

Supplementary Table SI. Detailed Search Strategy for the Embase Database

No.	Query	Results
#10	#7 AND #8 AND #9	283
#9	#5 OR #6	5025573
#8	#3 OR #4	2226
#7	#1 OR #2	55312
#6	aged':ab,ti OR 'aged patient':ab,ti OR 'aged patients':ab,ti OR 'aged people':ab,ti OR 'aged person':ab,ti OR 'aged subject':ab,ti OR 'elderly':ab,ti OR 'elderly patient':ab,ti OR 'elderly patients':ab,ti OR 'elderly people':ab,ti OR 'elderly person':ab,ti OR 'elderly subject':ab,ti OR 'senior citizen':ab,ti	1473699
#5	'aged'/exp	4187502
#4	'inotuzumab ozogamicin':ab,ti OR 'besponsa':ab,ti OR 'calicheamicin cd22 antibody conjugate':ab,ti OR 'cd22 antibody calicheamicin conjugate':ab,ti	838
#3	'inotuzumab ozogamicin'/exp	2188
#2	'b cell acute lymphoblastic leukemia':ab,ti OR 'acute lymphoblastic leukeamia':ab,ti OR 'acute lymphoblastic leukemia':ab,ti OR 'acute lymphoblastic leukemias':ab,ti OR 'acute lymphoblastic leukeamias':ab,ti OR 'leukemia, acute lymphoblastic':ab,ti OR 'leukaemia, acute lymphoblastic':ab,ti OR 'leukemias, acute lymphoblastic':ab,ti OR 'leukaemias, acute lymphoblastic':ab,ti	54403
#1	'b cell acute lymphoblastic leukemia'/exp	2839

Supplementary Table SII. Baseline Characteristics and Quality Assessment of Included Studies

Characteristics	INITIAL-1 (Stelljes et al., 2024)	EWALL-INO (Chevallier et al., 2024)	NCT01371630 (Kantarjian et al., 2018)
Study Phase	Phase II	Phase II	Phase II
Number of Patients (N)	43 (evaluable)	131	52
Age (years), median (range)	64 (56–80)	68 (55–84)	68 (60–81)
Sex (Male), n (%)	21 (49%)	61 (47%)	32 (62%)
Bone Marrow Blasts (%), median (range)	84 (27–100)	90 (20–100)	80 (25–96)*
CD22 Expression (%), median (range)	70 (21–99)	88 (2–100)	97 (27–100)
InO Administration Regimen Relative	Fractionated	Fractionated	Single-dose
Chemoimmunotherapy Intensity	Less intensive	Less intensive	More intensive
MINORS Quality Assessment Score	15 / 16	15 / 16	14 / 16

* Bone marrow blasts for NCT01371630 represent the previously untreated patient cohort (n=48). The MINORS Quality Assessment Scores reflect the methodological quality evaluation conducted independently during this meta-analysis.

Supplementary Table SIII. Study-level treatment protocols and clinical trial characteristics.

Characteristics	INITIAL-1	EWALL-INO	NCT01371630
Chemotherapy Regimen	Dexamethasone prephase/induction; age-adapted ID-MTX/AraC/Asparaginase consolidation	Low-intensity vincristine/dexamethasone (Induction 1) and cyclophosphamide/dexamethasone (Induction 2); AraC/MTX/cyclophosphamide/VP16 consolidation	mini-hyper-CVD (cyclophosphamide/dexamethasone/vincristine alternating with methotrexate/cytarabine)
InO Dose & Timing	Fractionated: 0.8 mg/m ² (d1), 0.5 mg/m ² (d8, 15) for cycle 1; 0.5 mg/m ² (d1, 8, 15) for cycles 2-3	Fractionated: 0.8 mg/m ² (d1), 0.5 mg/m ² (d8, 15) for cycle 1; 0.5 mg/m ² (d1, 8) for cycle 2	Single-dose per cycle (Day 3): 1.8 to 1.3 mg/m ² or 1.3 to 1.0 mg/m ² for the first 4 cycles
Number of Cycles	Up to 3 induction, 6 consolidation, 24 months maintenance	2 induction, up to 6 consolidation, 18 months maintenance	8 induction/consolidation, 36 months maintenance
Transplant Policy	Allowed in CR1 (performed in patients with persisting/relapsing MRD or after consolidation I)	Allowed after 3 consolidation cycles	At the discretion of the treating physician in first remission
Eligibility Criteria	Age ≥ 56 years, newly diagnosed Ph-negative B-ALL, CD22 ≥ 20%, adequate liver function	Age ≥ 55 years, newly diagnosed Ph-negative BCP-ALL, CD22 ≥ 20%, ECOG ≤ 2, no CNS involvement	Age ≥ 60 years, newly diagnosed Ph-negative B-ALL, ECOG 0-3, normal cardiac/organ function
Follow-up, median	32.4 months	31.3 months	29.0 months

Note: AraC, cytarabine; B-ALL, B-cell acute lymphoblastic leukemia; BCP-ALL, B-cell precursor acute lymphoblastic leukemia; CNS, central nervous system; CR1, first complete remission; CVD, cyclophosphamide, vincristine, dexamethasone; ECOG, Eastern Cooperative Oncology Group; ID, intermediate-dose; InO, inotuzumab ozogamicin; MRD, measurable residual disease; MTX, methotrexate; Ph-negative, Philadelphia chromosome-negative; VP16, etoposide.

**Supplementary Table SIV. Sensitivity analysis of overall survival estimates
utilizing alternative parametric survival distributions**

Parametric Distribution	Akaike Information Criterion (AIC)	Estimated 1-Year OS (95% CI)	Estimated 3-Year OS (95% CI)
Weibull	1,245.3	74.9% (69.5%–80.8%)	52.0% (45.2%–59.9%)
Log-normal	1,248.7	75.3% (69.8%–81.1%)	51.4% (44.8%–59.2%)
Log-logistic	1,251.2	74.5% (68.9%–80.4%)	52.8% (46.1%–60.5%)

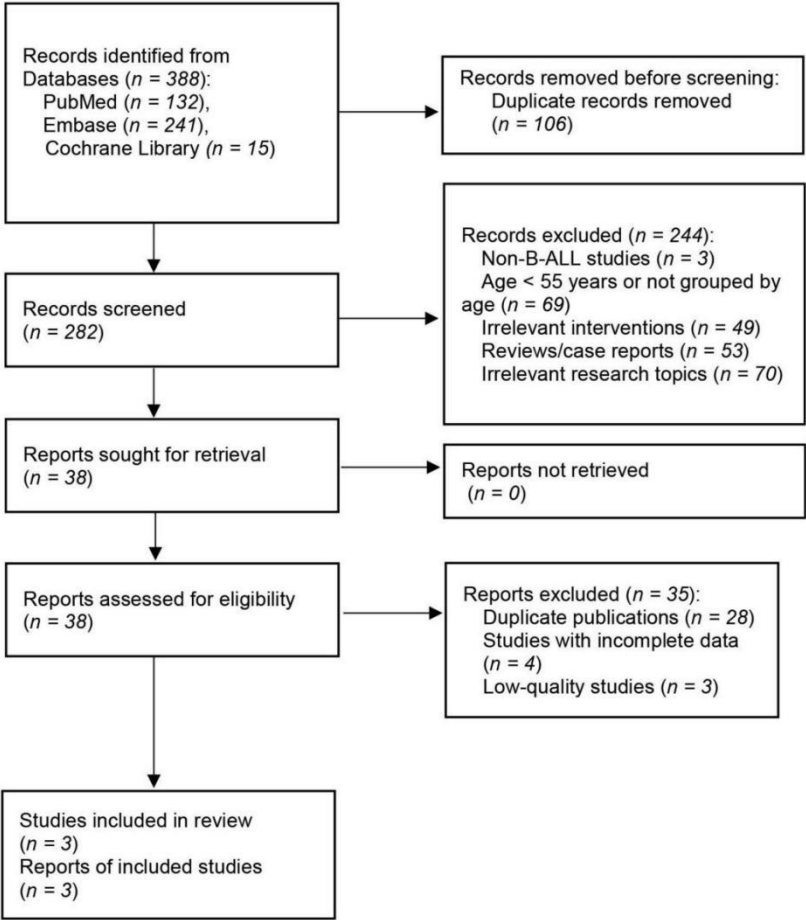
Note: The Weibull distribution was selected for the primary analysis as it demonstrated the lowest AIC, indicating the most optimal statistical fit for the reconstructed pseudo-individual survival data.

**Supplementary Table SV. Item-level Quality Assessment of Included Studies
according to the MINORS criteria**

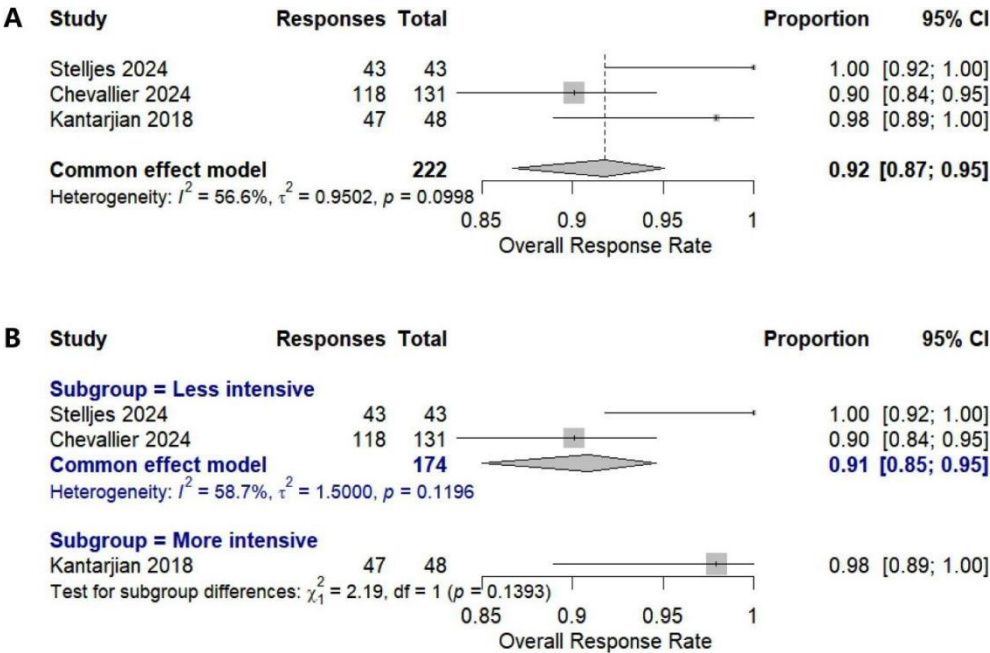
MINORS Criteria (Non-comparative studies)	INITIAL-1 (Stelljes)	EWALL-INO (Chevallier)	NCT01371630 (Kantarjian)
1. A clearly stated aim	2	2	2
2. Inclusion of consecutive patients	2	2	2
3. Prospective collection of data	2	2	2
4. Endpoints appropriate to the aim of the study	2	2	2
5. Unbiased assessment of the study endpoint	1	1	1
6. Follow-up period appropriate to the aim of the study	2	2	2
7. Loss to follow up less than 5%	2	2	2
8. Prospective calculation of the study size	2	2	1
Total Score (Maximum: 16)	15	15	14

Note: Items are scored as 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). Item 5 scored 1 uniformly across studies as these were open-label phase II trials lacking an independent blinded review committee for endpoints. Item 8 scored 1 for NCT01371630 as the sample size for this specific older adult cohort was not independently pre-calculated outside the broader trial design.

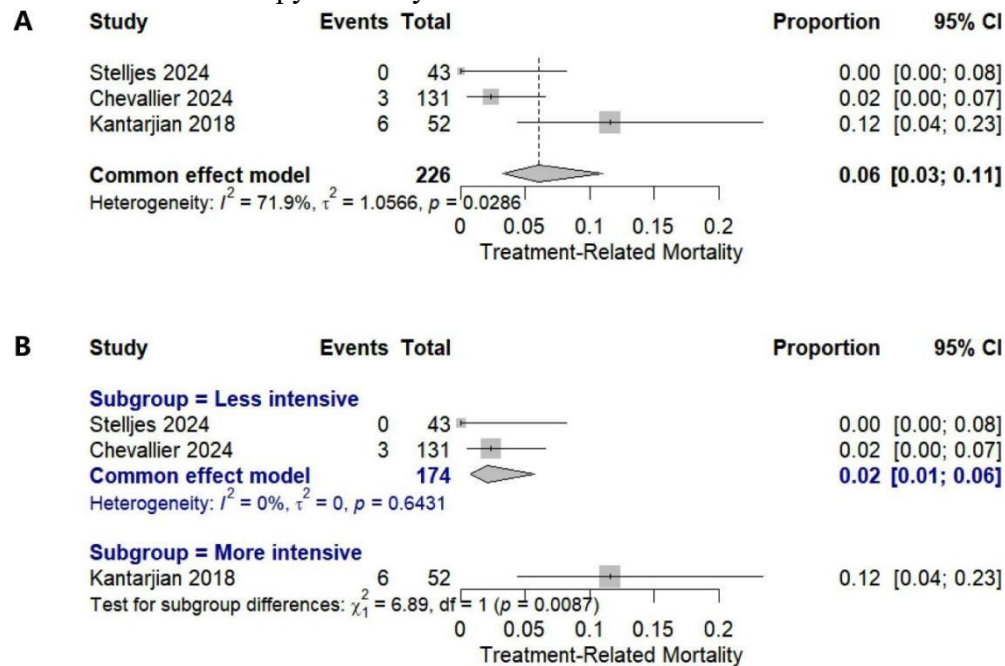
Supplementary Figure S1. PRISMA Flow Diagram of the Study Selection Process



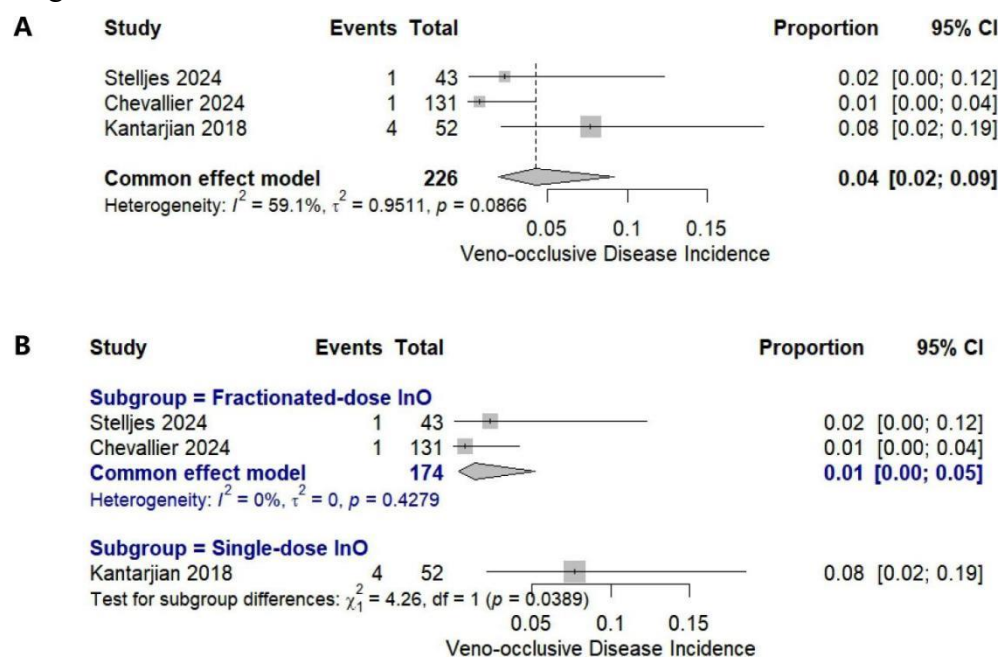
Supplementary Figure S2. Forest Plot of the Overall Response Rate. (A) Pooled Estimate. (B) Exploratory Cross-Study Comparison Stratified by Relative Chemoimmunotherapy Intensity



Supplementary Figure S3. Forest Plot of Treatment-Related Mortality. (A) Pooled Estimate. (B) Exploratory Cross-Study Comparison Stratified by Relative Chemoimmunotherapy Intensity



Supplementary Figure S4. Forest Plot of Veno-Occlusive Disease. (A) Pooled Estimate. (B) Exploratory Cross-Study Comparison Stratified by InO Administration Regimen



Supplementary Figure S5. Sensitivity analyses of binary efficacy and safety endpoints using a random-effects model. Forest plots display the exploratory cross-study comparisons calculated via the DerSimonian-Laird random-effects method for (A) overall response rate (ORR) stratified by relative chemoimmunotherapy intensity, (B) treatment-related mortality (TRM) stratified by relative chemoimmunotherapy intensity, and (C) veno-occlusive disease (VOD) incidence stratified by inotuzumab ozogamicin (InO) administration regimen

