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The importance of greater speed in drug development for advanced malignancies

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Abstract

It takes on average 6–12 years to develop new anticancer drugs from discovery to approval. Effective new agents prolong survival. To demonstrate the importance of rapid drug approval, we calculated life-years potentially saved if selected agents were approved more rapidly. As illustrative examples, we used 27 trials documenting improvements in survival. We multiplied improvement in median survival by numbers of patients dying annually and multiplied this by number of years from drug discovery until approval. For every year by which time to drug approval could have been shortened, there would have been a median number of life-years potentially saved of 79,920 worldwide per drug. Median number of life-years lost between time of drug discovery and approval was 1,020,900 per example. If we were able to use available opportunities to decrease the time required to take a drug from discovery to approval to 5 years, the median number of life-years saved per example would have been 523,890 worldwide. Various publications have identified opportunities to speed drug development without sacrificing patient safety. While many investigational drugs prove to be ineffective, some significantly prolong survival and/or reduce suffering. These illustrative examples suggest that a substantial number of life-years could potentially be saved by increasing the efficiency of development of new drugs for advanced malignancies.

Introduction

For new anticancer agents, the average time from drug discovery to marketing approval was 8 years in the 1960s [1], but had increased to 13.9 years from 2000 onwards [2], prior to recently decreasing for some drugs [3]. With "breakthrough drug" legislation [4], the US Food and Drug Administration (FDA) recently granted rapid approval for several promising new agents based on high response rates in phase I-II trials without requiring the time and expense of phase III trials [5–7]. For example, crizotinib and ceritinib gained accelerated approval for use in patients with ALK-rearranged nonsmall cell lung cancer (NSCLC) in 6.0 and 6.4 years, respectively, from date of patent application [8–11].

Potential Gains from Speeding Drug Development Processes

Several factors contribute to long time intervals between drug discovery and approval, and there are opportunities to reduce this time interval without sacrificing patient

safety or data integrity [12–17]. In addition, even if an effective new drug is approved for marketing, there can be long delays in some jurisdictions before payers agree to provide the drug to patients [18–20]. Reducing the time required for making new drugs available to relevant patients is of high importance, as it could reduce suffering while translating into a substantial number of life-years saved. To illustrate this, we took as examples selected new therapies that had undergone phase III clinical trials published between 2001 and 2015 [21–47], had demonstrated a statistically significant incremental improvement in overall survival in patients with metastatic malignancies, and had been approved for marketing in the United States. Our observations are relevant internationally (and not just in the United States) as many jurisdictions may use the same clinical trials to support drug approval.

To estimate the number of life-years that could potentially be saved for every year by which time from drug discovery to approval and funding could be reduced for these selected drugs (if all relevant patients were treated once the drug was approved), we multiplied the incremental improvement in median survival by the number of patients in North America [48, 49] and worldwide [50, 51] dying annually from the relevant malignancy, and then multiplied this by the estimated time from drug discovery until approval.

Where tumor subgroups were involved in the relevant study, death rates for the tumor and potential therapy benefits were adjusted based on published estimates of subgroup size.

NSCLC was calculated as 85% of all lung cancers, with squamous cell lung cancer comprising 25% and nonsquamous NSCLC 60% of all lung cancers [52]. HER2-positive breast cancer was calculated as 20% of all breast cancers [53]. Colorectal cancers expressing EGFR by immunohistochemistry were calculated as 97% of all colorectal cancers [54, 55]. HER2-positive gastric cancer was calculated as 21% of all gastric cancers [32]. Among malignant melanomas, about 50% are *BRAF*-mutant [43]. More than 90% of head and neck cancers are squamous cell [56].

We used date of initial US filing of a patent application as a surrogate for date of drug discovery. For drugs missing patent information, we instead used date of first synthesis, date of first publication on the agent, or (for some monoclonal antibodies) date that use of a similar antibody against the target was reported as being effective in animal models. We used date of approval by the US FDA as a surrogate for date of worldwide approval. This would generally underestimate the potential impact of gains in life-years worldwide as US approval on average occurs earlier than approval in many other countries [57].

In Table 1, we present the estimated life-years potentially gained in North America (USA plus Canada) and worldwide per year of acceleration of drug approval and payer funding for the 21 therapies in 11 malignancies from our illustrative examples. The gain in median overall survival across studies ranged from 0.12 to 1.31 years (median, 0.31 years). Across these examples, the median potential gain in life-years per year of acceleration of drug approval and payer funding would have been 5932 per example in North America and 79,920 worldwide if all relevant patients dying of the malignancy had been treated with the new agent and if all clinical trial results accurately reflected "real-world" outcomes.

Adjustment for Factors that Would Reduce "Real-World" Benefit

"Real-world" evidence suggests survival gains equivalent to those seen in clinical trials for some agents [58], but not others [59]. Furthermore, many patients might not be treated even if a drug were approved and payer-funded. Patients might elect not to proceed with treatment, even if it were offered, and the probability of a physician proposing treatment with the agent might be impacted by the physician's perception of the efficacy, cost-effectiveness, and toxicity of the drug, by the availability of an effective alternative, and by the patient's performance status, comorbidities, etc. For example, in the province of Ontario, Canada, only 24% of patients with metastatic NSCLC receive approved, government-funded systemic therapies [60], and there is much less access to effective new therapies in developing countries than in wealthier countries [18]. Overall, access to new therapies varies widely across drugs and across countries. Oncology drugs currently account for the highest dollar share of worldwide sales of any class of agents, with one of the most rapid rates of sales growth [61], but we were unable to find any firm data on proportion of patients receiving therapy across the spectrum of new agents. However, even if the proportion treated is low, there could still be substantial numbers of life-years saved by faster access to these effective new therapies.

Life-years Lost from Drug Discovery Until Approval

Table 2 shows life-years potentially lost from drug discovery or patent application until approval, had all relevant patients been treated. The median time from discovery/patent application until approval was 12 (range, 6.1–23.3) years for our illustrative examples. The median number of life-years lost worldwide between time of drug discovery and approval was 1,020,900 per example

Table 1. Life-years potentially gained per year of acceleration of drug approval for selected drugs.

Malignancy	Therapy (reference)	Median survival gain (years)	No. patients per year potentially eligible for the therapy[1]		Life-years potentially gained per year of acceleration of drug approval If all relevant patients were treated[2]	
			North America	Worldwide	North America	Worldwide
NSCLC	Erlotinib [21]	0.17	152,794	1,351,418	25,975	229,741
NSCLC (nonsquamous)	Bevacizumab [22]	0.17	95,559	953,941	16,245	162,170
NSCLC (squamous)	Nivolumab [23]	0.27	44,941	397,474	12,134	107,318
Breast	Eribulin [24]	0.21	45,529	521,900	9561	109,599
Breast (HER2+ve)	Trastuzumab [25]	0.40	9106	104,371	3643	41,742
Breast (HER2+ve)	Trastuzumab emtansine [26]	0.48	9106	104,371	4371	50,103
Breast (HER2+ve)	Pertuzumab [27]	1.31	9106	104,371	11,929	136,737
Colorectal	Bevacizumab [28]	0.39	59,100	693,900	23,248	270,621
Colorectal	Oxaliplatin [29]	0.38	59,100	693,900	22,652	263,682
Colorectal	Regorafinib [30]	0.12	59,100	693,900	7153	83,268
Colorectal (EGFR+ve)	Cetuximab [31]	0.13	57,823	673,086	7517	87,501
Gastric (HER2+ve)	Trastuzumab [32]	0.23	2748	151,852	632	34,926
Head/Neck (squamous)	Cetuximab [33]	0.23	8926	199,800	2053	45,954
Prostate	Cabazitaxel [34]	0.20	33,480	307,500	6,696	61,500
Prostate	Enzalutamide [35]	0.40	33,480	307,500	13,392	123,000
Prostate	Abiraterone [36]	0.38	33,480	307,500	12,722	116,850
Prostate	Sipuleucel-T [37]	0.36	33,480	307,500	12,053	110,700
Renal	Temsirolimus [38]	0.30	15,610	116,000	4683	34,800
Renal	Sunitinib [39]	0.38	15,610	116,000	5932	44,080
Renal[3]	Sorafenib [40]	0.29	15,610	116,000	4527	33,640
Melanoma	Ipilumumab [41]	0.31	10,760	46,000	3336	14,260
Melanoma (BRAF-mutant)	Vemurafenib [42]	0.33	5380	23,000	1775	7590
Melanoma (BRAF-wild type)	Nivolumab [43]	0.42	5380	23,000	2260	9660
Myeloma	Pomalidomide [44]	0.39	12,400	72,000	4836	28,080
Myeloma	Bortezomib [45]	1.11	12,490	72,000	13,864	79,920
Hepatocellular	Sorafenib [46]	0.23	24,050	745,500	5532	171,465
Cervix	Bevacizumab [47]	0.31	4400	265,700	1364	82,367
Median		0.31	15,610	265,700	5932	79,920
Cumulative (all sites/drugs combined)					240,085	2,541,274

[1]No. patients dying per year.
[2]Median survival gain (years) x no. patients dying per year.
[3]Control patients censored at time of cross-over.

(range, 51,612–6,143,791). As noted above, the actual number would be substantially lower than this as many relevant patients would not have been treated even if the drug were available, but even if the proportion who would have been treated was very low, the number of life-years lost from drug discovery to approval would nevertheless be expected to be high for many of these agents.

For the 27 drug-tumor pairs in our illustrative examples, the FDA approved the drug 0.17–6.5 (median, 1.1) years prior to publication of the phase III trial results for 18 drugs, and 0–3.17 (median, 0.33) years after publication of the phase III data for nine drugs. Hence, the major factor determining time to drug approval was the time required for preclinical and clinical assessments rather than the review time required by regulatory agencies.

Life-Years Saved if Average Time from Drug Discovery to Approval and Payer Coverage were Reduced to 5 years

As noted previously, while the length of time between drug discovery and approval lengthened progressively from the 1960s to the late 1990s, it has more recently begun to shorten for some agents [1–3, 18]. Recent experience indicates that it could be feasible to reduce the time between drug discovery and approval to around 4–7 years [8–11,

Table 2. Number of life-years potentially lost in North America and worldwide between time of drug patent application and drug approval.

Malignancy	Therapy	US Patent application date or drug discovery (reference)	FDA approval date (reference)	Patent to approval, years	Life-years lost from patent to approval	
					North America	Worldwide
NSCLC	Erlotinib	05-1996 [94]	11-2004 [95]	8.5	220,790	1,952,795
NSCLC (nonsquamous)	Bevacizumab	05-1995 [96]	10-2006 [97]	11.4	185,193	1,848,738
NSCLC (squamous)	Nivolumab	2002[1] [98]	03-2015 [99]	13	157,739	1,395,137
Breast	Eribulin	04-2001 [100]	11-2010 [101]	9.6	91,788	1,052,150
Breast (HER2+ve)	Trastuzumab	1990[2] [102]	09-1998 [103]	8	29,138	334,015
Breast (HER2+ve)	Trastuzumab emtansine	10-2004 [104]	02-2013 [105]	8.3	36,276	415,849
Breast (HER2+ve)	Pertuzumab	06-2000 [106]	06-2012 [107]	12	143,157	1,640,853
Colorectal	Bevacizumab	05-1995 [96]	02-2004 [97]	8.8	204,582	2,381,465
Colorectal	Oxaliplatin	10-1980[3] [108]	01-2004 [109]	23.3	527,787	6,143,791
Colorectal	Regorafinib	01-2000 [110]	02-2012 [111]	12.1	86,554	1,007,543
Colorectal (EGFR-+ve)	Cetuximab	09-1988 [112]	02-2004 [113]	15.4	115,760	1,347,512
Gastric (HER2+ve)	Trastuzumab	1990[2] [102]	10-2010 [114]	20	12,645	698,515
Head/Neck (squamous)	Cetuximab	09-1988 [112]	11-2011 [113]	23.2	47,630	1,066,133
Prostate	Cabazitaxel	11-1993 [115]	06-2010 [116]	16.6	111,154	1,020,900
Prostate	Enzalutamide	05-2006 [62]	08-2012 [63]	6.3	84,370	774,900
Prostate	Abiraterone	09-1994 [117]	04-2011 [118]	16.6	211,192	1,939,710
Prostate	Sipuleucel-T	09-1998 [119]	04-2010 [120]	11.6	139,815	1,284,120
Renal	Temsirolimus	04-1994 [121]	05-2007 [122]	13.1	61,347	455,880
Renal	Sunitinib	12-1999[4] [64]	01-2006 [65]	6.1	36,184	268,888
Renal[5]	Sorafenib	02-1999 [66]	12-2005 [67]	6.8	30,783	228,752
Melanoma	Ipilumumab	1997[6] [98]	03-2011 [123]	14	46,698	199,640
Melanoma (RAF-mutant)	Vemurafenib	12-2004 [68]	08-2011 [69]	6.8	12,073	51,612
Melanoma (RAF-wild type)	Nivolumab	2002[1] [98]	12-2014 [99]	12	27,115	115,920
Myeloma	Pomalidomide	07-1996 [124]	02-2013 [125]	16.6	80,278	466,128
Myeloma	Bortezomib	05-1995 [126]	06-2008 [127]	13.1	181,617	1,046,952
Hepatocellular	Sorafenib	02-1999 [66]	11-2007 [67]	8.8	48,677	1,508,892
Cervix	Bevacizumab	05-1995 [96]	08-2014	19.3	26,325	1,589,683
Median				12	80,278	1,020,900
Cumulative (all sites)					2,956,667	31,537,958

[1]Demonstration that PD-L1 expression in mouse tumors confers immune resistance and that human tumors have high expression of PD-L1.

[2]Creation of trastuzumab.

[3]First published report on oxaliplatin.

[4]Patent priority date.

[5]Control patients censored at time of cross-over.

[6]Treatment of mouse tumors with anti-CTLA-4.

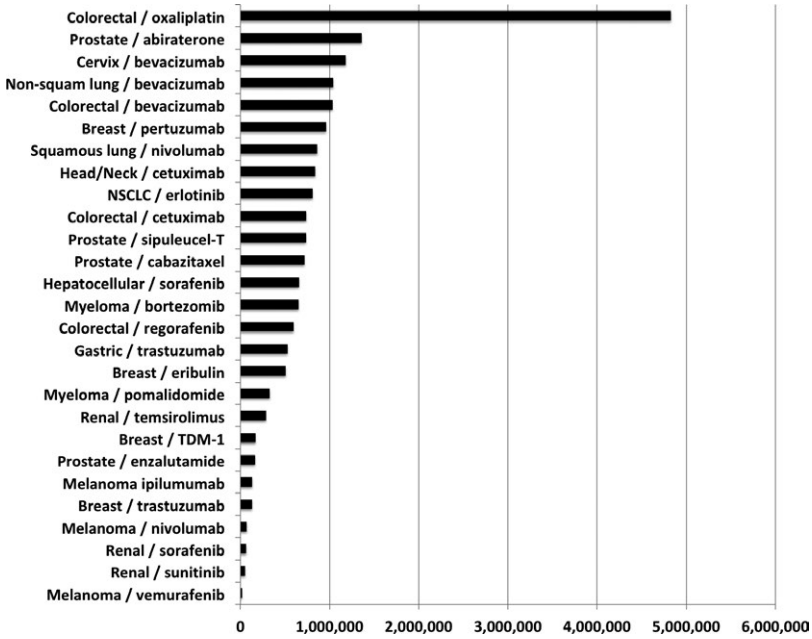

Figure 1. Cumulatively, across illustrative examples, more than 19,000,000 life-years could potentially have been saved worldwide if time from drug discovery to approval for these agents had been reduced to 5 years, or more than 1,900,000 if (for example) only 10% of all relevant patients were to be treated.

18, 62–69]. The median number of life-years potentially saved by reducing the time between drug discovery and approval/funding to 5 years per example would have been 43,981 for North America (range, 3195–414,532) and would have been 523,890 worldwide (range, 13,662–4,825,381) (Fig. 1), if all relevant patients were to be treated.

Discussion

Our analysis has the limitations that are inherent in any modeling study. However, we are also aware of five qualitative criticisms regarding the themes discussed in this manuscript. The first is that the data presented are of little ultimate importance as there are no feasible solutions that could speed drug development. The second is that many patients would not be able to access the new drug(s) even if they were approved, so correcting delays in approval would not accomplish much. The third is that important drug toxicity may be missed if clinical research approaches are changed. The fourth is that our work constitutes an unjustified attack on the FDA and other regulators. The fifth is that many investigational agents prove to be ineffective, and we do not take that into account.

However, these critiques, while each having some validity, do not diminish the importance of the themes presented. First, the nihilistic view that there are no feasible solutions that could speed drug development is not correct. Importantly, we will not solve the problem if we do not try. There will be a greater collective willingness to try to solve the problem if there is broad societal awareness that a problem actually does exist. The data we present here help illustrate how important this problem is. In addition, we and others have identified several pragmatic, feasible steps that could help [12–16], and we reiterate that the US FDA has taken a major step in the right direction with "breakthrough drug" approaches [4] that have markedly accelerated approval for selected effective agents. Breakthrough drug approval is a very important first step, but there are several other feasible value-added steps that could pay important dividends.

We have no major issue with the approaches taken in assessment of therapies for nonlethal conditions, but for lethal diseases, we need "progress-centered regulation," with the primary objective being the rapid, affordable identification of new, effective agents. The launching of the "Moonshot" Cancer Campaign [70] was an important step in this direction.

One example of a step that can be improved is preclinical toxicology. Expensive preclinical toxicology (that takes months or years to complete prior to initiation of any clinical trials) can often be of limited value: It either predicts the obvious (e.g., that the drug will cause myelosuppression) or predicts toxicity that does not occur in humans or it misses things that end up being important. There are relatively few examples of preclinical toxicology assessments providing an early warning about important

toxicity that might not have been anticipated from the drug mechanism of action or from toxicity of similar classes of agents already in clinical use. The solution for this part of the problem has already been tested and demonstrated to work: It has been shown that if one rapidly and inexpensively defines the dose of the agent that kills 10% of rodents (the LD10), then it is generally safe to use 1/10 the LD10 as the initial starting dose in clinical phase I trials [71, 72].

Once preclinical data are available, it can take months or years and hundreds of separate steps and processes (many with little added value) to take a clinical trial from initial concept to full activation. This needs to be markedly streamlined and accelerated [73, 74], and the US National Cancer Institute has implemented processes to begin to address this issue [75].

It can take months (or longer) and substantial resources for IRB approval and activation at each participating site, but, in the age of therapies targeting uncommon mutations, each site may accrue few or no patients after they have gone to the time and expense of activating the trial. What we need is "just-in-time" trial activation: If an accredited investigator identifies an eligible patient, they should be able to go online and immediately activate a trial that has already been approved elsewhere by an accredited IRB. That way, there is no delay in trial access and no wasted effort and expense activating a trial for which no patients are subsequently found at the individual institution [12–16]. Assessments of this approach have been initiated [76].

Excessively restrictive exclusion criteria need to be addressed so that clinical trials are not unnecessarily slowed by inability to rapidly identify eligible patients, and there has been recent progress on this front as well [77].

Patient selection for a trial should be possible using a research laboratory biomarker rather than requiring the many months and large expense of CLIA certification or Investigational Device approval for the biomarker before the trial can be launched and before one has any clinical data to indicate whether or not the biomarker will actually be a useful predictor of drug efficacy [12–16]. Use of research laboratory biomarkers to guide clinical trial accrual has proven to be feasible and effective [78].

We need to right size the currently massively excessive documentation that drives a large part of the rapidly escalating cost of clinical research, consumes hundreds of hours of investigator and research staff time and that often adds little value [12–16]. The cost and complexity of all the "paperwork," which is often not adequately reimbursed, is one important reason more oncologists do not participate in clinical trials. Work is underway to facilitate direct dumping of data from electronic medical records into research databases.

We need to rationalize the reporting of toxicity to reduce the huge effort that goes into reporting minor toxicity and to reduce the time and expense of producing and reviewing toxicity reports that often report once more a toxicity that is already well known or that present as possible toxicity events that are much more likely to be related to the underlying malignancy. To help address this issue, the FDA is currently working with pharmaceutical companies to rationalize the reporting of toxicity data. Furthermore, pragmatic postmarketing surveillance mechanisms have been proposed to monitor real-world drug toxicity (and efficacy) and to replace in part the extensive, expensive detailed documentation of minor toxicities currently required during early clinical trials [16].

We need to reduce the rapidly escalating burden of overly restrictive privacy regulation, and we need to rationalize consent and reconsent processes [12–16].

Finally, in the age of massive computer databases and robust correlative studies, we need to be able to use real-world data to gain approvals or add indications. A nascent example of such an approval is that of the checkpoint inhibitor pembrolizumab that was recently approved by the FDA for all solid tumors with high microsatellite instability (MSI-H) [79]. This approval went forward because of high response rates in these tumors. Importantly, it was in part based on retrospective data mining and correlative studies. The alterative would have been for the FDA to request a prospective study across tumor types, and this would have delayed approval and hence drug availability for years.

In summary, we have the tools to fix the problem. We just need to have the collective will to do so. Quantifying the size of the problem will hopefully help motivate change.

With respect to the question regarding drug pricing limiting drug availability and hence the usefulness of speeding discoveries, it is an undeniable disturbing fact that many patients both in North America and worldwide are unable to access effective new drugs even if they are approved. A life-year saved is every bit as important if it is gained by faster access to drug payment as if it is gained by faster drug approval. However, faster drug approval is an essential component of better drug access. Outside of a clinical trial (and fewer than 5% of North American adult cancer patients are able to enroll on a clinical trial [80]), regulatory approval of the drug is generally a prerequisite to broad access. Other factors such as drug funding and access to medical care may be of little consequence if the drug is not approved. Furthermore, the longer it takes the effective drug to get approved, the higher the likely price, as investors attempt to recoup expenses generated over multiple years and as duration of patent protection shrinks.

Once the drug is approved, rapidly escalating drug prices contribute to the inability of patients and healthcare systems to afford drug access. Drug development costs have been rising much faster than inflation, with little evidence that these increased costs translate into enhanced patient safety or better clinical trials [15, 81]. These rapidly rising drug development costs are driven in part by the same accelerating regulatory complexity that delays drug approval. For example, from 1999 to 2005, unique investigational study procedures grew by 6.5% each year, procedural frequency rose by 8.7% annually, and the number of eligibility criteria per protocol tripled [82]. Additionally, in phase I trials conducted between 2004 and 2007, an average of 45 safety monitoring processes/events were mandated in the first four weeks of the trial [83], while between 2009 and 2012, this had risen to a mean of 105 processes/events [84]. It has historically taken a median of 370–500 distinct processes and 26 months to take a cooperative group trial from initial concept to activation [73, 74]. Several separate phase I-III clinical trials may be required for drug approval [85], and these studies are often performed sequentially, with similar delays encountered with each sequential step.

The steps we have proposed above to speed drug development would also have the potential to markedly reduce drug development costs. If these costs could be reduced, savings could be invested instead in testing of other new ideas, and this could directly speed progress.

While drug development costs are not the only factor driving an explosion in drug prices, they are a major contributing factor. If drug development costs can be brought down, then there would be at least the potential to reduce drug prices without discouraging investment in new drug development. If prices can be brought down, this would translate into improved cost-effectiveness, better value for money, perhaps more willingness of physicians to prescribe these agents, and more rapid approval of payer coverage of effective new therapies. More rapid payer coverage would mean more life-years saved. Reducing drug prices by reducing drug development costs is particularly crucial if the benefits of new effective therapies are to be made available to patients in less wealthy countries where access to new therapies is currently often poor [18].

The third critique of the proposals herein is that important drug toxicity may be missed if clinical research approaches are changed. For this reason, we agree that effective regulation is essential. Current clinical research regulatory and methodological approaches are intended to ensure safety and informed consent for study participants, to clarify risks and toxicities, to guarantee an appropriate level of safety for patients treated once a new agent is approved, and to ensure that agents do not get approved unless they add value. However, while it is currently felt that a price of $50,000–$250,000 per life-year saved would be reasonable for a new drug [86], for participants in clinical trials, the cost per life-year saved by increasingly complex clinical research regulation is in the millions of dollars [15]. Furthermore, there has been little evidence that toxicity that was missed pre-approval has been a major problem with the overwhelming majority of anticancer drugs, including those agents undergoing accelerated approval [87], and one may question if it is ethical to pursue randomized trials to more fully assess toxicity when it has already been established that one arm of a trial is clearly more effective than the other [88]. Unquestionably, regulation is important and toxicity is important. Postmarketing surveillance of new agents is also important, and there is the potential for pragmatic ways to do this more effectively [16]. There has also been successful implementation of clinical trials using greatly simplified, low cost designs that could facilitate ongoing postmarketing assessment of recently approved new therapies [89, 90]. Overall, is it really justifiable to delay access to all effective new agents for lethal diseases based on the possibility that an important toxicity might initially be missed for a small proportion of patients being treated with a small proportion of these drugs?

The fourth common concern has been that our work constitutes an unjustified attack on the FDA and other regulators. Let us stress that this is far more than just a problem with the regulators. Clinical researchers, institutions, sponsors, institutional review boards, clinical research organizations, a number of government agencies outside of the FDA, and others all contribute to the problem in important ways, and all need to do their part by improving their efficiency, performance, and commitment to progress. From our discussions with people from both the FDA and Health Canada, we know that they know there are problems, and we know that they want as much as anyone to see these problems fixed. We all need to work together to fix them. As noted above, recent "breakthrough drug" approaches [4], permitting rapid approval of effective agents without phase III trials, are a major step in the right direction, and the enactment by the US Congress of the 21st Century Cures Act in December 2016 has the potential to help substantially [91]. However, some of these important steps are facing opposition from some individuals and groups outside of regulatory bodies [92], and it is highly important that we support regulators worldwide in the drive to facilitate development of effective new anticancer drugs.

Finally, a fifth critique of the themes presented herein is that the importance of rapid, cost-effective drug assessment is diminished by the fact that only a minority of new experimental agents prove effective [93]. However, we believe that it is as important to rapidly identify

ineffective agents as it is to quickly recognize effective agents. Inefficient studies of agents that ultimately prove to be ineffective compete for patients and other resources with studies of agents that ultimately prove to be effective: This slows progress. The suggestions herein should not serve to lower the bar so that ineffective drugs may be approved. Their purpose is to improve the efficiency and cost-effectiveness of the entire drug development process so that we can rapidly and inexpensively identify those drugs that work and those drugs that do not work.

In summary, improving the efficiency of new drug development and decreasing the regulatory burden could translate into large benefits for patients, while the potential reduction in drug development costs is in everyone's best interest.

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Conflict of Interest

Dr. D. J. Stewart has received advisory board fees from Amgen, Roche Canada, Pfizer Canada, Boehringer Ingleheim Canada, and Novartis Canada, honoraria from Pfizer Canada and from the International Association for the Study of Lung Cancer, research funding from Celgene, Pfizer Canada and Roche Canada, and is Lead Advisor on the Life-Saving Therapies Network. J.-P. Bradford is President of Bradford Bachinski Limited, CEO of the Life-Saving Therapies Network, cochair of the Advocacy Committee of Lung Cancer Canada, a member of the Cancer Care Advisory Committee of the Ottawa Regional Cancer Foundation, and a member of the Research Advisory Committee of the Canadian Partnership Against Cancer. Dr. R. Kurzrock has research funds from Incyte, Genentech, Merck Serono, Foundation Medicine, Guardant, Sequenom and Pfizer, as well as consultant fees from Acutate Therapeutics, XBiotech and Loxo, speaker fees from Roche, and an ownership interest in CureMatch Inc. Dr. J. H. Schiller is President of Free to Breathe, has done consulting and participated in advisory boards for Synta, Vertex, Genentech, Clovis, Biodesix, AVEO, Eisai, AbbVie, Lilly, Merck, and AstraZeneca, and has participated in clinical research with Clovis, AbbVie, Astex, Jannsen, Genentech, Synta, Sorono/EMD, Pfizer, PUMA, and Johnson & Johnson. Dr. G. Batist has received support for research from Pfizer and works in an academic-industry Consortium that includes Merck, Roche, Pfizer, Amgen, Bayer, Novartis. Dr. Paul Wheatley-Price is President of Lung Cancer Canada.

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