in collaboration with:

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ADDENDUM TO

Ramucirumab for treating advanced gastric cancer or gastro-oesophageal junction adenocarcinoma previously treated with chemotherapy

Addendum by the ERG in response to the questions raised by NICE

Details of additional analyses requested by NICE

- Clarification on the exploratory scenario analysis 3 undertaken by ERG (utilities directly taken from RAINBOW EQ-5D results)
    - Which states in the model are affected
    - Differences between the base case in the CS and Scenario 3
    - Utility values used in Scenario 3
- Pairwise comparisons for the Ramucirumab(RAM) vs. all comparators for the monotherapy model
- Ramucirumab+paclitaxel (RAM+PAC) vs Docetaxel (DOC) comparison for ERG base case and Scenario 1

ERG response to the questions raised by NICE

Clarification on the exploratory scenario analysis 3 undertaken by ERG (utilities directly taken from RAINBOW EQ-5D results)

States in the model that are affected
In this scenario analysis, mean EQ-5D scores collected at different time points in the RAINBOW trial, which were provided in Table 21 from the company submission, are implemented.[1]

Both pre-progression and post-progression state utilities of all interventions are updated according to the values from the RAINBOW trial in this scenario analysis.

Differences between the base case utilities in the CS and in Scenario 3
In the company submission, for the pre-progression state, the baseline mean EQ-5D index score is used for the entire RAINBOW intention to treat (ITT) population and UK weights are applied. Utility increments due to response and utility decrements due to adverse events are incorporated on top of this uniform pre-progression utility. For post progression state: the utility value is estimated using the mean EQ-5D score at the end of treatment for all patients who discontinued the treatment due to the progressive disease.

In the company submission, it is assumed pre-progression state utility remains constant, and the utility increments due to disease response lasts the whole pre-progression state period. In scenario 3, mean EQ-5D results measured at different time points are used and no utility increment due to treatment response is applied.

Utility values that were used in Scenario 3
The utility values used in Scenario 3 can be seen in Table 1.

Table 1 RAINBOW: EQ-5D Results

	RAM+PAC	OTHER COMPARATORS
EQ-5D Index Score, mean (SD)		
Baseline – Week 4, Pre-progression	0.741 (0.228)	0.732 (0.250)
Week 5-Week 6, Pre-progression	0.752 (0.226)	0.772 (0.227)
Week 7- Week 10, Pre-progression	0.743 (0.212)	0.767 (0.230)
Week 11- Week 12, Pre-progression	0.737 (0.241)	0.777 (0.189)
Week 13- Week 16, Pre-progression	0.708 (0.277)	0.756 (0.246)
Week 17- Week 18, Pre-progression	0.712 (0.241)	0.821 (0.135)
Week 19 and afterwards, Pre-progression	0.750 (0.236)	0.800 (0.191)
Post-progression	0.581 (0.335)	0.570 (0.366)

Abbreviations: SD = standard deviation. Based on a –0.59 to 1 scale, with 1 representing perfect health. Calculated based on the UK population-based preference weights for EQ-5D. These are based on values elicited from a representative national sample using the time trade-off (TTO) method.

The impact of using the direct utility values from the RAINBOW trial can be seen by comparing the Scenario 3 results in Table 5.35 with the ERG base case results in Table 5.31 in the ERG report.[2]

Pairwise comparisons for the RAM vs all comparators for the monotherapy model

Pairwise comparisons for RAM vs all comparators, including Irinotecan (IRI) and Folinic acid + flouracil + irinotecan (FOLFIRI), are provided below in Table 2.

Table 2 Pairwise comparisons for RAM vs all comparators.

Intervention	Comparator	Incr. QALY	Incr. Cost	ICER
RAM	Best Supportive Care (BSC)	0.12	£ 22,517	£ 188,437
	DOC	-0.07	£ 13,828	Dominated
	IRI	-0.29	£ 6,181	Dominated
	FOLFIRI	-0.45	-£ 417	FOLFIRI is more CE

RAM+PAC vs DOC comparison for ERG base case and Scenario 1

RAM+PAC vs DOC ICER results for the ERG base case (which excludes Roy et al.[3] in its evidence network) and Scenario 1 (in which Roy et al. was included) are given in Table 3 and Table 4 respectively.

Table 3 ERG base case (without Roy et al.), RAM+PAC vs DOC ICER results

Comparator	Costs	LYs	QALYs	ICER (per QALY)
DOC	£10,523	0.59	0.39	
RAM+PAC	£50,050	0.94	0.62	£168,164

Table 4 ERG Scenario 1 (without Roy et al.), RAM+PAC vs DOC ICER results

Comparator	**Costs**	**LYs**	**QALYs**	**ICER (per QALY)**
DOC	£11,121	0.68	0.44	
RAM+PAC	£50,050	0.94	0.62	£214,017

References:

[1] Eli Lilly and Company Ltd. Ramucirumab for treating metastatic gastric cancer or gastro-oesophageal junction adenocarcinoma after chemotherapy: Submission to National Institute of Health and Clinical Excellence. Single technology appraisal (STA). Eli Lilly and Company Ltd, 2015: 269.

[2] Riemsma R, Al M, Büyükkaramikli N, Armstrong N, Blommestein H, Clay F, et al. *Ramucirumab for treating advanced gastric cancer or gastro-oesophageal junction adenocarcinoma previously treated with chemotherapy*. York: Kleijnen Systematic Reviews Ltd, 2015

[3] Roy AC, Park SR, Cunningham D, Kang YK, Chao Y, Chen LT, et al. A randomized phase II study of PEP02 (MM-398), irinotecan or docetaxel as a second-line therapy in patients with locally advanced or metastatic gastric or gastro-oesophageal junction adenocarcinoma. *Ann Oncol* 2013;24(6):1567-73.