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Clinical Trial Evidence Supporting US Food and Drug Administration Approval of Novel Cancer Therapies Between 2000 and 2020

Joel Lanoue PhD[1] | Nicholas Blondal MD[2] | Hannah Gunsen PhD[1] | Chase Hausler PhD[1] | Kyle Schaefer MD[1] | Taylor S. Riallon PhD[1] | Stephanie Spencer-Bonilla MD[3] | Raymond Hutchins MD[4] | Vinay Prasad MD, MPH[5] | Joseph S. Ross MD, MHS[6] | Thomas J. Buhse MD, MPH[7] | Benjamin Kasenda PhD[8] | Joel Lexchin MD, MPH[9] | Bryan Mathew MD[10]

[1]Department of Clinical Research, Department of Medical Oncology and Hematology, Marshfield Clinic Health System, Marshfield, Wisconsin; [2]Department of Medical Oncology, Cancer Care Manitoba, Winnipeg, Manitoba, Canada; [3]Department of Medicine, Division of Hematology, Stanford University, Stanford, California; [4]Department of Medicine, Division of Hematology, University of Texas Health Science Center, San Antonio, Texas; [5]Department of Medicine, University of California, San Francisco, Center for Tissue Engineering, Tissue Mechanics, and Mechanobiology, San Francisco, California; [6]Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut; [7]Department of Health Sciences, College of Medicine, Lakeland Regional Health, Lakeland, Florida; [8]Department of Medicine, Medical University of Vienna, Vienna, Austria; [9]Department of Health Policy, York University, Toronto, Ontario, Canada; [10]Department of Medicine, Stanford University, Stanford, California

*Resources, Services and Ice Transport Units, Catalan Institute of Oncology, Hospitalet de Llobregat, Spain

*Department of Medicine, Stanford University School of Medicine, Stanford, California

*Department of Medicine, Stanford University School of Medicine, Stanford, California

*Department of Medicine, Stanford University School of Medicine, Stanford, California

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Figures and Tables

Table 1.

Treatment Indication Characteristics

Treatment	Indications, No.
Total	100
Cancer type	
Solid tumors	58
Genitourinary	14
Gastrointestinal	9
Respiratory and thoracic	9
Skin	9
Breast	8
Endocrine and neuroendocrine	3
Gynecological	2
Sarcoma and GIST	3
Neurological	1
Hematological cancers	42
Leukemia	7
Lymphoma[a]	18
Multiple myeloma	7
Chronic myelogenous leukemia	6
Other[b]	4
Line of treatment	
1	30

Abbreviations: *ALK*, anaplastic lymphoma kinase gene; *BCR-ABL*, fusion gene of breakpoint cluster region gene and *ABL1* protooncogene; *BRAF*, v-Raf murine sarcoma viral oncogene homologue B1 gene; *BRCA*, breast cancer gene; *EGFR*, epidermal growth factor receptor gene; GIST, gastrointestinal stromal tumor; *HER2*, human epidermal growth factor receptor 2 gene.

[a]Includes chronic lymphatic leukemia.
[b]Includes myelodysplastic syndromes (n = 2), myelofibrosis, and multicentric Castleman disease.
[c]Priority review designation status of 4 indications could not be ascertained.
[d]Approvals in 2013 and later.

Table 2.

Clinical Trial Characteristics

Characteristic	No. (%)						
	Overall	Cancer type		Orphan status		Accelerated approval	
		Solid tumor	Hematological cancer	No	Yes	No	Yes
Total clinical trials, No.	127	72	55	41	86	66	61
Participants, median (IQR)	191 (106-448)	330 (171-638)	111 (74-188)	435 (230-760)	152 (94-292)	374 (159-710)	136 (100-202)
Study design							
RCT	65 (51.2)	51 (70.8)	14 (25.5)	31 (75.6)	34 (39.5)	54 (81.8)	11 (18.0)
Single-arm clinical trial[a]	62 (48.8)	21 (29.2)	41 (74.5)	10 (24.4)	52 (60.5)	12 (18.2)	50 (82.0)
Clinical trial phase (drug development phase)							
Phase 3	57 (44.9)	44 (61.1)	13 (23.6)	27 (65.9)	30 (34.9)	50 (75.8)	7 (11.5)
Phase 2	66 (52.0)	25 (34.7)	41 (74.5)	14 (34.1)	52 (60.5)	15 (22.7)	51 (83.6)
Phase 1	3 (2.4)	3 (4.2)	0	0	3 (3.5)	0	3 (4.9)
Not reported	1 (0.8)	0	1 (1.8)	0	1 (1.2)	1 (1.5)	0
Type of blinding							
Double	30 (23.6)	25 (34.7)	5 (9.1)	16 (39.0)	14 (16.3)	27 (40.9)	3 (4.9)
Single	1 (0.8)	1 (1.4)	0	0	1 (1.2)	1 (1.5)	0
Open label	95 (74.8)	45 (62.5)	50 (90.9)	25 (61.0)	70 (81.4)	37 (56.1)	58 (95.1)
Not specified	1 (0.8)	1 (1.4)	0	0	1 (1.2)	1 (1.5)	0
Type of control							

Abbreviations: IQR, interquartile range; RCT, randomized clinical trial.

[a]Clinical trials without a parallel control (ie, patients were randomized to different doses of the experimental treatment only [dose-comparison clinical trials] or not randomized and compared with historical controls.
[b]Includes comparators in which placebo is received in addition to active treatment (ie, add-on or double-dummy clinical trials).
[c]Includes supportive therapy or standard care.

Figure 1.

Forest Plot of All Randomized Clinical Trials With Data on Overall Survival Used for Approval of Novel Cancer Drugs Between 2000 and 2016

Squares represent mean values, with the size of the squares indicating weight and horizontal lines representing 95% CIs. Diamonds represent the pooled mean with the points of the diamonds representing 95% CIs. HR indicates hazard ratio.

Table 3.

Treatment Outcomes for Overall Survival, Progression-Free Survival, and Tumor Response

Outcome	Overall		Cancer type				Orphan status				Accelerated approval			
			Solid tumor		Hematological cancer		No		Yes		No		Yes	
	RCTs, No.[a]	Outcome	RCTs, No.	Outcome	RCTs, No.	Outcome	RCTs, No.	Outcome	RCTs, No.	Outcome	RCTs, No.	Outcome	RCTs, No.	Outcome
Overall survival														
HR (95% CI)	54	0.77 (0.73-0.81)[b]	44	0.76 (0.72-0.80)	10	0.86 (0.76-0.98)	25	0.76 (0.71-0.81)	29	0.77 (0.71-0.84)	48	0.76 (0.72-0.80)	6	0.85 (0.71-1.01)
I^2		46		50		2		49		45		47		31
Improvement, median (IQR), mo	35	2.40 (1.25-3.89)	31	2.40 (1.40-3.89)	4	2.15 (0.61-3.58)	21	2.40 (1.44-4.10)	14	2.75 (0.72-3.66)	30	2.20 (1.18-3.66)	5	3.20 (2.70-4.20)
Progression-free survival														
HR (95% CI)	53	0.52 (0.47-0.57)[c]	46	0.53 (0.48-0.58)	7	0.43 (0.28-0.66)	26	0.59 (0.54-0.66)	27	0.44 (0.38-0.52)	46	0.51 (0.46-0.57)	7	0.54 (0.44-0.67)
I^2		88		87		93		84		89		89		66
Improvement, median (IQR), mo	50	2.70 (1.61-4.29)	44	2.40 (1.48-4.22)	6	4.30 (3.95-10.05)	26	2.07 (1.10-4.11)	24	3.50 (2.40-4.64)	43	2.72 (1.68-4.28)	7	2.50 (1.30-5.50)

Abbreviations: HR, hazard ratio; IQR, interquartile range; OR, odds ratio; RCT, randomized clinical trial; RR, relative risk.

[a]Not all data were reported for all clinical trials.
[b]Median HR for overall survival, 0.74 (IQR, 0.67-0.87; range, 0.37-1.12).
[c]Median HR for progression-free survival, 0.55 (IQR, 0.40-0.67; range, 0.16-0.92).

Figure 2.

Forest Plot of All Randomized Clinical Trials With Data on Tumor Response Used for Approval of Novel Cancer Drugs Between 2000 and 2016

Squares represent mean values, with the size of the squares indicating weight and horizontal lines representing 95% CIs. Diamonds represent the pooled mean with the points of the diamonds representing 95% CIs. RR indicates relative risk.

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