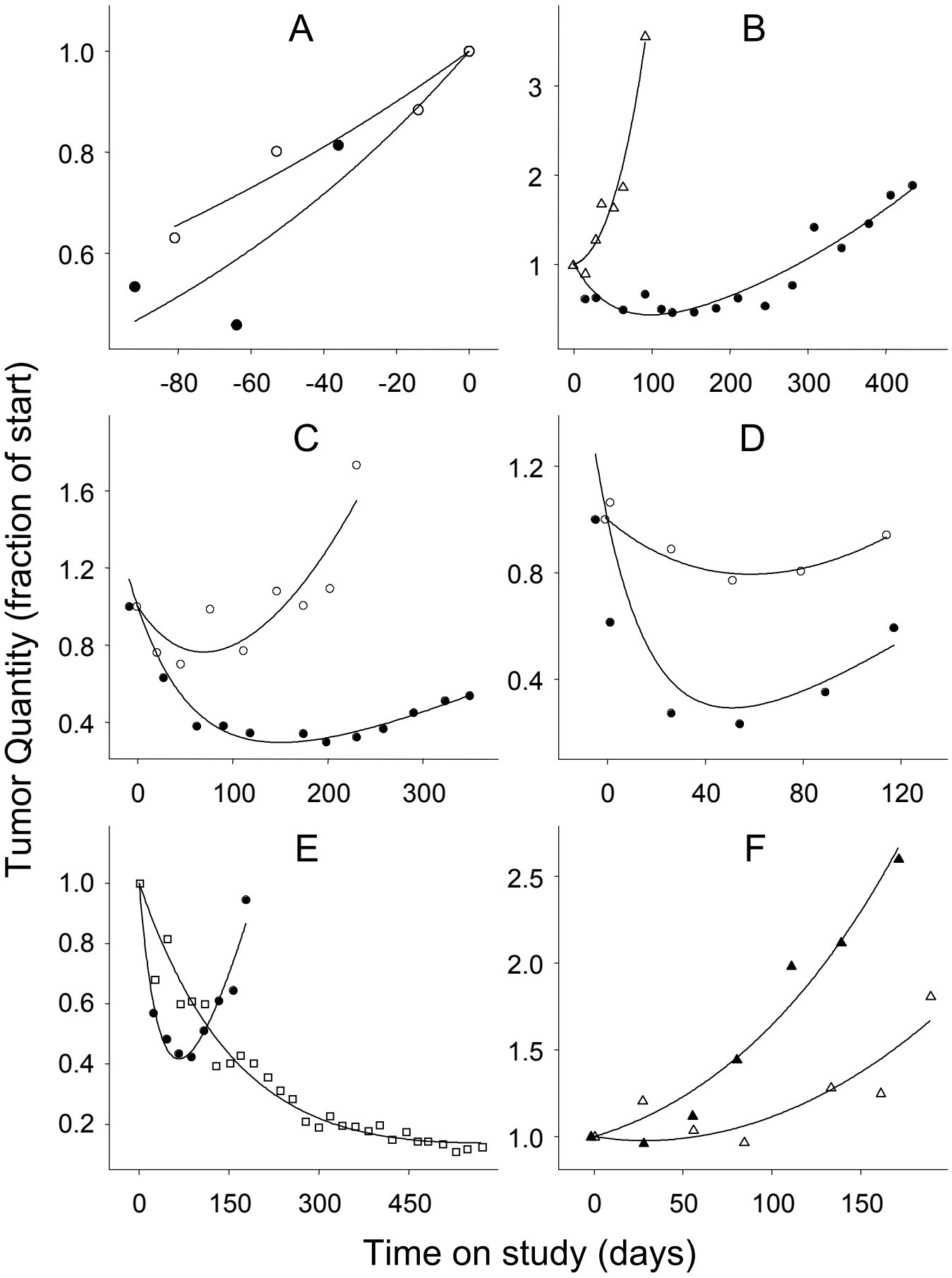
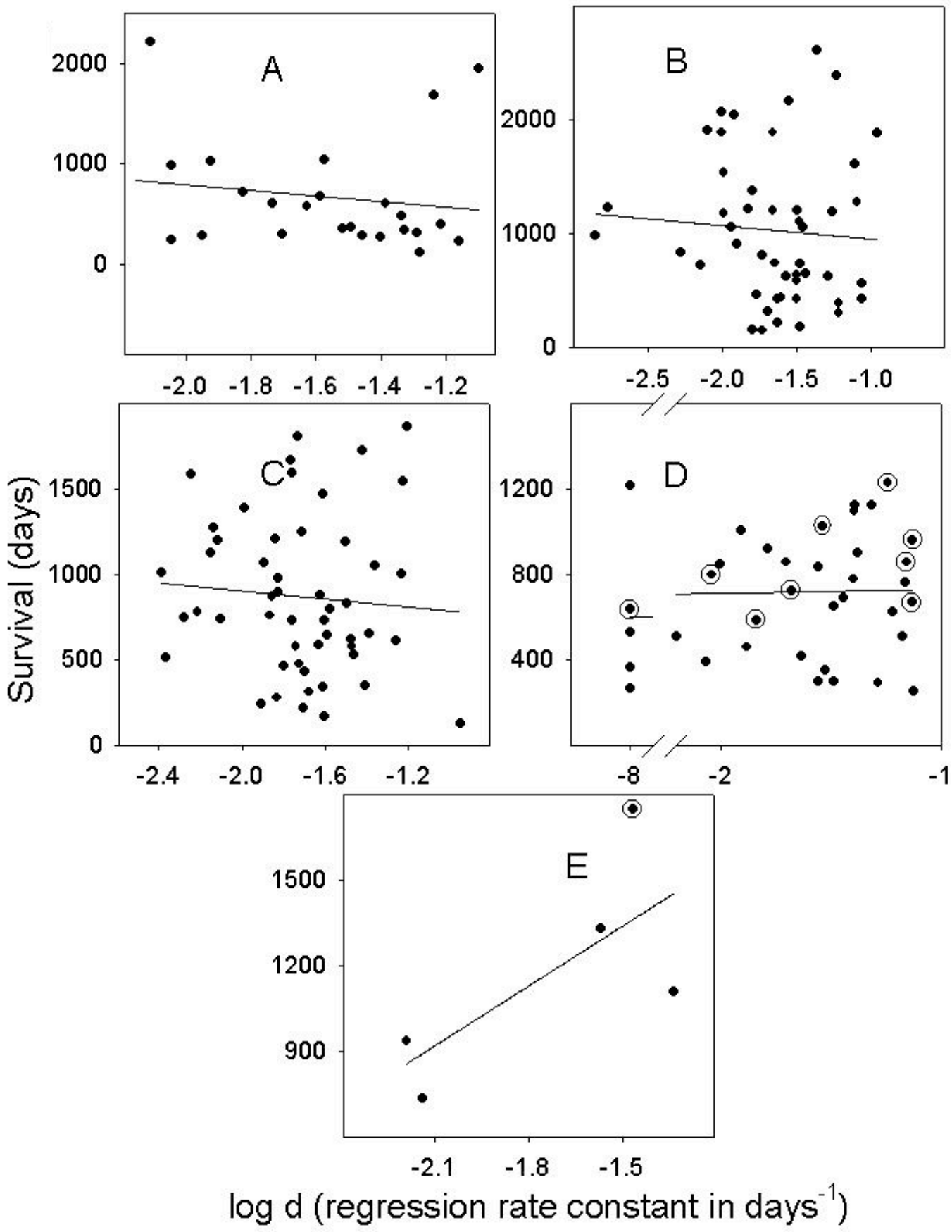
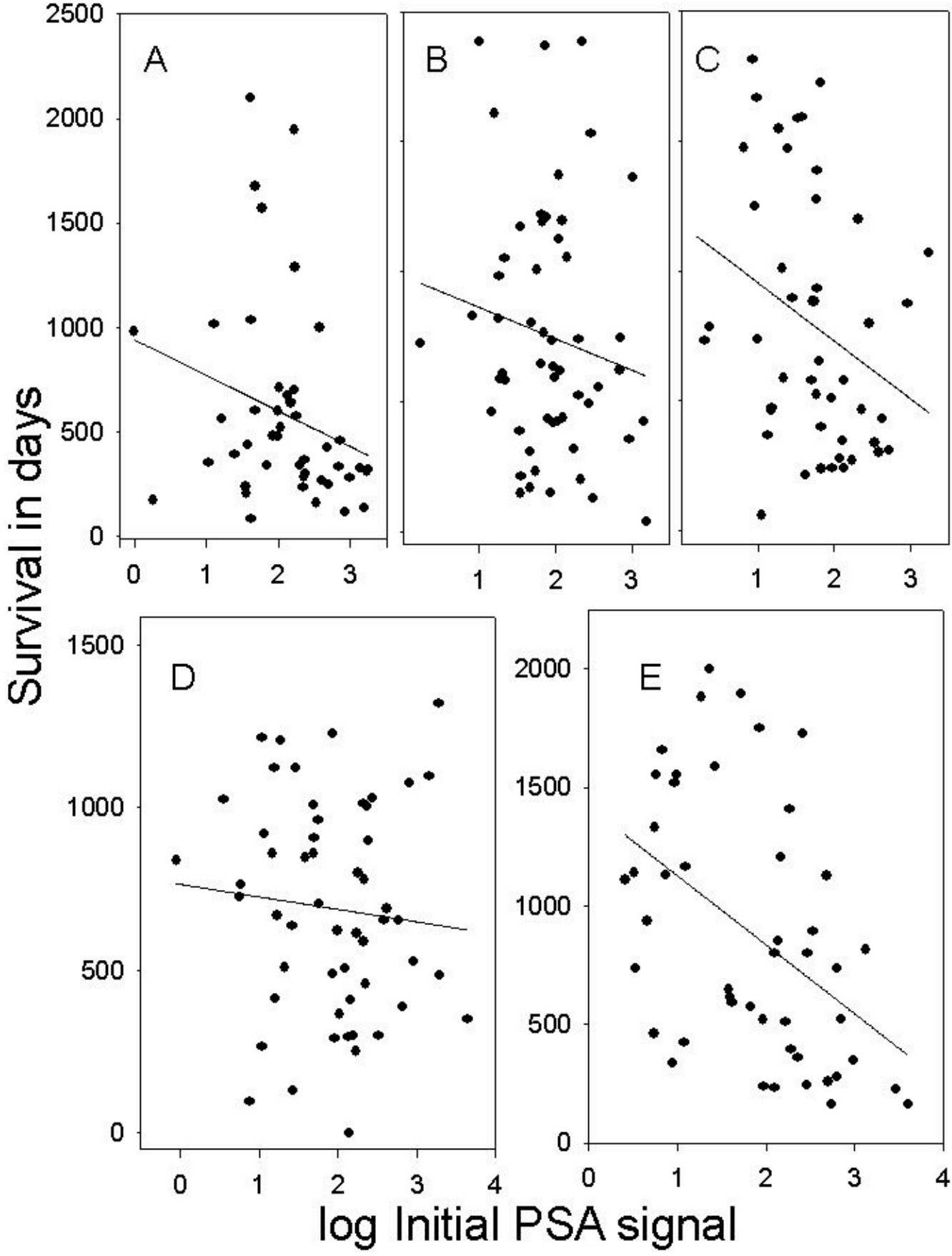


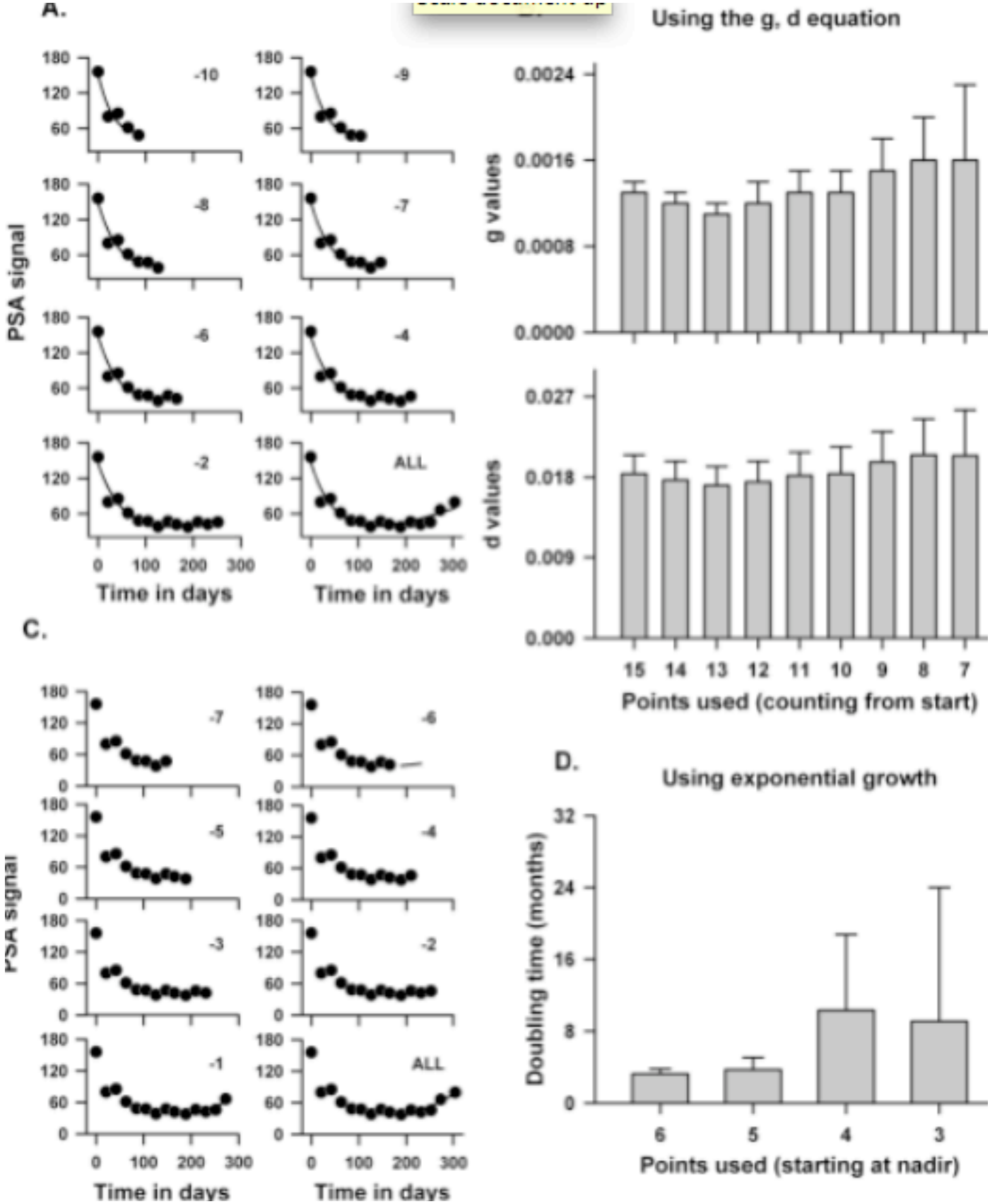
Stein et al, Supplemental Figure 1



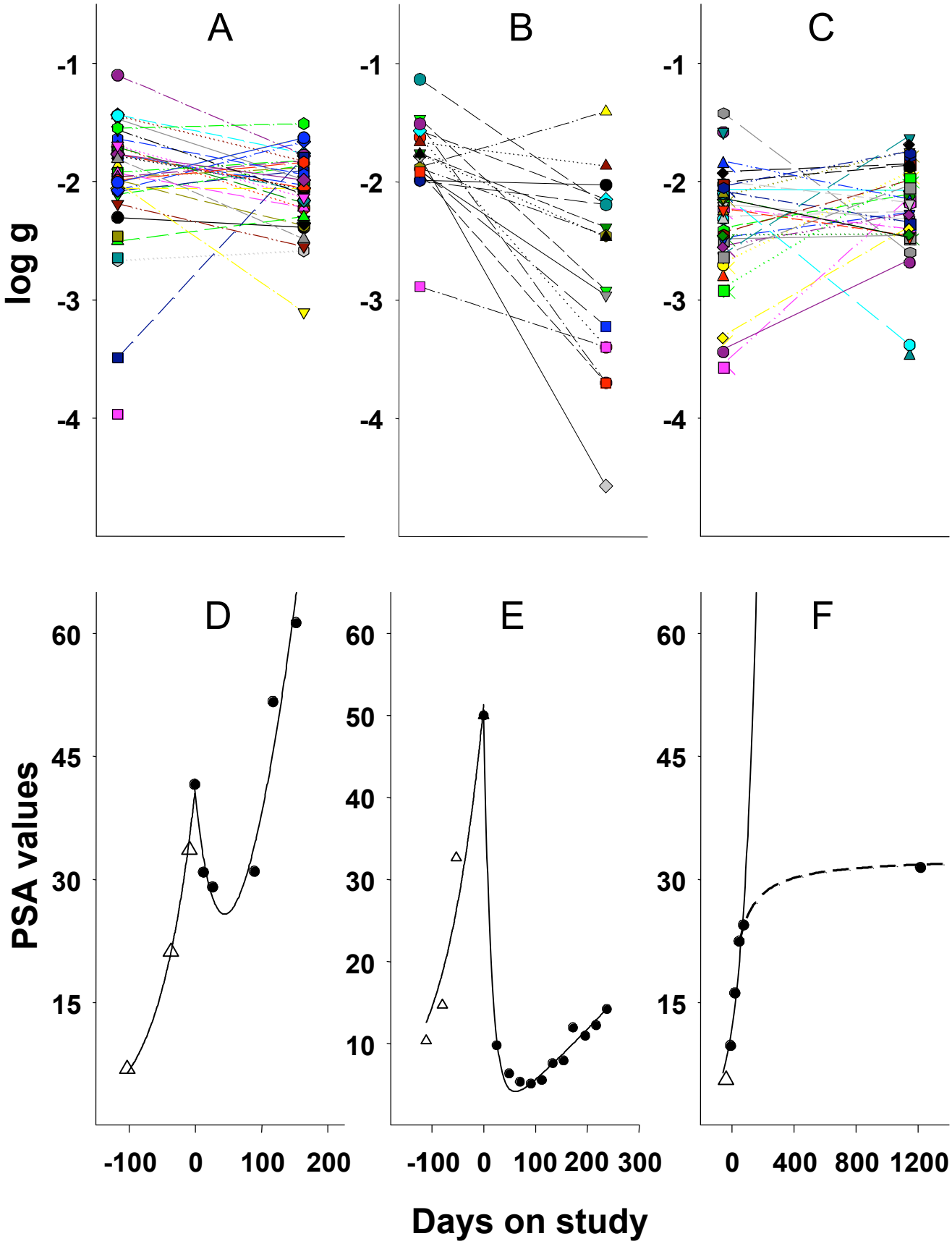
Stein et al, Supplemental Figure 2



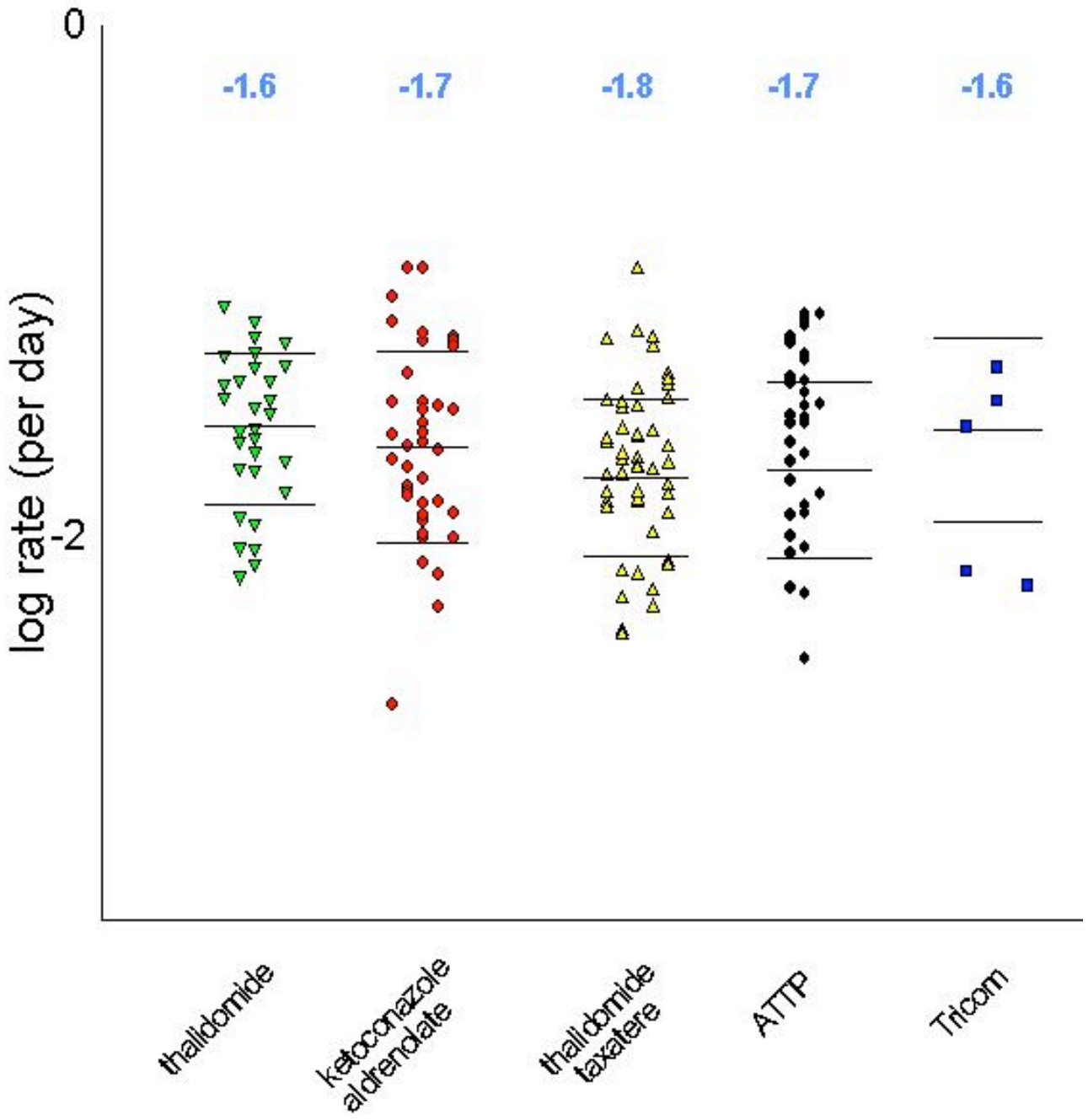
Stein et al, Supplemental Figure 3



Stein et al, Supplemental Figure 4



Stein et al, Supplemental Figure 5



Stein et al, Supplemental Figure 6

SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1: Plots for the regression/growth model using PSA data obtained from 12 representative patients treated (or not treated) with various therapies. The concomitant regression and growth curves added together give the solid line that fits the PSA values obtained in the clinical setting (solid circles or open circles, each depicting a different patient), and thus represents the sum of the fraction of tumor that is regressing and the fraction that is growing. Panel A depicts the pre-enrollment PSA profile of two patients whose PSA levels were available before treatment commenced at day 0. These two cases show only an upward growth curve, since no therapy had yet been given to these patients. Panels B through F show two patients from each of the five trials, depicting on-study data from the thalidomide, ketoconazole plus alendronate, thalidomide plus docetaxel, ATTP, and PSA-TRICOM trials, respectively. Clinical courses characterized by PSA regression (a downward trend) followed by re-growth (an upward trend) are found in most cases. For these, Eq. (1) gives an acceptable fit as shown by the solid lines through the data points. (Two earlier papers show the theoretical predictions of the individual terms of Eq. (1) and how these combine together to yield the solid lines drawn through the points in Figure 1 [4, 5]). In all of these cases, both the g and the d parameters of Eq. (1) were found with p values < 0.05. The figure also includes an example better described by Eq. (2), complete downward response without evidence of re-growth during the period on study (panel E, open circles), and also includes examples better described by Eq. (3), upward growth without regression (open circles panel B and open and

closed circles, panel F). Y-axis: PSA signal relative to initial on study value set at 1 for all patients. X-axis: time on study in days.

Supplemental Figure 2: (Lack of) dependence of patient survival (Y axis in days) on the log of the decay (regression) rate constants. All X-axes are logarithmic scales. Decay rate constants (**d**, per day) were derived using Eq. (1) or Eq. (2). (A) thalidomide (R = 0.15, p = 0.49); (B) ketoconazole plus alendronate (R = 0.074, p = 0.62); (C) thalidomide plus docetaxel (R = 0.080, p = 0.58); (D) ATTP (R = 0.15, p = 0.38); and (E) PSA-TRICOM (R = 0.71, p = 0.18) studies, respectively

Supplemental Figure 3: Dependence of patient survival (Y axis in days) on the initial tumor quantity. All X-axes are logarithmic scales. (A) thalidomide (R = 0.26, p = 0.087); (B) ketoconazole plus alendronate (R = 0.15, p = 0.28); (C) thalidomide plus docetaxel (R = 0.29, p = 0.050); (D) ATTP (R = 0.09, p = 0.52) and (E) PSA-TRICOM (R = 0.45, p = 0.0014) studies, respectively.

Supplemental Figure 4: A**n** example of one record of the PSA values over time is depicted to shown how a g value indistinguishable from that obtained using the full data set of PSA values can be obtained earlier in the clinical course than a value for PSA-DT. **(A)** Curve fitting with Sigmaplot using Eq. (1) at successive times from the fifth through the fifteenth data point, each time adding in additional data points, until all fifteen were used. In the upper histogram of **(B)** we depict the

results of this analysis with the ratio of the SE to the mean for the derived g values. As can be seen, the value of g derived in this set using only the first 8 data points is hardly different neither in absolute size nor in SE from that using all fifteen data points. Even using the first seven data points, gathered until just before the actual nadir, an acceptable value of g with an acceptable SE was obtained. The d values are similarly well derived as shown in the lower histogram of **(B)**. In contrast, as shown in **(C)** and **(D)** using these same data points fitted with the PSA-DT paradigm, rising from the nadir, four points beyond the nadir (13 counting from the start) are required to get a stable value for the PSA-DT, with an acceptable ratio of SE to the mean. In this example, then, an acceptable g value is obtained 18 weeks before a valid PSA-DT.

Supplemental Figure 5: Comparison of the pre-study and on study values for individual patients showing effect of therapy on the growth rate constant, g. Panels (A), (B), and (C) depict data from the thalidomide, ATTP, and PSA-TRICOM trials. In these patients pre-study PSA values were available and a growth rate constant could be determined for both periods. In each case, straight lines connect pre- and on-study g values, as logarithms, for individual patients (pre-study values on the left, on-study on the right). The lower panels depict PSA values in single, representative patients from the thalidomide (D), ATTP (E) and PSA-TRICOM (F) trials. The PSA data were fitted by Eqs. (1) or (3). In (D) and (E), pre-enrollment PSA values were available and are depicted as the points leading up to day 0 on the X-axes. The g values from the time of recurrence in

(D) and (E) are not significantly different from the pre-study rates. For both cases, the pre-treatment and re-growth rate constants do not differ significantly: (D), $p = 0.15$; (E), $p = 0.14$, by t-tests. In contrast, example (F) from the PSA-TRICOM trial shows the slowing in growth that apparently occurred after therapy had been discontinued. The solid line represents the predicted PSA values had the patient's tumor continued to grow with the on-study growth rate constant. The dashed line merely connects up the actual last and the second to last PSA values.

Supplemental Figure 6: Dot plots of the distribution of the best-fit decay (regression, d) rate constants in studies conducted over time. The horizontal lines in each set are the mean values and the SD. The Y-axis is the logarithm of the derived decay rate constant. The mean