1123PThe cost of expensive breast cancer drugs

Article *in* Annals of Oncology · September 2017

DOI: 10.1093/annonc/mdx375.011

5 authors, including:

Sofie Berghuis
University of Twente
10 PUBLICATIONS **6** CITATIONS
SEE PROFILE

Hendrik Koffijberg
University of Twente
120 PUBLICATIONS **1,610** CITATIONS
SEE PROFILE

Leon W M M Terstappen
University of Twente
371 PUBLICATIONS **22,681** CITATIONS
SEE PROFILE

Maarten IJzerman
University of Melbourne
351 PUBLICATIONS **5,572** CITATIONS
SEE PROFILE

accurately the EQ5D with ESAS, although we can replace two symptom questions within EQ5D with ESAS with high correlation.

Legal entity responsible for the study: Princess Margaret Cancer Centre, UHN, Toronto, Canada

Funding: Cancer Care Ontario

Disclosure: All authors have declared no conflicts of interest.

1121P Costs of dacomitinib versus placebo in pretreated unselected patients (pts) with advanced NSCLC: CCTG BR.26

S. Karim[1], K. Ding[2], P. Bradbury[3], P. Ellis[4], N. Mittman[5], X. Xiaoqun Sun[6], M. Millward[7], G. Liu[8], S. Sun[9], M.R. Stockler[10], V. Cohen[11], N. Blais[12], R. Sangha[13], M. Boyer[14], R. Sasidharan[15], C. Lee[16], F.A. Shepherd[8], G. Goss[17], L. Seymour[6], N.B. Leighl[18]

[1]Department of Medical Oncology, Queen's University, Kingston, ON, Canada, [2]Canadian Clinical Trials Division, Queen's University, Kingston, ON, Canada, [3]Medical Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada, [4]Department of Oncology, McMaster University, Hamilton, ON, Canada, [5]Sunnybrook Research Institute, University of Toronto, Toronto, ON, Canada, [6]NCIC Clinical Trials Group, Cancer Research Institute, Queen's University, Kingston, ON, Canada, [7]Medical Oncology, School of Medicine and Pharmacology Sir Charles Gairdner Hospital, Nedlands, Australia, [8]Department of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada, [9]Medical Oncology, BC Cancer Agency, Vancouver, BC, Canada, [10]Medical Oncology, NHMRC Clinical Trials Centre, Camperdown, Australia, [11]Oncology, Sir Mortimer B. Davis-Jewish General Hospital, Montreal, QC, Canada, [12]Medical Oncology, Notre Dame du CHUM, Montreal, QC, Canada, [13]Medical Oncology, University of Alberta Cross Cancer Institute, Edmonton, AB, Canada, [14]Medical Oncology, Chris O'Brien Lifehouse, Camperdown, Australia, [15]Medical Oncology, Auckland City Hospital, Auckland, New Zealand, [16]Medical Oncology, British Columbia Cancer Agency, Surrey, BC, Canada, [17]Oncology, The Ottawa Hospital Cancer Centre, Ottawa, QC, Canada, [18]Oncology, Cancer Clinical Research Unit (CCRU), Princess Margaret Cancer Centre, Toronto, ON, Canada

Background: Dacomitinib, a potent irreversible pan-HER kinase inhibitor, has activity in EGFR mutant (mt) lung cancer. BR.26, completed in 2013, compared dacomitinib versus placebo in unselected pts who had received both chemotherapy (1 or 2 lines) and a first-generation EGFR TKI for advanced NSCLC. Dacomitinib pts had significantly improved tumour response rate, PFS, and time to symptom deterioration but not improved survival (OS). A trend towards improved OS was seen in pts with KRAS wildtype (wt) tumours (KRAS unknown in 42%). A prospective economic evaluation was planned for Canadian and Australian pts.

Methods: Resource utilization and utility scores (EQ5D-3L) were collected prospectively in 385 trial participants from Canada and Australia. Direct medical costs were applied to resources in 2015 Canadian dollars (CAD) from the Canadian public health care payer perspective. Dacomitinib is not approved for marketing, thus we used a range of plausible drug costs (0-$120/mg). Restricted mean survival time, utility, and costs per arm were calculated, and explored in KRAS wt and EGFR mt subgroups.

Results: Incremental outcomes and costs by treatment arm are shown below. Mean utility scores were similar, although higher in dacomitinib-treated pts with KRAS wt or EGFR mt tumours (range u = 0.41- 0.55). Mean quality-adjusted survival was approximately 1 month longer with dacomitinib in both KRAS wt and EGFR mt subgroups. Direct medical costs excluding dacomitinib were similar between arms. Exploratory estimates of cost-utility ranged from $26,369-$184,701/QALY in KRAS wt, and $2,243-$133,953/QALY in pretreated EGFR mt pts.

Conclusions: Dacomitinib in previously treated, unselected NSCLC may yield minor gains in quality-adjusted survival without increasing other costs of care. Analyses of mutation status by ctDNA are ongoing.

Clinical trial identification: 2009-016509-41

Legal entity responsible for the study: Canadian Clinical Trials Group (CCTG)

Funding: Pfizer

Disclosure: P. Bradbury: Honorarium from Pfizer and Merck. P. Ellis: In the past two years, received honoraria for talks from Boehringer Ingelheim and Novartis. G. Liu: Honoraria from AstraZeneca, Pfizer, Novartis and Takeda. R. Sangha: Honoraria from: Pfizer, Boehringer Ingelheim, AstraZeneca, Roche, Eli-Lilly, Bristol-Myers Squibb and Merck. M. Boyer: I've received Honoraria (paid to my institution) from Pfizer, Boehringer Ingelheim and Astra Zeneca. G. Goss: Honoraria from Pfizer, AstraZeneca, Boehringer Ingelheim, Lilly, Bristol-Myers Squibb, and Celgene. L. Seymour: Pfizer provided funding for the BR.26 trial. N.B. Leighl: Research funding (institution) - Novartis Unrelated CME (not speaker's bureau) - travel/honoraria - AstraZeneca, Merck Sharpe Dohme, Pfizer, Bristol-Myers Squibb. All other authors have declared no conflicts of interest.

Table: 1121P

Incremental mean outcome with dacomitinib over placebo	All patients (n = 385)	*KRAS* wild type (*KRAS* known n = 165)	*EGFR* mutant (*EGFR* known n = 80)
Survival (ΔE, years)	0.0014	0.104	0.129
Quality-adjusted survival (ΔE, QALY)	0.011	0.069	0.088
Cost (ΔC, 2015 CAD) Set drug price at: $0/mg $40/mg $80/mg $120/mg	$524 $3,944 $7,363 $10,783	$1,829 $5,489 $9,149 $12,809	$199 $4,083 $7,968 $11,853

1122P Feasibility of routine collection of health state utilities using EQ-5D in a breast cancer outpatient clinic

S. Torres[1], M. Trudeau[1], K. Pritchard[1], N. Mitsakakis[2], N. Li[3], M. Krahn[2]

[1]Department of Medicine, Division of Medical Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [2]Toronto Health Economics and Technology Assessment Collaborative, University of Toronto, Toronto, ON, Canada, [3]Imaging Research, Sunnybrook Research Institute, Toronto, ON, Canada

Background: Routine collection of health state utilities in the clinical setting may produce data more representative of the real-world population for use in cost-utility models and guide decision making. We are currently carrying out a cross-sectional study to assess the feasibility of routine administration of EQ-5D to breast cancer patients in a multidisciplinary oncology clinic, in an academic cancer centre in Ontario, Canada.

Methods: English literate women undergoing treatment or on follow-up for their breast cancer (stage I to IV), are being recruited during their scheduled visit to the cancer centre, preferably after completing the implemented routine symptom screening using the Edmonton Symptom Assessment System (ESAS). Consenting patients complete EQ-5D-5L in tablets, followed by a socio-demographic questionnaire and feedback questions pertaining to study conduct. Answers are stored in a research database and linked to diagnostic and treatment data. Feasibility will be assessed primarily by the proportion of patients who fully complete EQ-5D and by their willingness to complete the instrument at each clinic visit.

Results: To date, 474 women were approached; 262 (55%) were eligible and consented to participate (target enrolment: 341). Median age of participants was 56 years (range:28-90); 24% had metastatic disease. All participants were English literate, but 59% were born outside Canada and speak primarily other languages at home. Ninety-eight percent of recruited patients completed EQ-5D, compared with 84% who completed ESAS on the same day (63% completed ESAS voluntarily prior to enrolment; 21% agreed on completing ESAS for study purposes only). Median time for EQ-5D completion was 84 seconds. Most patients (82%) had no problems using the tablet. Willingness to continue to complete EQ-5D at each clinic visit was not affected by disease status (stage I to III versus stage IV) and 74% would "definitely"/"very likely" continue to answer EQ-5D regularly at each clinic visit.

Conclusions: These preliminary results indicate that routine collection of EQ-5D in clinical practice might be feasible, although the completion rate might be overestimated by the cross-sectional design of the study.

Legal entity responsible for the study: Sofia Torres

Funding: None

Disclosure: All authors have declared no conflicts of interest.

1123P The cost of expensive breast cancer drugs

S. Berghuis[1], H. Koffijberg[1], L.W.M.M. Terstappen[2], S. Sleijfer[3], M.J. Ijzerman[1]

[1]Health Technology and Services Research, University of Twente, Enschede, Netherlands, [2]Medical Cell BioPhysics, University of Twente, Enschede, Netherlands, [3]Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands

Background: Increasing healthcare costs are a major challenge in medical oncology, since the total costs of oncology can account for up to 30% of the total hospital expenditures. As many novel (expensive) cancer treatments are being developed, it is important to be transparent about drug prices from an early research stage on. To assess the potential financial impact of pipeline drugs, their expected future prices can be deducted from prices of currently used drugs. As an overview of the standard prices of expensive breast cancer treatments in European countries is lacking, this review aimed to synthesize all evidence on costs of approved, expensive breast cancer drugs in the Netherlands.

Methods: A literature review was performed to create an overview of all approved, expensive drugs in the Netherlands. Standard drug costs were retrieved via the Dutch administrative health authority (ZINL). Drugs were considered expensive if the standard price of the drug was more than €10 per unit or if the cost of a treatment with that particular drug exceeded €1000 on average per patient.

Results: In the Netherlands 25 breast cancer drugs are approved with a standard price of more than €10 per unit. After excluding drugs with expected treatment costs less than €1000, 19 drugs were included in the analysis. The standard drug price is €7,943 on average (range €63 - €45,452), and the average number of cycles per patient is 10.5 (range 4 - 25.3 cycles). This results in average treatment costs per patient of expensive drugs of €17,968 (range €1,103 - €87,123). Four drugs that initially ranked low based on standard drug unit prices (rank 10-19), rank substantially higher (rank 1-10) when ranking total treatment costs.

Conclusions: Ranking standard drug prices per unit may not be very informative. It would be valuable to rank drug treatment costs, based on treatment length and dosage estimates. However, in the Netherlands the expected treatment length for a particular drug is not standardly reported in official approval reports. Furthermore, actual prices of expensive drugs may differ from standard drug prices, by which treatment costs might be deviant. Extending standardization of reporting and calculation of drug treatment costs would be valuable and particularly relevant when extending this type of cost calculations to other countries.

Legal entity responsible for the study: University of Twente - Health Technology and Services Research

Funding: None

Disclosure: All authors have declared no conflicts of interest.

1125P The cost-effectiveness of EndoPredict to inform adjuvant chemotherapy decisions in early breast cancer

S. Hinde[1], C. Theriou[2], S. May[3], L. Matthews[3], A. Arbon[4], L. Fallowfield[3], D. Bloomfield[4]

[1]Centre for Health Economics, University of York, York, UK, [2]Faculty of Medicine & Health Sciences, University of Nottingham, Nottingham, UK, [3]SHORE-C/BSMS, University of Sussex, Brighton, UK, [4]Oncology, Brighton&Sussex University Hospitals, Brighton, UK

Background: Chemotherapy alongside endocrine treatment in ER +ve breast cancer patients post resection of a primary tumour has been estimated to reduce mortality rates by up to 30%. However, the high cost of the therapies, heterogeneous nature of the disease and adverse event profile implies that not all patients should receive the treatment. Many existing prognostic tools such as the NPI, PREDICT, and Adjuvant! Online may not definitively estimate the risk profile of patients, resulting in an *indeterminate* risk classification. In such cases gene expression profiling tests such as EndoPredict can aid the treatment decision. It is important to examine if the test represents a cost-effective use of limited NHS resources in such intermediate risk patients.

Methods: This small (n = 151) multi-centre, two-stage study evaluated the cost-effectiveness of EndoPredict in patients with no clear treatment based on current prognostic criteria. The primary analysis examined whether EndoPredict test results increased or decreased the use and intensity of chemotherapy and the associated direct cost implications. Secondly, a mathematical model was constructed to determine how the change in treatment decisions impacted the long term health of the population, and the future cost implications to the NHS.

Results: A cost increase per patient treated with chemotherapy was identified when EndoPredict test results were available (£149), alongside no significant change in the total number being prescribed chemotherapy. However, chemotherapy was offered to a very different patient population, with 36.9% of patients having a change in treatment decision. The long term analysis found the use of EndoPredict to be associated with greater total costs but a potential increase in population health, resulting in an incremental cost-effectiveness ratio of £26,836 per quality adjusted life year.

Conclusions: While EndoPredict was found to be more expensive overall, the ability of the EPClin score to affect a more optimal allocation of chemotherapy, resulted in long term health gains. However, this result was on the margin of what is conventionally considered a cost-effective use of limited NHS resources and subject to significant uncertainty.

Clinical trial identification: ISRCTN69220108

Legal entity responsible for the study: Sussex Health Outcomes Research and Education in Cancer

Funding: Myriad

Disclosure: S. Hinde C. Theriou, S. May, L. Matthews, A. Arbon, L. Fallowfield, D. Bloomfield: This research was funded through an unrestricted educational grant from Myriad.

1126P The evolution of value with filgrastim in oncology

P. Cornes[1], A. Krendyukov[2]

[1]Comparative Outcomes Group, Bristol, UK, [2]Hexal AG, Holzkirchen, Germany

Background: The value of drugs will evolve over time as new evidence for risks and benefits emerge and the price of a drug changes.

Methods: A NICE Evidence Search on March 1, 2017 revealed 25 systematic reviews and 55 economic evaluations of filgrastim.[1]

Results: Initial Health Technology Assessments (HTA) suggested low value due to high drug cost and no evidence for significant gain in Overall Survival (OS). More recent metanalyses of placebo-controlled randomized trial data show absolute OS gains of 3.2% (95% CI:2.1—4.2%) from filgrastim support of cytotoxic chemotherapy[2] and falling costs due to biosimilar competition.

Conclusions: Physicians and payers need to be aware that HTA decisions need constant re-evaluation, especially following the launch of biosimilar alternatives. This explains the first inclusion of filgrastim in the WHO essential Drug List for cancer more than 20 years after its original approval in 1991,[3] and demonstrates the power of biosimilar medicines in transforming healthcare. References [1] NICE Database search "filgrastim", performed March 1, 2017. URL: https://www.evidence.nhs.uk/search?q=filgrastim. [2] Lyman GH, Dale DC, Culakova E, et al. The impact of the granulocyte colony-stimulating factor on chemotherapy dose intensity and cancer survival: a systematic review and meta-analysis of randomized controlled trials. *Annals of Oncology*. 2013;24(10):2475-2484. doi:10.1093/annonc/mdt226. [3] WHO Model Lists of Essential Medicines, 19th Edition Reviewed November 2015.URL: http://www.who.int/medicines/publications/essentialmedicines/en/. Accessed March 1, 2017.

Legal entity responsible for the study: N/A

Funding: None

Disclosure: P. Cornes: PC: Honoraria from Accord Healthcare, Amgen, Bernstein, BMJ, European Generics Association, Global Academy of Health Sciences, Hospira/Pfizer, Janssen, Lilly, Merck Serono, Napp, National Cancer Society Malaysia, PhAMA, Roche, Sandoz, Teva. A. Krendyukov: Employee of Hexal AG, Holzkirchen, Germany.

1127P Tyrosine kinase inhibitors (TKI): Awareness of drug-drug interaction

N. Ozdemir[1], S. Toptas[2], M.A.N. Sendur[1], O. Yazici[2], B. Öksüzoğlu[3], K. Silay[4], N. Zengin[2]

[1]Department of Medical Oncology, Ankara Yıldırım Beyazıt Universtiy Faculty of Medicine, Ankara, Turkey, [2]Medical Oncology, Ankara Numune Education and Research Hospital, Ankara, Turkey, [3]Medical Oncology, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Ankara, Turkey, [4]Department of Geriatrics, Ankara Yıldırım Beyazıt Universtiy Faculty of Medicine, Ankara, Turkey

Background: Since TKI are metabolized with cytochrome P450 system which is a common pathway for drug-drug interactions. However, these interactions might be overlooked by clinicians. The aim of this study is to evaluate the drug-drug interactions in patients receiving TKI.

Methods: Between May 2007 and March 2015, the data of 265 patients receiving TKI for any reason were evaluated retrospectively. All prescribed medications (PMs) received during TKI therapy for 6 months period were noted and drug-drug interactions with TKI were evaluated. Additionally the nature of interaction was described as 'increase or decrease in TKI level or cautious use of TKI recommended'. The interaction between TKI and PMs was checked from Up-To-Date web site or "medscape.com/drug-interaction checker".

Results: In the study, 265 patients who are taking TKI were noted. 251 patients (94.8%) have been taking PMs additional to TKI. The median age was 56 year (17-87), most common diagnosis was gastrointestinal stromal tumor (27.5%) followed by kidney tumor (26.3%). Most common TKI has been used was Imatinib (21.9%) and Lapatinib (21.9%). The most common PM groups during 6 months period was non-steroidal anti inflammatory and acetaminophen (50.2%), proton pomp inhibitors (41.4%), antibiotics (33.1%), cardiovascular system drugs (33.5%) and narcotic analgesics (21.1%). The interaction rate between TKI and PMs was 54.2%. The nature of interaction was; decrease in TKI level in 39.7% of patients and increase in TKI level in 30.1% of patients. 77.1% of patients have been warned as cautious use of TKI due to increase risk of side effect. The side effect was emphasized as QT prolongation.

Conclusions: TKI drug interaction is usually overlooked by clinicians. Our study revealed that more than 90% of patients who are taking TKI are also prescribed another medication. There is a drug-drug interaction between TKI and prescribed medications in more than half of these patients. TKI-prescribed drug interaction has been caused decrease effectiveness of treatment and increase the rate of side effects and medical cost. The TKI –drug interaction risk might be decreased by increasing the knowledge of the physicians from other specialties about recent molecular treatments.

Legal entity responsible for the study: Ankara Numune Education and Research Hospital

Funding: None

Disclosure: All authors have declared no conflicts of interest.