Submitted by [redacted] on behalf of:
NCRI Breast CSG, RCP, RCR, ACP, JCCO

Comments coordinated by [redacted]

LAPATINIB REVISED ACD

We have reviewed the draft recommendations announced by NICE in the second technology appraisal consultation document (ACD) that suggests that lapatinib (Tyverb) should not be used in the NHS, except within the context of clinical trials. This recommendation seems to be based on an economic argument that continues to disregard the reality of the current clinical situation in the UK where trastuzumab is frequently given beyond progression with capecitabine or other cytotoxic regimens.

To illustrate the extent of unlicensed use of trastuzumab beyond progression the NCRI Breast Cancer Study Group conducted an e-mail poll of UK oncologists. Oncologists were asked whether they used trastuzumab beyond progression, and if they did, to provide both an estimate of the proportion of patients seen and the absolute numbers per year in their care who receive trastuzumab for progressive systemic disease, other than those with brain metastases where the use beyond progression is less contentious (Appendix 1).

Due to time constraints only a four-day response time was allowed, but this generated replies from 81 clinical and medical oncologists with special expertise in the management of advanced breast cancer. These replies came from 28 English and 3 Welsh service networks as well as, 2 Scottish networks and 1 from Northern Ireland.

Of 81 respondents 33 admitted to use of trastuzumab in >75% of their patients, 20 in 50-74%, 8 in 25-49%, 12 in 1-24% and only 8 either never used trastuzumab beyond progression or had no clinical experience of this particular clinical situation. Minimum estimates of numbers of patients receiving trastuzumab beyond progression totaled 745 patients per year. Bearing in mind that not all oncologists involved in the treatment of advanced breast cancer responded and that around 20% of patients progress first in brain and will also receive trastuzumab beyond progression, it is clear that considerably more than 50% of patients in the country are receiving this treatment (Appendix 2).

In recognition that the first ACD from NICE did not consider lapatinib to be cost effective in treating this patient population, Glaxo Smith Kline (GSK) proposed an innovative patient access programme, where the company would bear the cost of lapatinib for all eligible patients, for up to the first 12 weeks of treatment. The NHS would commence payment only for the patients who continue to receive clinical benefit beyond 12 weeks. This programme was designed to provide access to all eligible patients and deliver cost-effectiveness at a threshold that should have been acceptable to NICE. We

consider that this is a very responsible acknowledgement of the cost pressures of incorporating another expensive drug into routine NHS practice and tips the economic argument firmly in favour of lapatinib in place of the current standard of care.

In our view the use of lapatinib plus capecitabine will ultimately reduce the costs to the UK health system compared to the established but unlicensed clinical practice of continuing to use trastuzumab once a patient's disease has progressed. The relevant merits of lapatinib or trastuzumab beyond progression are clearly an important research question that the UK oncology community would be happy to address in a well-designed randomised clinical trial.

Appendix 1: Questionnaire to breast oncologists – October 2008.

Dear Colleague

We need to inform NICE of the usage of trastuzumab beyond progression in advanced HER2+ breast cancer as part of the response to the Lapatinib ACD. We realise this is neither licensed, or specifically funded but know that use in this setting is considerable. Please answer these three questions.

1. Do you use trastuzumab beyond progression in advanced HER2+ breast cancer in the absence of brain metastases?

YES/NO

(>75% of cases)
(50-74% of cases)
(25-49% of cases)
(1-24% of cases)

2. Please estimate the number of patients in your practise per year with advanced breast cancer who progress after initial trastuzumab treatment. (This is to allow an estimate of overall mean for the use of trastuzumab beyond progression and to estimate the proportion of the advanced breast cancer population included in our survey).

3. What is the name of your network?

Appendix 2: Anonymised results from questionnaire

Yes/No	%age of cases	No. of Cases	Network	Comments
No	-		Mount Vernon	So far I have not encountered a patient of this nature of the 20 metastatic on Herceptin
No		3	Peninsular	
Yes	1-24	5	Yorkshire	
Yes	25-49	4	ASWCS	
Yes	50-74	5	Sussex	
Yes	25-49	8	Greater Midlands	
Yes	>75	20	Peninsular	
Yes	>75	5-10	Kent & Medway	
Yes	1-10	10	Berkshire	Only very rare because no funding agreement
Yes	>75	5	North of England	
Yes	>75	5-10	Leics, Northants & Rutland	
Yes	25-49	15	3 Counties	
Yes	1-24	2-3	North London	
Yes	>75	20-25	Greater Midlands	
Yes	1-24	5-10	W Anglia	
Yes	50-74	5	ASWCS	
Yes	>75	20	ASWCS	
Yes	50-74	25	Merseyside & Cheshire	
Yes	>75	10	SW London	
No		4	NE London	
Yes	50-74	10	NE London	
Yes	50-74	10	3 Counties	
Yes	50-74		ASWCS	
Yes	>75	10	Greater Midlands	
Yes	50-74	15	Sussex	
Yes	25-49	5	Merseyside & Cheshire	
Yes	50-74	30	Mount Vernon	

Yes	50-74	15	ASWCS	
Yes	50-74	3	Anglia	
Yes	1-24	30	SE Wales	
Yes	>75	20	W Anglia	
Yes	>75	5	North Trent	
Yes	>75	10	ASWCS	
Yes	50	6-8	SE Essex	
Yes	>75	2	SW Wales	
Yes	>75	5	Arden	
Yes	50	10	Peninsular	
Yes	1-24	5-10	N Wales	
Yes	>75	2-3	SW Thames	
Yes	>75	5-10	Thames Valley	
Yes	50-74		Humber & Yorkshire	
No		4-8	Northern Ireland	We are specifically forbidden from using Trastuzumab through progression in NI as not funded
Yes	>75	7	Sussex	
Yes	>75	5	ASWCS	
Yes	1-24		North Trent	
Yes	>75	25	West Scotland	
No		3	SE Wales	
Yes	>75	10	South Essex	
No			Central South Coast	I have had so few numbers yet that nobody has had Trastzumab after progression
Yes	25-49	4	Greater Midlands	
Yes	1-24	5-10	North of England	
Yes	>75	5-7	Lancs & S Cumbria	
Yes	1-24	5-10	West of Scotland	
No			W Anglia	We don't use Herceptin after progression although some parts of the network do
Yes	>75	5	Kent & Medway	
Yes	50-74	30	Lancs & S Cumbria	
Yes	>75	20	SW London	
Yes	>75	30	Merseyside & Cheshire	

Yes	>75	5	NE Cumbria	
Yes	1-24	<5	3 Counties	
Yes	>75	5-7	Greater Manchester & Cheshire	
Yes	30	10	North London	
Yes	50-74	3-5	Sussex	
Yes	>75	6	North London	
Yes	50-74	6-10	North Trent	
Yes	50-74	4	SE London	
Yes	50-74	20	Yorkshire	
Yes	>75	10-15	Yorkshire	
Yes	50-74	5	NECN	
Yes	>75	20	Thames Valley	
Yes	50-74	8	W Anglia	
Yes	>75	30-50	Lancashire & S Cumbria	I quite agree. Don't have accurate numbers on relapse rates
No		15	South Essex	
Yes	1-24	2-3	Pan Birmingham	
Yes	>75	10-15	W Anglia	
Yes	25-49	15	SCAN	
Yes	25-49	5	Greater Manchester & Cheshire	
Yes	>75	4	SCAN	
Yes	1-24	10-15	Mid Trent	
No			W London	We stick to licence but know we are unusual
Yes	>75	10	Yorkshire	
Yes	>75		West of Scotland	
Yes	25-49	6	North Trent	