

Should we treat newly diagnosed patients with CLL differently after ASH 2019?

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## Abbreviations

BR, bendamustine + rituximab; CLL, chronic lymphocytic leukemia; FCR, fludarabine + cyclophosphamide + rituximab; obi, obinutuzumab

	CLL10 <sup>1</sup>		CLL11 <sup>2</sup>		CLL14⁴		RESONATE-2 <sup>5</sup>		iLLUMINATE <sup>6,*</sup>		ALLIANCE A041202 <sup>7</sup>			ECOG-ACRIN E1912 <sup>8,*</sup>	
Median FU	37.1 months		CG vs Clb: 62.5 months CG vs R-Clb: 59.4 months		28.1 months		29 months		31.3 months		38 months			33.6 months	
Treatment	FCR	BR	CG vs Clb	CG <i>vs</i> R-Clb	VenG	CG	I	Clb	IG	CG	BR	I.	IR	FCR	IR
PFS (%)	mPFS 55.2 m	mPFS 41.7 m	5-year 25 <i>vs</i> 2	5-year 23 <i>vs</i> 9	24-month 88.2	24-month 64.1	24-month 89%	24-month 34%	30-month 79	30-month 31	2-year 74	2-year 87	2-year 88	3-year 72.9	3-year 89.4
OS (%)	3-year 92	3-year 91	5-year 66 <i>vs</i> 53	5-year 66 <i>v</i> s 57	24-month 91.8	24-month 93.3	24-month 95%	24-month 84%	30-month 86	30-month 85	2-year 95	2-year 90	2-year 94	3-year 91.5	3-year 98.8
ORR (%)	95	96	CG: 77.3; Clb: 31.4; R-Clb: 65.7 <sup>3</sup>		84.7	71.3	92	_	88	85	81	93	94	81.1	95.8
CR (%)	40	31	CG: 22.3 R-Cll	3; Clb: 0; p:7.3 <sup>3</sup>	49.5	23.1	18	—	22	8	26	7	12	30.3	17.2
Safety	Severe neutropenia and infections more frequently observed with FCR compared with BR (84% vs 59% and 39% vs 25%, respectively)		Grade 3-5 AEs: 74% vs 51%. Prolonged neutropenia: 3% vs 9%. Late onset neutropenia: 17% vs 11%	Grade 3-5 AEs: 72% vs 60%. Prolonged neutropenia: 2% vs 4%. Late onset neutropenia: 15% vs 12%	Grade 3/4 neutropenia: 52.8% VenG group and 48.1% CG group. Grade 3/4 infections: 17.5% VenG group and 15.0% CG group		Most frequent AEs with ibrutinib: diarrhea (45%), fatigue (33%), cough (28%), anemia (23%), nausea (23%). Grade ≥ 3 AEs generally more frequent during the first 12 months of ibrutinib therapy and generally decreased over time		Most common Grade 3/4 AEs in both groups: neutropenia and thrombocytopenia		Higher rate of Grade 3–5 hematologic AEs with BR (61%) vs I (41%) and IR (41%). Lower rate of non-hematologic AEs with BR (63% vs 74% for each I-containing regimen)			Grade ≥3 infectious complications more common with FCR (20.3%) vs IR (10.5%)	

\* In the iLLUMINATE trial, patients were aged  $\geq$ 65 years and in the ECOG-ACRIN E1912 trail, patients were aged  $\leq$ 70 years (in all the other trials patient age was >18 years)

## Abbreviations

AE, adverse event; BR, bendamustine + rituximab; Clb, chlorambucil; CG, chlorambucil + obinutuzumab; CR, complete response; FC, fludarabine + cyclophosphamide; FCR, fludarabine + cyclophosphamide + rituximab; FU, follow-up; I, ibrutinib; IG, ibrutinib + obinutuzumab; IR, ibrutinib + rituximab; mPFS, median progression-free survival; ORR, overall survival; PFS, progression-free survival; R, rituximab; VenG, venetoclax + obinutuzumab; VR, venetoclax + rituximab

**1.** Eichhorst B., *et al. Lancet Oncol.* 2016;17:928–42; **2.** Goede V., *et al.* EHA 2018. Abstract S151; **3.** Goede V., *et al. N Engl J Med.* 2014;370:1101–10; **4.** Fischer K., *et al. N Engl J Med.* 2019;380:2225–36; **5.** Barr P.M., *et al. Haematologica.* 2018;103:1502–10; **6.** Moreno C., *et al. Lancet Oncol.* 2019;20:43–56; **7.** Woyach J., *et al. N Engl J Med.* 2018;379:2517–28; **8.** Shanafelt T.D., *et al. N Engl J Med.* 2019;381:432–43



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