

# THE LANCET Oncology

## Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.  
We post it as supplied by the authors.

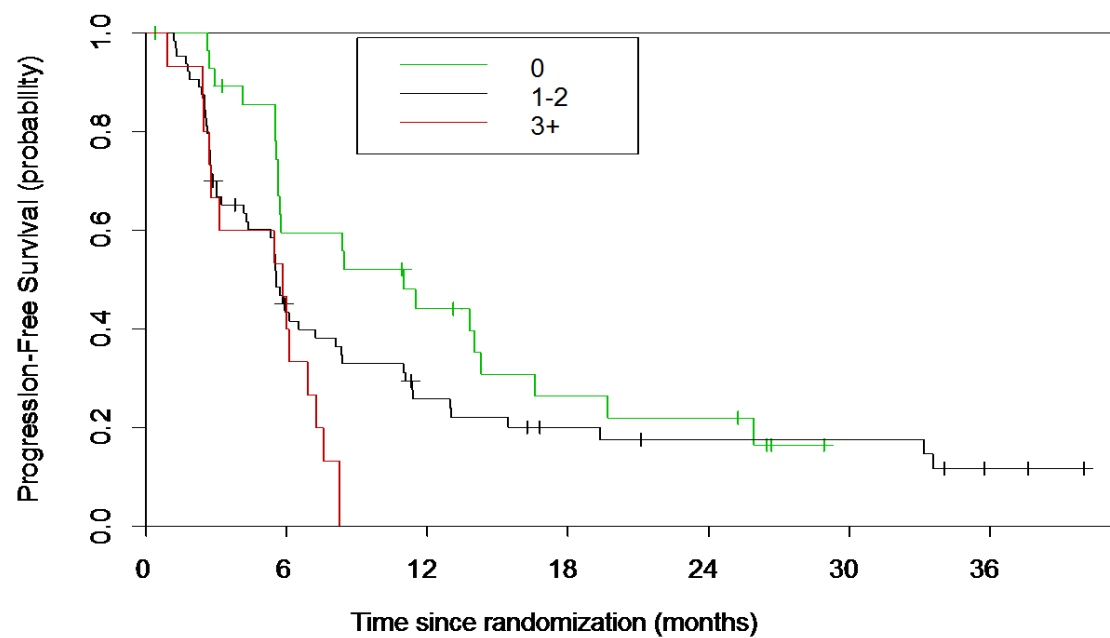
Supplement to: Armstrong AJ, Halabi S, Eisen T, et al. Everolimus versus sunitinib for patients with metastatic non-clear cell renal cell carcinoma (ASPEN): a multicentre, open-label, randomised phase 2 trial. *Lancet Oncol* 2016; published online Jan 12. [http://dx.doi.org/10.1016/S1470-2045\(15\)00515-X](http://dx.doi.org/10.1016/S1470-2045(15)00515-X).

## Appendix

| Principal Investigator       | Site   | Patients Enrolled |
|------------------------------|--|-------------------|
| Tim Eisen                    | University of Cambridge, Cambridge, United Kingdom                                 | 15                |
| Walter M. Stadler            | University of Chicago, Chicago, IL USA   | 13                |
| Robert J. Jones              | The Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom                | 13                |
| Jorge A. Garcia              | Cleveland Clinic, Cleveland, OH USA  | 12                |
| Andrew J. Armstrong          | Duke University and the Duke Cancer Institute, Durham, NC                          | 11                |
| Ulka N. Vaishampayan         | Karmanos Cancer Institute, Wayne State University, Detroit, MI USA                 | 10                |
| Joel Picus                   | Washington University in St. Louis, St. Louis, MO USA                              | 6                 |
| Robert E. Hawkins            | Christie Cancer Research Centre, Manchester, United Kingdom                        | 5                 |
| John D. Hainsworth           | Sarah Cannon Research Institute, Nashville, TN USA                                 | 4                 |
| Christian K. Kollmannsberger | BC Cancer Agency, Vancouver Cancer Centre, Vancouver, BC Canada                    | 4                 |
| Theodore F. Logan            | Indiana University Melvin and Bren Simon Cancer Center, Indianapolis, IN USA       | 3                 |
| Igor Puzanov                 | Vanderbilt University Medical Center, Nashville, TN USA                            | 3                 |
| Lisa M. Pickering            | Royal Marsden Hospital, London, United Kingdom                                     | 3                 |
| Christopher W. Ryan          | Oregon Health & Science University, OHSU Knight Cancer Institute, Portland, OR USA | 2                 |
| Andrew Protheroe             | University of Oxford Medical Oncology Department, Oxford, United Kingdom           | 2                 |
| Mary Mackenzie               | London Health Sciences Center, London Ontario Canada                               | 1                 |
| Omar Din                     | Cancer Clinical Trial Centre, Weston Park Hospital, Sheffield, UK                  | 1                 |

**Table 1.** List of participating sites and accruals.

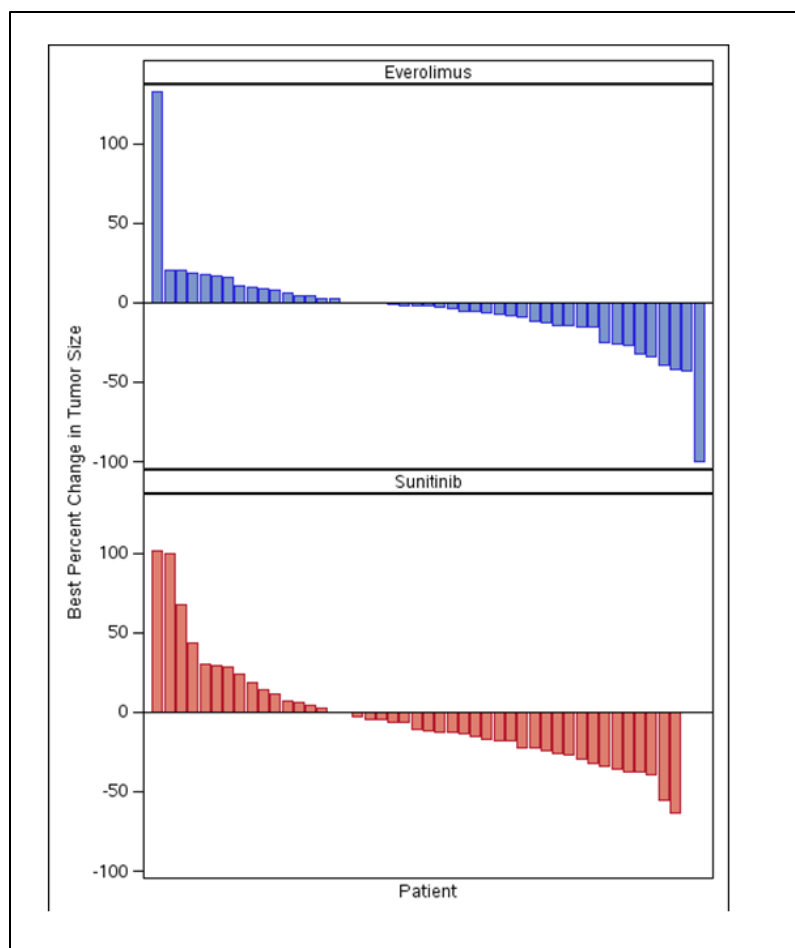
## Overall Survival Curves by Motzer Criteria



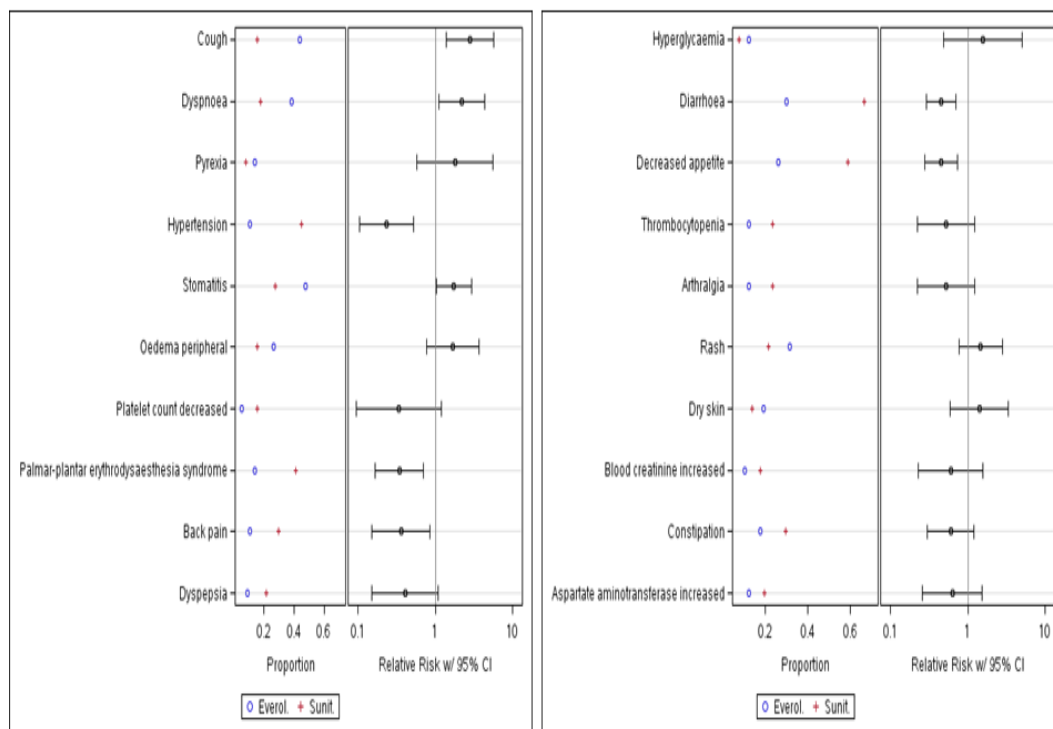
### Number of Patients at Risk

|     |    |    |    |   |   |   |   |
|-----|----|----|----|---|---|---|---|
| 0   | 29 | 16 | 11 | 6 | 5 | 0 | 0 |
| 1-2 | 64 | 25 | 14 | 8 | 6 | 6 | 2 |
| 3+  | 15 | 6  | 0  | 0 | 0 | 0 | 0 |

**Supplementary Figure 1.** Kaplan-Meier estimates of PFS according to 2002 MSKCC risk groups.



**Supplementary Figure 2.** Waterfall plots of best overall RECIST 1.1 response according to treatment group. Tumor shrinkage post-treatment is represented below the x-axis, while tumor growth is portrayed as above the x-axis, and patients are arranged in increasing order on the x-axis.



**Supplementary Figure 3.** Forest plot of toxicity, with relative risks of a given toxicity displayed with sunitinib as the reference group (i.e.  $RR > 1.0$  indicates a higher risk of developing a toxicity for everolimus treated patients).

A. Overall FACT-KSI.

| Treatment / Visit | n   | Mean (SD)    | Observed          | Min, Max   | n  | Change from Randomization |                    |             |
|-------------------|-----|--------------|-------------------|------------|----|---------------------------|--------------------|-------------|
|                   |     |              | Median (Q1, Q3)   |            |    | Mean (SD)                 | Median (Q1, Q3)    | Min, Max    |
| Everolimus        |     |              |                   |            |    |                           |                    |             |
| Randomization     | 54  | 46.5 (9.20)  | 47.5 (42.9, 53.0) | 23.0, 59.0 |    |                           |                    |             |
| Cycle 3           | 31  | 43.6 (8.63)  | 44.0 (37.0, 50.0) | 25.0, 60.0 | 30 | -3.5 (9.61)               | -4.5 (-9.0, 1.0)   | -25.0, 28.0 |
| Cycle 6           | 13  | 47.2 (6.64)  | 49.0 (42.0, 51.0) | 38.0, 60.0 | 13 | -4.4 (6.37)               | -2.0 (-9.0, 1.0)   | -18.5, 4.0  |
| End of Treatment  | 33  | 41.5 (11.42) | 43.9 (32.0, 50.0) | 15.0, 59.0 | 32 | -6.6 (7.83)               | -7.5 (-12.4, -2.0) | -19.0, 11.0 |
| Sunitinib         |     |              |                   |            |    |                           |                    |             |
| Randomization     | 47  | 43.6 (7.78)  | 45.0 (39.0, 49.0) | 26.8, 56.0 |    |                           |                    |             |
| Cycle 3           | 33  | 42.7 (8.46)  | 43.0 (36.4, 49.0) | 22.5, 59.0 | 31 | -0.9 (7.19)               | -1.0 (-4.5, 4.1)   | -23.6, 11.0 |
| Cycle 6           | 19  | 41.6 (9.18)  | 44.0 (35.0, 48.0) | 27.0, 57.0 | 17 | -2.1 (6.69)               | -1.0 (-5.0, 1.0)   | -20.0, 8.3  |
| End of Treatment  | 31  | 39.4 (10.02) | 41.8 (31.0, 48.0) | 23.0, 56.0 | 30 | -6.4 (10.04)              | -5.0 (-12.0, 1.0)  | -27.0, 9.0  |
| Overall           |     |              |                   |            |    |                           |                    |             |
| Randomization     | 101 | 45.2 (8.65)  | 46.0 (41.0, 51.0) | 23.0, 59.0 |    |                           |                    |             |
| Cycle 3           | 64  | 43.1 (8.49)  | 43.0 (36.7, 49.5) | 22.5, 60.0 | 61 | -2.2 (8.49)               | -3.0 (-7.0, 2.0)   | -25.0, 28.0 |
| Cycle 6           | 32  | 43.9 (8.59)  | 44.5 (37.0, 50.0) | 27.0, 60.0 | 30 | -3.1 (6.55)               | -2.0 (-7.0, 1.0)   | -20.0, 8.3  |
| End of Treatment  | 64  | 40.5 (10.74) | 42.0 (31.5, 49.5) | 15.0, 59.0 | 62 | -6.5 (8.89)               | -5.5 (-12.0, -2.0) | -27.0, 11.0 |

B. FACT-KSI Disease related symptoms (DRS) subscale.

| Observed          |     |             |                   |            | Change from Randomization |             |                   |             |
|-------------------|-----|-------------|-------------------|------------|---------------------------|-------------|-------------------|-------------|
| Treatment / Visit | n   | Mean (SD)   | Median (Q1, Q3)   | Min, Max   | n                         | Mean (SD)   | Median (Q1, Q3)   | Min, Max    |
| Everolimus        |     |             |                   |            |                           |             |                   |             |
| Randomization     | 54  | 29.9 (5.42) | 31.0 (28.0, 34.0) | 17.0, 36.0 |                           |             |                   |             |
| Cycle 3           | 31  | 27.7 (5.52) | 29.0 (24.0, 32.0) | 16.0, 36.0 | 30                        | -2.6 (6.27) | -2.0 (-5.0, 1.0)  | -19.1, 15.0 |
| Cycle 6           | 13  | 29.8 (3.76) | 29.0 (27.0, 32.0) | 22.0, 36.0 | 13                        | -2.5 (4.77) | -2.0 (-5.0, 1.0)  | -14.0, 4.0  |
| End of Treatment  | 33  | 26.6 (6.85) | 28.0 (23.0, 32.0) | 10.3, 36.0 | 32                        | -4.6 (4.03) | -4.0 (-7.4, -2.0) | -16.0, 3.0  |
| Sunitinib         |     |             |                   |            |                           |             |                   |             |
| Randomization     | 47  | 28.9 (4.97) | 29.0 (25.0, 33.0) | 15.0, 36.0 |                           |             |                   |             |
| Cycle 3           | 33  | 28.3 (5.01) | 29.0 (25.9, 32.0) | 12.4, 36.0 | 31                        | -0.1 (5.42) | -1.0 (-3.1, 3.0)  | -18.6, 11.0 |
| Cycle 6           | 19  | 27.6 (4.37) | 27.0 (25.0, 31.0) | 19.0, 35.0 | 17                        | -0.4 (5.23) | 1.0 (-3.0, 3.0)   | -11.0, 7.0  |
| End of Treatment  | 31  | 26.6 (6.13) | 28.0 (22.0, 32.0) | 12.0, 35.0 | 30                        | -3.3 (6.30) | -2.0 (-5.0, 0.0)  | -18.0, 8.0  |
| Overall           |     |             |                   |            |                           |             |                   |             |
| Randomization     | 101 | 29.4 (5.22) | 31.0 (26.0, 34.0) | 15.0, 36.0 |                           |             |                   |             |
| Cycle 3           | 64  | 28.0 (5.23) | 29.0 (24.9, 32.0) | 12.4, 36.0 | 61                        | -1.3 (5.93) | -1.0 (-4.0, 2.0)  | -19.1, 15.0 |
| Cycle 6           | 32  | 28.5 (4.22) | 28.0 (26.5, 32.0) | 19.0, 36.0 | 30                        | -1.3 (5.07) | -1.5 (-4.0, 2.0)  | -14.0, 7.0  |
| End of Treatment  | 64  | 26.6 (6.46) | 28.0 (22.5, 32.0) | 10.3, 36.0 | 62                        | -4.0 (5.25) | -3.0 (-7.0, -1.0) | -18.0, 8.0  |

**Supplementary Table 2.** Quality of life Data based on FACT-KSI overall (A) and the disease related symptom (DRS) subscale (B).