

Early and metastatic HER2-positive breast cancer: subcutaneous trastuzumab

Evidence summary

Published: 13 March 2013

[nice.org.uk/guidance/esnm13](https://www.nice.org.uk/guidance/esnm13)

Overview

The content of this evidence summary was up-to-date in March 2013. See [summaries of product characteristics \(SPCs\)](#), [British national formulary \(BNF\)](#) or the [MHRA](#) or [NICE](#) websites for up-to-date information.

Key points from the evidence

Trastuzumab is a monoclonal antibody licensed for intravenous administration to treat people with breast cancers that show overexpression of the human epidermal growth factor receptor 2 (HER2) protein or HER2 gene amplification. HER2 overexpression has been linked with a poorer outcome in people with breast cancer.

An application for an extension to the product licence for a subcutaneous formulation of trastuzumab (with hyaluronidase as an excipient) to treat HER2-positive early and metastatic breast cancer was filed with the European Medicines Agency in March 2012.

An open-label randomised controlled trial was conducted in 596 women with non-metastatic (clinical stage I–III) HER2-positive breast cancer (the HannaH study). All women received trastuzumab for 24 weeks neo-adjuvant treatment (that is, before surgery) as well as 1 year of adjuvant, post-surgical therapy. This study found that subcutaneous trastuzumab was non-inferior to intravenous trastuzumab for the primary efficacy outcome of pathological complete response (the absence of invasive neoplastic cells in the breast; remaining ductal carcinoma in situ was

accepted). It was also not inferior for the co-primary outcome of pharmacokinetic serum trough concentration in pre-dose cycle 8 (before surgery). Pathological complete response has been associated with long-term clinical benefit but there has yet to be a formal validation of it as a surrogate outcome. The analysis for both outcomes was on the per-protocol population: statistical analysis of results in the intention-to-treat population was not reported in the published paper. Data for patient-oriented outcomes, event-free survival and overall survival were not available.

The same proportion of women in both study groups experienced at least 1 severe or worse adverse event. There were numerically more grade 3 and grade 4 events in the intravenous group than in the subcutaneous group, but those that occurred in the subcutaneous group were more likely to be classed as serious, chiefly because women who experienced them were more likely to be admitted to hospital. No phase III trials which compare the intravenous and subcutaneous formulations of trastuzumab in women with metastatic breast cancer have been conducted.

The manufacturer estimates that using subcutaneous instead of intravenous trastuzumab would lead to savings in acquisition costs. Subcutaneous administration of trastuzumab is quicker and less invasive than intravenous administration, and could be done in people's homes or in community settings. This may be preferred by some people and might lead to savings in hospital resources. However, these benefits may not be realised if trastuzumab is combined with other drugs given intravenously, such as taxanes.

Local decision makers will need to consider the available evidence when making decisions about using subcutaneous trastuzumab, in the setting of their local care pathways and usual trastuzumab-containing treatment schedules, and local patients' preferences regarding whether they prefer to be treated at home or in a day hospital. The likely benefits of its use will need to be balanced against the possible risks and the absence of direct patient-oriented outcomes in early breast cancer, and the absence of phase III studies in metastatic breast cancer.

Key evidence

Ismael G, Hegg R, Muehlbauer S et al. (2012) [Subcutaneous versus intravenous administration of \(neo\)adjuvant trastuzumab in patients with HER2-positive, clinical stage I-III breast cancer \(HannaH study\): a phase 3, open-label, multicentre, randomised trial](#). *The Lancet Oncology* 13: 869-78

About this evidence summary

'Evidence summaries: new medicines' provide summaries of key evidence for selected new medicines, or for existing medicines with new indications or formulations, that are considered to be

of significance to the NHS. The strengths and weaknesses of the relevant evidence are critically reviewed within this summary to provide useful information for those working on the managed entry of new medicines for the NHS, but this summary is not NICE guidance.

Relevance to NICE guidance programmes

Subcutaneous trastuzumab was not considered appropriate for a NICE technology appraisal and is not currently planned within any other NICE work programme.

Guidance issued by NICE which recommends trastuzumab as an option in breast cancer in certain circumstances was based on consideration of the evidence relating to intravenous administration of the drug:

- [The use of trastuzumab for the treatment of advanced breast cancer](#) (NICE technology appraisal guidance 34).
- [Early and locally advanced breast cancer: diagnosis and treatment](#) (NICE clinical guideline 80), which updated [Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer](#) (NICE technology appraisal guidance 107).
- [Advanced breast cancer: diagnosis and treatment](#) (NICE clinical guideline 81).

[Lapatinib or trastuzumab in combination with an aromatase inhibitor for the first-line treatment of metastatic hormone-receptor-positive breast cancer that overexpresses HER2](#) (NICE technology appraisal guidance 257) does not recommend trastuzumab in combination with an aromatase inhibitor for first-line treatment in postmenopausal women with metastatic hormone-receptor-positive breast cancer that overexpresses HER2.

Introduction

Early breast cancer is subdivided into 2 major categories: in situ disease (mainly in the form of ductal carcinoma in situ), and invasive cancer. Both are heterogeneous processes with very variable appearances, biology and clinical behaviour (see the [early and locally advanced breast cancer full guideline](#) for more information).

Invasive breast cancer is the most common type of cancer in the UK and is by far the most common cancer among women. Cancer Research UK reported that 49,961 people were diagnosed with [invasive breast cancer](#) in the UK in 2010, more than 99% of whom were women. In the same year, 5765 women in the UK were diagnosed with [in situ breast cancer](#).

Metastatic breast cancer is an advanced stage of the disease when it has spread to other organs. An estimated 5% of people with newly diagnosed breast cancer have metastatic breast cancer, and approximately 30% of people with newly diagnosed localised breast cancer will later develop metastatic breast cancer. Common sites of metastasis include bone, liver, lung and brain (see the NICE technology appraisal on [lapatinib and trastuzumab](#)).

Various prognostic factors are considered when planning the management of breast cancer. Tumours that overexpress the human epidermal growth factor receptor 2 (HER2) protein grow and divide more quickly, so women with HER2-positive tumours generally have a worse prognosis than women with HER2-negative tumours (see the NICE technology appraisal on [lapatinib and trastuzumab](#)). HER2 positivity is seen in approximately 15% of early invasive breast cancer (see the [early and locally advanced breast cancer full guideline](#)).

Product overview

Drug action

Trastuzumab is a recombinant humanised IgG1 monoclonal antibody that binds to HER2. The subcutaneous formulation (Herceptin SC 600 mg/5 ml solution for injection, Roche Products Limited) contains hyaluronidase as an excipient. This temporarily breaks down hyaluronan in the subcutaneous space, increasing the volume that can be administered.

Proposed therapeutic indications

An application for an extension to the product licence for a subcutaneous formulation of trastuzumab plus hyaluronidase as an excipient was filed with the European Medicines Agency in March 2012. The manufacturer's proposed therapeutic indications for the subcutaneous formulation of trastuzumab are the same as for the intravenous formulation. Subcutaneous trastuzumab should be used only in people with metastatic or early breast cancer whose tumours have either HER2 overexpression or HER2 gene amplification as determined by an accurate and validated assay (Roche Products Limited: personal communication December 2012).

Early breast cancer

Subcutaneous trastuzumab fixed-dose formulation is proposed as a treatment for HER2-positive early breast cancer (Roche Products Limited: personal communication December 2012):

- after surgery, chemotherapy (neoadjuvant or adjuvant) and radiotherapy (if applicable)

- after adjuvant chemotherapy with doxorubicin and cyclophosphamide, in combination with paclitaxel or docetaxel
- in combination with adjuvant chemotherapy consisting of docetaxel and carboplatin
- in combination with neoadjuvant chemotherapy followed by adjuvant trastuzumab therapy, for locally advanced (including inflammatory) disease or tumours over 2 cm in diameter.

Metastatic breast cancer

Subcutaneous trastuzumab fixed-dose formulation is proposed as a treatment for HER2-positive metastatic breast cancer (Roche Products Limited: personal communication December 2012):

- as monotherapy in people who have received at least 2 chemotherapy regimens for their metastatic disease. Prior chemotherapy must have included at least an anthracycline and a taxane unless these treatments are unsuitable for the person. People with hormone-receptor-positive breast cancer must also have had an inadequate response from hormonal therapy, unless these treatments are unsuitable for them
- in combination with paclitaxel in people who have not received chemotherapy for their metastatic disease and in whom an anthracycline is not suitable
- in combination with docetaxel in people who have not received chemotherapy for their metastatic disease
- in combination with an aromatase inhibitor in postmenopausal women with hormone-receptor-positive metastatic breast cancer that has not been previously treated with trastuzumab.

Proposed course and cost

The recommended dose of subcutaneous trastuzumab is 600 mg irrespective of the person's body weight. Each fixed dose is delivered by injection over a period of up to 5 minutes, every 3 weeks. No loading dose is required. In early breast cancer, treatment with subcutaneous trastuzumab should continue for 1 year or until disease recurrence, whichever occurs first. In metastatic breast cancer it should continue until progression of disease (Roche Products Limited: personal communication December 2012).

The manufacturer states that subcutaneous trastuzumab is expected to have a list price of £1222.20 per 600 mg fixed-dose vial (Roche Products Limited: personal communication December 2012). In people with early breast cancer, the estimated cost per course of treatment is £22,000

(assuming a full treatment course of 18 cycles per person). In people with metastatic breast cancer, the estimated cost per course of treatment is £21,022 (assuming a mean of 17.2 cycles per person [Roche Products Limited: personal communication December 2012]).

Evidence review

This evidence review is based on a published phase III study that compared the subcutaneous and intravenous formulations of trastuzumab in women with HER2-positive, non-metastatic clinical stage I–III breast cancer (HannaH study; [Ismael et al. 2012](#); see table 1).

- Design: 81-centre, open-label, non-inferiority randomised controlled trial. Review of pathological tumour assessment results was done by a medical reviewer masked to the women's treatment allocation.
- Population: 596 women (18 years or over, mean 50 years) with newly diagnosed, non-metastatic, HER2-positive, primary invasive breast cancer (clinical stage I to IIIC). About half of the women had negative oestrogen receptor status and about half had cancer of clinical stage T1b–T3, N0–N1.
- Intervention and comparison: subcutaneous trastuzumab (fixed dose of 600 mg in a volume of 5 ml plus 10,000 units rHuPH-20 [hyaluronidase]) injected into the thigh with a hand-held syringe by the nursing team at a steady rate over about 5 minutes at alternating sites every 3 weeks, compared with intravenous trastuzumab (8 mg/kg loading dose, 6 mg/kg maintenance dose) given every 3 weeks. Concurrently, all women received 8 cycles of chemotherapy: 4 cycles of docetaxel (75 mg/m²) every 3 weeks followed by 4 cycles of fluorouracil (500 mg/m²), epirubicin (75 mg/m²) and cyclophosphamide (500 mg/m²) every 3 weeks. After chemotherapy, surgery was performed according to local practice. In the adjuvant phase, radiotherapy and hormonal therapy were administered as per local practice. Trastuzumab was continued after surgery until women had completed 18 cycles of treatment.
- Outcomes: antitumour efficacy and pharmacokinetics were co-primary outcomes, analysed in the per-protocol population. Efficacy was assessed using the pathological complete response (pCR: the absence of invasive neoplastic cells in the breast; remaining ductal carcinoma in situ was accepted). The primary pharmacokinetic outcome was pre-dose serum concentration of trastuzumab (C_{trough}) recorded at cycle 8 before surgery. The primary analyses were done when all women had completed surgery (unless prematurely withdrawn) and at least 100 women in each study group had completed 1 year of treatment. The median duration of follow-up was 12.2 months (range 1.0–20.8) in the intravenous group and 12.4 months (range 0.3–20.4) in

the subcutaneous group. In each group, 116 women had completed full treatment at the time of the published analysis.

Table 1 Summary of the HannaH study

	Subcutaneous trastuzumab	Intravenous trastuzumab	Analysis
Randomised	n=297	n=299	
Co-primary outcomes			
<i>Efficacy: per protocol set^a</i>	n=260	n=263	
Primary efficacy outcome, pCR ^b	45.4% (118/260)	40.7% (107/263)	Treatment difference: 4.7% (95% CI -4.0 to 13.4%) Non-inferiority criteria met: lower limit of the 2-sided 95% CI for the difference greater than pre-specified non-inferiority margin of -12.5%
<i>Efficacy: Intention-to-treat set^c</i>	n=294	n=297	
Primary efficacy outcome, pCR ^b	42.2% (124/294)	37.4% (111/297)	Statistical analysis not reported
<i>Pharmacokinetics: per protocol set^d</i>	n=234	n = 235	
Primary pharmacokinetic outcome: pre-surgery geometric mean serum C _{trough} (microgram/ml; percentage coefficient of variation)	69 (55.8%)	51.8 (52.5%)	Geometric mean ratio: 1.33 (90% CI 1.24 to 1.44) Non-inferiority criteria met: lower limit of the 2-sided 90% CI of the geometric mean ratio C _{trough} subcutaneous/ C _{trough} intravenous was greater than the pre-specified margin of 0.8 or more

Selected secondary outcomes, per protocol set:			
Total pathological complete response ^e	39.2% (102/260)	34.2% (90/263)	Treatment difference: 5.0% (95% CI -3.5 to 13.5)
Median time to response (weeks) ^f	6.0 (2 to 28) n=225	6.0 (3 to 25) n=231	
Safety outcomes: safety analysis set^g	n=297	n=298	
Women reporting ≥1 adverse event (any grade)	97.3% (289/297)	93.9% (280/298)	p value for comparison not reported
Women reporting ≥1 adverse event (grade 3-5) ^h	51.9% (154/297)	52.0% (155/298)	p value for comparison not reported
Women reporting ≥1 serious adverse event	20.9% (62/297)	12.4% (37/298)	p value for comparison not reported
Women with adverse events leading to death	1.0% (3/297)	<1% (1/298)	p value for comparison not reported

Abbreviations: CI, confidence interval; pCR, pathological complete response (absence of residue invasive disease in the breast; remaining ductal carcinoma in situ was accepted).

^a Subset of the intention-to-treat population with the following exclusions: women with less than 8 cycles of trastuzumab/chemotherapy treatment, metastatic breast cancer before study entry, previous anticancer therapy, HER2-negative breast cancer.

^b Clinical tumour response was assessed by ultrasound or clinical examination at baseline and on day 1 of cycles 3, 5, and 7, and before surgery.

^c All women with at least 1 efficacy assessment after first study drug administration.

^d All women randomised and adherent to the protocol.

^e Absence of invasive neoplastic cells in the breast and ipsilateral lymph nodes.

^f The time from first drug administration to the date of the first clinical complete or partial response.

^g All women who received at least 1 dose of trastuzumab: includes information from neoadjuvant and adjuvant phases.

^h Graded according to the US National Cancer Institute's common terminology criteria for adverse events (v3.0), from 1 (mild), through 3 (severe) to 5 (fatal).

Clinical effectiveness

The [HannaH study](#) evaluated the efficacy and pharmacokinetics of 2 formulations of trastuzumab as neoadjuvant therapy in addition to chemotherapy. Subcutaneous trastuzumab was non-inferior to intravenous trastuzumab for the primary efficacy outcome of pathological complete response in the per-protocol analysis. This outcome was defined as the absence of invasive neoplastic cells in the breast; remaining ductal carcinoma in situ was accepted.

Subcutaneous trastuzumab was also non-inferior to intravenous trastuzumab for the primary pharmacokinetic outcome of pre-dose serum concentration at cycle 8 (before surgery) in the per-protocol analysis.

Among the secondary outcomes, there was no significant difference between the treatment groups for total pathological complete response (defined as the absence of invasive neoplastic cells in the breast and ipsilateral lymph nodes), and the median time to show a response to treatment (defined as the time from first drug administration to the date of the first clinical complete or partial tumour response) in the per-protocol analysis. Event-free survival and overall survival were described as secondary outcomes but data on these outcomes were not reported; the authors stated that the data were immature at the time of the analysis.

Safety

Statistical analysis of safety data was not undertaken which limits the interpretations which can be drawn.

The severity of adverse events was graded according to the US National Cancer Institute's [common terminology criteria for adverse events \(v3.0\)](#), from 1 (mild), through 3 (severe) to 5 (fatal). Similar numbers of women in each group experienced an adverse event of any grade of severity. The most common adverse events were alopecia, nausea, neutropenia, diarrhoea, asthenia and fatigue.

The same proportion of women in each group (52%) experienced at least 1 adverse event of grade 3 (severe) or worse. There were numerically more grade 3 adverse events and grade 4 adverse events in the intravenous group compared to the subcutaneous group (273 versus 254, and 81 versus 73, respectively) but the number of women experiencing the different grades of adverse events was not stated. Most grade 3 or worse adverse events were haematological toxic effects (most commonly neutropenia, leucopenia, and febrile neutropenia), followed by gastrointestinal disorders: the pattern of adverse events of grade 3 or worse appears similar between the study groups. Four adverse events were fatal (grade 5 severity): 1 in the intravenous group and 3 in the subcutaneous group, all of which occurred during the pre-surgery neoadjuvant phase. Of these 3 deaths, 2 were considered potentially treatment related: 1 from a myocardial infarction and 1 from septic shock.

In addition to grading by severity as above, an adverse event was classed as serious if it was fatal, life-threatening, required inpatient hospital admission or extension of existing hospital admission, resulted in persistent or significant disability or incapacity, was a congenital anomaly or birth defect, was medically significant, or required intervention to prevent any of these outcomes.

More women in the subcutaneous group than in the intravenous group had serious adverse events: new or extended hospital admissions were by far the most common reasons for an adverse event to be classified as serious. Data presented as a graph in the appendix published on line suggest that a greater proportion of serious adverse effects in the subcutaneous group than in the intravenous group related to hospital admission or prolonged stay, whereas a greater proportion of serious adverse effects in the intravenous group than the subcutaneous group were noted as being medically significant (actual numbers not reported).

The proportion of grade 3 adverse events classified as serious was numerically greater in the subcutaneous than in the intravenous group (46/254 grade 3 events [18.1%] compared with 21/273 grade 3 events [7.7%]). This was also the case for grade 4 (life-threatening or disabling) events

(21/73 grade 4 events [28.8%] compared with 19/81 grade 4 events [23.5%]). In the subcutaneous group, 8.1% of serious adverse events related to 'infections and infestations' compared with 4.1% of serious adverse events in the intravenous group. However, the authors state that no infection was associated with a subcutaneous trastuzumab injection site. The most common serious adverse events were febrile neutropenia and neutropenia.

The [summary of product characteristics](#) states that cardiotoxicity (heart failure) at New York Heart Association (NYHA) class II–IV is a common adverse reaction associated with the use of intravenous trastuzumab, occurring in up to 2% of people. It states that all candidates for treatment with trastuzumab should undergo a baseline cardiac assessment. In the [HannaH study](#), cardiac function was monitored by echocardiography or multiple-gated acquisition scan and electrocardiogram every 3 months. No cases of symptomatic congestive heart failure (NYHA class III or IV) were reported. In the subcutaneous trastuzumab group, 2 women developed congestive heart failure NYHA class II, and both had pre-existing risk factors (obesity and hypertension). The authors state that the rate of symptomatic congestive heart failure was in line with previous reports for patients with early operable or locally advanced HER2-positive breast cancer treated with trastuzumab concurrently with an anthracycline.

The authors report that the safety profiles of the intravenous and subcutaneous formulations were similar and consistent with the known safety profile of intravenous trastuzumab. See the section of this evidence summary on the [evidence strengths and limitations](#) for a discussion of the safety data. Safety and tolerability of subcutaneous trastuzumab as adjuvant therapy after surgery in women with early HER2-positive breast cancer is being assessed in the open label, non-randomised SafeHer trial ([ClinicalTrials.gov identifier: NCT01566721](https://clinicaltrials.gov/ct2/show/study/NCT01566721)).

Evidence strengths and limitations

The study design and analysis of results demonstrated non-inferiority of subcutaneous trastuzumab compared with intravenous trastuzumab in early (non-metastatic) breast cancer, in terms of a surrogate antitumour efficacy measure and a pharmacokinetic outcome measure. It should be noted that the treatment schedule used in the study included 24 weeks of neo-adjuvant (that is, before surgery) treatment with trastuzumab, and the pharmacokinetic outcome measure was the trastuzumab C_{trough} level recorded at the end of this neoadjuvant period. Specialists have said that this is different from normal UK practice where surgery is done first unless downstaging is required or preferred.

The analysis was based on the per-protocol data set. The surrogate efficacy outcome appeared similar in the intention-to-treat analysis, but statistical analysis was not reported. The [European](#)

Medicines Agency states that non-inferiority studies should be analysed using both the per-protocol and the intention-to-treat data sets.

The authors of the HannaH study note that although pathological complete response has been associated with long-term clinical benefit, there has yet to be a formal validation of it as a surrogate outcome. The lack of available data on event-free and overall survival measures means that the efficacy of the subcutaneous formulation of trastuzumab has not been proven for patient-oriented outcomes. In addition, the HannaH study relates only to women with early breast cancer, whereas the proposed marketing authorisation also includes women with metastatic breast cancer. No phase III trials which compare the intravenous and subcutaneous formulations of trastuzumab in women with metastatic breast cancer have been conducted (Roche Products Limited: personal communication January 2013).

The same proportion of women in both study groups experienced at least 1 severe (grade 3) or worse adverse events. There were numerically more grade 3 and grade 4 events in the intravenous group than in the subcutaneous group, but those that occurred in the subcutaneous group were more likely to be classed as serious. HannaH had an open-label study design because the different delivery methods of intravenous and subcutaneous administration prevented blinding. The study authors argue that awareness of treatment assignment may have affected the investigators' management of adverse events, leading them to take a more cautious approach with the investigational product and be more likely to admit women receiving the subcutaneous formulation of trastuzumab to hospital compared with those receiving the intravenous formulation. They imply that this explains why similar proportions of women in both study groups had 'severe' adverse events but there were more 'serious' adverse events in the subcutaneous group. However, alternative explanations include the possibility that admission to hospital was clinically justified more often in women in the subcutaneous group.

Context

Treatment alternatives

The subcutaneous formulation of trastuzumab provides an alternative route of administration to the intravenous route. There are currently no other NICE-approved biological treatments for HER2-positive breast cancer.

Costs of treatment alternatives

For intravenous trastuzumab, the cost of a 150 mg vial of powder concentrate for solution for infusion is £407.40. The total cost of an 18-cycle course of treatment, assuming a body weight of 70 kg, is £22,407. Each dose is delivered by infusion over a 30-minute period, every 3 weeks. An initial loading dose over a 90-minute period is also required.

These costs are based on prices published in [MIMS](#) February 2013. Costs may vary in different settings because of negotiated procurement discounts. The costs do not include the staff costs and consumables associated with administering intravenous infusions.

Estimated impact for the NHS

Likely place in therapy

The subcutaneous formulation of trastuzumab is a potential alternative to intravenous trastuzumab in people for whom trastuzumab treatment is appropriate and offers a quicker, less invasive mode of administration. Patient convenience, patient preference for the route of administration, and medical resource use is being assessed in the PrefHer trial ([ClinicalTrials.gov identifier: NCT01401166](https://clinicaltrials.gov/ct2/show/study/NCT01401166)).

A [comment article](#) published with the HannaH study discussed the convenience of subcutaneous administration of trastuzumab in terms of the benefit to people of receiving treatment at home or in the community, and the potential savings in hospital resources. The commentators note that these benefits may not be realised if trastuzumab is combined with other drugs given intravenously, such as taxanes. Savings may also be offset if women receiving subcutaneous trastuzumab are more likely to be admitted to hospital to manage adverse effects, as was seen in the HannaH study. In addition, some women may prefer to receive treatment in a day hospital setting where they can access other support, while some women may prefer to receive treatment at home.

The patent for intravenous trastuzumab [expires in 2014](#) and it is possible that biosimilar products will become available then. However, information on whether such products are in development, their likely licensed route of administration and cost is not available at present.

Local decision makers will need to consider the available evidence when making decisions about using subcutaneous trastuzumab, in the setting of their local care pathways and usual trastuzumab-containing treatment schedules, and local patients' preferences regarding whether they prefer to be treated at home or in a day hospital. The likely benefits of its use will need to be balanced against

the possible risks and the absence of direct patient-oriented outcomes in early breast cancer, and the absence of phase III studies in metastatic breast cancer.

Estimated usage

The manufacturer has used data from the [Quality and Outcomes Framework](#), [Hospital Episodes Statistics](#) and the [National Cancer Intelligence Network](#) to estimate the likely potential use of subcutaneous trastuzumab. It estimates that in the UK in 2012 there were about 5500 people with early-stage HER2-positive breast cancer and about 2200 people with HER2-positive metastatic breast cancer that was suitable for trastuzumab treatment. Using modelling derived from its market research data, which takes account of the distribution of patient weight (and hence the costs of intravenous trastuzumab), and assuming no vial-sharing for the intravenous product, the manufacturer estimates that treating all these people with subcutaneous trastuzumab rather than intravenous trastuzumab would lead to total UK drug cost savings of about £12.5 million over 18 cycles of treatment for early breast cancer and about £4.7 million over a mean treatment duration of 17.2 cycles for metastatic breast cancer (Roche Products Limited: personal communication February 2013). Local decision makers will need to estimate the potential savings for their organisations, because this depends on the weight of patients treated locally and hence the doses and numbers of vials of intravenous trastuzumab used.

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