SUPPLEMENTARY APPENDICES

Evaluating the clinical effectiveness and safety of various HER2-targeted regimens after prior taxane/trastuzumab in patients with previously treated, unresectable, or metastatic HER2-positive breast cancer: a systematic review and network meta-analysis

Authors:
Noman Paracha, Adriana Reyes, Véronique Diéras, Ian Krop, Xavier Pivot, Ander Urruticoechea

Corresponding author:
Noman Paracha
F. Hoffmann-La Roche AG
Grenzacherstrasse 124
4070 Basel
Switzerland

Tel: +41 61 688 2661

Email: noman.paracha@roche.com
### Online Resource 5: Appendix 5. Data inputs for NMA

#### Data inputs – PFS and OS

| Study name         | Treatment 1       | Treatment 2       | PFS HR (95% CI) Treatment 1 vs 2 | OS HR (95% CI) Treatment 1 vs 2 | XO Adj. OS HR (95% CI) Treatment 1 vs 2 |
|--------------------|-------------------|-------------------|-----------------------------------|----------------------------------|----------------------------------------|
| EMILIA [43]        | T-DM1             | LapCap            | 0.65 (0.55, 0.77)                 | 0.75 (0.64, 0.88)                | 0.69<sup>a</sup> (0.58, 0.85)          |
| EGF100151 [36]     | LapCap            | Cap alone         | 0.55 (0.40, 0.74)                 | 0.87 (0.70, 1.08)                | 0.80<sup>b</sup> (0.64, 0.99)          |
| GBG 26 [32]        | TrasCap           | Cap alone         | 0.68 (0.48, 0.96)                 | 0.94 (0.65, 1.35)                | NR                                     |
| Martin et al., 2013 [39] | Neratinib        | LapCap            | 1.19 (0.89, 1.60)                 | 1.25 (0.83, 1.86)                | NR                                     |
| CEREBEL [17]       | LapCap            | TrasCap           | 1.13 (0.85, 1.50)                 | 1.18 (0.76, 1.18)                | NR                                     |
| PHEREXA [26]       | PerTrasCap        | TrasCap           | 0.83 (0.68, 1.02)                 | 0.76 (0.60, 0.98)                | NR                                     |
| ELTOP [40]         | LapCap            | TrasCap           | 0.81 (0.55, 1.21)                 | 0.58 (0.26, 1.31)                | NR                                     |

<sup>a</sup>Using RPSFTM – see NICE appraisal [43]

<sup>b</sup>XO as time dependent covariate; a subsequent follow-up analysis determined that HR for OS in EMILIA allowing for treatment crossover was 0.75 (95% CI: 0.64, 0.88)

Cap capecitabine, CI confidence interval, HR hazard ratio, LapCap lapatinib plus capecitabine, NR not reported, OS overall survival, PFS progression-free survival, PerTrasCap pertuzumab plus trastuzumab plus capecitabine, T-DM1 trastuzumab emtansine, TrasCap trastuzumab plus capecitabine
| Study name\(^a\) | Treatment  | Event (r) | Evaluable (n) | %   |
|----------------|------------|-----------|---------------|-----|
| EMILIA [10]    | T-DM1      | 173       | 397           | 44% |
| EMILIA [10]    | LapCap     | 120       | 389           | 31% |
| EGF100151 [38] | LapCap     | 47        | 198           | 24% |
| EGF100151 [38] | Cap        | 28        | 201           | 14% |
| GBG 26 [32]    | TrasCap    | 37        | 77            | 48% |
| GBG 26 [32]    | Cap        | 20        | 74            | 27% |
| Martin et al., 2013 [39] | Neratinib | 34        | 117           | 29% |
| Martin et al., 2013 [39] | LapCap   | 47        | 116           | 41% |
| PHEREXA [26]   | PerTrasCap | 73        | 163           | 45% |
| PHEREXA [26]   | TrasCap    | 61        | 164           | 37% |
| ELTOP [40]     | TrasCap    | 16        | 40            | 40% |
| ELTOP [40]     | LapCap     | 15        | 37            | 41% |

\(^a\)Data for CEREBEL not available

*Cap* capecitabine, *LapCap* lapatinib plus capecitabine, *ORR* overall response rate, *PerTrasCap* pertuzumab plus trastuzumab plus capecitabine, *T-DM1* trastuzumab entansine, *TrasCap* trastuzumab plus capecitabine
## Data inputs – adverse events

| Study name* | Treatment       | Evaluable (n) | Anemia | Diarrhea | Fatigue | Increased ALT | Increased AST | Mucosal inflammation | Nausea | Neutropenia | PPE | Thrombocytopenia | Vomiting |
|-------------|----------------|---------------|--------|----------|---------|---------------|---------------|---------------------|--------|-------------|-----|----------------|---------|
| EMILIA [13] | T-DM1          | 490           | 19     | 9        | 12      | 15            | 22            | 1                   | 4      | 11          | 0   | 70            | 5       |
| EMILIA [13] | LapCap         | 488           | 11     | 103      | 17      | 9             | 7             | 11                  | 13     | 21          | 87  | 2             | 24      |
| EGF100151   | LapCap         | 198           | 2      | 28       | 6       | 4             | 6             | 0                   | 4      | 8           | 24  | 2             | 4      |
| EGF100151   | Cap            | 191           | 2      | 19       | 7       | 2             | 4             | 4                   | 6      | 27          | 4   | 4             | 4      |
| GBG 26 [32] | TrasCap        | 77            | 0      | 12       | 3       | 3             | 5             | 1                   | 1      | 4           | 25  | 0             | 1      |
| GBG 26 [32] | Cap            | 74            | 2      | 14       | 4       | 2             | 2             | 3                   | 3      | 18          | 1   | 3             |        |
| Martin et al., 2013 [39] | | 116 | NR | 33 | 3 | 4 | 4 | NR | 5 | 2 | 0 | NR | 5 |
| Martin et al., 2013 [39] | LapCap | 115 | NR | 11 | 3 | 1 | 3 | NR | 4 | 4 | 16 | NR | 2 |
| PHEREXA [26] | PerTrasCap    | 228           | 3      | 37       | 6       | 3             | NR            | 6                   | 6      | 9           | 23  | 3             | 4      |
| PHEREXA [26] | TrasCap       | 218           | 6      | 22       | 3       | 1             | NR            | 7                   | 7      | 13          | 48  | 1             | 7      |
| ELTOP [40]  | TrasCap        | 43            | 0      | 4        | NR      | 2             | 1             | NR                  | NR     | 2           | 9   | NR            | NR     |
| ELTOP [40]  | LapCap         | 43            | 0      | 7        | NR      | 1             | 3             | NR                  | NR     | 1           | 9   | NR            | NR     |

*ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *Cap* capecitabine, *LapCap* lapatinib plus capecitabine, *NR* not reported, *PerTrasCap* pertuzumab plus trastuzumab plus capecitabine, *PPE* palmar–plantar erythrodysesthesia, *T-DM1* trastuzumab emtansine, *TrasCap* trastuzumab plus capecitabine
| Study name* | Treatment       | Event (r) | Evaluable (n) | Grade 3 and above | Serious AEs | Tx disc. due to AEs |
|------------|-----------------|-----------|---------------|-------------------|-------------|-------------------|
| EMILIA [13]| T-DM1           | 490       | 233           | 92                | 50          |                   |
| EMILIA [13]| LapCap          | 488       | 291           | 99                | 59          |                   |
| EGF100151  | LapCap          | 198       | 12*           | NR                | 28          |                   |
| EGF100151  | Cap             | 191       | 12*           | NR                | 27          |                   |
| GBG 26 [32]| TrasCap         | 77        | 49            | 13                | 8           |                   |
| GBG 26 [32]| Cap             | 74        | 49            | 18                | 10          |                   |
| Martin et al., 2013 [39]| Neratinib | 116       | NR            | 31                | 7           |                   |
| Martin et al., 2013 [39]| LapCap         | 115       | NR            | 25                | 20          |                   |
| PHEREXA [26]| PerTrasCap     | 228       | 118           | 56                | 48          |                   |
| PHEREXA [26]| TrasCap        | 218       | 130           | 52                | 42          |                   |
| ELTOP [40]| TrasCap         | 43        | NR            | NR                | 5           |                   |
| ELTOP [40]| LapCap          | 43        | NR            | NR                | 12          |                   |

*These data are given for grade 4 and above

AE adverse event, Cap capecitabine, LapCap lapatinib plus capecitabine, NR not reported, PerTrasCap pertuzumab plus trastuzumab plus capecitabine, T-DM1 trastuzumab emtansine, TrasCap trastuzumab plus capecitabine