PCN36

OVERALL COMPLETE REMISSION RATE (OCRR) AND COMPLETE REMISSION RATE (CR) OF STANDARD OF CARE (SoC) IN RELAPSED/REFRACTORY (R/R) ADULT ACUTE LYMPHOBLASTIC LEUKEMIA (aALL): A META-ANALYSIS

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BACKGROUND

- Acute lymphoblastic leukemia (ALL) is a heterogeneous group of lymphoid disorders that results from the clonal proliferation of immature lymphocytes of B-cell or T-cell lineage in the blood, bone marrow, and other organs.[1]
- Effective treatment options for R/R B-precursor ALL are limited, and approximately half of adult patients are refractory or relapse after receiving first-line treatment.[2]

RESEARCH OBJECTIVES

- To better understand treatment effectiveness beyond first-line, this study aims to estimate OCRR (CR or CR with incomplete hematologic recovery) and CR in R/R aALL from published trials on approved and recommended standard of care (SoC) treatments.

METHODS

- A meta-analysis was conducted using published data from clinical trials of latest European Society for Medical Oncology (ESMO)[3] and National Comprehensive Cancer Network (NCCN)[4] guideline-recommended agents in R/R aALL patients. Publications identified through a systematic literature review (SLR) conducted in June 2019 were evaluated for meta-analysis inclusion based on the following criteria:
  - Interventions and comparator treatments were licensed within both European Union and the United States for R/R aALL, including salvage chemotherapy, blinatumomab, inotuzumab, and tyrosine kinase inhibitors (TKI)-based regimens
  - Report of OCRR or CR outcome
  - Patient population age is ≥18 years with refractory or relapsed ALL
  - Study has a (randomized) clinical trial design
- The best fitting model (fixed, random effect models) was used to estimate pooled CR and OCRR. Analysis of the variability in the studies by means of I^2 and Bayesian Information Criterion (BIC) demonstrated that the random effects model was the preferred model.
- The base case analysis included all eligible studies.
- A scenario analysis was performed for studies representing more severe patient populations.
  - ≥ 50% of patients having received 2 or more prior lines of treatment
  - Heavy bone marrow blast (BMB) burden; median BMB burden ≥50% or ≥50% of trial patients with BMB ≥50%

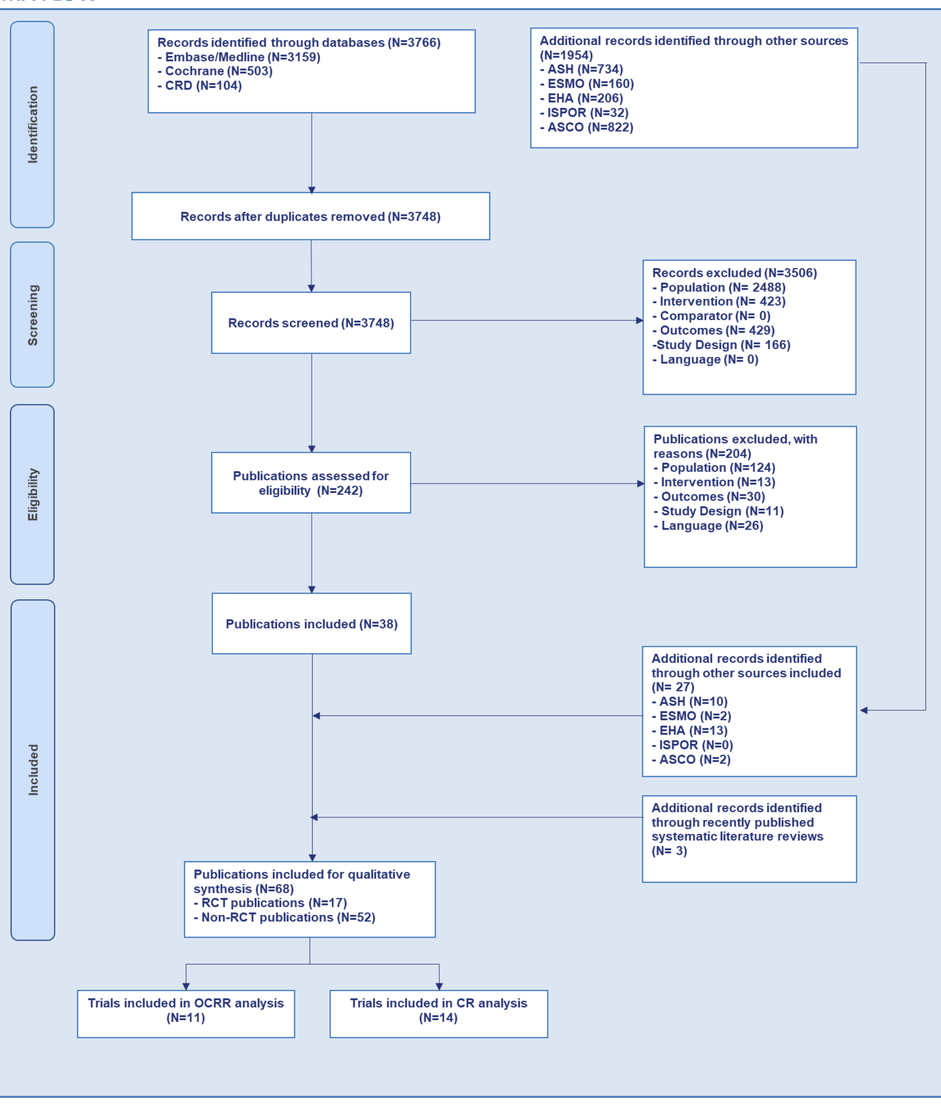
RESULTS

- The SLR identified 68 eligible publications through Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). In the base case, 11 and 14 trials were included for the OCRR- and CR meta-analysis, respectively (Figure 1).

BASELINE CHARACTERISTICS

- 1,197 treated patients were included in the OCRR analysis. The weighted average age was 42 years old. The weighted BMB was 72%. 57% patients received 3 or more prior lines of therapies.
- 1,204 treated patients were included in the CR pooled analysis. The weighted average age was 42 years old. The weighted average BMB was 74%. 58% received 3 or more prior lines of therapies.
- Study and treatment-specific patient baseline characteristics are summarized in Table 1.

FIGURE 1: PRISMA FLOW



OCRR META-ANALYSES

- Eleven studies, comprising a total of thirteen treatment arms were included in the primary analysis (Table 1).
- In the base case (Figure 2), pooling all treatments resulted in an OCRR of 51% (95% CI: 42%-59%).
- In the scenario analysis (Figure 2), pooling resulted in a OCRR of 47% (95% CI: 37%-57%).

CR META-ANALYSES

- Fourteen studies, comprising a total of sixteen treatment arms were included in the primary analysis (Table 1).
- In the base case (Figure 2), pooling all treatment arms resulted in a CR of 38% (95% CI: 28%-49%).
- In the scenario analysis (Figure 2), pooling resulted in a CR of 30% (95% CI: 23%-36%).

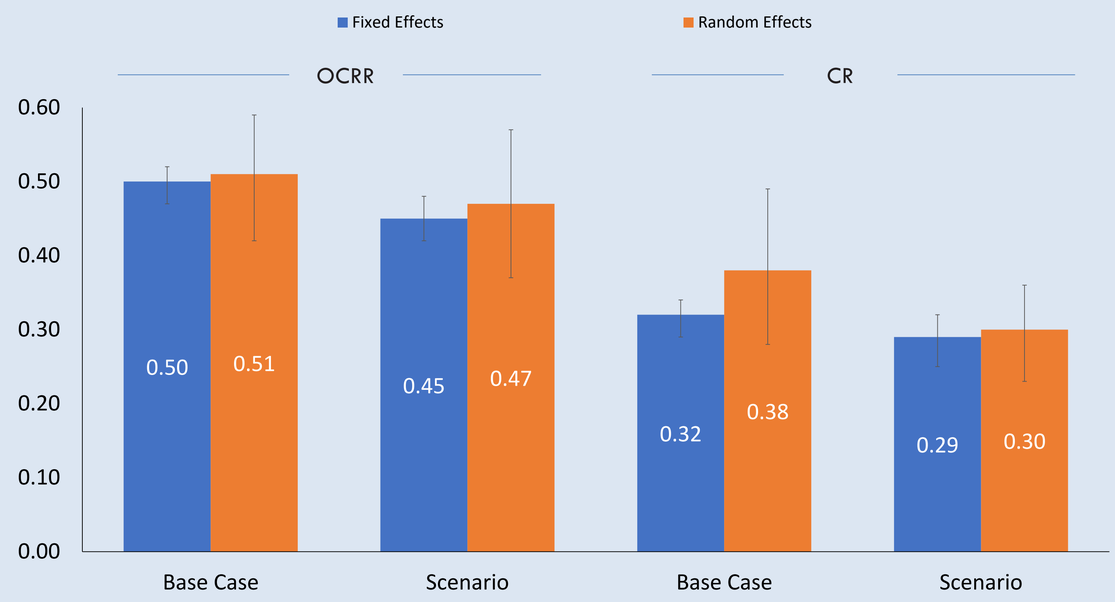
RESULTS Cont.

TABLE 1: OVERVIEW OF INCLUDED TRIALS: BASELINE CHARACTERISTICS AND RESPONSE OUTCOMES

	Study	Treatment	Treated (N)	Age	LoT at baseline (% patients)	BMB ≥50% (% patients)	Median BMB (%)	OCRR/ CR	B	S	OCRR/ CR (% patients)
Salvage chemotherapy	GIMEMA	Salvage chemotherapy	27	39 (median)	2L+ (NR)	NR	73%	OCRR, CR	✓		OCRR: 62% CR: 19%
	SWOG S0910	Salvage chemotherapy	31	41 (median)	2L+ (NR)	NR	NR	OCRR, CR	✓		OCRR: 52% CR: 32%
	INO-VATE	Salvage chemotherapy	109	47 (median)	2L+ (2L: 63%, 3L: 36%, NA: 1%)	70%	NR	OCRR, CR	✓		OCRR: 35% CR: 17%
	TOWER	Salvage chemotherapy	134	41 (mean)	2L+(2L:49%, 3L:32%, 4L+:19%)	78%	NR	OCRR, CR	✓	✓	OCRR: 30% CR: 16%
	Kadja et al. 2015	Salvage chemotherapy	24	42 (median)	2L+ (2L:32%, 3L:38%, 4L+:30%)	NR	79%	CR	✓	✓	CR: 17%
Blina- or InO-based regimens, regardless of SCT status	INO-VATE	InO	109	47 (median)	2L+ (2L:68%, 3L: 31%, NA: 1%)	66%	NR	OCRR, CR	✓		OCRR: 74% CR: 36%
	TOWER	Blina	271	41 (mean)	2L+ (2L:42%, 3L:33%, 4L+:25%)	74%	NR	OCRR, CR	✓	✓	OCRR: 45% CR :34%
	NCT01371630	InO+CT	59	35 (median)	2L+ (2L:56%, 3L:22%, 4L+:22%)	71%	NR	OCRR, CR	✓		OCRR: 61% CR: 59%
	NCT01363297	InO	72	45 (median)	2L+ (2L:22%, 3L: 40%, 4L:25%, 5L+:13%)	81%	NR	OCRR, CR	✓	✓	OCRR: 68% CR: 32%
	Aboudalle et al. 2018	Blina	35	28 (median)	2L+ (2L:29%, 3L:20%, 4L:29%, 5L+:22%)	NR	69%	OCRR, CR	✓	✓	OCRR: 49% CR: 37%
	NCT02000427	Blina	45	55 (median)	2L+ (2L: 16%, 3L:47%, 4L: 29%, 5L: 9%)	76%	NR	OCRR, CR	✓	✓	OCRR: 36% CR: 31%
	Kobayashi et al. 2018	Blina	21	43 (median)	3L+ (3L:33%, 4L:19%, 5L:14%)	NR	69%	OCRR	✓	✓	OCRR: 38%
	NCT01209286	Blina	36	32 (median)	2L+ (2L:42%, 3L+:58%)	NR	77%	OCRR, CR	✓	✓	OCRR: 69% CR: 42%
	NCT01466179	Blina	189	39 (median)	2L+ (2L:20%, 3L: 41%, 4L:22%, 5L+:17%)	69%	NR	OCRR, CR	✓	✓	OCRR: 43% CR: 33%
	Yoon et al., 2019	Blina	32	NR	2L+ (NR)	NR	NR	CR	✓		CR: 72%
	NCT00198978	Blina	20	NR	2L+ (NR)	NR	NR	CR	✓		CR: 60%
	Sokolov et al., 2018	Blina+TKI	11	39 (median)	2L+ (NR)	NR	NR	CR	✓		CR: 91%

Key: 2L, second line; 3L, third line; 4L, fourth line; 5L, fifth line; B, base case analysis; Blina, blinatumomab; BMB, bone marrow blast; CR, complete remission rate; InO, inotuzumab ozogamicin; LoT, line of treatment; NE, not estimable; NR, not reported; OCRR, overall complete remission rate; OS, overall survival; S, scenario analysis; TKI, tyrosine kinase inhibitor; *Range: 0.2-68

FIGURE 2: META-ANALYSIS RESULTS



Arm (N)	13	8	16	8
I^2	88%	86%	93%	72%
BIC	69.14 -6.53	12.92 -3.26	91.68 1.13	-1.85 -9.56

Key: BIC, Bayesian Information Criterion; CR, complete remission rate N, number; OCRR, overall complete remission rate
Error bar in figure represents 95% confidence interval

LIMITATIONS

- Results are representative of unadjusted baseline characteristics across studies. There was some heterogeneity in terms of sex and prior line of treatments, and the results might not be representative of a given real world population.
- The number of treated patients among the included studies varies from 21 to 267 per study arm, which may not reflect the treatment landscape in the real world setting.

CONCLUSIONS

- SoC for R/R aALL patients comprises multiple therapeutic options, none providing optimal response.
- The study confirms the unmet needs for the care of R/R aALL patients require better treatment options.

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