SUPPORTING INFORMATION: Estimating the self-renewal capacity in hierarchically organized tumors

Benjamin Werner[1,2], Jacob G. Scott[3,4], Andrea Sottoriva[2], Alexander R.A. Anderson[3], Arne Traulsen[1], Philipp M. Altrock[5,6•]

[1]Department of Evolutionary Theory, Max Planck Institute for Evolutionary Biology, Plön, Germany
[2] Centre for Evolution and Cancer, The Institute of Cancer Research, 15 Cotswold Rd, Sutton, London, SM2 5NG, UK
[3] Integrated Mathematical Oncology Department, H. Lee Moffit Cancer Center and Research Institute, Tampa, FL 33612, USA
[4] Wolfson Centre for Mathematical Biology, University of Oxford, Oxford, UK
[5] Dana-Farber Cancer Institute, Boston, MA 02215, USA and Harvard School of Public Health, Boston, MA 02115, USA
[6] Program for Evolutionary Dynamics, Harvard University, Cambridge, MA 02138, USA

•paltrock@jimmy.harvard.edu

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Figure S1. Flow chart for the linear regression to estimate cancer stem cell fractions from individual treatment response data. From all patients that qualify with a prominent bi-phasic reduction of tumor burden during continued treatment we calculated a distribution of the two slopes of tumor decay. Additionally, we calculated the offset (at tumor detection) of the second phase. In the meantime, we estimated the initial tumor growth rate at early tumor development (way before detection) using patients with clear relapse. All four values together yield a distribution of cancer stem cell fractions at the beginning and in the second phase of treatment (see main text for equations). We assumed a constant tumor size at detection (10^{12} cells), and an expected tumor age at diagnosis of 5 years.

Figure S2. Individual treatment response of chronic myeloid leukemia patients to Imatinib. Shown are treatment responses (dots) for all patients that meet the criteria of a complete follow up and no visible resistance. For each patient we estimate the slopes σ_1 (dashed line) and and the slope σ_2 (line) from linear regression (lines). The second linear regressions also provides the offset η_t that allows us to estimate cancer stem cell fractions for each patient.

Figure S3. Relapse of chronic myeloid leukemia. Shown is the relapse of 7 patients under Imatinib treatment due to an expanding resistant subclone. Linear regression (line) is used to infer the slope of the growing clone and is used as estimate for the initial fast tumor growth s_1.

Figure S4. Parameter estimates from linear regression analysis. **A** the slope s_1 inferred from the linear regression of the relapse in the seven patients from Fig. SI3. **B,C** the slopes and the offsets inferred from the linear regressions of patients with bi-phasic decline in disease burden from Fig. SI2. **D** Estimates for the growth of the tumor s_2 before treatment, inferred via the conservative relationship $s_2 = \sigma_2/\sigma_1 s_1$, see Methods for details.

Figure S5. Variation of cancer stem cell (CSC) fraction estimates with tumor age. We can perform a linear regression analysis on each patient (as described in the main text) under the consideration of a range of tumor age at diagnosis. The typical time from the initiating mutational hit until diagnosis in approximately 72 months in CML. **A** CSC fraction at diagnosis. **B** CSC fraction at end of treatment.