JNCCN

JOURNAL OF THE NATIONAL COMPREHENSIVE CANCER NETWORK

Supplemental online content for:

Associations With Definitive Outcomes and Clinical Benefit of Cancer Drugs at the Time of Marketing Approval and in the Postmarketing Period

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J Natl Compr Canc Netw, doi: 10.6004/jnccn.2021.7003

eTable 1: Predictors of Benefit in the Noncurative Setting

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Univariable Analysis

Variable	OS Benefit[a] OR (95% CI)	OS Benefit[a] *P* Value[e]	QoL Benefit[b] OR (95% CI)	QoL Benefit[b] *P* Value[e]	ASCO-VF Clinical Benefit[c] OR (95% CI)	ASCO-VF Clinical Benefit[c] *P* Value[e]	ESMO-MCBS Clinical Benefit[d] OR (95% CI)	ESMO-MCBS Clinical Benefit[d] *P* Value[e]
Regular approval (vs accelerated approval)	**4.00 (1.29–12.38)**	**.016**	0.46 (0.15–1.44)	.18	0.64 (0.23–1.83)	.40	0.56 (0.20–1.53)	.26
Orphan drug designation (vs not)	0.55 (0.23–1.30)	.17	1.86 (0.65–5.29)	.25	1.27 (0.53–3.02)	.59	1.30 (0.55–3.10)	.55
Priority review designation (vs not)	1.00 (0.18–5.70)	.99	2.86 (0.87–9.46)	.08	2.92 (0.99–8.57)	.05	2.02 (0.70–5.82)	.19
Breakthrough therapy designation	0.85 (0.20–3.71)	.83	0.85 (0.20–3.71)	.83	3.00 (0.37–24.50)	.305	**15.38 (1.73–136.67)**	**.01**
Initial approval (vs supplemental)	0.79 (0.34–1.84)	.58	2.71 (0.94–7.81)	.06	**5.39 (2.11–13.78)**	**<.001**	2.11 (0.87–5.08)	.09
Multiple trials supporting approval (vs 1 trial)	0.36 (0.09–1.48)	.16	3.52 (0.63–19.84)	.15	2.23 (0.52–9.59)	.28	**4.32 (1.03–18.08)**	**.04**
Sample size per 100 patients	**1.47 (1.22–1.76)**	**<.001**	1.50 (0.54–4.17)	.44	**0.88 (0.77–0.99)**	**.04**	0.98 (0.86–1.11)	.74
Lung, breast, colorectal, and prostate cancer (vs others)	**2.46 (1.04–5.85)**	**.04**	7.27 (0.79–66.60)	.008	0.95 (0.40–2.25)	.91	1.58 (0.66–3.77)	.30
Immunotherapy (vs standard and target therapy)	7.55 (0.88–64.27)	.06	**4.98 (1.36–18.23)**	**.001**	4.12 (0.80–21.26)	.090	**6.61 (1.28–34.06)**	**.02**
Companion diagnostic (vs none)	1.21 (0.43–3.44)	.72	**6.53 (1.25–34.03)**	**.02**	**6.74 (1.76–25.74)**	**.005**	**22.67 (4.74–108.42)**	**<.001**
Single-arm (vs randomized)	**0.13 (0.03–0.63)**	**.01**	**5.88 (1.42–24.36)**	**.01**	**9.94 (1.18–83.54)**	**.03**	2.03 (0.62–6.67)	.24
Phase I–II (vs phase III)	**0.17 (0.04–0.67)**	**.01**	0.58 (0.10–3.44)	.55	**7.33 (1.51–35.58)**	**.01**	2.31 (0.77–6.97)	.14
Approval based on subgroup analysis (vs not)	2.50 (0.46–13.65)	.29	**4.75 (1.52–14.85)**	**.007**	2.16 (0.37–12.51)	.39	2.22 (0.46–10.62)	.32
Open-label (vs double-blind)	1.12 (0.47–2.65)	.80	**4.41 (1.20–16.14)**	**.02**	1.58 (0.65–3.79)	.31	**3.37 (1.30–8.80)**	**.01**
Crossover (vs not)	**0.25 (0.09–0.71)**	**.01**	2.11 (0.70–6.35)	.18	2.10 (0.87–5.06)	.09	1.42 (0.52–3.90)	.49
Later lines (vs first-line)	0.83 (0.35–1.99)	.68	2.04 (0.72–5.77)	.18	2.25 (0.84–6.04)	.11	1.06 (0.44–2.57)	.90
OS (vs intermediate endpoints)	—	—	2.19 (0.70–6.85)	.18	**4.54 (1.70–12.11)**	**.003**	1.35 (0.57–3.23)	.49
QoL (vs not)	0.59 (0.17–2.06)	.41	—	—	**34.00 (3.61–320.10)**	**.002**	**40.00 (5.82–274.76)**	**<.001**

Multivariable Analysis

Variable	OS Benefit[a] OR (95% CI)	OS Benefit[a] *P* Value[f]	QoL Benefit[b] OR (95% CI)	QoL Benefit[b] *P* Value[f]	ASCO-VF Clinical Benefit[c] OR (95% CI)	ASCO-VF Clinical Benefit[c] *P* Value[f]	ESMO-MCBS Clinical Benefit[d] OR (95% CI)	ESMO-MCBS Clinical Benefit[d] *P* Value[f]
Companion diagnostic (vs none)	4.66 (1.13–19.25)	.033	5.94 (1.56–22.56)	.009	7.78 (2.00–30.29)	.003	30.84 (46.21–153.14)	<.001
Immunotherapy (vs standard and target therapy)	28.52 (2.65–306.62)	.006	9.85 (1.02–95.04)	.04	5.45 (1.02–29.05)	.04	12.35 (2.20–68.71)	.004
Sample size per 100 patients	1.70 (1.34–2.16)	<.001	—	—	—	—	—	—

Bold indicates statistically significant *P* value.

Abbreviations: ASCO-VF, ASCO Value Framework; ESMO-MCBS, ESMO-Magnitude of Clinical Benefit Scale; OR, odds ratio; OS, overall survival; QoL, quality of life.

[a]A drug was considered to have shown an OS benefit if a statistically significant benefit was observed with experimental therapy.

[b]A drug was considered to have shown a QoL benefit if a statistically significant difference was reported between the drug and experimental arm among randomized controlled trials and between baseline and after treatment in single-arm trials.

[c]High clinical benefit for ASCO-VF was considered a threshold score of ≥45.

[d]High clinical benefit for ESMO-MCBS was considered a grade of A or B for trials of curative intent and a grade of 4 or 5 for those of palliative intent.

[e]Based on univariable logistic regression. All *P* values are 2-sided.

[f]Multivariable models were adjusted for variables with *P* values <.05 in the univariable model and showing benefit for at least 2 benefit outcomes: sample size (continuous), companion diagnostic (yes vs no), immunotherapy (yes vs no), and type of trial (single-arm vs randomized).