

Table 1. Characteristics of included randomized clinical trials

Study	Tumor type and disease setting	Study design	Participants	Intervention	Comparator	Main outcomes extracted
Vergote et al., 2025; ENGOT-ov50/GO G-3029/INNOVAT E-3	Platinum-resistant epithelial ovarian cancer	Phase III, randomized, open-label, multicenter trial	Adults with PROC, ECOG PS 0–1, ≤5 prior lines; N=558	Tumor Treating Fields plus weekly paclitaxel	Weekly paclitaxel	OS, PFS, adverse events
Assouline et al., 2023	High-eIF4E refractory or relapsed acute myeloid leukemia	Phase II, randomized, open-label, multicenter trial	Adults with AML after primary treatment failure, relapse, or ineligibility for intensive induction; N=23	Vismodegib, ribavirin, and decitabine	Vismodegib and ribavirin	Overall response, molecular response, safety
Bauer et al., 2022; INTRIGUE	Advanced gastrointestinal stromal tumor after imatinib failure or intolerance	Phase III, randomized, open-label, international multicenter trial	Adults with advanced GIST previously treated with imatinib; N=453	Ripretinib	Sunitinib	PFS, ORR, safety, patient-reported outcomes
Brose et al., 2021; COSMIC-311	Radioiodine-refractory differentiated thyroid cancer after prior VEGFR-targeted therapy	Phase III, randomized, double-blind, placebo-controlled trial	Patients with radioiodine-refractory DTC previously treated with lenvatinib or sorafenib; N=187	Cabozantinib	Placebo	ORR, PFS, adverse events
Heudobler et al., 2021; ModuLung	Advanced non-small cell lung cancer treated in second or later line	Phase II, randomized, open-label, multicenter trial	Patients with stage IIIB/IV NSCLC after failure of platinum-based chemotherapy; N=37	Biomodulatory therapy with treosulfan, pioglitazone, and clarithromycin	Nivolumab	PFS, OS, ORR, treatment-related adverse events
Mukai et al., 2021; SELECT BC-CONFIRM	HER2-negative, endocrine-resistant metastatic breast cancer	Phase III, randomized, open-label, non-inferiority trial	Women aged 20–75 years with metastatic HER2-negative breast cancer and no prior chemotherapy for advanced disease; N=230	S-1	Anthracycline-containing regimen	OS, PFS, treatment failure, safety
Zhao et al., 2024; INO-VATE molecular analysis	Relapsed or refractory B-cell acute lymphoblastic leukemia	Exploratory molecular analysis from a phase III, randomized, open-label trial	Adults with CD22-positive R/R B-cell ALL in first or second salvage therapy; N=326 randomized, genomic subset N=91	Inotuzumab ozogamicin	Standard chemotherapy	CR/CRi, MRD negativity, OS, molecular subgroup efficacy
Locke et al., 2022; ZUMA-7	Early relapsed or refractory large B-cell lymphoma	Phase III, randomized, international trial	Adults with LBCL refractory to or relapsed ≤12 months after first-line chemoimmunotherapy; N=359	Axicabtagene ciloleucel	Standard second-line therapy with salvage chemoimmunotherapy followed by high-dose chemotherapy and autologous SCT in responders	EFS, ORR, CR, OS, safety
Ying et al., 2021; RELIANCE	Heavily pretreated relapsed or refractory large B-cell lymphoma	Randomized dose-level, single-arm, open-label, multicenter CAR-T trial	Adults with CD19-positive R/R LBCL; N=68 enrolled, 59 treated	Relma-cel 100 × 10 ⁶ CAR-positive T cells	Relma-cel 150 × 10 ⁶ CAR-positive T cells	3-month ORR, DOR, PFS, OS, CRS, neurotoxicity
San-Miguel et al., 2023; CARTITUDE-4	Lenalidomide-refractory multiple myeloma after	Phase III, randomized, open-label,	Patients with lenalidomide-refractory multiple myeloma; N=419	Ciltacabtagene autoleucel	Physician's choice standard care with PVd or DPd	PFS, ORR, complete response or better, MRD

	one to three previous lines	multicenter trial				negativity, OS, safety
Lentz et al., 2024	Refractory microsatellite-stable, BRAF wild-type metastatic colorectal cancer	Phase II trial with randomized treatment-schedule cohorts	Patients with disease progression after ≥ 2 prior lines; N=50 treated	Pembrolizumab, binimetinib, and bevacizumab with binimetinib run-in	Same triplet started concurrently	ORR, disease control, PFS, OS, safety
Shoji et al., 2022; JGOG3023	Platinum-resistant ovarian, fallopian tube, or primary peritoneal cancer previously treated with bevacizumab	Phase II, randomized, open-label, multicenter trial	Patients with bevacizumab-pretreated platinum-resistant disease; N=103	Chemotherapy plus bevacizumab	Chemotherapy alone	PFS, OS, ORR, safety
Andreadis et al., 2025; Alliance A051301/BMT-CT N 1201	Relapsed or refractory activated B-cell type diffuse large B-cell lymphoma undergoing autologous HSCT	Phase III, randomized, double-blind, placebo-controlled trial	Patients with R/R ABC-DLBCL eligible for autologous HSCT; N=88 randomized	Ibrutinib added to conditioning and maintenance therapy	Placebo added to conditioning and maintenance therapy	2-year PFS, OS, safety
Metzger et al., 2026; PATINA	Hormone receptor-positive, HER2-positive advanced breast cancer after induction therapy	Phase III, randomized, open-label, international trial	Patients without progression after chemotherapy plus anti-HER2 induction; N=518	Palbociclib plus anti-HER2 and endocrine maintenance therapy	Anti-HER2 and endocrine maintenance therapy	PFS, OS, response, clinical benefit, grade ≥ 3 adverse events
Powles et al., 2021; EV-301	Previously treated locally advanced or metastatic urothelial carcinoma	Phase III, randomized, open-label, global trial	Patients previously treated with platinum chemotherapy and PD-1/PD-L1 inhibitor; N=608	Enfortumab vedotin	Investigator-choice chemotherapy	OS, PFS, ORR, safety
Voorthuis et al., 2026; POSEIDON	Hormone receptor-positive, HER2-negative metastatic breast cancer refractory to endocrine therapy	Phase II, randomized, double-blind, placebo-controlled trial	Patients with HR-positive/HER2-negative metastatic breast cancer; N=152	Taselisib plus tamoxifen	Placebo plus tamoxifen	PFS, ORR, clinical benefit, ctDNA biomarkers, safety
Bardia et al., 2021; ASCENT	Relapsed or refractory metastatic triple-negative breast cancer	Phase III, randomized, open-label trial	Patients with metastatic triple-negative breast cancer previously treated with chemotherapy; primary efficacy population without brain metastases, N=468	Sacituzumab govitecan	Physician-choice single-agent chemotherapy	PFS, OS, ORR, adverse events
Bishop et al., 2022; BELINDA	Aggressive B-cell lymphoma refractory to or relapsed within 12 months	Phase III, randomized, open-label, international trial	Adults with aggressive B-cell lymphoma after first-line treatment failure or early relapse; N=322	Tisagenlecleucel with optional bridging therapy	Salvage chemotherapy followed by autologous HSCT in responders	EFS, response, OS, safety

	after first-line therapy					
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