MAYO CLINIC

COMMENTARY

The UK Cancer Drugs Fund Experiment and the US Cancer Drug Cost Problem: Bearing the Cost of Cancer Drugs Until It Is Unbearable

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Earlier this year, under increasing budgetary pressure, the United Kingdom through its Cancer Drugs Fund (CDF) declined to pay for 45 cancer indications. This decision is estimated to affect more than 5000 patients.[1] Then, on April 1, 2016, the entire UK CDF underwent an overhaul with plans to integrate with the existing National Institute for Health and Clinical Excellence (NICE) appraisal program.[2] Although critics of the government's policy argue that this action will limit patients' access to important drugs, defenders point out that these choices are inevitable as we continue to witness the rapidly escalating cost of cancer treatments in a world of finite budgets.[1] The reasons for and implications of the United Kingdom's action provide important lessons regarding the price of cancer drugs.

The CDF

The CDF was created in 2010 as a mechanism to bypass the United Kingdom's strict standards of demonstrated cost-effectiveness of new therapies. Through the CDF, drugs that had been denied by the United Kingdom's NICE as low value could still receive funding, and patients who receive these drugs would bear no additional copay. However, because the CDF inherently subverts the guiding principle of the UK system—do the most good with the money you have—critics alleged from the outset that the CDF "undermines the entire concept of a rational and evidence-based approach to the allocation of finite health-care resources" and is "already intellectually bankrupt."[3,389]

Unlike the situation in the United States, the UK CDF negotiates the price of drugs with the pharmaceutical industry. The magnitude of discount is not revealed and is protected by confidentiality agreements. However, in some cases, negotiations have stalled because companies were unwilling to reach an agreement with the United Kingdom on what some call "realistic prices,"[4] making rejection necessary.

Earlier this year, before restructuring, to protect the solvency of the CDF, 45 indications were cut from the fund (Table). Many excluded drugs offer real, albeit marginal, benefits, and the US Food and Drug Administration (FDA) has approved all of the 45 drug indications. Seventeen excluded drug indications (38%) improve overall survival, a standard that exceeds the percentage of new FDA drug approvals that meet this mark (19 of 63, 30%).[5] Other denied drugs, such as ibrutinib and brentuximab, are able to achieve responses in patients refractory to all other therapies, serving as a bridge to potentially beneficial treatment, such as stem cell transplant. In short, if cost were not an issue, we believe that most oncologists would not hesitate to prescribe many of these drugs in the appropriate setting. Yet, in each of these cases, cost is the deciding factor.

It is instructive to highlight the ocean of difference between the discussion of cost in the United Kingdom versus the United States. Take, for example, brentuximab, a monoclonal antibody to CD30, which is overexpressed in several forms of lymphoma. One month of brentuximab therapy costs approximately £9000 in the United Kingdom (equivalent of approximately $13,000 in the United States). The CDF has stated that it is unable to pay for brentuximab for patients with relapsed Hodgkin and anaplastic large cell lymphoma. In the United States, brentuximab was approved for this purpose in 2011, and it has been universally embraced by oncologists. However, with median progression-free survival in pivotal trials of approximately 6 months, a rough estimate of total cost per patient in the United States

TABLE. Cancer Drug Indications That Were Removed From the UK Cancer Drugs Fund in 2015[a]

Drug	Indication	Median OS-(mo)		Change in OS (mo)	Cost per cycle	
		Control	Experimental		£[b]	$[b]
Drugs With a Proven Survival Benefit						
Ibrutinib	Relapsed CLL	81% (1-y survival, median not reached)	90% (1-y survival, median not reached)	9%	5151	7512
Pemetrexed	Second line for nonsquamous NSCLC	8.0	9.3	1.3	1728	2520
Pemetrexed	Maintenance therapy for nonsquamous NSCLC	11.0	13.9	2.9	1728	2520
Bevacizumab	Second/third line for metastatic colon cancer	10.8	12.9	2.1	1109	1617
Bevacizumab	First line for metastatic colon cancer with irinotecan-based chemotherapy	15.6	20.3	4.7	1109	1617
Cabazitaxel	Refractory metastatic prostate cancer	12.7	15.1	2.4	4435	6462
Nabpaclitaxel	First line for metastatic pancreas cancer	6.6	8.7	2.1	2657	3871
Eribulin	Third line for breast cancer	10.5	13.2	2.7	2365	3446
Nintedanib	Metastatic adenocarcinoma of the lung after first line	7.9	10.9	3.0	2581	3761
Radium-223	Metastatic prostate cancer	11.3	14.9	3.6	4848	7064
Bevacizumab	Advanced cervical cancer	13.3	17.0	3.7	3328	4849
Abiraterone	Chemotherapy-naive metastatic prostate cancer	30.3	34.7	4.4	3282	4782
Aflibercept	Second line for metastatic colon cancer	13.5	12.1	1.4	1064	1550
Pomalidomide	R/R MM (beyond third line)	8.1	13.1	5.0	10,661	15,534
Pazopanib	Previously treated soft-tissue sarcoma	10.7	12.5	1.8	2511	3659
Trastuzumab Emtansine	Further treatment of Her2+ MBC	25.1	30.9	5.8	5908	8608
Lenalidomide	Second line for MM	31.6	38.0	6.4	5242	7638
Drugs With Unknown Effects on Survival						
Bendamustine	Relapsed mantle cell lymphoma	NA	NA	NA	1162	1693
Bendamustine	Relapsed CLL	NA	NA	NA	829	1208
Bendamustine	Refractory indolent non-Hodgkin lymphoma	NA	NA	NA	1491	2173
Bosutinib	AP-CML	NA	NA	NA	4124	6009
Bosutinib	Blast phase CML	NA	NA	NA	4124	6009
Bosutinib	CP-CML refractory to nilotinib/dasatinib	NA	NA	NA	4124	6009
Dasatinib	Blast phase CML	NA	NA	NA	2806	4089
Brentuximab	Relapsed ALCL	NA	NA	NA	9000	13,114
Brentuximab	Relapsed Hodgkin lymphoma	NA	NA	NA	9000	13,114
Dasatinib	Ph+ ALL	NA	NA	NA	2806	4089
Ibrutinib	Relapsed MCL	NA	NA	NA	6868	10,007
Pepide receptor radionucleotide	GEP NET	NA	NA	NA	67,200	97,914
Liposomal doxorubin	Angiosarcoma	NA	NA	NS	1710	2492
Liposomal doxorubicin	Fibromatosis	NA	NA	NA	1710	2492
Liposomal doxorubin	Primary sarcomas of the heart and great vessels	NA	NA	NA	1710	2492
Bortezomib	Relapsed WM	NA	NA	NA	3659	5331
Bortezomib	Relapsed mantle cell lymphoma	NA	NA	NA	3659	5331
Bortezomib	Retreatment in relapsed myeloma	NA	NA	NA	3659	5331
Ofatumumab	Relapsed/refractory CLL	NA	NA	NA	4368	6364
Drugs for Which Best Evidence Suggests No Improvement in OS						
Bevacizumab	TNMBC	25.2	26.7	NS	2219	3233
Bevacizumab	First line for metastatic colon cancer with oxaliplatin-based chemotherapy	19.9	21.3	NS	1109	1616
Bevacizumab	First line for metastatic colon cancer with single-agent fluoropyrimidine	12.9	16.6	NS	1692	2465
Bevacizumab	With combination chemotherapy in recurrent platinum-sensitive ovarian cancer	33.7	33.4	NS	3328	4849
Everolimus	ER-positive breast cancer	26.6	31.0	NS	3326	4846

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