Genomic screening costs in modelling: a penalty for innovation?

Karissa Johnston,[1] Greta Lozano-Ortega,[1] Matt Hodgson,[2] Florian Csintalan,[2] Clarissa Zerbini,[2] Julian Nam[2]
[1]Broadstreet HEOR, Vancouver, Canada; [2] Hoffmann-La Roche Limited

BACKGROUND

- Advances in precision oncology towards genomically-guided treatment with targeted therapies have contributed to greater efficacy and safety outcomes among individuals with actionable mutations.
- "Genomic testing"—which may be comprised of single-gene tests, or panel tests for multiple known mutations—are required to identify individuals as candidates for corresponding targeted therapies.
- However, at the population level, the cost of testing can be considerable. For a rare mutation, a substantial number of tests will be required to detect each positive case.
- Based on principles of pharmacoeconomic evaluation, the costs of genomic testing may be included in economic evaluations of targeted therapies if they are associated with introducing new genomic tests that are not currently in routine use.
- If including the cost of testing in economic modelling is dependent on whether a test is already in routine use, treatments that target a novel mutation, which are associated with the introduction of new testing, consequently absorb the additional costs.
- Conversely, subsequent therapies targeting the same mutation may benefit from "spillover effect" in which existing testing practices provide the necessary diagnostic information without the need for additional costs to be included.
- The objective of this study was to further explore this dynamic, and assess the impact of attributing genomic testing costs to a novel targeted therapy for rare oncological mutations, when subsequent entrants are anticipated.

METHODS

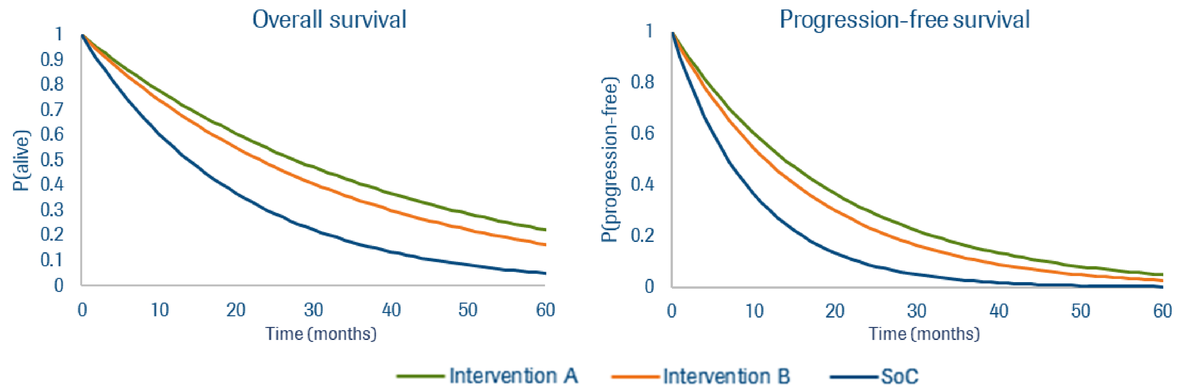
- A simulated example was developed to demonstrate that by including the cost of new testing in economic evaluation of a targeted therapy, the first-to-market drug can appear less cost-effective than subsequent entrants, even in situations where the second entrant is less efficacious and / or more costly.
- A deterministic partitioned-survival cost-utility analysis was developed for a hypothetical cancer with a rare gene mutation "mutation X" (assumed prevalence of 0.29%).
- Intervention A, a novel targeted therapy, was assumed to launch with evidence of a net clinical benefit vs. standard of care (SOC), reflected by a hazard ratio (HR) of 0.5 for overall survival (OS) and progression-free survival (PFS). Second-entrant targeted therapy, intervention B, had a slightly less favourable clinical profile, reflected by a HR of 0.6 relative to the SOC for both OS and PFS. (**Figure 1**).
- Intervention B was priced at parity to intervention A ($8,000 / month), both at a premium relative to SOC ($5,000 / month).
- Genomic testing for mutation X was assumed not to be routinely conducted at the time of intervention A entering the market, but was assumed to be routinely conducted at the time of entry of intervention B to market.
- Consequently, in cost-effectiveness analysis, the cost of testing ($1,500 / genomic test, with 345 tests required to identify each individual with the mutation) was absorbed by intervention A, and the cost-utility analysis included the cost of testing mutation positive and negative patients.
- As intervention B was a subsequent entrant at a time when the test would be routinely used, the cost of testing was not considered in evaluations of intervention B.
- Utility values were health state-specific, and were assumed to be 0.9 in pre-progression and 0.5 in post progression.
- The incremental cost-utility ratio (ICUR) was estimated over a 5-year time horizon.
- Several sensitivity analyses were conducted by varying reference case parameters (**Table 1**).

Table 1. Parameters varied in sensitivity analysis

	Lower value	Reference	Upper value
Intervention A HRs (OS and PFS) vs SOC	0.4	0.5	0.6
Post-progression utility	0.3	0.5	0.7
Prevalence of mutation X		0.29%	4%
Unit cost of test	$500	$1,500	$2,000
Intervention A cost	$6,400	$8,000	$9,600

HR: hazard ratio; PFS: progression-free survival; OS: overall survival; SOC: standard of care.

Figure 1. Overall and progression-free survival assumptions

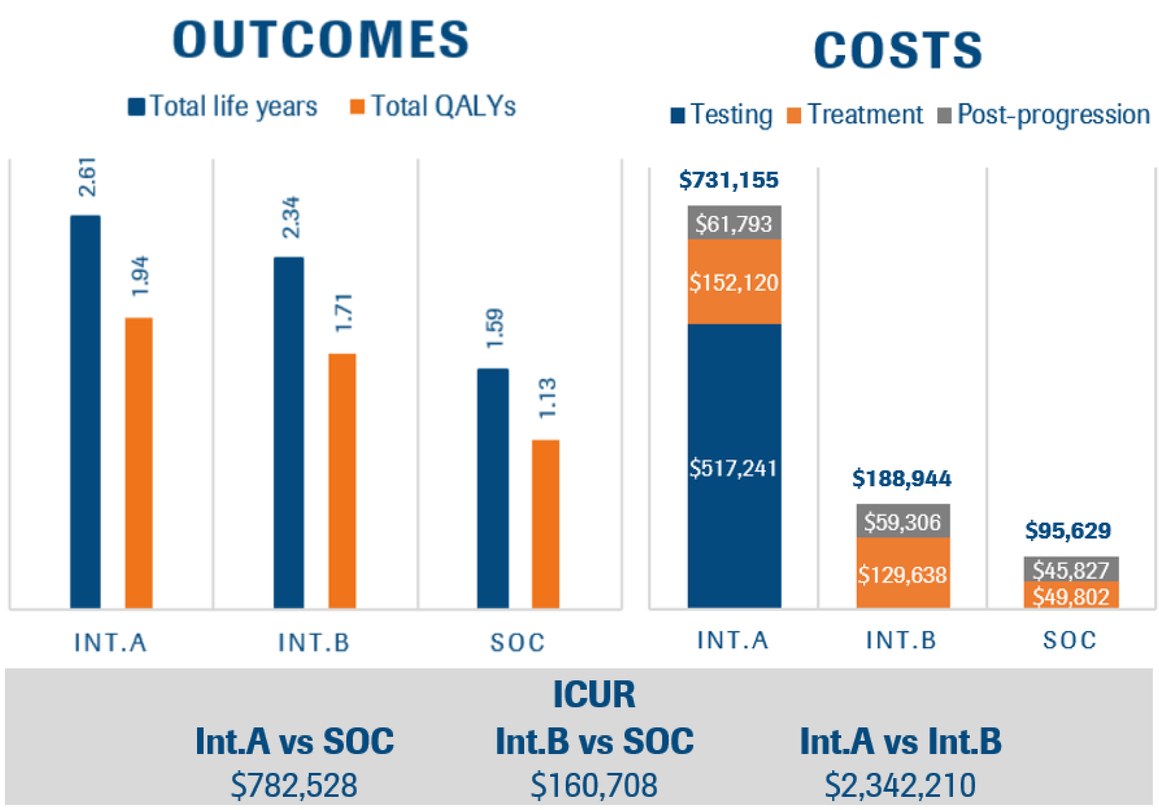


Targeted therapies A and B are both superior to SOC, and first entrant therapy A is slightly superior to second entrant therapy B.

SoC: standard of care.

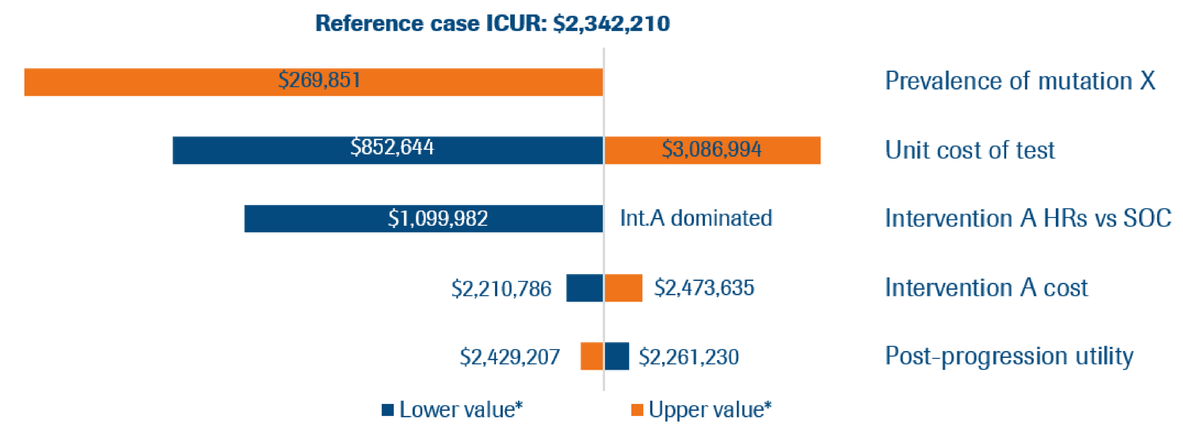
RESULTS

Figure 2. Cost-utility analysis results



Int.A: intervention A; Int.B: intervention B; ICUR: incremental cost-utility ratio; QALYs: quality adjusted life years; SoC: standard of care.

Figure 3. Sensitivity analysis for the comparison of intervention A vs. intervention B (ICUR)



* Lower and upper values used in sensitivity analysis are described in Table 1

ICUR: incremental cost-utility ratio; Int.A: intervention A; SOC: standard of care.

- Intervention A resulted in greater life years and QALYs relative to both Intervention B and SOC, however it was also associated with considerably greater costs, attributable to the cost of testing. Intervention A was also associated with a small increase in treatment costs than intervention B due to its favourable PFS (**Figure 2**).
- The ICUR of intervention A vs. intervention B was highly reduced when the prevalence of the mutation was increased to 4% (**Figure 3**).
- Results were also sensitive to differences in survival relative to SOC; however, a variation range of possible values in the cost of the test also led to substantial variations to the estimated ICUR (**Figure 3**).

CONCLUSIONS

- Testing creates spillover effects that can benefit multiple subsequent therapies.
- By attributing the cost of the new test as an element in the economic evaluation of treatments, novel therapies are penalized. The rarer the mutation, the greater the penalty to the innovator therapy.
- As an alternative, the cost-effectiveness of testing strategies could be evaluated independently of individual treatments.