52) | 13 (65) | |
| Presence of metastases (de novo) at initial diagnosis | | | | |
| | No | 16 (53) | 6 (30) | 0.1480 |
| | Yes | 14 (47) | 14 (70) | |
| Baseline LDH | ≤1.5 × ULN | 28 (93) | 19 (95) | 1.0000 |
| | >1.5 × ULN | 2 (7) | 1 (5) | |
| Baseline Hb | ≥LLN | 19 (63) | 12 (60) | 1.0000 |
| | <LLN | 11 (37) | 8 (40) | |
| Baseline Neu | ≤ULN | 28 (93) | 15 (75) | 0.1003 |
| | >ULN | 2 (7) | 5 (25) | |
| Baseline Plt | ≤ULN | 29 (97) | 17 (85) | 0.2885 |
| | >ULN | 1 (3) | 3 (15) | |

Abbreviations: ECOG PS Eastern Cooperative Oncology Group performance status, Hb

haemoglobin, LDH lactate dehydrogenase, LLN lower limit of normal, NA not applicable Neu

neutrophil, OS overall survival, Plt platelet, ULN upper limit of normal

^a Excluded 6 patients who were censored <24 months in OS.

^b Fisher's exact test was used for all, except weight, for which Cochran-Armitage trend test was used.

^c 1 patient in the OS≥24 months group did not have any measurable target lesion; hence, was not included in the analysis.