

## Oncology drug costs—the imaginary crisis?

R. Turck

*TurckBio LLC, Montclair, NJ, USA*

### introduction

Oncology drug costs keep going in only one direction—up. Complaints about cancer drug costs are manifold. Increasing drug costs are obviously not a new phenomenon, but costs of individual therapy frequently exceeding 6-digit figures is a recent trend. Containing those costs and thus potentially denying individual patients treatment that could extend their lives or cure them becomes a very personal matter as opposed to abstract healthcare policy. While there is excess in some cases and a significant financial burden for patients it appears that the outrage is not always well informed.

### is there really a crisis?

Here are some facts (see Table 1):

[1–5]

Cancer drug costs have gone up by 6.5% CAGR globally in the last 5 years [3], increasing the share of oncology to 11.3% (from 10.7%) of drug costs in US and 14.7% in the EU (from 13.3%) [3]. Costs could go up at a 7–12% CAGR in 2016–2020 [3, 6] (see also Figure 1).

Cancer care costs increased for a number of reasons (see Table 2) with cancer drugs being a significant driver representing 20% of cancer care costs in 2014 compared with 15% in 2004 [4]. However, over the 2004–2014 time period, cost of cancer care in general increased in line with that of general healthcare cost when adjusted for the increasing incidence of cancer. This means that increasing cancer drug costs are associated with decreasing costs in other healthcare areas. Modern cancer drugs help to reduce healthcare costs in other areas—reduce hospitalization, ER visits, surgery and radiation—this has always been the promise of the pharmaceutical industry—to leverage the 10% drug costs to bring down the 90% other healthcare costs while simultaneously improving outcomes [4, 7].

Cancer drug costs represent <1% of overall healthcare costs [1, 5], yet it is estimated that 83% of increased cancer survival can be attributed to new treatments including medications [8]. Propelled by new tools and technologies, science has made unprecedented progress and our deep understanding of cancer helps to identify more and more promising targets. The better tumor biology is understood, the more pathways and targets are identified and the better patients likely to respond can be identified with biomarkers, the more cancer therapy becomes

individualized and the better the outcomes in terms of survival and tolerability. As a consequence cancer death rates continue to decline, the number of cancer survivors is at record high (Table 3) and cure is within reach for some cancers [9].

In particular, with cancer immunotherapy, the industry does what the public seems to expect—develop more breakthrough drugs as opposed to incremental innovation and me-toos. The breakthrough paradigm demanded by society, regulators and payers takes hold and delivers treatments that provide not only a statistical separation of curves but clinically meaningful benefits for patients.

Attitudes about how to manage healthcare cost differ dramatically in EU and USA. Europeans and Canadians have long had to accept rationing and governments capping the price paid for a year of life gained. US Americans have much freer access, provided they have healthcare coverage—the concept of attaching a monetary value to life is politically toxic and legally impossible. Conversely, healthcare disparity is philosophically anathema to Europeans and Canadians (although it does exist) while it is not to Americans.

Once a product is approved in Europe reimbursement is negotiated country by country or even region by region. EU countries typically assess cost-effectiveness based on comparable therapies and some maximum value they are willing to pay for a year of quality adjusted life gained (QALY). Drugs become available within the confines of the reimbursement decision that often limits use to a subset of patients, off-label use is usually not reimbursed and sales are capped in some countries. Utilization of expensive therapies can be further restricted by insurances and providers. Access to cancer drugs varies considerably between countries [10] as some drugs that do not meet the criteria are not made available.

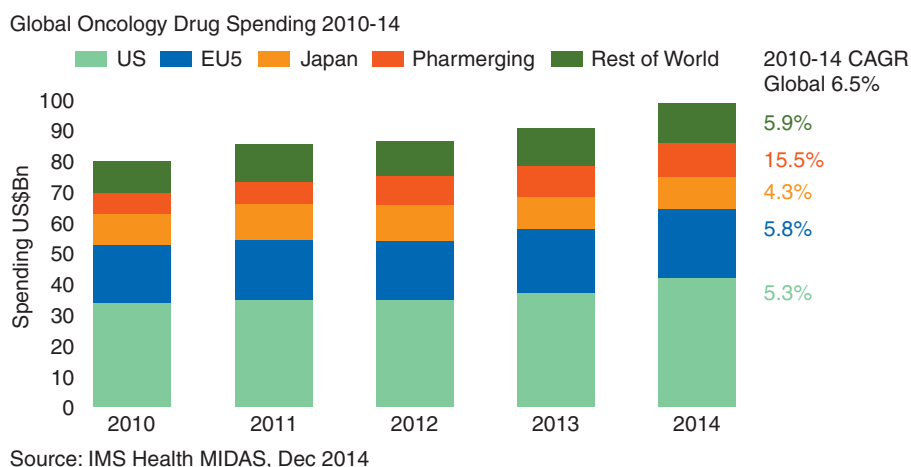
In USA, oncology drugs often become available the day they are FDA approved. They are either covered by public payers, such as Medicare (covering most Americans 65 and older) that operates under a legal mandate to fund ‘all or substantially all’ [11] cancer drugs, the Veterans Administration (VA) and Medicaid or by commercial insurances. The latter try to negotiate prices for a drug and implement other strategies to manage cost and Medicare benefits from the price concessions they negotiate. Reimbursement for off-label use is possible if high quality data supporting the indication are available.

Significant co-pays for drugs shouldered by the patients make drug costs highly visible contrary to medical benefits and divert attention from total healthcare cost. Oncology drugs escaped payer’s pressure to some extent in US, not only due to the Medicare mandate. But as cancer drug costs increase, payers are more and more pressed to manage them aggressively. Payers have a portfolio of established and emerging strategies preventing costs from spinning out of control. The challenge is to grant access to novel cancer

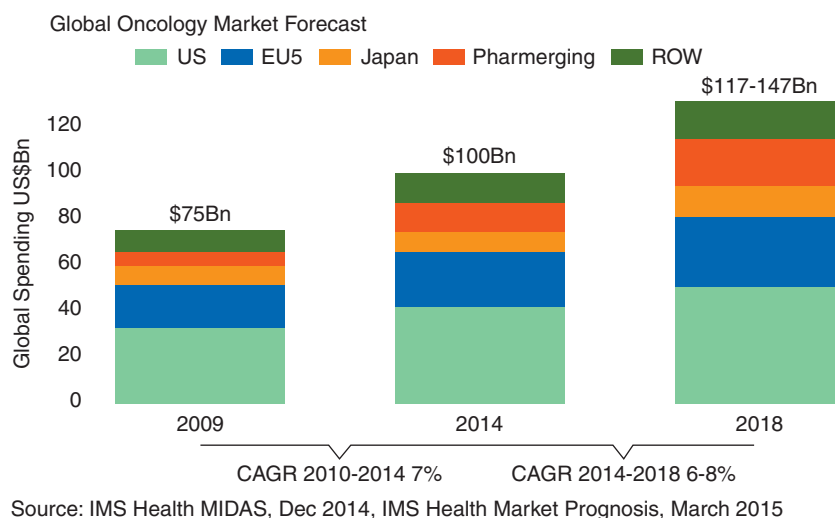
Correspondence to: Dr Roland Turck, TurckBio—Consulting, 24 Prospect Ave, Montclair, NJ 07042, USA. Tel: +1-973-610-1528; E-mail: roland.turck@turckbio.com

**Table 1.** Oncology facts

		Ref
Assets in clinical development	~800	[1]
New approvals (2015, US, inc. new indications)	18	[2]
Global Sales (2014, inc. supportive care)	100 Bio US\$	[3]
Percentage of cancer drug costs of overall drug costs (US 2014)	11.3%	[3]
Percentage of drug costs of overall cancer care cost (US 2014)	18–20%	[4]
Percentage of cancer drug costs of overall healthcare costs (US)	<1%	[1]
Percentage of cancer drug costs of overall healthcare costs (EU)	<1.5%	[5]



**Figure 1.** Global oncology drug spending 2010–2014.



**Figure 2.** Global oncology market forecast.

drugs to everyone in need but to make sure that those therapies are used in the most cost-effective way.

**current strategies to manage costs and improve outcomes**

The traditional fee-for-drug system is said to be coming to an end; yet, it is still the dominant reimbursement mechanism. The big advantage that will keep fee-for-drug alive is its simplicity.

Novel drug combinations are simply reimbursed individually whatever the aggregated cost of therapy. Adoptive, gene therapy and other high cost procedures would be paid up-front like regular drugs.

Fee-for-service tends to lead to over-utilization, a risk counterbalanced by various managed care strategies. They use different pivots varying with regard to the degree that various stakeholders share risk.

**Table 2.** Oncology trends

	Trends	Cost impact
Ageing population, cancer incidence	↑	↑
New drugs (targeted therapy, new chemo, adoptive therapy)	↑	↑
Treatment duration and number of treatments	↑	↑
Novel drug combinations	↑	↑
Biosimilars	↑	↓
Inpatient services	↓	↓
Cancer surgery	↓	↓
Shift from chemo administration from MD office to outpatient setting	↑	↑

**Table 3.** Progress in cancer care [4]

Cancer death rates peaked in 1991 and decreased by 20% since (US, annual change rate, 2002–2011)		
Men	Women	0–19 year olds
–1.8%	–1.4%	–2.1%
5-year relative survival rate (US, 1975–2010, all cancers)		
1975	2010	
49%	68%	
Cancer survivors (US, 2014 estimate): 14.5 millions		
Incidence (US, 2015 estimate): 1.7 millions		
Cancer death (US, 2015 estimate): 590 000		

- lowering drug acquisition cost, tendering, reducing utilization
- improving ‘input’ parameters, e.g. incentivizing cost-effective therapies or
- rewarding positive outcomes.

Managed care typically lowers cost of drug acquisition while simultaneously reducing usage potentially resulting in more appropriate but also under-usage. Mechanisms such as

- utilization management (prior authorization, step therapy, formularies, limited quantities),
- network design (preferred provider networks, specialty pharmacies) and
- benefit design (prescription drug tiers, co-payments and co-insurance) [12].

are widespread in oncology; in particular patient co-pays are widely criticized and sometimes viewed as ‘financial toxicity’... Payers encourage moving drugs from medical to pharmaceutical benefits that are managed more rigorously [13] and try to eliminate potential conflict of interest by removing the provider’s margin on drugs [14, 15].

Generics and biosimilars, but also competing drugs are leveraged to lower costs, a mechanism that proved effective, e.g. in HCV where comparable novel drugs compete directly for the same indication, a situation rarely found in oncology.

Pathways and guidelines foster standardized cancer care to improve outcome and providers are rewarded for being compliant (or penalized if not). This strategy creates some practical

complexities since different payers often prefer different, competing guidelines. In order to increase acceptance, some flexibility is needed [8]; guidelines have to be adjusted for new data, new drugs and changed standard of care [10]. While assuring appropriate use of novel drugs and potentially better outcomes, guidelines do not reduce costs of appropriate use. Biomarker identified sub-populations further help to ensure most cost-effective drug use.

Emerging models—incentivizing cost-effective use of health-care resources.

- Pay for performance (PFP) & value-based pricing (VBP) [16]

Although used for years to some extent both in Europe and US, VBP is often viewed as the way of the future: drugs are priced according to expected outcome (e.g. quality of life adjusted OS or HR) and reimbursement adjusted based on real life performance thus creating a risk share between payer and manufacturer. A variation of the theme is adjusting reimbursement by indication. Harder, real life endpoints could be used for reimbursement instead of surrogate endpoints produced in clinical trials. Performance metrics can also include cost reductions in other healthcare areas (e.g. reduction of hospitalization).

One of the conceptual issues with VBP is how to deal with outcomes that cannot be clearly attributed to a particular drug, as in combination therapy. This is particularly challenging in oncology where checkpoint inhibitors, e.g. could become a backbone for many combination therapies. One great benefit of VBP is that value can be increased in various negotiated ways, e.g. by reducing side effects or improving adherence. VBP is viewed as a method for setting the right incentives for manufacturers.

Differentiated payment by indication, adjustments for deviations between real life and clinical trial performance, and incentives to use most cost-effective regimens where there is direct comparison of outcomes can help assuring cost-effective use of novel therapies and support outcome-based rational pricing.

While aligning stakeholders' interest to a great degree, implementation is a challenge. There needs to be agreement on the relevant parameters to be monitored and methodology for value assessment as well as on a cost-effective way of monitoring. Availability of and access to data and the ability to track patients for some period of time becomes critical—which with no coherent medical records system in US proves difficult. Reactions of CMS and payers have been mixed, but there is general agreement that VBP will be enacted in some way.

Real life data are essential for VBP. In order to allow all stakeholders to optimize their contribution to healthcare, it seems desirable that anonymized patient data are broadly shared by payers, providers, distributors, manufacturers and academia. Recognizing that these data represent economic value, this is likely to be a contentious issue. Allowing key stakeholders to mine such data might have a disruptive impact on cancer management and cost-effectiveness, however.

Within the framework of VBP, various tools (ASCO, NCCN, Drug Abacus, ICER and ESMO-MCBS) have been proposed [17–21]. While helpful, they all have their limitations and focus on comparative cost-effectiveness of drug therapy without looking at overall cost of care (except for ICER). They also sidestep the issue of setting a value for a QALY—which is not acceptable in US—and do not necessarily reflect what outcomes matter for patients.

- Accountable care organizations

A more comprehensive approach is mandated by 'Obamacare' that attributes a core role to Accountable Care Organizations (ACOs). Provider organizations contract with CMS to provide healthcare for a certain population, savings are shared and there will be penalties if agreed upon costs are exceeded [22]. As a result, risk is shifted from payer to provider. In the future, population-based capitated payments—flat fees per patient for some period of time—are envisioned. The vision is to shift the incentive to preserving health rather than fixing health problems. Experience with ACOs models in oncology is very limited [14]. While offering the major advantage of optimizing overall cost of care it is unclear how the model can be applied to oncology. There may be some role for first line therapy that is fairly standardized and driven by guidelines as opposed to more advanced disease stages that are extremely diverse and require intensive therapy. The savings potential may be limited however.

- Bundling, Capitation and Episode-of-care

Most of the above applies too to various bundling models—lump-sum payments covering medication or care for a course of therapy (e.g. capitated drug budgets) or some period of time (episode-of-care) regardless of what drugs (or care) a patient actually receives. There is limited experience thus far in the community setting but some interesting examples [15]. DRG codes for hospitals tend to penalize providers for using novel, expensive therapies and to slow adoption before fees are adjusted or new codes created. In general, these models are best suitable for treatments that can be

standardized; one advantage is that generics and biosimilars could directly contribute to creating budget for novel therapies. A particular challenge is combination of novel drug therapies that would leave it up to the manufacturers to figure out how to divide the fees—there is certainly no mechanism to deal with that at the moment.

ACOs as well as any capitated model share the same ethical dilemma: it is unclear how providers can avoid a conflict of interest between achieving best outcomes for patients and staying within the confines of capitated payments even when adjusted for better outcomes.

## discussion

In recent years, innovative cancer drugs have improved patient survival while costs have increased significantly [3]. As long as oncology progresses at the current pace and as long as new drugs meaningfully improve patients' outcomes, costs will continue to increase and so will the pressure to manage them.

The challenge is to provide those cancer drugs that best address a patient's needs but to do so in the most cost-effective manner. There is no single mechanisms assures that the best possible care is effectively delivered to the largest possible number of patients at the lowest possible price, not surprising given the absence of a true market.

To limit cost increases by capping the price per QALY and other rationing like in Europe is unlikely to find broad acceptance in US for the foreseeable future. Whether the heavy handed European approach contains costs any better than US approach is doubtful.

In USA, a multitude of tools and strategies creates a system of checks and balances that can foster cost-effective use of cancer drugs. Moving from 'cost' to 'value' focus and optimizing expenditure across healthcare categories makes sense. Established cost management strategies will be combined with some VBP. Differentiated payment by indication, adjustments for deviations between real life and clinical trial performance and incentives to use most cost-effective regimens where there is direct comparison can all help assuring cost-effective use of novel therapies.

Realistically, VBP will not lower costs of individual therapy *per se* and it is unlikely to prevent overall cancer drug costs from soaring. But novel and expensive therapies will be provided to those patients who benefit most—biomarkers play a significant role—while the use in patients expected to benefit marginally will continue to be disincentivized. This may be the best way to assure some cost containment while at the same time improving outcomes and hopefully maintaining overall cost of cancer care. Importantly, biosimilars in addition to generics and competing drugs offer a chance to limit cost increase without compromising care by making room in budgets for novel therapies.

One can only hope that patient co-pays will be reduced as drugs help contain total cancer care cost. Resistance to what payers, providers, legislators and patients perceive as price gouging will increase and the threshold of what is being considered meaningful progress in patient outcomes will continue to be pushed upwards thus contributing to limit cost increases. But manufacturers that embrace the cost-effectiveness paradigm will hopefully see their innovation appropriately rewarded with VBP.

To accept that costs for innovative drugs go up in oncology as outcomes improve while avoiding more aggressive cost management, is a rational strategy as payers have more to gain by reducing waste in healthcare areas that progress less. The complexity, the variability of individual cases, the specific situation of cancer patients and the fact that so much progress in cancer treatment is occurring at the moment makes it ill-suited for intrusive cost containment experiments. The argument is further strengthened by the fact that cost in other areas of cancer care decrease as novel drugs are being used.

It is noteworthy that healthcare administration costs account for >30% [23] of overall healthcare cost in US compared to ~1% in US and EU [1, 5] spent on oncology drugs that provide most medical advancement in cancer treatment—it is estimated that new treatments and drugs contribute 83% to increased life expectancy in cancer patients [8]. As the rate of progress slows, more competing drugs will come to market, drugs will lose exclusivity and generics and biosimilars will eventually lower drug costs like in other spaces. Hopefully, prevention will slow increasing demand. The rising cost until then will be the price society has to pay for extraordinary progress that could dramatically change the fate of patients and will finally convert cancer into a chronic disease or cure it. Ensuring access to novel therapies for patients in need is the challenge. Creating workable solutions to assure that novel treatments are used in the most cost-effective way is the answer to rising costs rather than blanket cost containment and more administration.

## funding

None declared.

## disclosure

Author serves as consultant to numerous public and private oncology companies.

## references

1. PhRMA 2014. Cancer Report. PhRMA Pharmaceutical Research and Manufacturers of America. <http://www.phrma.org/sites/default/files/pdf/2014-cancer-report.pdf> (3 November 2016, date last accessed).
2. <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm430302.htm> (3 November 2016, date last accessed).
3. IMS HI, Oncology Trend Report. IMS Health Institute 2015.
4. Pyenson BS, Fitch KV, Pelizzari PM. Cost Drivers of Cancer Care: A Retrospective Analysis of Medicare and Commercially Insured Population Claim Data 2004–2014. Seattle, WA, USA: Milliman Report 2016.
5. Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol* 2013; 14(12): 1165–1174.
6. IMS HI, Global Use of Medicines. IMS Health Institute 2020.
7. Roebuck MC, Liberman JN, Gemmill-Toyama M et al. Medication adherence leads to lower health care use and costs despite increased drug spending. *Health Affairs* 2011; 30(1): 91–99.
8. Sun E, Lakdawalla D, Reyes C et al. The determinants of recent gains in cancer survival: an analysis of the Surveillance, Epidemiology, and End Results (SEER) Database. *J Clin Oncol* 2008; 26, No 15S (May 20 Supplement), 2008: 6616.
9. American Association for Cancer Research. AACR Cancer Progress Report 2015. *Clin Cancer Res* 2015; 21(Suppl 1): S1–S128.
10. Bergmann L, Enzmann H, Thirstrup S et al. Access to innovative oncology medicines in Europe. *Ann Oncol* 2016; 27(2): 353–356.
11. Medicare Modernization Act Final Guidelines Formularies: Guidelines for Reviewing Prescription Drug Plan Formularies and Procedures. Centers for Medicare & Medicaid Services, USA Federal Government.
12. Paul H, Keckley, et al. Value Based Pricing for Pharmaceuticals, Implications of the Shift from Volume to Value. Deloitte Center for Health Solutions 2012.
13. Olivier Leclerc, et al. Strategies in Oncology: Spotlight on Clinical Pathways. *Oncology Knowledge Bulletin*, McKinsey & Co 2012.
14. Leprai C, Levine E, Sozdatelev A, Vaskov D. Designing and Implementing An Integrated Oncology Care Management Program. New York City, NY, USA: McKinsey & Co 2015.
15. Newcomer LN, Gould B, Page RD et al. Changing physician incentives for affordable, quality cancer care: results of an episode care payment model. *J Oncol Practice* 2014; 10(5): 322–6.
16. Used synonymously.
17. Schnipper LE, Davidson NE, Wollins DS et al. American Society of Clinical Oncology. American Society of Clinical Oncology statement: a conceptual framework to assess the value of cancer treatment options. *J Clin Oncol* 2015; 33: 2563–2577.
18. Chery, Sullivan R, Dafni U et al. A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). *Ann Oncol* 2015; 26(8): 1547–1573.
19. [www.drugabacus.org](http://www.drugabacus.org) (3 November 2016, date last accessed).
20. [NCCN.org/evidenceblocks](http://www.nccn.org/evidenceblocks) (3 November 2016, date last accessed).
21. <http://www.icer-review.org/wp-content/uploads/2014/01/Slides-on-value-frame-work-for-national-webinar1.pdf> (22 April 2016, date last accessed).
22. CMS <https://innovation.cms.gov/initiatives/bundled-payments/index.html> (22 April 2016, date last accessed).
23. Woolhandler S, Campbell T, Himmelstein DU. Costs of Health Care Administration in the United States and Canada. *N Engl J Med* 2003; 349: 768–775.