**Supplementary Table 1: Summary Table of Full Text Articles of Biomarker Studies**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trial Name | Study Type | First Author | Year | Total Patients (n) | Investigational Therapy (n) | Standard Therapy (n) | Line of Therapy | Trial Phase |
| KEYNOTE 426 | Primary Trial Result | Rini [3] | 2018 | 861 | pembrolizumab + axitinib (432) | sunitinib (429) | 1 | 3 |
| Substudy: Biomarkers | Rini [66] | 2019 |  | | | | |
| JAVELIN RENAL 101 | Primary Trial Result | Choueiri [4] | 2020 | 886 | avelumab + axitinib (442) | sunitinib (444) | 1 | 3 |
| Substudy: Biomarkers | Choueiri [31] | 2019 |  | | | | |
| Substudy: Biomarkers | Motzer [15] | 2020 |
| CheckMate 9ER | Primary Trial Result | Choueiri [6] | 2020 | 651 | cabozantinib + nivolumab (323) | sunitinib (328) | 1 | 3 |
| CheckMate 214 | Primary Trial Result | Tannir [2] | 2020 | 1096 | nivolumab + ipilimumab (550) | sunitinib (546) | 1 | 3 |
| Substudy: Biomarkers | Motzer [16] | 2020 |  | | | | |
| CheckMate 025 | Primary Trial Result | Motzer [11] | 2020 | 821 | nivolumab (410) | everolimus (411) | 2 | 3 |
| Primary Trial Result | Motzer [14] | 2015 |  | | | | |
| Substudy: Biomarkers | Ficial [67] | 2020 |
| Substudy: Biomarkers | Braun [68] | 2020 |
| Substudy: Biomarkers | Braun [38] | 2020 |
| IMmotion 150 | Primary Trial Result | Atkins [69] | 2017 | 305 | atezolizumab + bevacizumab (101) / atezolizumab (103) | sunitinib (101) | 1 | 2 |
| Substudy: Biomarkers | McDermott [10] | 2018 |  | | | | |
| IMmotion 151 | Primary Trial Result | Rini [1] | 2019 | 915 | atezolizumab + bevacizumab (454) | sunitinib (461) | 1 | 3 |
| Substudy: Biomarkers | Rini [57] | 2018 |  | | | | |
| Substudy: Biomarkers | Rini [70] | 2020 |
| RECORD-3 | Primary Trial Result | Knox [71] | 2017 | 471 | everolimus (238) | sunitinib (233) | 1 | 3 |
| Substudy: Biomarkers | Hseih [43] | 2015 |  | | | | |
| Substudy: Biomarkers | Hsieh [30] | 2017 |
| Substudy: Biomarkers | Voss [22] | 2019 |
| COMPARZ | Primary Trial Result | Motzer [12] | 2013 | 1110 | pazopanib (557) | sunitinib (553) | 1 | 3 |
| Substudy: Biomarkers | Choueiri [8] | 2015 |  | | | | |
| Substudy: Biomarkers | Hakimi [56] | 2019 |
| AXIS | Primary Trial Result | Rini [72] | 2011 | 723 | axitnib (362) | sorafenib (361) | 2+ | 3 |
| Substudy: Biomarkers | Murphy [73] | 2020 |  | | | | |
| TARGET | Primary Trial Result | Escudier [27] | 2009 | 903 | sorafenib (451) | placebo (452) | 2+ | 3 |
| Substudy: Biomarkers | Choueiri [28] | 2013 |  | | | | |
| CABOSUN | Primary Trial Result | Choueiri [5] | 2018 | 157 | cabozantinib (79) | sunitinib (78) | 1 | 2 |
| METEOR | Primary Trial Result | Choueiri [9] | 2016 | 658 | cabozantinib (330) | everolimus (328) | 2+ | 3 |
| Substudy: Biomarkers | Flaifel [13] | 2019 |  | | | | |
| BIONIKK | Primary Trial Result | Vano [59] | 2020 | 202 | nivolumab + ipilimumab (101), nivolumab (61) | sunitinib/pazopanib (40) | 1 | 2 |

**Supplementary Table 2. IHC Based Biomarker Results**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| First Author | Year | Trial Name | Biomarker | OS Result | Significant Results: mPFS, months (95% CI) | | |
| Treatment | Biomarker (+)  mPFS (95% CI) | Biomarker (-)  mPFS (95% CI) |
| Choueiri [31] | 2020 | JAVELIN Renal 101 | PD-L1 | HR 0.80 (95% CI, 0.62 - 1.02) ITT  one-sided P=0.0392  HR 0.83 (95% CI, 0.60 - 1.15) PD-L1 (+)  one-sided P=0.13 | AXI + AVE | 13.3 (9.8 - NE) | 12.5 (9.9 - 15.3) |
| SUN | 8.2 (6.9 - 8.5) | 11.1 (9.7 - 13.8) |
| Motzer [16] | 2020 | CheckMate 214 | PD-L1 | HR 0.73 (95% CI 0.56 - 0.96) PD-L1 (-)  HR 0.45 (95% CI 0.29 - 0.71) PD-L1 (+)  \*Int-Poor Risk patients | NIVO + IPI | 22.8 | 11.0 |
| SUN | 5.9 | 10.4 |
| Rini [3] | 2019 | KEYNOTE 426 | PD-L1 | HR 0.59 (95% CI, 0.34 - 1.03) PD-L1 (-)  HR 0.54 (95% CI, 0.35 - 0.84) PD-L1 (+) | AXI + PEM | 15.3 (12.6 - NE) | 15.0 (12.4 - NE) |
| SUN | 8.9 (7.6 - 11.3) | 12.5 (11.0 - NE) |
| Rini [1] | 2019 | IMmotion 151 | PD-L1 | HR 0.93 (95% CI, 0.76 - 1.14) ITT, P=0.4751  HR 0.84 (95% CI, 0.62 - 1.15) PD-L1 (+), P=0.2857 | ATEZ + BEV | 11.2 (8.9 - 15.0) | 11.2 (8.6 - 13.7) |
| SUN | 7.7 (6.8 - 9.7) | 9.5 (8.2 - 10.9) |
| McDermott [10] | 2018 | IMmotion 150 | PD-L1 | N/A | ATEZ + BEV | 11.1 (8.1 - 16.7) | 11.1 (8.2 - 13.5)\* |
| ATEZ | 5.5 (3.0 - 13.9) | 5.5 (3.0 - 8.4) \* |
| SUN | 7.0 (5.6 - 1.2) | 7.8 (5.7 - 11.2)\* |
| Motzer [11]  Motzer [14] | 2020  2015 | CheckMate 025 | PD-L1 | HR 0.77 (95% CI, 0.60 - 0.97) PD-L1 (-)  HR 0.79 (95% CI, 0.53 - 1.17) PD-L1 (+) | NIVO | 21.8 (16.5 - 28.1) | 27.4 (21.4 - NE) |
| EVE | 18.8 (11.9 - 19.9) | 21.2 (17.7 - 26.2) |
| Choueiri [8] | 2015 | COMPARZ | PD-L1 | N/A | PAZO | 15.1 (9.4 - 45.1) | 35.6 (27.2 - 40.8) |
| SUN | 15.3 (11.2 - 30.5) | 27.8 (23.7 - 30.5) |
| Flaifel [9, 13] | 2019 | METEOR | PD-L1 | HR 0.58 (95% CI, 0.38-0.88) PD-L1 (-)  HR 0.82 (95% CI, 0.47-1.41) PD-L1 (+) | CABO | 5.6 (4.5 - 7.4) | 8.5 (7.2 - 13.5) |
| EVE | 3.7 (2.0 - 5.3) | 4.1 (3.7 - 6.0) |
| Choueiri [5] | 2016 | CABOSUN | PD-L1 | HR 0.47 (95% CI, 0.26 - 0.86) PD-L1 (-)  HR 0.46 (95% CI, 0.18-1.21) PD-L1(+) | CABO | 8.4 (1.1 - 16.6) | 11.0 (6.8 - 15.6) |
| SUN | 3.1 (1.6 - 10.1) | 5.0 (3.0 - 12.9) |
| Voss [22] | 2018 | RECORD-3 | PTEN | N/A |  | PTEN (+)  mOS (95% CI) | PTEN (-) loss  mOS (95% CI) |
| SUN | 10.9 (8.1 - 14.5) | 10.3 (7.2 - 16.9) |
| EVE | 5.3 (2.9 - 8.1) | 10.5 (8.1 - 13.9) |
| Stratified PFS HR = 2.5 (1.5 - 4.1) in arm. P=0.0004 | | |

AVE: avelumab, AXI: axitinib, PEMBRO: pembrolizumab, NIVO: nivolumab, IPI: ipilimumab, ATEZ, atezolizumab; AVEL, avelumab; AXI, axitinib; BEV, bevacizumab; CI, confidence interval; EVE, everolimus; HR, hazard ratio; IPI, ipilimumab; M, median; mOS, median overall survival; mPFS, median progression free survival; mo, months; mOS, median overall survival; NIVO, nivolumab; NR, not reached; N/A, not available; ORR, overall response rate; PEM, pembrolizumab; SUN: sunitinib; \* Total population (PD-L1 positive and Negative)

**Supplementary Table 3. Genomic Biomarker Results**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Gene | Study | First Author | Year | Treatment | Endpoint, Result | |
|  | | | | | mPFS (95% CI) mo  WT | mPFS (95% CI) mo  MT |
| *PBRM1* | CheckMate 214 | Motzer [16] | 2020 | NIVO + IPI | N/A | N/A |
| Stratified HR NR; PFS p= 0.76, OS P=0.11 | | |
| SUN | N/A | N/A |
| Stratified HR NR; PFS p = 0.40, OS P=0.96 | | |
| IMmotion 150 | McDermott [10] | 2018 | ATEZO | 8.15 | 5.49 |
| HR 1.33 (95% CI, 0.73 - 2.42) P=0.358 | | |
| ATEZ + BEV | 8.31 | 14.09 |
| HR 0.67 (95% CI, 0.36 - 1.25) two-sided P=0.205 | | |
| SUN | 5.85 | 21.82 |
| HR 0.38 (95% CI 0.20 - 0.73) two-sided P=0.003 | | |
| RECORD 3 | Hsieh [30] | 2017 | EVE | 5.5 (3.1 - 8.4) | 12.8 (8.1 - 18.4) |
| HR 0.53 (95% CI, 0.3-0.8) log rank P=0.002 | | |
| SUN | 8.3 (5.8 - 12.9) | 11.0 (8.3 - 13.8) |
| HR 0.79 (95% CI, 0.5-1.3) log rank P=0.3 | | |
| CheckMate 025, 010, 009 | Braun [38] | 2018 | NIVO | N/A | N/A |
| Stratified HR NR; PFS P=0.0056, OS P=0.00093 | | |
| EVE | N/A | N/A |
| Stratified HR NR; PFS P=0.32, OS P=0.27 | | |
| JAVELIN Renal 101 | Motzer [15] | 2020 | AXI + AVEL | N/A | N/A |
| Stratified HR 1.14 (95% CI, 0.81 - 1.61) P=0.4485 | | |
| SUN | N/A | N/A |
| Stratified HR 0.88 (95% CI, 0.65 - 1.20) P=0.4273 | | |
| COMPARZ, RECORD3 | Voss [39] | 2018 | EVE, SUN, PAZ | 8.2 (5.5 - 8.4) | 11.1 (9.5 - 16.5) |
| PFS HR 0.67 (95% CI, 0.51- 0.88) P=0.004 | | |
| EVE, SUN, PAZ | 23.8 (18.7 - 28.2) | 35.5 (28.0 - NR) |
| OS HR 0.63 (95% CI, 0.47 - 0.85) P=0.0019 | | |
| *VHL* | IMmotion 150 | McDermott [10] | 2018 | ATEZ + BEV | 11.73 | 13.73 |
| HR 1.02 (95% CI, 0.55 - 1.90) P=0.951 | | |
| ATEZ | 5.45 | 11.04 |
| HR 0.67 (95% CI, 0.37 - 1.23) P=0.196 | | |
| SUN | 5.72 | 10.71 |
| HR 0.54 (95% CI, 0.29 - 1.00) P=0.050 | | |
| RECORD 3 | Hsieh [30] | 2017 | EVE | 6.5 (3.1 - 10.9) | 8.4 (5.3 - 11.2) |
| HR 0.77 (95% CI, 0.5-1.3) log rank P=0.2 | | |
| SUN | 10.9 (5.4 - 27.3) | 10.8 (8.1 - 13.3) |
| HR 0.88 (95% CI, 0.5-1.5) log rank P=0.5 | | |
| JAVELIN Renal 101 | Motzer [15] | 2020 | AXI + AVEL | N/A | N/A |
| Stratified HR 0.98 (95% CI, 0.71 - 1.35) P=0.9092 | | |
| SUN | N/A | N/A |
| Stratified HR 1.09 (95% CI, 0.82 - 1.45) P=0.5657 | | |
|  | | | | | TMB (High) | TMB (Low) |
| TMB | CheckMate 025, 010, 009 | Braun [38] | 2020 | Anti PD-1 | N/A | N/A |
| Stratified HR N/R; PFS P=0.74, OS P=0.38 | | |
| mTOR | N/A | N/A |
| Stratified HR N/R; PFS P=0.12, OS P=0.13 | | |
| CheckMate 214 | Motzer [16] | 2020 | NIVO + IPI | N/A | N/A |
| Stratified HR N/R; PFS P=0.76, OS P=0.11 | | |
| SUN | N/A | N/A |
| Stratified HR N/R; PFS P=0.40, OS P=0.96 | | |
| JAVELIN Renal 101 | Motzer [15] | 2020 | AXI + AVEL | N/A | N/A |
| HR 1.09 (95%CI, 0.79 - 1.50) P=0.6084 | | |
| SUN | N/A | N/A |
| HR 0.79 (95% CI, 0.60 - 1.05) P=0.1092 | | |
|  | | | | | WT | MT |
| *SETD2* | RECORD 3 | Hsieh [30] | 2017 | EVE | 8.4 (6.5 - 11.1) | 6.6 (3.0 - 12.1) |
| HR 1.19 (95% CI, 0.7 - 1.9) log rank P=0.2 | | |
| SUN | 9.8 (8.1 - 12.4) | 11.5 (8.1 - 16.9) |
| HR 0.99 (95% CI, 0.6 - 1.6) log rank P=0.3 | | |
| *BAP1* | RECORD3 | Hsieh [30] | 2017 | EVE | 10.5 (7.3 - 12.9) | 4.9 (2.9 - 8.1) |
| HR 1.84 (95% CI, 1.1 - 3.2) log rank P=0.02 | | |
| SUN | 11.0 (8.3 - 13.8) | 8.1 (3.1 - 11.3) |
| HR 1.69 (95% CI, 0.9 - 3.2) log rank P=0.06 | | |
| JAVELIN Renal 101 | Motzer [15] | 2020 | AXI + AVEL | N/A | N/A |
| HR 0.68 (95% CI, 0.43 - 1.09) P=0.1099  ); log rank p = 0.002 | | |
| SUN | N/A | N/A |
| HR 1.34 (95% CI, 0.92 - 1.94) log rank P=0.1220 | | |
| *KDM5C* | RECORD3 | Hsieh [43] | 2017 | EVE | 8.2 (5.3 - 10.9) | 9.8 (2.2 - 16.6) |
| HR 1.06 (95% CI, 0.5 - 2.1) log rank P=0.5 | | |
| SUN | 8.3 (7.8 - 11.0) | 20.6 (12.4 - 27.3) |
| HR 0.57 (95% CI, 0.3 - 1.1) log rank P=0.03 | | |
| *PTEN* | RECORD3 | Hsieh [30] | 2017 | EVE | 8.3 (5.5 - 10.7) | 9.1 (2.1 - 28.4) |
| HR 1.06 (95% CI, 0.5 - 2.1) log rank P=0.4 | | |
| SUN | 10.8 (8.1 - 13.8) | 10.6 (5.8 - 12.4) |
| HR 1.52 (95% CI, 0.8 - 2.8) log rank P=0.1 | | |
| JAVELIN Renal 101 | Motzer [15] | 2020 | AXI + AVEL | N/A | N/A |
| HR 2.64 (95% CI, 1.56 - 4.46) log rank P=0.002 | | |
| SUN | N/A | N/A |
| HR 1.20 (95% CI, 0.74 - 1.93) log rank P=0.4571 | | |
| *mTOR/TSC1/TSC2* | RECORD-3 | Voss [22] | 2019 | EVE | 8.1 (5.4 - 10.5) | 10.3 (2.2 - 13.9) |
| HR 1.1 (95% CI, 0.6 - 2.1) P=0.8056 | | |
| Unstratified HR 0.25 (95% CI, 0.0 - 0.79) two-sidedP=0.0109 | | |
| SUN | 8.5 (8.2 - 9.7) | 5.6 (2.8 - N/A) |
| Unstratified HR 1.19 (95% CI, 0.58 - 2.42) two-sided P=0.6363 | | |

AVE: avelumab, AXI: axitinib, PEMBRO: pembrolizumab, NIVO: nivolumab, IPI: ipilimumab, ATEZ, atezolizumab; AVEL, avelumab; AXI, axitinib; BEV, bevacizumab; CI, confidence interval; EVE, everolimus; HR, hazard ratio; IPI, ipilimumab; M, median; mOS, median overall survival; mPFS, median progression free survival; mo, months; NIVO, nivolumab; NR, not reached; N/A, not available; ORR, overall response rate; PEM, pembrolizumab; PTEN, Phosphatase and tensin homolog; SUN, sunitinib; TMB, Tumour mutational burden

**Supplementary Table 4: Gene Expression Biomarkers**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| First Author | Trial Name | Biomarkers Assessed | Pertinent Results | | PFS Results | | | | |
| Murphy [73] | AXIS | *CCR7*  *CXCR4*  *TLR3* |  | | Treatment, biomarker | | ≥Median  mPFS (95% CI) mo | | <Median  mPFS (95% CI) mo |
| AXI, *CXCR4* | | 9.0 (2.8 - 15.7) | | 2.8 (1.4 - 6.5) |
| PFS HR 0.98 HR: 0.3 (95% CI, 0.1 - 0.8); P=0.011 | | | | |
| AXI, *TLR3* | | 9.0 (2.7 - 15.7) | | 4.5 (1.7 - 6.5) |
| PFS HR: 0.4 (95% CI, 0.2 - 0.9) P=0.023 | | | | |
| SOR, *TLR3* | | 4.5 (1.6 - 6.1) | | 11.9 (3.4 - 27.5) |
| PFS HR 3.9 (95% CI, 1.4 - 10.7) P=0.005  OS HR: 3.0 (95% CI, 1.1 - 8.0) P=0.022 | | | | |
| AXI, *CCR7* | | 13.3 (6.8 - 18.5) | | 32.4 (20.0 - NR) |
| OS HR 3.9 (95% CI, 1.4 - 10.3) P=0.005 | | | | |
| Hakimi [56] | COMPARZ | Gene Signatures  Angiogenic  Macrophage | angio High v angio Low; PFS HR 0.68 (95% CI, 0.53 - 0.88) P=0.0023  angio High v angio Low; OS HR 0.68 (95% CI, 0.52 - 0.90) P=0.0058 | |  | | | | |
| McDermott [10] | IMmotion 150 | Angiogenic  T effector | HR (ATEZ + BEV versus SUN)  angio High 1.36 (95% CI, 0.78 - 2.36)  angio Low 0.59 (95% CI, 0.35-0.98)  HR (ATEZ + BEV versus SUN)  Teff High 0.55 (95% CI, 0.32 - 0.95)  Teff Low 1.41 (95% CI, 0.85 - 2.36) | |  | | angio GES (High)  mPFS (95% CI) mo | | angio GES (Low)  mPFS (95% CI) mo |
| ATEZO + BEV | | 11.4 | | 11.3 |
| Stratified HR 0.90 (95% CI, 0.51 - 1.51) | | | | |
| SUN | | 19.52 | | 3.71 |
| Stratified HR 0.31 (95% CI, 0.18 - 0.55) P<0.001 | | | | |
|  | | Teff (High)  mPFS (95% CI) mo | | Teff (Low)  mPFS (95% CI) mo |
| ATEZO + BEV | | 21.68 | | 5.65 |
| Stratified HR 0.50 (95% CI, 0.30 - 0.86) | | | | |
| SUN | | 7.79 | | 10.81 |
| Stratified HR 1.31 (95% CI, 0.77 - 2.23) | | | | |
| Rini [57] | IMmotion 151 | IMmotion150 signature  Teff, angio  Gene expression signatures. | HR (ATEZ + BEV versus SUN)  angio High 0.95 (95% CI, 0.76 - 1.19)  angio Low 0.68 (95% CI, 0.52 - 0.88)  HR (ATEZ + BEV versus SUN)  Teff High 0.76 (95% CI, 0.59 - 0.99)  Teff Low 0.91 (95% CI, 0.73 - 1.14) | |  | | angio (High)  mPFS (95% CI) mo | | angio (Low)  mPFS (95% CI) mo |
| ATEZO + BEV | | 12.4 | | 8.9 |
| Unstratified HR 0.86 (95% CI, 0.76 - 1.1) | | | | |
| SUN | | 10.1 | | 6.0 |
| Unstratified HR 0.59 (95% CI, 0.47 - 0.75) | | | | |
|  | | Teff (High)  mPFS (95% CI) mo | | Teff (Low)  mPFS (95% CI) mo |
| ATEZO + BEV | | 12.4 | | 9.7 |
| Unstratified HR N/A | | | | |
| SUN | | 8.3 | | 8.4 |
| Unstratified HR N/A | | | | |
| Motzer [15] | JAVELIN Renal 101 | 26 gene JAVELIN Renal 101 |  | |  | | angio (≥M)  mPFS (95% CI) mo | | angio (<M)  mPFS (95% CI) mo |
| AXI + AVE | | 12.5 (9.7 - 15.2) | | 12.5 (9.7 - NE) |
| Unstratified HR 0.98 (95% CI, 0.71 - 1.34) two-sided P=0.88 | | | | |
| SUN | | 9.8 (8.4 - 12.6) | | 6.9 (4.4 - 8.3) |
| Unstratified HR 0.56 (95% CI, 0.42 - 0.74) two-sided P<0.0001 | | | | |
|  | | immuno (≥M)  mPFS (95% CI) mo | | immuno (<M)  mPFS (95% CI) mo |
| AXI + AVE | | 15.2 (12.5 - NE) | | 9.8 (8.6 - 12.2) |
| Unstratified HR 0.60 (95% CI, 0.44 - 0.83) two-sided P=0.0019 | | | | |
| SUN | | 8.3 (7.0 - 11.1) | | 9.0 (7.1 - 9.8) |
| Unstratified HR 0.89 (95% CI, 0.67 - 1.17) two-sided P=0.3973 | | | | |
| Motzer [16] | CheckMate 214 | IMmotion 150 Angiogenesis  JAVELIN Renal 101  Tumour Inflammation Signature (TIS)  IMmotion 150 T-effector  IMmotion 150 Myeloid  Teff/Myeloid composite |  | |  | | angio GES (≥M)  mOS (95% CI) mo | | angio GES (<M)  mOS (95% CI) mo |
| NIVO + IPI | | NR (30.2 - NR) | | 49.2 (25.3 - N) |
| Unstratified HR 1.23 (95% CI, 0.79 - 1.92) | | | | |
| SUN | | 39.7 (29.0 - NR) | | 33.6 (19.3 - 52.3) |
| Unstratified HR 0.58 (95% CI, 0.37 - 0.92) P<0.05 | | | | |
|  | | immuno (≥M)  mPFS (95% CI) mo | | immuno (<M)  mPFS (95% CI) mo |
| NIVO + IPI | | 15.2 (12.5 - NE) | | 9.8 (8.6 - 12.2) |
| Unstratified HR 0.60 (95% CI, 0.44 - 0.83) two-sided P=0.0019 | | | | |
| SUN | | 8.3 (7.0 - 11.1) | | 9.0 (7.1 - 9.8) |
| Unstratified HR 0.89 (95% CI, 0.67 - 1.17) two-sided P=0.3973 | | | | |
| Vano [59] | BIONIKK | ccrcc 1-4 |  | |  | ORR (%) | | PFS (mo) | |
|  | ccrcc1 | NIVO | 21 | | 4.6 | |
| NIVO + IPI | 39 | | 8.0 | |
| ccrcc2 | TKI | 48 | | NR | |
| NIVO + IPI | 54 | | 10.4 | |
| ccrcc3 | NIVO + IPI | 25 | | N/A | |
| TKI | 0 | | N/A | |
| ccrcc4 | NIVO + IPI | 50 | | 12.2 | |
| NIVO | 53 | | 7.8 | |

Angio, angiogenesis; ATEZ, atezolizumab; AVEL, avelumab; AXI, axitinib; BEV, bevacizumab; CABO: cabozantinib; CI, confidence interval; EVE, everolimus; GES, gene expression signature; HR, hazard ratio; IPI, ipilimumab; M, median; mOS, median overall survival; mPFS, median progression free survival, mo, months; mOS, median overall survival; NIVO, nivolumab; NR, not reached; N/A, not available; ORR, overall response rate; PEM, pembrolizumab; SUN, sunitinib; Teff, T effector

**Supplementary Materials:**Electronic Database Searches

**MEDLINE (Ovid)**

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to August 12, 2020

August 13, 2020

3580 records

1. kidney neoplasms/ or exp carcinoma, renal cell/ or ((kidney\* or renal or nephroid) adj3 (cancer\* or tumo?r\* or neoplas\* or carcinoma\* or adenocarcinoma\* or malignanc\*)).ab,ti,kf

2. molecular targeted therapy/ OR immunotherapy/ OR (immunotherap\* or immuno therap\* or immunooncology or immuno oncology or monoclonal or targeted therap\*).ab,kf,ti OR ((checkpoint or check point) adj3 (inhibit\* or block\*)).ab,kf,ti

3. ipilimumab.nm or tremelimumab.nm or exp nivolumab/ or pembrolizumab.nm or atezolizumab.nm or avelumab.nm or durvalumab.nm or sunitinib.nm or pazopanib.nm or exp axitinib/ or lenvatinib.nm or exp sorafenib/ or cabozantinib.nm or exp everolimus/ or temsirolimus.nm or tivozanib.nm or (ipilimumab or tremelimumab or ticilimumab or nivolumab or pembrolizumab or atezolizumab or avelumab or durvalumab or sunitinib or pazopanib or axitinib or lenvatinib or sorafenib or cabozantinib or everolimus or temsirolimus or tivozanib or rapalog\*).ab,kf,ti

4. exp antibodies, monoclonal/ OR "antagonists and inhibitors".fs OR (monoclonal OR inhibit\* OR antagonist\*).ab,kf,ti

5. exp programmed cell death 1 receptor/ or exp programmed cell death 1 ligand 2 protein/ or ctla4 protein, human.nm or exp ctla-4 antigen/ or exp b7-h1 antigen/ or exp receptors, vascular endothelial growth factor/ or exp tor serine-threonine kinases/ or (pd 1 or pd1 or cd279 or programmed cell death ligand or pd l1 or pdl1 or pd l2 or pdl2 or cd273 or b7-d7 or b7d7 or cd274 or cytotoxic t-lymphocyte-associated protein 4 or ctla 4 or ctla4 or b7 h1 or b7h1 or vascular endothelial growth factor or vegf or target of rapamycin or mtor).ab,kf,ti

6. exp biomarkers/ OR exp genetic phenomena/ or exp genetic techniques/ or exp histological techniques/ or (polymorphism\* or genetic\* or genotype\* or gene or genes or allele\* or locus or loci or expression or mircoarray or high throughput or genom\* or genotyp\* or dna or rna or mrna or variant\* or sequenc\* or chromosome\* or chromatin or mutation\* or transcription\* or snp or snps or polymorphism\* or polymerase chain reaction\* or pcr\* or short tandem repeat\* or phenotyp\* or rnaseq or differential display or transcriptom\* or epigenet\* or methylation or hypermethylation or hypomethylation or biomarker\* OR marker\* or bioindicator\* or biological indicator\* or molecular correlat\* or histolog\* or pathohistolog\* or histopatholog\* or immunohistochem\*).ab,kf,ti

7. prognosis/ or predictive value of tests/ or (prognos\* or predict\* or correlat\* or associat\*).ab,kf,ti

8. 1 and (2 or 3 or (4 and 5)) and 6 and 7

**Embase (Elsevier, 1974 - )**

August 13, 2020

4004 Records

1. 'kidney cancer'/de OR 'kidney carcinoma'/de OR 'renal cell carcinoma'/de OR 'kidney metastasis'/de or ((kidney\* or renal or nephroid) NEAR/3 (cancer\* or tumor\* or tumour\* OR neoplas\* or carcinoma\* or adenocarcinoma\* or malignanc\*)):ab,kw,ti

2. ('molecularly targeted therapy'/exp OR 'immunotherapy'/exp OR 'checkpoint inhibitor'/exp) OR (immunotherap\* or 'immuno therap\*' or immunooncology or 'immuno oncology' or monoclonal or 'targeted therap\*'):ab,kw,ti OR ((checkpoint or 'check point') NEAR/3 (inhibit\* or block\*)):ab,kw,ti

3. 'ipilimumab'/mj OR 'ticilimumab'/mj OR 'nivolumab'/mj OR 'pembrolizumab'/mj OR 'atezolizumab'/mj OR 'avelumab'/mj OR 'durvalumab'/mj OR 'sunitinib'/mj OR 'pazopanib'/mj OR 'axitinib'/mj OR 'lenvatinib'/mj OR 'sorafenib'/mj OR 'cabozantinib'/mj OR 'everolimus'/mj OR 'temsirolimus'/mj OR 'tivozanib'/mj or (ipilimumab or tremelimumab or ticilimumab or nivolumab or pembrolizumab or atezolizumab or avelumab or durvalumab or sunitinib or pazopanib or axitinib or lenvatinib or sorafenib or cabozantinib or everolimus or temsirolimus or tivozanib or rapalog\*):ab,kw,ti

4. 'monoclonal antibody'/de OR 'antagonists and inhibitors'/de OR (monoclonal OR inhibit\* OR antagonist\*):ab,kw,ti

5. 'programmed death 1 receptor'/de OR 'programmed death 1 ligand 2'/de OR 'ctla4 protein human'/de OR 'cytotoxic T lymphocyte antigen 4'/de OR 'programmed death 1 ligand 1'/de OR 'vasculotropin receptor'/de OR 'target of rapamycin kinase'/de or ('pd 1' or pd1 or cd279 or 'programmed cell death ligand' or 'pd l1' or pdl1 or 'pd l2' or pdl2 or cd273 or 'b7-d7' or b7d7 or cd274 or 'cytotoxic t-lymphocyte-associated protein 4' or 'ctla 4' or ctla4 or 'b7 h1' or b7h1 or 'vascular endothelial growth factor' or vegf or 'target of rapamycin' or mtor):ab,kw,ti

6. 'biological marker'/exp OR 'molecular genetic phenomena and functions'/exp OR 'genetic procedures'/exp OR 'histochemistry'/exp OR 'immunohistochemistry'/exp or (polymorphism\* or genetic\* or genotype\* or gene or genes or allele\* or locus or loci or expression or mircoarray or 'high throughput' or genom\* or genotyp\* or dna or rna or mrna or variant\* or sequenc\* or chromosome\* or chromatin or mutation\* or transcription\* or snp or snps or polymorphism\* or 'polymerase chain reaction\*' or pcr\* or 'short tandem repeat\*' or phenotyp\* or rnaseq or 'differential display' or transcriptom\* or epigenet\* or methylation or hypermethylation or hypomethylation or biomarker\* OR marker\* or bioindicator\* or 'biological indicator\*' or molecular correlat\* or histolog\* or pathohistolog\* or histopatholog\* or immunohistochem\*):ab,kw,ti

7. 'cancer prognosis'/exp OR 'predictive value'/de or (prognos\* or predict\* or correlat\* or associat\*):ab,kw,ti

8. #1 AND (#2 OR #3 OR (#4 AND #5)) AND #6 AND #7

9. #8 NOT 'conference abstract'/it

**Web of Science (Clarivate)**

Indexes=SCI-EXPANDED, ESCI Timespan=All years

August 13, 2020

4349 Records

1. TS=(("kidney\*" OR "renal" OR "nephroid") NEAR/3 ("cancer\*" OR "tumor\*" OR "tumour\*" OR "neoplas\*" OR "carcinoma\*" OR "adenocarcinoma\*" OR "malignanc\*"))

2. TS=("immunotherap\*" OR "immuno therap\*" OR "immunooncology" OR "immuno oncology" OR "monoclonal" OR "targeted therap\*" OR (("checkpoint" OR "check point") NEAR/3 ("inhibit\*" OR "block\*")))

3. TS=("ipilimumab" OR "tremelimumab" OR "ticilimumab" OR "nivolumab" OR "pembrolizumab" OR "atezolizumab" OR "avelumab" OR "durvalumab" OR "sunitinib" OR "pazopanib" OR "axitinib" OR "lenvatinib" OR "sorafenib" OR "cabozantinib" OR "everolimus" OR "temsirolimus" OR "tivozanib" OR "rapalog\*")

4. TS=("monoclonal" OR "inhibit\*" OR "antagonist\*")

5. TS=("pd 1" OR "pd1" OR "cd279" OR "programmed cell death ligand" OR "pd l1" OR "pdl1" OR "pd l2" OR "pdl2" OR "cd273" OR "b7-d7" OR "b7d7" OR "cd274" OR "cytotoxic t-lymphocyte-associated protein 4" OR "ctla 4" OR "ctla4" OR "b7 h1" OR "b7h1" OR "vascular endothelial growth factor" OR "vegf" OR "target of rapamycin" OR "mtor")

6. TS=("polymorphism\*" OR "genetic\*" OR "genotype\*" OR "gene" OR "genes" OR "allele\*" OR "locus" OR "loci" OR "expression" OR "mircoarray" OR "high throughput" OR "genom\*" OR "genotyp\*" OR "dna" OR "rna" OR "mrna" OR "variant\*" OR "sequenc\*" OR "chromosome\*" OR "chromatin" OR "mutation\*" OR "transcription\*" OR "snp" OR "snps" OR "polymorphism\*" OR "polymerase chain reaction\*" OR "pcr\*" OR "short tandem repeat\*" OR "phenotyp\*" OR "rnaseq" OR "differential display" OR "transcriptom\*" OR "epigenet\*" OR "methylation" OR "hypermethylation" OR "hypomethylation" OR "biomarker\*" OR "marker\*" OR "bioindicator\*" OR "biological indicator\*" OR "molecular correlat\*" OR "histolog\*" OR "pathohistolog\*" OR "histopatholog\*" OR "immunohistochem\*")

7. TS=("prognos\*" OR "predict\*" OR "correlat\*" OR "associat\*")

8. #1 AND (#2 OR #3 OR (#4 AND #5)) AND #6 AND #7

Refined by: [excluding] DOCUMENT TYPES: (PROCEEDINGS PAPER OR MEETING ABSTRACT)