Cost-Effectiveness of *TP53* and *IGHV* Biomarker Testing Prior to First-Line Treatment With Novel Agents for Chronic Lymphocytic Leukemia

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Background

- Tumor suppressor p53 (*TP53*) aberrations (including mutations and deletions of 17p) and unmutated immunoglobulin heavy chain (*IGHV*-U) are associated with reduced survival and resistance to chemoimmunotherapy (CIT) regimens such as fludarabine, cyclophosphamide and rituximab (FCR) combination therapy for patients with chronic lymphocytic leukemia (CLL)[1].
- Novel agents such as ibrutinib represent an alternative effective treatment choice for patients with *TP53* aberrations and/or *IGHV*-U[2].
- While ibrutinib is reimbursed in Australia for first-line treatment in patients with deletions of 17p, i.e., del(17p), a subgroup of high-risk patients with CLL is potentially without effective treatment[3].

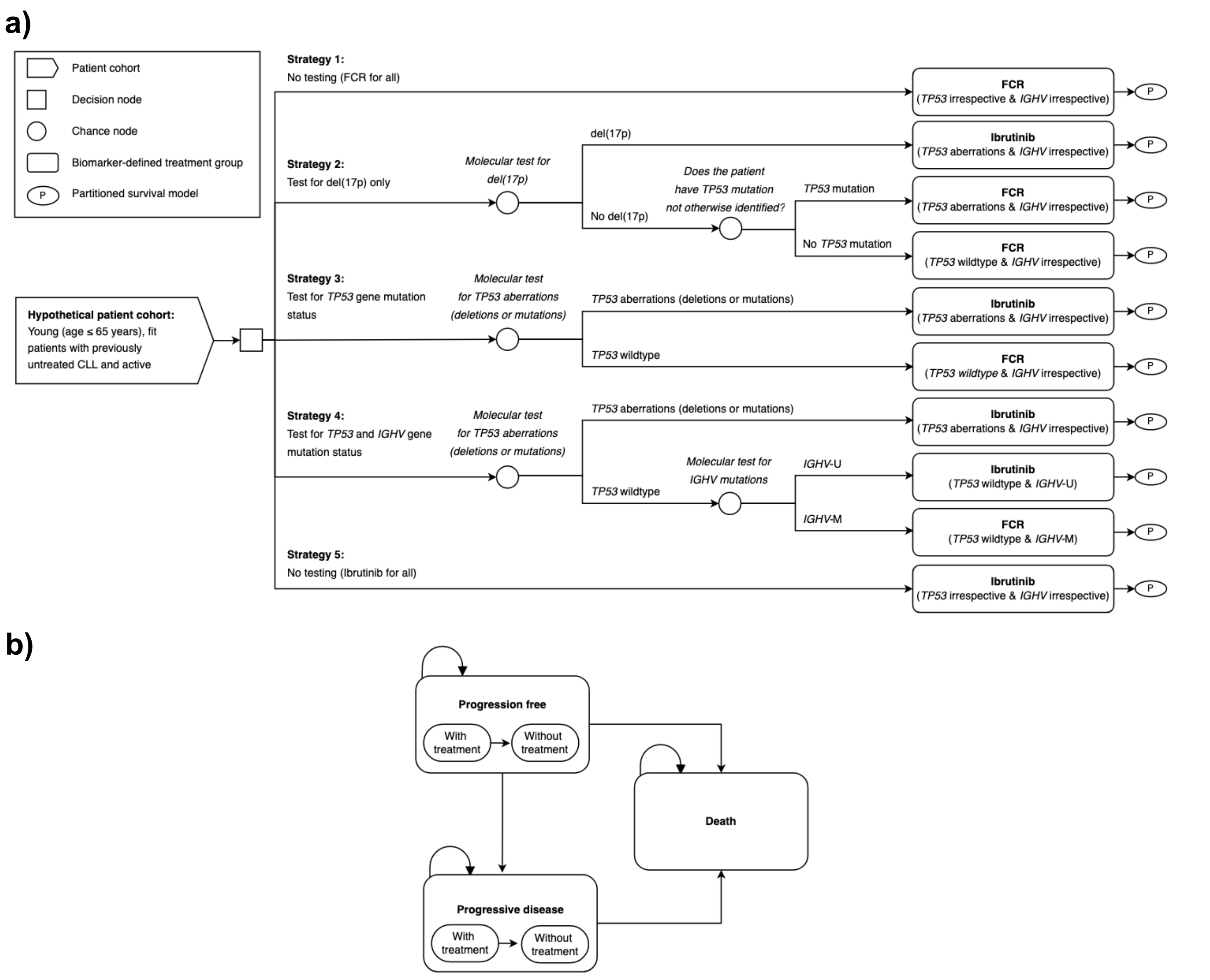
Objective

- This study assessed the cost-effectiveness of strategies for first-line treatment in CLL:
  - Strategy 1: no testing (FCR for all)
  - Strategy 2: test for del(17p) only
  - Strategy 3: test for *TP53* gene mutation status
  - Strategy 4: test for *TP53* and *IGHV* gene mutation status
  - Strategy 5: no testing (ibrutinib for all).

Method

- Decision analytic model consisting of a decision tree and partitioned survival model (PSM) evaluated the lifetime costs and health consequences of first-line treatment (either FCR or ibrutinib) in a hypothetical cohort of young (age ≤ 65 years) fit patients with active CLL disease (Figure 1).
- Perspective of the Australian healthcare system over a lifetime horizon and discounted at an annual rate of 5%. Model cycle length of four weeks were used to reflect a typical CLL treatment cycle.
- State membership estimated from indirect treatment comparisons and survival analysis using public literature.
- Costs, utility scores and adverse events derived from public literature.
- Model outcomes included incremental cost-effectiveness ratio (ICER) and net monetary benefit (NMB) with a willingness-to-pay (WTP) threshold of 100,000 Australian dollars (AUD) per quality-adjusted life year (QALY) gained.
- Deterministic sensitivity and probabilistic analyses quantified the impact of model assumptions and uncertainties on outcomes.

Figure 1. Decision analytic model: a) decision tree and b) partitioned-survival model



Conclusion

- Testing for *TP53* and *IGHV* gene mutation status improved health outcomes for patients with CLL
- Testing for *TP53* and *IGHV* gene mutation status could be cost-effective at a WTP threshold of 155,000 AUD per QALY gained or at lower per cycle treatment cost of ibrutinib

References

1. Fischer K, Bahlo J, Fink AM, *et al.* Blood. 2016;127(2):208-15.
2. Boddy CS, Ma S. Curr Hematol Malig Rep. 2018;13(2):69-77.
3. Pharmaceutical Benefit Schedule. https://www.pbs.gov.au/pbs/industry/listing/elements/pbac-meetings/psd/2019-11/ibrutinib-capsule-140-mg-imbruvica. Accessed 9 June 2022.

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Results

Table 1. Health economic outcomes from probabilistic analysis

Strategy	Mean discounted cost (AUD) (95% CI)	Mean discounted effectiveness (QALY) (95% CI)	Incremental cost (AUD) (95% CI)	Incremental effectiveness (QALY) (95% CI)	ICER (AUD per QALY gained)	NMB (AUD)*
Strategy 1	458,836 (236,792-786,314)	5.69 (2.85-10.22)	-	-	-	110,454
Strategy 2	496,076 (276,922-812,501)	5.96 (3.14-10.43)	37,240 (12,579-69,118)	0.27 (0.03-0.56)	138,698	100,064
Strategy 3	510,821 (293,728-823,194)	6.07 (3.24-10.53)	14,745 (4,779-29,580)	0.11 (0.01-0.24)	140,013	95,850
Strategy 4	742,038 (566,610-1,042,805)	7.47 (4.21-11.83)	231,217 (38,258-430,793)	1.41 (-1.06-3.51)	164,462	5,224
Strategy 5	861,394 (669,429-1,264,748)	7.58 (3.84-12.24)	119,356 (2,722-263,980)	0.11 (-1.06-1.16)	1,124,983	-103,523

* NMB calculated using a WTP threshold of 100,000 AUD per QALY gained

Figure 2. Cost-effectiveness plane

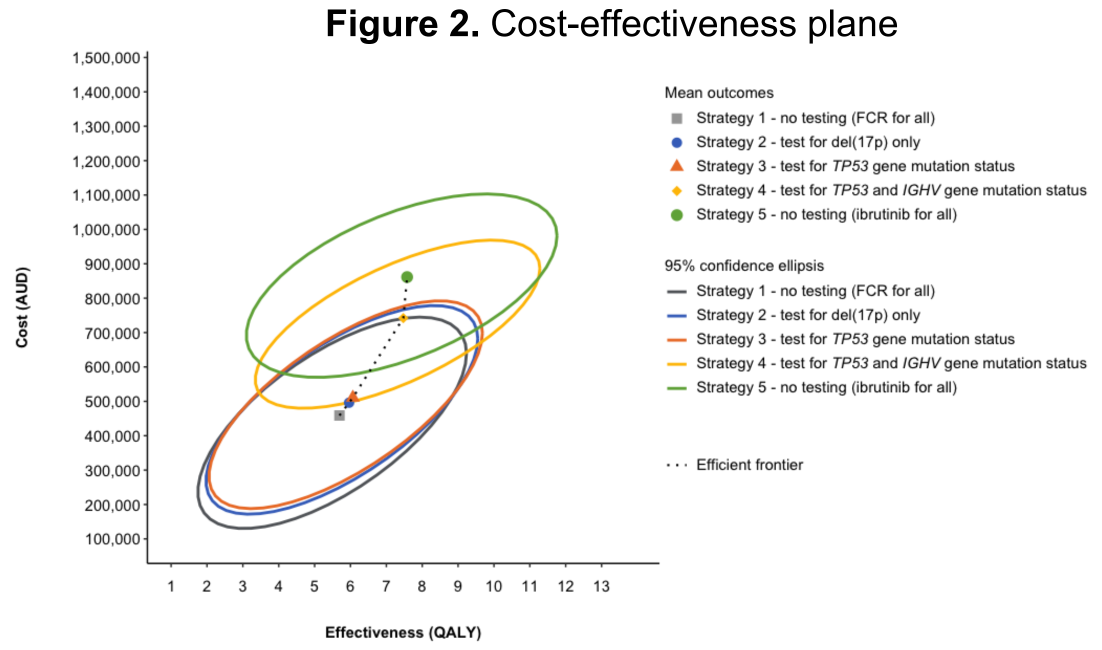


Figure 3. Cost-effectiveness acceptability curve*

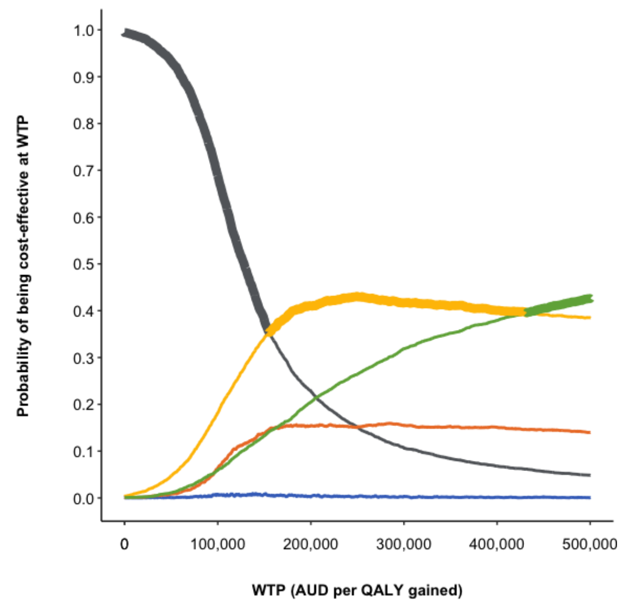
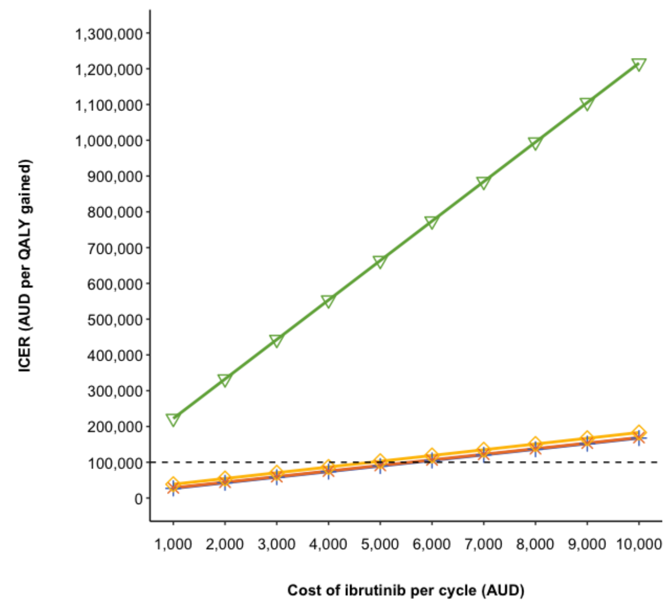


Figure 4. Threshold analysis of cost of ibrutinib



* Thick border line corresponds to the cost-efficient frontier.

Figure 5. Tornado diagram of deterministic sensitivity analysis