Supplementary Online Content

Unger JM, LeBlanc M, Blanke CD. The effect of positive SWOG treatment trials on survival of patients with cancer in the US population. *JAMA Oncol.* Published online June 5, 2017. doi:10.1001/jamaoncol.2017.0762

eFigure 1. Survival Functions Indicating Life-Years Gained Calculations for a Representative Positive SWOG Phase III Trial (S9008) by Age Category

eFigure 2. Study Flow Diagram Indicating the Disposition of the Studies Examined and Their Cancer Type
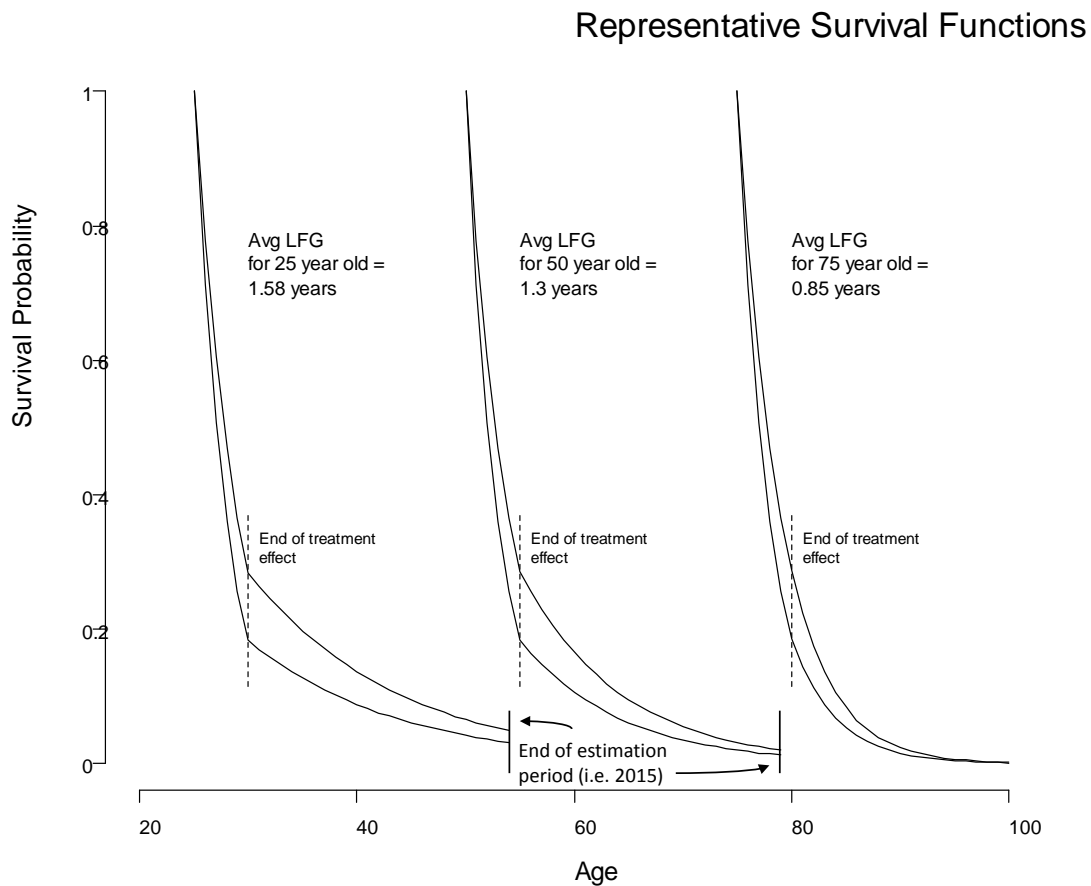
eFigure 3. Life-Years Gained by Treatment Duration and Effectiveness

eMethods. Supplemental Methods

eTable. SWOG Studies With Statistically Significant Benefit of Experimental Therapy on Overall Survival
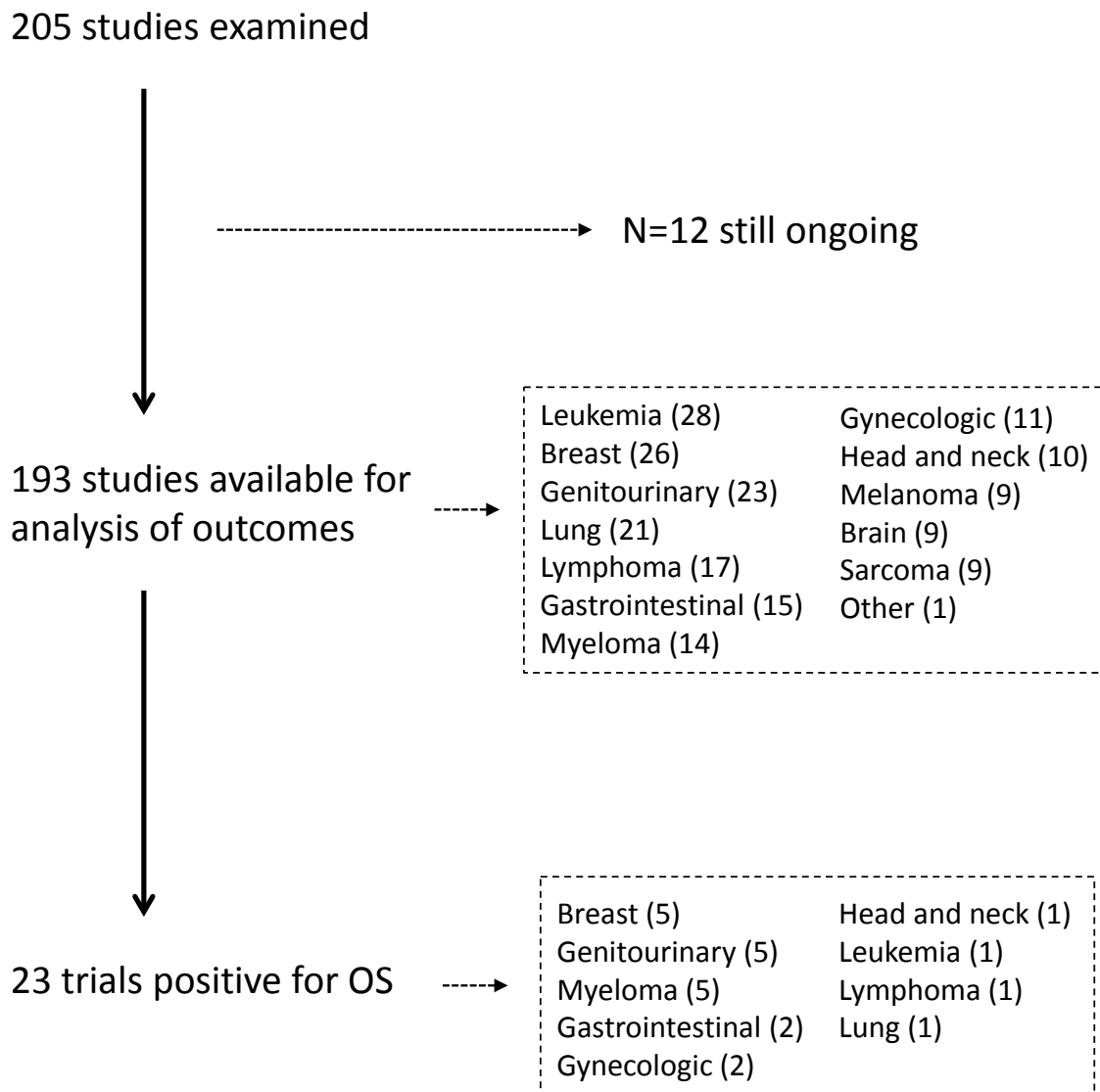
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Survival Functions Indicating Life-Years Gained Calculations for a Representative Positive SWOG Phase III Trial (S9008) by Age Category. Life-years gained is the difference in the area under the survival curve between individuals receiving standard versus experimental therapy. The survival functions for the effect of the new treatment is based on trial parameters; residual life years continue to accrue beyond the treatment impact period (i.e. 5 years) given more individuals are alive. Survival in the post-treatment effect period is assumed to exhibit exponential decay, with maximum survival at the half-life using life table data, out to the end of the estimation period.

Representative Survival Functions

Avg LFG
for 25 year old =
1.58 years

Avg LFG
for 50 year old =
1.3 years

Avg LFG
for 75 year old =
0.85 years

End of treatment
effect

End of treatment
effect

End of treatment
effect

End of estimation
period (i.e. 2015)

Survival Probability

Age

Study Flow Diagram

205 studies examined

N=12 still ongoing

193 studies available for analysis of outcomes

Leukemia (28)	Gynecologic (11)
Breast (26)	Head and neck (10)
Genitourinary (23)	Melanoma (9)
Lung (21)	Brain (9)
Lymphoma (17)	Sarcoma (9)
Gastrointestinal (15)	Other (1)
Myeloma (14)	

23 trials positive for OS

Breast (5)	Head and neck (1)
Genitourinary (5)	Leukemia (1)
Myeloma (5)	Lymphoma (1)
Gastrointestinal (2)	Lung (1)
Gynecologic (2)	

eFigure 3. Life-Years Gained by Treatment Duration and Effectiveness. Each dot indicates an estimate of life-years gained across all 23 positive trials based on the duration of the treatment effect (3 to 7 years by one year intervals), the efficiency of the translation of the treatment effect to the treatment population (75% to 100%), and the weight parameter (uniformly within five category ranges of 1:10, 11:50, 50:100, 100:200, and 200:1000).

Life Years Gained
By Treatment Duration and Effectiveness

Effectiveness
- 75% to 80%
- 80% to 85%
- 85% to 90%
- 90% to 95%
- 95% to 100%

Proportion of estimates above 2 million: 95%

Life Years Gained (millions)

Duration of Treatment Effect
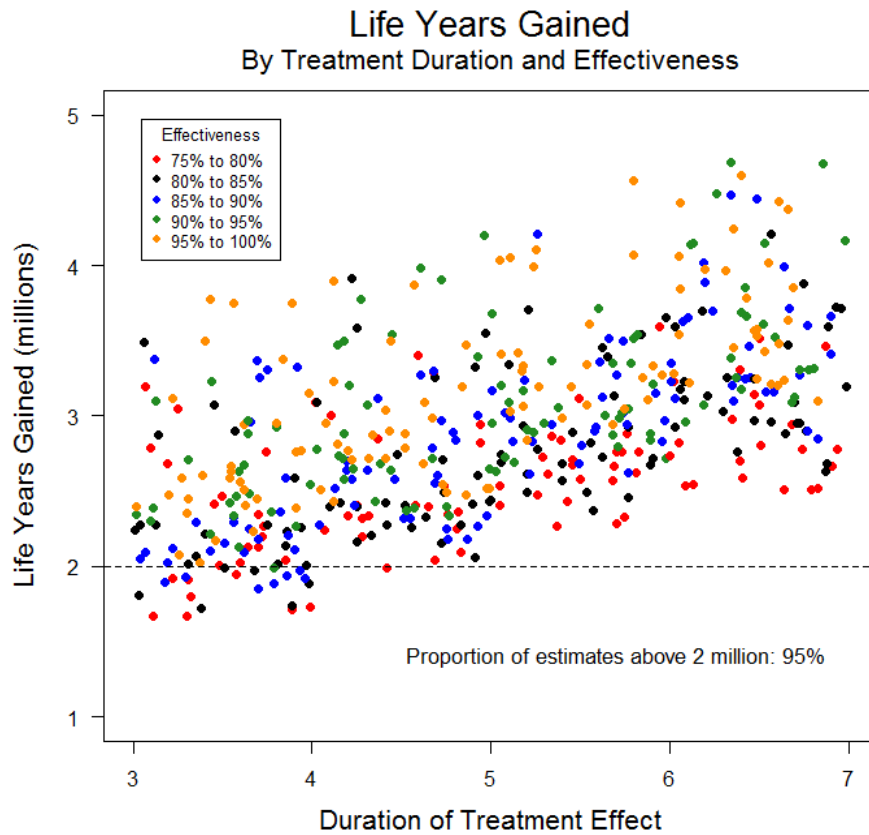
eMethods. Supplemental Methods

Methods regarding adjusting hazard functions to better reflect population cancer outcomes

An adjustment factor was derived by identifying the relative benefit of trial participation on OS from the data used to generate Figure 4 in Unger, 2014. The relative benefit of trial participation differed by year (and was especially strong in the first year but waned over time) and according to prognosis. We estimated the relative benefit for each year out to 5 years and according to prognosis in 10% increments.

Methods regarding calculation of years of life lost due to cancer in U.S.

To estimate years of life due to cancer in the United States, we relied on data from multiple reports.

Horm and Sondik (American Journal of Public Health, 1989; 79(11); 1490-1993) estimated the years of

life lost due to cancer in the United States in 1970 as 5,303,668, and in 1984 as 6,881,281. Data from the

most recent Cancer Trends Progress Report from the National Institutes of Health indicates that

9,186,000 life years were lost due to cancer in the United States in 2013. A simple linear projection

regression line was estimated from these data points, and the area under the curve from 1969-2016 was

estimated as the total life years lost due to cancer during the period, giving an estimate of 356,829,000.

References:

- Horm JW, Sondik EJ. Person-years of life lost due to cancer in the United States, 1970 and 1984. American Journal of Public Health November 1989: Vol. 79, No. 11, pp. 1490-1493.
- Cancer Trends Progress Report, National Cancer Institute, NIH, DHHS,Bethesda, MD, January 2017, http://progressreport.cancer.gov

eTable. SWOG Studies With Statistically Significant Benefit of Experimental Therapy on Overall Survival

Cancer Study No.	Major Eligibility Criteria	Treatment Comparison (Experimental therapy vs. Standard therapy)	Accrual Years	1st Year of Publication	Std. Arm Hazard[a]	HR	N
Myeloma (SWG01)[14]	Multiple myeloma; previously untreated	Melphalan + prednisone vs. melphalan alone	1965-1968	1969	0.678[1]	1.60[1]	183
Breast (SWG02)[15]	Carcinoma; disseminated (refractory)	Adriamycin vs. oral nitrosoureas	1972-1972	1974	2.870[1]	1.87[1]	110
Breast (S7436)[16]	Modified or radical mastectomy, node(+), no metastatic disease	CMFVP vs. intermittent L-PAM	1975-1979	1982	0.110[1]	1.76[1]	364
Myeloma (S7704)[17]	Multiple myeloma; previously untreated	VMCP and (VCAP or VBAP) vs. melphalan + prednisone	1977-1979	1983	0.422[1]	1.65[1]	275
Testis (S7817)[18]	Germ cell; metastatic; no prior chemotherapy	High dose cisplatin + vinblastine/bleomycin vs. low dose cisplatin + vinblastine/bleomycin	1978-1981	1984	0.269[2]	2.33[2]	114
Prostate (S8494)[19]	Carcinoma; previously untreated, stage D2	Leuproline + flutamide vs. leuprolide alone	1985-1986	1988	0.709[1]	1.28[1]	603
Ovarian (S8501)[20]	Epithelial; previously untreated, stage III	Intraperitoneal cisplatin + cyclophosphamide vs. intravenous cisplatin + cyclophosphamide	1986-1992	1995	0.236[2]	1.32[3]	546
Colon (S8591)[21]	Adenoma; resected; stage C	Levamisole + 5FU vs. levamisole or observation	1984-1987	1990	0.182[2]	1.49[3]	971
Myeloma (S8624)[22]	Multiple myeloma; previously untreated	Chemotherapy plus dose intensive corticosteroids vs. chemotherapy plus standard dose corticosteroids	1987-1990	1992	0.356[2]	1.32[2]	507
Bladder (S8710)[23,c]	Transitional cell carcinoma; stages T2–T4A	M-VAC plus cystectomy vs. cystectomy alone	1988-1997	2001	0.223[2]	1.33[3]	307
NHL (S8736)[24]	Intermediate and high grade NHL; stage I-IIE (non-bulky disease)	CHOP plus radiotherapy vs. CHOP alone	1988-1995	1996	0.070[2]	1.70[3]	401
Cervix (S8797)[25,d]	Squamous cell, adeno-, or adenosquamous carcinoma; stages IA2, IB, or IIA	Cisplatin/5-FU plus radiation therapy vs. radiation therapy alone	1990-1996	1999	0.101[2]	1.96[3]	243
Breast (S8814)[26]	Adenocarcinoma; hormone-receptor positive; stage T1-T3; postmenopausal; node positive (N1 or N2)	CAF followed by tamoxifen or CAF with concurrent tamoxifen vs. tamoxifen alone	1989-1995	1997	0.041[2]	1.20[3]	1477
HN (S8892)[27]	Nasopharyngeal; stage III-IV(M0)	Cisplatin/5-FU plus radiation therapy vs. radiation therapy alone	1989-1996	1996	0.257[2]	2.50[3]	148
Breast (S8897)[28,d]	Adenocarcinoma; stage T1-T3a; node negative	CAF vs. CMF	1989-1993	1995	0.020[2]	1.19[3]	2695
Renal (S8949)[29]	Carcinoma; metastatic	Nephrectomy plus interferon alfa-2b vs. interferon alfa-2b alone	1989-1998	2000	1.296[2]	1.30[2]	241
Gastric (S9008)[30]	Adenocarcinoma; stage IB–IV (M0); prior en bloc surgery	Surgery plus 5-FU/leucovorin/radiation therapy vs. surgery alone	1991-1998	2000	0.340[2]	1.35[3]	556
Leukemia (S9126)[31]	Acute myeloid leukemia; refractory/relapse or secondary	Ara C-DNR plus CsA vs. Ara C-DNR alone	1993-1998	1998	1.742[2]	1.28[3]	226
Myeloma (S9210)[32,e]	Multiple myeloma; previously untreated	Prednisone 50 mg vs. prednisone 10 mg (for remission maintenance)	1993-1998	1998	0.205[2]	1.41[2]	126

NSCLC (S9308)[33]	Any NSCLC; stage IIIB or IV	Cisplatin plus vinorelbine vs. vinorelbine alone	1993-1995	1997	2.070^2	1.44^2	415
Prostate (S9916)[34]	Adenocarcinoma; advanced (metastatic) refractory	Docetaxel plus estramustine vs. mitoxantrone plus prednisone	1999-2003	2004	0.714^2	1.25^3	684
Breast (S0226)[35]	Hormone-receptor positive; metastatic; postmenopausal; no prior systemic therapy	Anastrozole and fulvestrant vs. anastrozole alone	2004-2009	2011	0.224^2	1.25^3	695
Myeloma (S0777)[36]	Multiple myeloma; previously untreated; no intent to treat with autologous stem cell transplant	Bortezomib, lenalidomide, & dexamethasone vs. lenalidomide + dexamethasone	2008-2012	2015	0.117^2	1.50^3	474
TOTAL (23 trials)			**1965-2012**				**12,361**

HR = hazard ratio; OS = overall survival; CI = confidence interval; NHL = non-Hodgkin's lymphoma; VAD = vincristine, doxorubicin and dexamethasone; M-VAC = methotrexate, vinblastine, doxorubicin and cisplatin; CHOP = cyclophosphamide, doxorubicin, vincristine, and prednisone; 5-FU = fluorouracil; Ara C = Cytarabine; DNR = daunorubicin; CsA = cyclosporine-A; NSCLC = non-small cell lung cancer; CAF = cyclophosphamide, doxorubicin, and 5-fluorouracil; HN = head and neck; CMF = cyclophosphamide, methotrexate, and fluorouracil

a – Adjusted for a trial effect

1 – Calculated using overall survival point estimates from the published manuscript.

2 – Calculated using patient-level data from the SWOG database.

3 – Reported in the primary manuscript.

[b] HR estimate not reported; estimate calculated from primary manuscript dataset.

[c] The study was considered positive even though the p-value for the overall survival comparison was marginally greater than .05, based on the totality of the examinations of the overall survival endpoint.

[d] Study reported one-sided results per design specifications; reported as 2-sided here for consistency with other studies.

e – A median of 9 mos was added for induction to survival function; assumes 50% respond based on half of patients going on to maintenance

f – Limited to stage C