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Figure 1: Flow chart for cohort selection of each real-world cohort
Table 1: ORRs vs rwRRs in real-world cohorts before and after weighting

Supplemental Figure 1. Flow chart for cohort selection of each real-world cohort

Trial	Step 1: Limit to patients with same treatment as trial control arm initiated during trial enrollment window	Step 2: Implement trial I/E criteria with available RWD	Step 3: Apply inverse odds weights on trials' published summary baseline characteristics where feasible
ALEX	● Initiated first line Crizotinib monotherapy between 2014-08-18 and 2016-01-20	● Advanced or metastatic NSCLC at initial diagnosis or recurrence ● ALK + ● Age ≥ 18 ● ECOG = 0, 1 or 2. ● Adequate organ function based on labs (e.g. plt, ANC, hgb, CrCl, ALT, AST etc) ● no h/o HIV / AIDS	● Age ● Gender ● ECOG ● Smoking status
KEYNOTE-021	● Initiated first line carboplatin and pemetrexed alone between 2014-11-25 and 2016-01-25	● Advanced or metastatic NSCLC at initial diagnosis or recurrence ● Age ≥ 18 ● no EGFR mutations or ALK translocations ● ECOG = 0 or 1 ● Adequate organ function based on labs (e.g., ANC, plt, hgb, Serum Cr OR CrCl, bilirubin, AST, ALT, Alk Phos) ● no h/o HIV or Hepatitis B/C	● Age ● Gender ● Race ● ECOG ● Smoking status
KEYNOTE-177	● Initiated first line FOLFOX/FOLFIRI +/- Bevacizumab or Cetuximab between 2016-02-11 and 2018-02-19	● Metastatic colorectal cancer at initial diagnosis or recurrence ● Age ≥ 18 ● dMMR or MSI-H ● ECOG = 0 or 1 ● Adequate organ function based on labs (e.g,. ANC, plt, hgb, Creatinine / GFR / CrCl, bilirubin , AST, ALT, Albumin) ● no h/o HIV or Hepatitis B/C	● Age ● Gender ● ECOG ● Treatment
PALOMA-2	● Initiated first line Letrozole between 2013-02-01 and 2014-07-31	● Age >= 18 and female ● Metastatic breast cancer at initial diagnosis or recurrence ● ER+, HER2- ● ECOG = 0-2	● Age ● Race ● ECOG ● Stage at initial diagnosis ● Number of metastasis

		• Adequate organ function based on labs (e.g., ANC, plt, hgb, SCr, bilirubin, AST, ALT, Alk Phos) • no known brain or CNS metastases • no prior neoadjuvant or adjuvant treatment • no h/o HIV		• Sites of metastasis

Supplemental Table 1: ORRs vs rwRRs in real-world cohorts before and after weighting

Trial name	Include vs Exclude patients with no response assessments as non-responders	Trial Results		Real-world cohort before weighting			Real-world cohort after weighting		
		N	ORR (%)	N	rwRR (%)	rwRR with confirmation (%)	N	rwRR (%)	rwRR with confirmation (%)
ALEX	Include	151	75.5 (67.8, 82.1) **w/o confirmation	106	38.7% (30.0, 48.2)	29.2 (21.4, 38.5)	64.6	37.9 (27.1, 50.1)	29.9 (20.1, 42.0)
	Exclude	--	--	85	48.2 (37.9, 58.7)	36.5 (27.0, 47.1)	56.8	43.2 (31.1, 56.1)	34.1 (23.1, 47.0)
KEYNOTE-122	Include	63	28.6 (18, 41) **w/ confirmation	384	42.7 (37.9, 47.7)	28.6 (24.4, 33.4)	308.3	43.9 (38.5, 49.5)	31.3 (26.4, 36.7)
	Exclude	--	--	321	51.1 (45.6, 56.5)	34.3 (29.3, 39.6)	263.6	51.4 (45.4, 57.4)	36.6 (31.1, 42.6)

KEYNOTE-177	Include	154	33.1 (25.8, 41.1) **w/ confirmation	1251	49.6 (46.9, 52.4)	35.2 (32.6, 37.9)	1040.0	51.8 (48.8, 54.9)	37.0 (34.1, 39.9)
	Exclude	--	--	1027	60.5 (57.4, 63.4)	42.8 (39.8, 45.9)	870.2	62.0 (58.7, 65.1)	44.2 (40.9, 47.5)
PALOMA-2	Include	222	34.7 (28.4, 41.3) **w/ confirmation	268	27.6 (22.6, 33.3)	19.0 (14.8, 24.2)	58.971 33	35.9 (24.9, 48.7)	19.3 (11.2, 31.1)
	Exclude	--	--	198	37.4 (30.9, 44.3)	25.8 (20.2, 32.3)	45.199 34	46.9 (33.1, 61.1)	25.2 (14.8, 39.4)