Table 4 — Main Safety Results of the Included Studies

Study	Intervention / Comparator	Grade ≥3 or ≥3/4 AEs	Serious Events / Deaths	Discontinuation due to Toxicity	Neutropenia	Diarrhea	Hematological & Specific Events
Vergote et al., 2025; INNOVATE-3	TTFields + paclitaxel vs paclitaxel	Frequency of grade ≥3 AEs similar between groups	No new safety signals	NR	NR	NR	Device-related skin AEs (grade 1/2) in 83.6% of patients treated with TTFields
Assouline et al., 2023	Vismodegib + ribavirin + decitabine vs vismodegib + ribavirin	No substantial relevant toxicity described	NR	NR	NR	NR	Small study in R/R AML; safety described predominantly qualitatively
Bauer et al., 2022; INTRIGUE	Ripretinib vs sunitinib	Grade 3/4 AEs: 41.3% vs 65.6%; Treatment-related grade 3/4 AEs: 26.5% vs 55.2%	Treatment-emergent SAEs: 25.6% vs 25.8%; Treatment-related SAEs: 7.6% vs 9.0%	3.6% vs 7.7%	Grade 3/4 neutropenia or decreased neutrophils: 0% vs 13.1%	Grade 3/4: 0.9% vs 2.7%	Lower toxicity with ripretinib; grade 3/4 hypertension: 8.5% vs 26.7%; hand-foot syndrome: 1.3% vs 10%
Brose et al., 2021; COSMIC-311	Cabozantinib vs placebo	Grade 3/4 AEs: 57% vs 26%; Grade 4: 6% vs 3%	Treatment-related SAEs: 16% vs 2%; no treatment-related deaths	Treatment-related discontinuation due to fatigue, arthralgia, diarrhea, hypercalcemia, hypertension, intestinal perforation, liver alteration, myalgia, or renal injury	NR	Grade 3/4: 7% vs 0%	Grade 3/4 hand-foot syndrome: 10% vs 0%; hypertension: 9% vs 3%; fatigue: 8% vs 0%; hypocalcemia: 7% vs 2%
Heudobler et al., 2021; ModuLung	Oral biomodulation vs nivolumab	Treatment-related grade 3–5 AEs: 10% vs 29%	NR	NR	NR	NR	Tolerability profile described as favorable for biomodulation, though study was terminated early
Mukai et al., 2021; SELECT BC-CONFIRM	S-1 vs anthracycline or taxane	NR	NR	NR	NR	NR	Detailed safety data not available in the main extracted excerpt
Zhao et al., 2024; INO-VATE molecular	Inotuzumab ozogamicin vs standard chemotherapy	NR	NR	NR	NR	NR	Molecular analysis derived from INO-VATE; did not add independent safety details in the extracted excerpt
Locke et al., 2022; ZUMA-7	Axicabtagene ciloleucel vs standard therapy	Grade ≥3 AEs: 91% vs 83%	No deaths attributed to CRS or neurological events	NR	NR	NR	CAR-T: Grade ≥3 CRS in 6%; grade ≥3 neurological events in 21%

Ying et al., 2021; RELIANCE	Relma-cel; dose comparison	NR	NR	NR	NR	NR	CD19 CAR-T; safety evaluated by dose, no classic comparator. Events of interest include CRS, neurotoxicity, infections, and cytopenias
San-Miguel et al., 2023; CARTITUDE-4	Cilta-cel vs standard care	Most patients presented grade 3/4 AEs	CRS without grade 5 events; total deaths: 39 vs 46 patients	NR	NR	NR	CAR-T: CRS in 76.1% (grade 3/4 in 1.1%); ICANS in 4.5% (all grade 1/2); cranial nerve palsy in 9.1%; CAR-T-associated peripheral neuropathy in 2.8%
Lentz et al., 2024	Pembrolizumab + binimetinib + bevacizumab	Grade 3 AEs: 56%; Grade 4: 8%	NR	NR	NR	NR	Most common grade 3/4 events: rash 12% and increased AST 12%; study without classic comparator
Shoji et al., 2022; JGOG3023	Chemotherapy + bevacizumab vs chemotherapy	Treatment-related grade ≥3 AEs: 54.9% vs 42.0%	NR	Events leading to discontinuation: 12 vs 2	Grade ≥3 neutrophil reduction: 37.3% vs 32.0%; febrile neutropenia: 2.0% vs 6.0%	NR	Grade ≥3 thrombocytopenia: 9.8% vs 14.0%; anemia: 9.8% vs 8.0%; proteinuria, hypertension, and oral mucositis occurred only in the bevacizumab arm at low frequencies
Andreadis et al., 2025	Ibrutinib + AutoHCT vs placebo + AutoHCT	Grade ≥3 AEs: 76.9% vs 73.7%	Four grade 5 events in ibrutinib arm, all infectious; deaths due to infection: 4 vs 0	Discontinuation due to AE: 18% vs 16%	Neutropenia: 36% vs 37%; febrile neutropenia: 28% vs 24%	10% vs 8%	Thrombocytopenia: 28% vs 18%; leukopenia: 26% vs 16%; anemia: 23% vs 13%; oral mucositis: 13% vs 3%; sepsis: 10% vs 5%
Metzger et al., 2026; PATINA	Palbociclib + anti-HER2 + endocrine therapy vs anti-HER2 + endocrine therapy	Grade 3 AEs: 79.7% vs 30.6%; Grade 4: 10.0% vs 3.6%	No treatment-related deaths	NR	Main toxicity associated with palbociclib; predominant neutropenia	Grade 2/3 diarrhea reported in palbociclib arm	Clear increase in hematological toxicity, mainly neutropenia; febrile neutropenia rare
Powles et al., 2021; EV-301	Enfortumab vedotin vs chemotherapy	Treatment-related grade ≥3 AEs: 51.4% vs 49.8%	Treatment-related deaths: 2.4% vs 1.0%	Peripheral sensory neuropathy led to dose reduction in 7.1%, interruption in 15.5%, and withdrawal in 2.4% in the enfortumab arm	NR	Grade ≥3: 3.4% vs 1.7%	Grade ≥3 peripheral sensory neuropathy: ~3%; grade ≥3 maculopapular rash: 7.4%; hyperglycemia in 6.4% (including 11 grade 3 cases and 1 death)
Voorthuis et al., 2026; POSEIDON	Taselisib + tamoxifen vs placebo + tamoxifen	NR	NR	22% vs 3%	NR	Any-grade diarrhea: 40% in taselisib arm	Significant toxicity; benefit magnitude did not outweigh the poor tolerability of the combination

Bardia et al., 2021; ASCENT	Sacituzumab govitecan vs chemotherapy	Treatment-related grade 3 AEs: 45% vs 32%; Grade 4: 19% vs 15%	Three AE-related deaths in each group; none considered related to sacituzumab	NR	Grade ≥3 neutropenia: 51% vs 33%; febrile neutropenia: 6% vs 2%	Grade ≥3: 10% vs <1%	Grade ≥3 leukopenia: 10% vs 5%; anemia: 8% vs 5%; myelosuppression and diarrhea were more frequent with sacituzumab
Bishop et al., 2022; BELINDA	Tisagenlecleucel vs standard therapy	NR in extracted excerpt	Deaths due to adverse events: 10 vs 13 patients	NR	NR	NR	CAR-T: Study evaluated safety, but specific CRS/ICANS events did not appear in the extracted excerpt; interpret descriptively