Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

Region	Agency	Website
Europe	EMA	https://www.ema.europa.eu/en/medicines
Canada	HC	https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html
Australia	TGA	https://www.tga.gov.au/ws-auspar-index
USA	FDA	https://www.accessdata.fda.gov/scripts/cder/daf/

Table e1 Marketing Authorization Data Sources

FDA: US Food and Drug Administration, EMA: European Medicines Agency, HC: Health Canada, TGA: Therapeutics Goods Administration.

	US (FDA)		EU (EMA)		Canada (HC)		Australia (TGA)		
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	*P-Value*
A) Regulatory									
Approval Type									*<.001*
Standard	52	(54.2%)	74	(80.4%)	41	(47.7%)	72	(86.8%)	
Conditional Approval	28	(29.2%)	12	(13.1%)	23	(26.7%)	3	(3.6%)	
Priority Review	16	(16.6%)	6	(6.5%)	22	(25.6%)	8	(9.6%)	
Orphan Designation									*<.001*
No	49	(51.0%)	70	(76.1%)	NA	NA	75	(90.4%)	
Yes	47	(49.0%)	22	(23.9%)	NA	NA	8	(9.6%)	
MA Supporting Trial †									*<.001*
No	57	(59.4%)	25	(27.2%)	48	(55.8%)	50	(60.2%)	
Phase 1	7	(7.3%)	14	(15.2%)	5	(5.8%)	2	(2.4%)	
Phase 2	15	(15.6%)	28	(30.4%)	13	(15.1%)	19	(22.9%)	
Phase 3	17	(17.7%)	25	(27.2%)	20	(23.3%)	12	(14.5%)	
B) Pivotal Trial									
Trial Design ‡									*0.822*
Phase 1	4	(4.2%)	3	(3.2%)	5	(5.8%)	3	(3.6%)	
Phase 2	25	(26.0%)	18	(19.6%)	23	(26.8%)	19	(21.7%)	
Phase 3	67	(70.8%)	71	(77.2%)	58	(67.4%)	61	(74.7%)	
Primary Endpoint									*0.985*
Surrogate	63	(66.6%)	58	(63.0%)	60	(69.8%)	56	(67.5%)	
Clinical	17	(17.7%)	18	(19.6%)	14	(16.3%)	14	(16.9%)	
Co-Primary	16	(16.7%)	16	(17.4%)	12	(13.9%)	13	(15.6%)	
MCBS									*0.488*
Score of 1, 2, or 3	54	(56.2%)	55	(59.8%)	42	(48.8%)	48	(57.8%)	
Score of 4 or 5	42	(43.8%)	37	(40.2%)	44	(51.2%)	35	(42.2%)	
Enrolled Patients									
Mean	563	[479-647]	600	[525-685]	556	[463-648]	579	[485-673]	
Trial Length (months)									
Mean	33	[30-37]	30	[27-33]	34	[30-39]	32	[28-36]	
C) Treatment									
Treatment Type									*0.709*
Combination	17	(17.7%)	18	(19.6%)	12	(14.0%)	12	(14.5%)	
Monotherapy	79	(82.3%)	74	(80.4%)	74	(86.0%)	71	(85.5%)	
Line of Treatment									*0.959*
2nd, 3rd, 4th line	61	(63.5%)	55	(59.8%)	53	(62.6%)	52	(62.7%)	
1st line	35	(36.5%)	37	(40.2%)	33	(38.4%)	31	(37.3%)	
Observations	**96**	**(100%)**	**92**	**(100%)**	**86**	**(100%)**	**83**	**(100%)**	

Table e2 Regulatory Approval Characteristics of Targeted Drugs Across the US (FDA), EU (EMA), Canada (HC), and Australia (TGA) – Continued

P-values calculated based on χ^2-tests. FDA: US Food and Drug Administration, EMA: European Medicines Agency, HC: Health Canada, TGA: Therapeutics Goods Administration, MCBS: Magnitude of Clinical Benefit Scale (1: *low* benefit to 5: *high* benefit). † Highest Phase of *supporting* trials disclosed in the regulatory approval report (No supporting trial: 0, Phase 1: 1, Phase 2: 2, Phase 3: 3). ‡ Highest Phase *pivotal* trial disclosed in the regulatory approval report (Phase 1: 1, Phase 2: 2, Phase 3: 3).

		(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
(1)	FDA Approval Sequence	1.00											
(2)	Conditional Approval	0.18***	1.00										
(3)	Priority Review	0.09	-0.20***	1.00									
(4)	Orphan Designation	0.21***	0.20***	0.13*	1.00								
(5)	Supporting Trials †	0.26***	0.07	-0.06	0.01	1.00							
(6)	Phase ‡	-0.18***	-0.48***	0.11*	-0.22***	0.03	1.00						
(7)	Primary Endpoint	-0.13*	-0.14**	-0.03	-0.31***	-0.01	0.34***	1.00					
(8)	MCBS Score	0.17**	0.32***	-0.10	0.29***	0.15**	-0.61***	-0.52***	1.00				
(9)	Enrolled Patients	-0.04	-0.23***	0.03	-0.35***	0.05	0.48***	0.46***	-0.36***	1.00			
(10)	Trial Length (months)	-0.12*	0.17***	-0.08	-0.01	-0.09	-0.40***	-0.12*	0.18***	0.03	1.00		
(11)	Monotherapy	0.20***	0.08	0.06	0.21***	0.08	-0.26***	-0.51***	0.37***	-0.38***	0.01	1.00	
(12)	1st Line Treatment	-0.11*	-0.23***	0.04	-0.12*	0.03	0.27***	0.10	-0.12*	0.11*	-0.03	-0.35***	1.00

Table e3 Pearson Correlation Coefficients of Collected Variables

Indication approval sequence was determined by the FDA approval date (initial indication: 1, supplementary indication: 0). P-values: * *p<0.05*, ** *p<0.01*, *** *p<0.001*. MCBS: Magnitude of Clinical Benefit Scale (1: *low* benefit to 5: *high* benefit). † Highest Phase of supporting trials disclosed in the regulatory approval report (No supporting trial: 0, Phase 1: 1, Phase 2: 2, Phase 3: 3). ‡ Highest Phase pivotal trial disclosed in the regulatory approval report (Phase 1: 1, Phase 2: 2, Phase 3: 3).