in collaboration with:

ERASMUS UNIVERSITEIT ROTTERDAM
INSTITUTE OF HEALTH POLICY & MANAGEMENT

Maastricht University

Ribociclib in combination with an aromatase inhibitor for previously untreated advanced or metastatic hormone receptor-positive, HER2-negative breast cancer

1st ADDENDUM

ERG base-case and scenario analysis results with the new PAS

Produced by

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1 Exploratory and sensitivity analyses undertaken by the ERG with the new PAS

The company provided a new PAS, which offers a [redacted] discount on the list price of the ribociclib. In their new PAS submission, the company applied this new PAS price to a different base-case from the ERG preferred base-case explained in the ERG report (all changes in the ERG base case were implemented except for the third-line treatment costs and PFS gain/OS gain relationship. Third-line treatment costs were assumed to be £2,000 per month and OS gain was assumed to be the same as the PFS gain). Therefore, in this addendum, we reconstructed the ERG preferred base-case and the scenario analyses from Section 5.3 of the ERG report with the new PAS price.

1.1 Results from the ERG preferred base-case with the new PAS

The results from the ERG preferred base-case are presented in Table 1.1. After the new PAS, the incremental QALYs gained did not change and remained 0.53, whereas the incremental costs with the new PAS is [redacted], and the corresponding ICER is [redacted] per QALY gained.

Table 1.1: ERG base-case cost effectiveness results (with patient access scheme)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus baseline (QALYs)
Letrozole monotherapy	[redacted]	[redacted]	[redacted]				
Ribociclib plus letrozole	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.53	[redacted]
ICER, incremental cost-effectiveness ratio; LYG, life years gained; QALYs, quality-adjusted life years							

The results of 1,000 PSA iterations are shown in Table 1.2 and the figures below. The cost effectiveness planes show the incremental QALYs and costs of ribociclib plus letrozole relative to letrozole monotherapy (Figure 1.1). In addition, the cost effectiveness acceptability curves (CEAC) are presented, showing the likelihood of ribociclib plus letrozole being cost effective at different willingness-to-pay thresholds (Figure 1.2). For the £30,000 per QALY gained threshold, the probability that ribociclib is cost-effective compared to the letrozole alone is [redacted]

Mean incremental QALYs from ribociclib plus letrozole were around 0.53. When taking into account the new patient access scheme, the incremental costs decreased to [redacted], and the corresponding probabilistic ICER was [redacted] (comparable to the deterministic, base-case ICER of [redacted]). The mean (incremental) results from the 1000 iterations are provided below:

Table 1.2: ERG PSA base-case cost effectiveness results (with the new patient access scheme)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus baseline (QALYs)
Letrozole monotherapy	[redacted]	[redacted]	[redacted]				
Ribociclib plus letrozole	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.53	[redacted]
ICER, incremental cost-effectiveness ratio; LYG, life years gained; QALYs, quality-adjusted life years							

Figure 1.1: Cost effectiveness plane (with the new PAS price)

Figure 1.2 Cost effectiveness acceptability curve (with PAS)

1.2 Results from the ERG additional exploratory scenario analyses

The results of the additional scenarios described in section 5.3.1 of the ERG report, which are now performed on the ERG preferred base-case with the new PAS prices, are provided in Table 1.3 below.

Table 1.3: Results from the additional scenario analyses conducted on the ERG preferred base-case (with the new PAS price)

Scenarios	Ribociclib in combination with letrozole		Letrozole monotherapy		Incr. costs	Incr. QALYs	ICER
	Total costs	Total QALYs	Total costs	Total QALYs			
New CS base-case	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.89	[redacted]
ERG preferred base-case	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.53	[redacted]
Scenario 1 (Weibull function for PFS1 and TTD)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.41	[redacted]
Scenario 2a (Third-line treatment costs = £0)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.53	[redacted]
Scenario 2b (Third-line treatment costs = £2,000 per month)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.53	[redacted]
Scenario 3 (Drug acquisition costs from cycle 11 onwards based on mean costs of cycle 11 to 26)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.53	[redacted]
Scenario 4 (Full OS surrogacy)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.89	[redacted]
Scenario 5 (Full OS surrogacy and Weibull function for PFS 1 and TTD)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.74	[redacted]
Scenario 6 (similar second-line treatments)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.50	[redacted]

QALYs = quality adjusted life years; ICER = incremental cost effectiveness ratio; CS = company submission; PFS = progression-free survival; TTD = time to treatment discontinuation.

Among the scenarios above, with the new PAS price, the largest impact on the ERG base-case ICER occurred in scenario 1, i.e. when the base-case PFS/TTD distributions for the first-line were changed from exponential to Weibull, which led to a substantial increase in the ICER. Since in section 5.2.6.1 of the ERG report, it was previously discussed that the Weibull distribution can be as plausible as the

company’s preferred exponential distribution, the ERG stresses that this scenario might be reflective of the uncertainty of the cost effectiveness of ribociclib.

Using higher (£2,000) or none (£0) third-line treatment costs resulted in substantial changes in ICER as well. A higher third-line treatment cost decreases the ICER.

Finally, assuming full OS surrogacy instead of partial OS surrogacy also decreases the ICER.

Table 0.4: Revised base-case cost effectiveness analysis, incorporating corrections and amendments identified by the ERG (with the new PAS)

Scenarios	Ribociclib plus letrozole		letrozole alone		Incr. costs	Incr. QALYs	ICER
	Total costs	Total QALYs	Total costs	Total QALYs			
0. New CS base-case	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.89	[redacted]
(1). Using post-progression costs from TA239 (fulvestrant)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.89	[redacted]
(2). Changing PFS gain / OS gain = 1 assumption	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.53	[redacted]
(1 to 2 all): ERG preferred base-case	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	0.53	[redacted]

CS = Company submission; ERG = Evidence review group; ICER = incremental cost effectiveness ratio; Incr. = incremental; LYG = life years gained; QALYs = quality adjusted life years.