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Feasibility and safety of venetoclax-obinutuzumab in fit and unfit CLL patients: comparison of CLL13/CLL14 pooled analysis with an Italian clinical practice cohort

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INTRODUCTION

- Based on the CLL13 and CLL14 clinical trials (CT), **fixed-duration venetoclax–obinutuzumab (VO)** became a **standard first-line treatment** for chronic lymphocytic leukemia (CLL) patients, both fit and with comorbidities.
- However, **longitudinal data in clinical practice (CP)** on VO feasibility and outcomes remain largely **unexplored.**

AIM

To compare the **feasibility and safety** of fixed-duration VO in Clinical Practice versus Clinical Trials.

METHODS

- **Separate descriptive analyses** for the **pooled CLL13/CLL14 CT** patients **and a multicenter, retrospective Italian CP cohort** (55 university/community hospitals, from May 2022 to June 2023).
- **Patients grouped by fitness status** (unfit:CIRS>6 and/or CrCL<70 ml/min; fit:CIRS≤6 and CrCl≥70 ml/min)
- **Toxicity and schedule modifications assessed by treatment phases** (early combination EaC; cycles, C1–2; combination COMB; C3–6; maintenance MAINT; C7 to end of treatment +28 days).
- **Adverse events** (AE) prospectively graded per Common Terminology Criteria for AE in CT and retrospectively collected in CP cohort.
- Patients visits **in CP** followed **site-specific standards of care.**

RESULTS

711 patients, median follow-up 72.3 months for CT and 29.3 months for CP.

Baseline characteristics according to cohort

Comparison of characteristics	Clinical Trials, n= 440	Clinical Practice, n=271
Female Sex, n (%)	313 (71.1)	179 (66.1)
Median Age, years (IQR)	67 (58-73)	65.8 (58-73.6)
ECOG ≥ 1, n (%)	**187 (42.5)**	**80 (29.5)**
CIRS > 6, n (%)	**183 (41.6)**	**56 (20.7)**
Number concomitant medications, median (IQR)	1 (0-4)	1 (0-3)
Creatinine clearance ml/min, median (IQR)	77.1 (60.1-95-1)	77 (61.9-91.7)
Unmutated IGHV status, n (%)	**249 (59)**	**130 (51.2)**
TP53 mutation/17p deletion, n (%)	25 (5.7)	10 (3.8)
Hemoglobin g/L, median (IQR)	116 (00-130.4)	118 (100-132)
Absolute Neutrophil count 10^9/L, median (IQR)	4.1 (2.5-6.4)	4.1 (2.76.4)
Platelet count 10^9/L, median (IQR)	141.5 (104-193.8)	145 (96-200)
Tumor Lysis Syndrome high risk, n (%)	60 (14)	60 (22.1)
Unfit patients, n (%)	**257 (58.5)**	**133 (49.1)**

Feasibility and treatment management outcomes according to cohort

	C1-2	C3-6	C7-EoT + 28 days
V dose intensity <70% in CT, %	22.7	18.9	22.9
V dose intensity <70% in CP, %	7	10.4	11.8
O dose intensity <100% in CT, %	11.8	9.5	
O dose intensity <100% in CP, %	13.5	8.4	

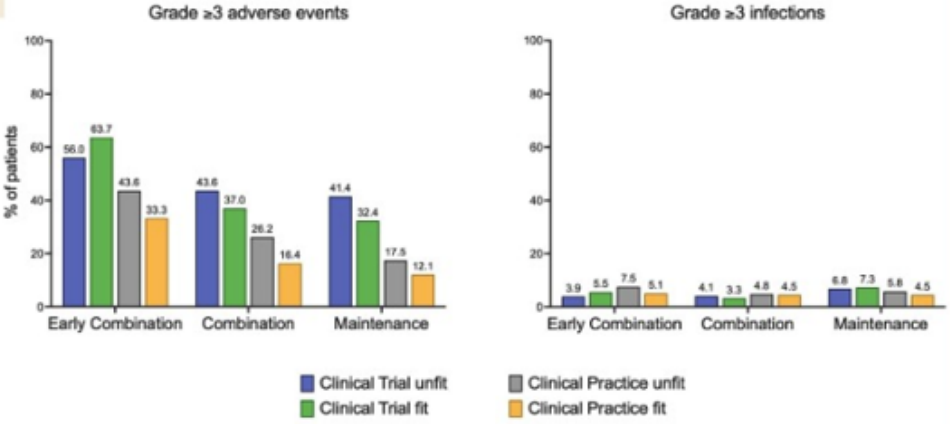
	Clinical Trial (CT)	CT unfit	CT fit	Clinical Practice (CP)	CP unfit	CP fit
Treatment completion, %	86.6	81.7	93.4	89.3	88	90.6
Toxicity-driven discontinuation, %	8	10.5	4.4	10	11.3	8.7
Tumor lysis syndrome, %	6.6	Not analyzed	Not analyzed	5.9	Not analyzed	Not analyzed
Infusion Related Reactions, %	48.6	Not analyzed	Not analyzed	36.9	Not analyzed	Not analyzed

Time-to-event exploratory endpoints at 24 months

	CLinical Trial unfit %	Clinical Trial fit %	Clinical Practice unfit%	Clinical Practice fit %
Progression-free survival	88.7	92.8	87.7	96.3
Overall survival	92.5	99.4	89.2	98.5
Time to next treatment	95.9	97.8	97.7	97.8
Treatment-free survival	89.7	97.2	87.7	96.3

Grade ≥3 AEs occurred more frequently in CT than CP during EaC (59.3% vs 38.4%), COMB (40.9% vs 21.2%) and MAINT (37.3% vs 14.7%).
G≥3 infections occurred in 4.5%, 3.8% and 7% during EaC, COMB and MAINT in CT, and in **6.3%, 4.6% and 5.2% in CP, respectively.**

Rates of grade ≥3 adverse events and infections by fitness status and treatment phase



CONCLUSIONS

- In this large comparative analysis, **VO** appeared **consistent with trials and feasible in clinical practice.**
- Although G≥3 AE and V dose intensity reductions were numerically higher in CT cohort, **rates of severe infections and discontinuations due to toxicity were consistent** between cohorts.
- Despite the more systematic reporting in clinical trials and the short FU time of the CP data**, the analysis supports VO use as frontline treatment in routine clinical practice.**

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