

**Supplemental Table 3 Comparison of cystic/papillary lesions in *Tsc2*<sup>+/-</sup> mice by histological analysis**

(Wilcoxon rank-sum test)

**A. Lesion number (cystic/papillary lesions)**

| Treatment*             | Number of mice | Median | Range | Z (P) (compared with Vehicle) | Z (P) (compared with Everolimus+Sorafenib) |
|------------------------|----------------|--------|-------|-------------------------------|--|
| Vehicle                | 10             | 55.0   | 28-65 |                               |  |
| Everolimus             | 10             | 25.5   | 17-50 | 3.10 (0.002)                  | 0.15 (0.881)                               |
| Sorafenib              | 10             | 47.5   | 28-71 | 1.06 (0.289)                  | 2.68 (0.007)                               |
| Everolimus + Sorafenib | 7              | 28.0   | 14-38 | 2.93 (0.003)                  |  |

**B. Lesion size cystic/papillary lesions)**

| Treatment*             | Number of mice | Median (mm <sup>2</sup> ) | Range (mm <sup>2</sup> ) | Z (P) (compared with Vehicle) | Z (P) (compared with Everolimus+Sorafenib) |
|------------------------|----------------|---------------------------|--------------------------|-------------------------------|--|
| Vehicle                | 10             | 20.056                    | 13.766-44.852            |                               |  |
| Everolimus             | 10             | 11.865                    | 2.405-14.329             | 3.36 (0.001)                  | 0.54 (0.589)                               |
| Sorafenib              | 10             | 17.198                    | 7.209-28.849             | 2.00 (0.046)                  | 2.49 (0.013)                               |
| Everolimus + Sorafenib | 7              | 9.215                     | 2.898-14.932             | 3.27 (0.001)                  |  |

**C. Lesion cellular area (cystic/papillary lesions)**

| Treatment*             | Number of mice | Median (mm <sup>2</sup> ) | Range (mm <sup>2</sup> ) | Z (P) (compared with Vehicle) | Z (P) (compared with Everolimus+Sorafenib) |
|------------------------|----------------|---------------------------|--------------------------|-------------------------------|--|
| Vehicle                | 10             | 7.214                     | 4.726-24.364             |                               |  |
| Everolimus             | 10             | 1.187                     | 0.123-7.190              | 3.36 (0.001)                  | 0.34 (0.728)                               |
| Sorafenib              | 10             | 5.975                     | 2.112-14.349             | 1.93 (0.054)                  | 3.36 (0.001)                               |
| Everolimus + Sorafenib | 7              | 1.024                     | 0.583-1.830              | 3.36 (0.001)                  |  |

\* Treatment was started from 11 month old and continued for two months.