Table 5. GRADE Summary of Findings for outcomes rated as high certainty

No.	Study / therapeutic context	Outcome rated as high certainty	Main effect estimate	Certainty of evidence	GRADE justification
1	Brose et al.; COSMIC-311 — cabozantinib in radioiodine-refractory differentiated thyroid cancer	Progression-free survival	Median PFS: not reached vs 1.9 months; HR 0.22, 95% CI 0.13–0.36; p<0.0001	High ⊕⊕⊕⊕	Large randomized, double-blind, placebo-controlled phase III trial; direct resistant population after VEGFR-targeted therapy; objective radiologic endpoint; large and precise treatment effect; no serious downgrading.
2	San-Miguel et al.; CARTITUDE-4 — cilta-cel in lenalidomide-refractory multiple myeloma	Progression-free survival	Median PFS: not reached vs 11.8 months; HR 0.26, 95% CI 0.18–0.38; p<0.001	High ⊕⊕⊕⊕	Randomized phase III trial; direct population with lenalidomide-refractory disease; large effect size; narrow confidence interval; clinically meaningful endpoint; no serious imprecision.
3	San-Miguel et al.; CARTITUDE-4 — cilta-cel in lenalidomide-refractory multiple myeloma	Overall response	ORR: 84.6% vs 67.3%	High ⊕⊕⊕⊕	Large randomized trial with clear comparator; response advantage consistent with PFS benefit; direct applicability to refractory myeloma; estimate clinically relevant and directionally robust.
4	San-Miguel et al.; CARTITUDE-4 — cilta-cel in lenalidomide-refractory multiple myeloma	Depth of response / complete response or better	Complete response or better: 73.1% vs 21.8%; MRD negativity: 60.6% vs 15.6%	High ⊕⊕⊕⊕	Very large magnitude of effect; direct and clinically meaningful marker of deep response; internally consistent with PFS and ORR; no serious indirectness.
5	Locke et al.; ZUMA-7 — axi-cel in early relapsed or refractory large B-cell lymphoma	Event-free survival	Median EFS: 8.3 vs 2.0 months; HR 0.40, 95% CI 0.31–0.51; p<0.001	High ⊕⊕⊕⊕	International randomized phase III trial; prespecified primary endpoint; direct R/R population; large and precise benefit; central review; no serious downgrading.
6	Locke et al.; ZUMA-7 — axi-cel in early relapsed or refractory large B-cell lymphoma	24-month event-free survival	24-month EFS: 41% vs 16%	High ⊕⊕⊕⊕	Clinically meaningful long-term disease-control endpoint; large absolute difference; consistent with median EFS and response outcomes; direct population.
7	Locke et al.; ZUMA-7 — axi-cel in early relapsed or refractory large B-cell lymphoma	Overall response	ORR: 83% vs 50%	High ⊕⊕⊕⊕	Large randomized comparison; objective response endpoint; large absolute effect; consistency with EFS and PFS; no serious imprecision.
8	Locke et al.; ZUMA-7 — axi-cel in early relapsed or refractory large B-cell lymphoma	Complete response	CR: 65% vs 32%	High ⊕⊕⊕⊕	Large absolute difference in complete response; directly applicable to second-line R/R LBCL; consistent with survival endpoints; no serious indirectness.
9	Locke et al.; ZUMA-7 — axi-cel in early relapsed or refractory large B-cell lymphoma	Progression-free survival	Median PFS: 14.7 vs 3.7 months; HR 0.49, 95% CI 0.37–0.65	High ⊕⊕⊕⊕	Objective time-to-event endpoint; precise estimate; consistent direction of benefit across EFS, response, and subgroup analyses; no serious downgrading.
10	Bardia et al.; ASCENT — sacituzumab govitecan in metastatic triple-negative breast cancer without brain metastases	Progression-free survival	Median PFS: 5.6 vs 1.7 months; HR 0.41, 95% CI 0.32–0.52; p<0.001	High ⊕⊕⊕⊕	Randomized phase III trial; blinded independent central review; direct refractory metastatic TNBC population; large and precise effect; no serious downgrading.

11	Bardia et al.; ASCENT — sacituzumab govitecan in metastatic triple-negative breast cancer without brain metastases	Overall survival	Median OS: 12.1 vs 6.7 months; HR 0.48, 95% CI 0.38–0.59; p<0.001	High ⊕⊕⊕⊕	Hard clinical endpoint; large survival gain; precise estimate; direct comparison with physician-choice chemotherapy; no serious indirectness or imprecision.
12	Bardia et al.; ASCENT — sacituzumab govitecan in metastatic triple-negative breast cancer	Progression-free survival, overall evidence set	Benefit consistent in the full randomized population; central-review PFS also favored sacituzumab govitecan: 5.5 vs 1.7 months; HR 0.35, 95% CI 0.28–0.44	High ⊕⊕⊕⊕	Consistent benefit across main and sensitivity analyses; objective endpoint; large effect; precise estimate; findings support robustness of PFS benefit.
13	Bardia et al.; ASCENT — sacituzumab govitecan in metastatic triple-negative breast cancer	Objective response	ORR: 35% vs 5%	High ⊕⊕⊕⊕	Large absolute response difference; objective endpoint; direct refractory population; response benefit consistent with PFS and OS.
14	Bardia et al.; ASCENT — sacituzumab govitecan in metastatic triple-negative breast cancer	Hematologic toxicity	Grade ≥3 neutropenia: 51% vs 33%; leukopenia: 10% vs 5%; anemia: 8% vs 5%; febrile neutropenia: 6% vs 2%	High ⊕⊕⊕⊕	High certainty of harm: frequent, clearly defined, treatment-related hematologic events; large randomized safety population; consistent toxicity pattern; no serious imprecision.
15	Bardia et al.; ASCENT — sacituzumab govitecan in metastatic triple-negative breast cancer	Grade 3 diarrhea	Grade ≥3 diarrhea: 10% vs <1%; no grade 4 diarrhea	High ⊕⊕⊕⊕	High certainty of harm: clear direction and magnitude of toxicity; clinically relevant adverse event; direct comparison; precise and well-characterized safety signal.
16	Metzger et al.; PATINA — palbociclib in HR-positive/HER2-positive advanced breast cancer	Grade 3/4 adverse events	Grade 3 AEs: 79.7% vs 30.6%; grade 4 AEs: 10.0% vs 3.6%; mainly neutropenia	High ⊕⊕⊕⊕	High certainty of harm: large randomized phase III trial; very large absolute increase in toxicity; biologically expected hematologic profile; precise and direct safety finding.
17	Powles et al.; EV-301 — enfortumab vedotin in previously treated advanced urothelial carcinoma	Overall survival	Median OS: 12.88 vs 8.97 months; HR 0.70, 95% CI 0.56–0.89; p=0.001	High ⊕⊕⊕⊕	Randomized phase III trial; hard survival endpoint; direct population after platinum and PD-1/PD-L1 therapy; precise estimate; no serious downgrading.
18	Powles et al.; EV-301 — enfortumab vedotin in previously treated advanced urothelial carcinoma	Progression-free survival	Median PFS: 5.55 vs 3.71 months; HR 0.62, 95% CI 0.51–0.75; p<0.001	High ⊕⊕⊕⊕	Objective time-to-event endpoint; precise treatment effect; direct comparator; benefit consistent with OS; no serious indirectness.
19	Powles et al.; EV-301 — enfortumab vedotin in previously treated advanced urothelial carcinoma	Objective response	Confirmed ORR: 40.6% vs 17.9%; p<0.001	High ⊕⊕⊕⊕	Large absolute response difference; objective RECIST-based outcome; consistent with survival benefit; direct resistant/pretreated population.