



Appendix 13 - CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

Approved settings/ treatment line	Chemotherapy protocols	Drugs in abbreviation	Evidence Category
1st line CLL with del(17p)/ TP53 mutation	Ibrutinib		Category 2A, Preferred
	Venetoclax + Obinutuzumab		Category 2A, Preferred
	Alemtuzumab ± Rituximab		Category 2A
	Obinutuzumab		Category 2A
	HD MethylPrednisolone + Rituximab		Category 2A
1st line CLL with del(17p)/ TP53 mutation	Ibrutinib		Category 2A, Preferred
	Venetoclax + Obinutuzumab		Category 2A, Preferred
	Alemtuzumab ± Rituximab		Category 2A
	Obinutuzumab		Category 2A
	HD MethylPrednisolone + Rituximab		Category 2A
1st line CLL without del(17p)/ TP53 mutation for patients with comorbidities*	Ibrutinib		Category 1, Preferred
	Venetoclax + Obinutuzumab		Category 2A, Preferred
	Bendamustine + Rituximab		Category 2A
	Bendamustine + Obinutuzumab		Category 2A
	Chlorambucil + Obinutuzumab		Category 2A
	HD MethylPrednisolone + Rituximab		Category 2B
	Ibrutinib + Obinutuzumab		Category 2B
	Obinutuzumab		Category 2B
	Chlorambucil		Category 3
Rituximab		Category 3	
1st line CLL without del(17p)/ TP53 mutation for patients without comorbidities*	Ibrutinib		Category 1, Preferred
	Venetoclax + Obinutuzumab		Category 2A, Preferred
	Bendamustine + Rituximab		Category 2A
	Bendamustine + Obinutuzumab		Category 2A
	FCR	Fludarabine, Cyclophosphamide, Rituximab	Category 2A
	FR	Fludarabine, Rituximab	Category 2A
	HD MethylPrednisolone + Rituximab		Category 2B
	Ibrutinib + Rituximab		Category 2B
Maintenance therapy CLL without del(17p)/ TP53 mutation**	Lenalidomide		Category 2A



	Chemotherapy protocols	Drugs in abbreviation	Evidence Category
Relapsed/ refractory CLL without del(17p)/ TP53 mutation for patients with comorbidities*	Ibrutinib		Category 1, Preferred
	Venetoclax + Rituximab		Category 1, Preferred
	Alemtuzumab ± Rituximab		Category 2A
	Chlorambucil + Rituximab		Category 2A
	Reduced dose FCR	Fludarabine, Cyclophosphamide, Rituximab	Category 2A
	HD MethylPrednisolone + Rituximab		Category 2A
	Lenalidomide ± Rituximab		Category 2A
	Obinutuzumab		Category 2A
	Ofatumumab		Category 2A
	Venetoclax		Category 2A
	Dose-dense Rituximab		Category 2B
	Bendamustine + Rituximab ± Ibrutinib		Category 2B
Relapsed/ refractory CLL without del(17p)/ TP53 mutation for patients without comorbidities*	Ibrutinib		Category 1, Preferred
	Venetoclax + Rituximab		Category 1, Preferred
	Alemtuzumab ± Rituximab		Category 2A
	Bendamustine + Rituximab		Category 2A
	FC + Obinutuzumab	Fludarabine, Cyclophosphamide	Category 2A
	FCR	Fludarabine, Cyclophosphamide, Rituximab	Category 2A
	HD MethylPrednisolone + Rituximab		Category 2A
	Lenalidomide ± Rituximab		Category 2A
	Obinutuzumab		Category 2A
	Ofatumumab		Category 2A
	Venetoclax		Category 2A
	Bendamustine + Rituximab + Ibrutinib		Category 2B
Post 2nd line maintenance therapy CLL without del(17p)/ TP53 mutation	Lenalidomide		Category 2A
	Ofatumumab		Category 2B

* (Inability to tolerate purine analogues, Age ≥ 65 years, CrCl < 70 ml/min

** Blood MRD ≥ 10⁻² or ≥ 10⁻⁴ and < 10⁻² with unmutated IGHV after 1st line therapy