PCN177

IMPACT OF TOLERABILITY PROFILES ON HTA DECISION MAKING IN ONCOLOGY

Kreeftmeijer J[1], Ryan J[2], Van Engen A[1], Heemstra L[1]

[1]*Quintiles Consulting, Hoofddorp, The Netherlands,* [2]*AstraZeneca, Cheshire, The Netherlands*

OBJECTIVES: To highlight the impact of tolerability profiles on Health Technology Assessment (HTA) decision making in non-small cell lung cancer (NSCLC), ovarian cancer and prostate cancer from three European HTA agencies. **METHODS:** HTA assessments on NSCLC, ovarian cancer and prostate cancer products marketed since 2011 were selected from HAS (France), G-BA (Germany) and NICE (UK). 14 reports on NSCLC, 5 on ovarian cancer and 14 on prostate cancer were selected for in-depth analysis. **RESULTS:** In the UK, safety profiles of the investigated drugs did not seem to have major impact on the recommendation. It was however seen that drugs with a good safety profile were more often recommended. Low impact of safety outcomes on the final decision from NICE was, for example, seen in the assessment of afatinib, where a significant increase in serious adverse events did not negatively impact the recommendation because clinical benefits outweighed safety concerns. Safety data and patient-relevance of endpoints is of high importance in Germany. A beneficial safety profile resulted in a higher benefit rating, whereas a negative safety profile lowered the G-BA rating. Case examples are evaluations of afatinib and crizotinib, where a negative safety profile lowered the benefit rating. Efficacy outcomes were weighted against safety outcomes in all assessments in France. An unfavourable safety profile appeared to have a negative impact on the ASMR rating from HAS, while a favorable profile did not have a positive impact. An example is the assessment of cabazitaxel, where the safety data presented at the initial submission was unfavorable, resulting in a lower ASMR rating (IV), however a resubmission with additional safety data resulted in a higher rating (III). **CONCLUSIONS:** Different EU payers seem to have a different view on safety profiles, with the highest impact seen in Germany and the lowest impact seen in the UK.

PCN179

HIERARCHY OF CLINICAL ENDPOINTS IN HTA DECISION MAKING IN ONCOLOGY

Kreeftmeijer J[1], Ryan J[2], Van Engen A[1], Heemstra L[1]

[1]*Quintiles Consulting, Hoofddorp, The Netherlands,* [2]*AstraZeneca, Cheshire, The Netherlands*

OBJECTIVES: To highlight the hierarchy of clinical endpoints in Health Technology Assessment (HTA) decision making in NSCLC, ovarian cancer and prostate cancer from three European HTA agencies. **METHODS:** HTA assessments on non-small cell lung cancer (NSCLC), ovarian cancer and prostate cancer products marketed since 2011 were selected from HAS (France), G-BA (Germany) and NICE (UK). 14 reports on NSCLC, 5 on ovarian cancer and 14 on prostate cancer were selected for in-depth analysis. In addition ASCO and ESMO guidelines were reviewed for recommendations around endpoints. **RESULTS:** HTA agencies base their decisions on the significance of the presented outcomes, but an analysis of NSCLC assessments showed that when the effect sizes in overall survival (OS) and progression-free survival (PFS) were deemed to be clinically irrelevant, recommendations were less positive. Significant improvements in OS and PFS can still be rejected in the UK because of unacceptable cost-effectiveness. Assessments demonstrating improvements only in PFS were most of the time rejected. Significant improvements in OS were associated with a higher ASMR rating in France. Assessments with improvements in surrogate outcomes, including PFS and overall response rate, were also accepted. OS and quality of life (QoL) are the main outcomes contributing to the benefit rating in Germany. A combination of OS and QoL improvements was associated with a higher G-BA benefit rating. When OS or QoL data were absent, the benefit rating was lower. **CONCLUSIONS:** OS data is considered the gold standard for clinical benefit in oncology, but surrogate outcomes and QoL benefits were also accepted when non-significant OS results were seen. In addition, it seems that statistical significance in itself is not enough, as payers want to see a clinical meaningful difference. Further research in pancreatic, breast and colon cancer, for which thresholds for clinical relevance have been published recently, could validate these results.

PCN180

IS THERE AN IMPACT OF THE ORPHAN DESIGNATION IN ONCOLOGY ON MARKET ACCESS IN EUROPE?

Boiziau SC

EMAUD, Claude Bernard Lyon 1 University, Villeurbanne cedex, France

OBJECTIVES: Orphan drugs (ODs) benefit from incentives from EMA for their development, but in a context of economical restrictions payers are more and more worried by highly priced medicines. The aim of this research was to evaluate whether the orphan designation has an impact on the reimbursement and pricing for drugs in oncology in European coutries. **METHODS:** First, a literature review was performed to identify specific methodologies or consideration applied for the evaluations of ODs. Second, a comparative analysis of HTA recommendations for drugs registered for their first indication in oncology between 2006 and 2013 and appraised by four agencies (HAS, G-BA, NICE, SMC) was performed, as well as coverage decisions, treatment cost, and delay between approval and price agreement. **RESULTS:** In the selected countries, there is no specific methods to assess ODs. However some special considerations are made to accept higher level of uncertainty. 49 drugs were included in the analysis. Significant inter-country variability in the HTA recommendations exists: 20% of drugs received heterogeneous recommendations across countries. The highest concordance scores were obtained between NICE and SMC for ODs (0.9 kappa score), for others concordance was poor. The percentage of rejection for ODs was not higher than the one for non-ODs. Average treatment costs were in favour of orphan oncology drugs, still it was not significant. There was correlation between treatment cost and population size for the non-ODs, but it was not the case for ODs. Delay of appraisal for ODs was slightly shorter, but never significant, except for NICE. **CONCLUSIONS:** In this study we did not show a significant advantage or disadvantage in the market access of ODs in oncology. However, as more ODs will obtain regulatory approval on an accelerated or conditional licensing, providing expanded evidence package to show the value for money to payer will become harder.

PCN181

OPTIMISING MARKET ACCESS OF CANCER DRUGS IN CANADA: A STUDY OF ECONOMIC REVIEWS BY THE PAN-CANADIAN ONCOLOGY DRUG REVIEW (PCODR) EXPERT COMMITTEE

Qu KQ[1], Jiang Y[2], Gauthier A[2]

[1]*Amaris, Toronto, ON, Canada,* [2]*Amaris, London, UK*

OBJECTIVES: pCODR was established in 2010 to guide drug funding decisions through assessing the clinical, patient perspectives and cost-effectiveness (CE) information of new drugs. A considerable number of oncology drugs do not get recommended or get conditional recommendation. This study aims to analyse the comments provided in pCODR final recommendations and act as a guidance for manufacturers to improve the preparation of pCODR submissions. **METHODS:** A review of pCODR assessments was completed evaluating all recommendations made available between May 2012 and December 2014 (N=36) relating to 29 oncology drugs. The comments regarding CE estimates were extracted and analysed based on the assessments made available on the website. **RESULTS:** In the reviewed recommendations, 3 drugs received a positive unconditional recommendation (8%), 26 received a positive recommendation, conditional on the cost-effectiveness being improved to an acceptable level (72%) and 7 were not recommended for funding (20%). Comments on CE estimates were analysed and summarised, the most prevalent comments received included lengthy time horizon (n=13), uncertainty (clinical benefits, large variability in the estimates, ICER sensitive to changes in overall survival) (n=11), lack of clinical evidence (n=9), inadequate model structure (n=5), invalid clinical assumptions (n=5) and the effects of potential wastage on ICER (n=3). **CONCLUSIONS:** This review suggests that in order to minimise comments that might hinder a favourable recommendation, manufacturers need to focus on demonstrating the CE of a drug over a time period in which parameters are more certain (e.g. trial horizon), as well as trying to generate clinical evidence to prove benefits of a drug beyond trial period. The investigators are currently evaluating other aspects of the review deliberative framework (clinical benefit, patient-based values and adoption feasibility) with the aim to develop a more comprehensive guideline for manufacturer's future submissions.

PCN182

USE OF MOLECULAR TESTING PRIOR TO FIRST-LINE ERLOTINIB THERAPY AMONG MEDICARE PATIENTS WITH STAGE IV NON-SMALL CELL LUNG CANCER

Romanus D[1], Cutler D[1], Keating NL[1], Lennes IT[2], Lamont E[1], Gazelle GS[2], Landrum MB[1]

[1]*Harvard University, Boston, MA, USA,* [2]*Massachusetts General Hospital, Boston, MA, USA*

OBJECTIVES: The extent to which individual lung cancer patients undergo guideline-recommended molecular testing in routine care prior to initiation of first-line erlotinib is not known. Prevalence and factors associated with testing and erlotinib therapy were determined in Stage IV non-small cell lung cancer (NSCLC). **METHODS:** We identified incident cases diagnosed between 2007-2009 using SEER-Medicare data. Multivariable models were used to identify factors independently associated with (1) molecular testing and (2) receipt of first-line erlotinib therapy. **RESULTS:** Only 6.5% (500/7,678) were treated with first-line erlotinib and of those, only 8.6% underwent a molecular test. Testing and erlotinib therapy were independently associated with phenotypic enrichment using correlates of epidermal growth factor receptor (EGFR) mutations (female gender, Asian ethnicity, non-squamous-cell histology). Older age, Medicaid enrollment, and admission to hospice decreased likelihood of testing but increased probability of erlotinib therapy. **CONCLUSIONS:** Vast majority of NSCLC patients did not undergo molecular testing prior to treatment. Clinical enrichment criteria were influential in patient selection for erlotinib therapy and testing, but these attributes do not adequately discriminate between EGFR mutation positive and wild type tumors. Provider education and payer mandates to submit test results before reimbursement for targeted therapies may encourage guideline-recommended implementation of these technologies.

PCN183

ONCOLOGY DRUGS RECEIVING BREAKTHROUGH THERAPY DESIGNATION: CLINICAL TRIAL CHARACTERISTICS, DRUG PRICING, AND APPROVAL PROCESS

Park Y[1], Vegesna A[2], Ray D[3], Tsang Y[4]

[1]*University of Maryland College of Pharmacy, Baltimore, MD, USA,* [2]*Thomas Jefferson University, Philadelphia, PA, USA,* [3]*Rutgers University, Piscataway, NJ, USA,* [4]*University of Maryland Baltimore, Baltimore, MD, USA*

OBJECTIVES: The Food and Drug Administration (FDA) grants breakthrough therapy designation (BTD) to facilitate faster approval of drug products are intended to treat a serious or life-threatening condition or provide substantial improvement over existing therapies. The purpose of this review is to compare time to approval, treatment cost and key clinical design characteristics of BTD drugs to non-BTD drugs in oncology. **METHODS:** This narrative review used publicly reported data from drug manufacturers' and FDA websites to examine all oncology drugs approved between November 2013 and December 2014. Median time-to-approval was assessed for new molecular entities (NMEs) and monthly treatment cost was calculated for approved indications based on wholesale acquisition cost (WAC) from Analysource. Approved oncology drugs were categorized as BTD and non-BTD drugs for comparison. **RESULTS:** A total of 25 FDA indications for oncology drugs were approved from November 2013 to December 2014. Nine indications were granted BTD, while 16 were approved through non-BTD pathways. For NMEs, median time from phase 1 trial initiation to indication approval was 2 times longer for non-BTD drugs (3414 days) compared to BTD drugs (1732 days). Pivotal trials had a median sample size of 173 participants and 213 participants for BTD and non-BTD drugs, respectively. For BTD drugs, pivotal trials were 44% phase 2, 44% single-arm, and 89% open-label studies. For non-BTD drugs, pivotal trials were 44% phase 2, 28% single-arm, and 69% open-label studies. Median treatment cost was $9,249 per month for BTD drugs and $10,099 per month for non-BTD drugs. **CONCLUSIONS:** The BTD approval pathway has offered a considerably shorter time-to-approval for oncology drugs. Trials leading to approval for BTD drugs had a higher proportion of single-arm and open-label studies compared to non-BTD drugs. Our findings suggest that oncology drugs with BTD are not related to higher treatment cost.

PCN184
TREATMENT PATTERNS AMONG ELDERLY METASTATIC COLORECTAL CANCER PATIENTS - A SEER-MEDICARE ANALYSIS
Parikh RC, Du XL, Morgan RO, Lairson DR
University of Texas Health Science Center at Houston, Houston TX, USA
OBJECTIVES: Colorectal cancer (CRC) ranks third in prevalence and cancer deaths among all cancers in the United States. Nearly one fourth of CRC patients are diagnosed at metastatic stage (mCRC), which has a poor prognosis and an overall survival of 5% to 8% at five years. Over the last decade multiple chemotherapies and targeted biologics have been approved for mCRC and patients receive an array of these treatments in various combinations, with limited evidence. The study examines current usage patterns by line of treatment for elderly mCRC patients. **METHODS:** A retrospective observational cohort study was conducted for mCRC patients diagnosed from January 2004 through December 2009 using the Surveillance Epidemiology and End Results-Medicare linked database. Systemic chemotherapies and targeted biologics currently approved by the Food and Drug Administration for treatment of mCRC patients were included. The first three lines of treatment administered to elderly mCRC patients were empirically identified. **RESULTS:** The most common first line of treatment for mCRC patients (n=4,603) was bevacizumab + fluorouracil + oxaliplatin (24%), followed by fluorouracil + oxaliplatin (23%). Bevacizumab + fluorouracil + oxaliplatin (18%) and bevacizumab + fluorouracil + irinotecan (15%) were the most administered second line of treatments, while cetuximab + irinotecan and bevacizumab + fluorouracil + irinotecan were the commonly administered third line regimens (15% each). Of 4,603 mCRC patients who received first a line of treatment, 2,708 (59%) continued to receive a second line of treatment, 1,480 (32%) received a third line of treatment, and 1,895 (41%) did not receive any further line of treatment. **CONCLUSIONS:** In accordance with current recommendations and previous studies, fluorouracil + oxaliplatin/irinotecan based regimens with bevacizumab were the most common first and second line treatments. Further exploration of the comparative effectiveness of line of treatments sequencing may yield important information for improving the quality of cancer treatment.

PCN185

WITHDRAWN

PCN186
CURRENT TREATMENT PATTERNS AND SURVIVAL IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA: FINDINGS FROM A BRIEF SURVEY OF EUROPEAN PHYSICIANS
Davis KL[1], Lin HM[2], Zhang S[3], Kaye JA[4]
[1]*RTI Health Solutions, Research Triangle Park, NC, USA,* [2]*Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Cambridge, MA, USA,* [3]*Takeda Pharmaceuticals International, Inc., Deerfield, IL, USA,* [4]*RTI Health Solutions, Waltham, MA, USA*
OBJECTIVES: Little data from real-world clinical settings in Europe are available describing treatment patterns and survival of relapsed/refractory multiple myeloma (RRMM) patients. This study begins to address this knowledge gap using data from a brief physician survey. **METHODS:** A cross-sectional survey of 61 physicians treating RRMM in France (n=21), Germany (n=20), and the United Kingdom (n=20) was conducted in November 2014. The survey collected physicians' opinions on typical treatment patterns and survival of RRMM patients in the relapse/refractory setting (i.e., following disease progression during/after completion of first-line therapy). Analyses were descriptive. **RESULTS:** Specialty distribution among the respondents was 44% hematology, 51% onco-hematology, and 5% medical oncology. Teaching hospitals were the most common practice setting (59%). The respondents' mean (SD) past-year multiple myeloma (MM) caseload was 53.0 (33.0) patients (range: 12-150); 21% of these patients were reported to have high-risk disease based on ISS stage and cytogenetics. Bortezomib-based regimens were first-line treatment for 73% of stem cell transplant (SCT)-eligible patients and 60% of SCT-ineligible patients; in second-line (post-onset of relapsed/refractory MM), lenalidomide/dexamethasone (33%) and bortezomib/dexamethasone (15%) were most common for patients previously receiving SCT (similar results reported for patients not receiving SCT). More than half of physicians estimated that typical second-line treatment duration is <6 months, with progression cited (~75% of respondents) as the main reason for second-line discontinuation. For high-risk patients, 52% of physicians judged median survival to be <10 months from RRMM onset. **CONCLUSIONS:** Bortezomib-based regimens are the predominant choice of first-line MM treatment; while bortezomib is also frequently chosen in second-line (post-RRMM onset), lenalidomide-based regimens are the most common. Survival prospects for RRMM patients remain limited, particularly for high-risk patients, and second-line therapy is typically of short duration (<6 months). Patient-level studies are needed to formally characterize unmet medical needs suggested in our findings for European RRMM patients.

PCN187
TREATMENT PATTERNS OF ENDOCRINE THERAPY AND CHEMOTHERAPY AMONG POST-MENOPAUSAL WOMEN WITH HR+/HER2- METASTATIC BREAST CANCER
Lin PL[1], Hao Y[2], Signorovitch JE[1], Kelley C[1], Macalalad AR[1], Ohashi E[1], Zhou Z[1], Wu EQ[1]
[1]*Analysis Group, Inc., Boston, MA, USA,* [2]*Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA*
OBJECTIVES: Initial endocrine therapy (ET) is preferred for most post-menopausal women with hormone receptor positive human epidermal growth factor receptor 2 negative metastatic breast cancer (HR+/HER2- mBC), and guidelines recommend reserving chemotherapy (CT) for patients with symptomatic visceral disease or no clinical benefit after 3 sequential ET regimens. This study describes treatment patterns among post-menopausal HR+/HER2- mBC patients previously treated with adjuvant therapy (recurrent patients) or not (de novo patients). **METHODS:** Charts from a network of US community-based oncology practices were reviewed for post-menopausal women with HR+/HER2- mBC who progressed to mBC between 1/1/2004 and 9/30/2010. Extracted chart data included demographic characteristics, treatment history, and outcomes. **RESULTS:** Patients (n=144) had a median age of 65 years at mBC diagnosis. They received a median of 2 lines of ET, and <10% had 3 or more lines of ET before receiving CT. De novo patients (n=69) and recurrent patients (n=75) received a median of 2 lines and 1 line of ET, respectively. The recurrent group had a lower proportion of patients receiving 1st-line single agent ET compared with the de novo group (65% vs. 71%). Unlike de novo patients, who had non-steroidal aromatase inhibitors (NSAIs) as the most frequent 1st-line ET (letrozole (35%), anastrozole (26%)), recurrent patients predominantly received fulvestrant (23%) in the 1st-line setting, possibly due to prior adjuvant NSAI. In addition, a higher proportion of recurrent patients received CT as 1st-line therapy compared with de novo patients (27% vs. 20%). **CONCLUSIONS:** The majority of de novo patients received 1st-line NSAIs, but recurrent patients were less likely to receive NSAIs and more likely to receive 1st-line CT. Recurrent patients also received fewer total lines of ET. Most mBC patients did not receive the guideline-recommended 3 lines of ET. The unmet need for improved ET options was particularly pronounced among recurrent patients.

GASTROINTESTINAL DISORDERS – Clinical Outcomes Studies

PGI1
AN EVALUATION OF CLINICAL REMISSION AND SAFETY AMONG BIOLOGICS FOR MODERATE-TO-SEVERE CROHNS DISEASE: A BAYESIAN NETWORK META-ANALYSIS
Bounthavong M[1], Bae YH[2], Vanness DJ[3], Kazerooni R[4], Devine B[5]
[1]*Univer, Seattle, WA, USA,* [2]*Western University of Health Sciences, Pomona, CA, USA,* [3]*University of Wisconsin-Madison, Madison, WI, USA,* [4]*Veterans Affairs San Diego Healthcare System, San Diego, CA, USA,* [5]*University of Washington, Seattle, WA, USA*
OBJECTIVES: To evaluate the efficacy and safety of FDA-approved biologics for moderate-to-severe Crohn's disease (CD). **METHODS:** We conducted a literature search using PubMed, EMBASE, and Cochrane library, and identified articles from inception to October 10, 2014. The combination of search terms included: "infliximab," "adalimumab," "certolizumab pegol," "vedolizumab," and "Crohn's disease." Studies were selected if they were randomized placebo-controlled trials >/= 50 weeks of follow-up; that evaluated one or more biologics of interest, provided results about clinical remission (defined as CD Activity Index<150 points), serious infections and/or serious adverse events; and was conducted in adults. The principal aim was to compare clinical remission at the end of the study period between biologics. Secondary aims included the probability of experiencing a serious infection or serious adverse event. Bayesian network meta-analyses were performed to synthesize results; and comparisons were summarized using odds ratios (OR) and 95% credible intervals (CrI). **RESULTS:** Among 324 articles identified, 11 met inclusion criteria. The odds of achieving clinical remission were greater with adalimumab than with vedolizumab (OR=1.33; 95%CrI: 0.67-2.42), infliximab (OR=1.40; 95%CrI: 0.86-2.53) and certolizumab pegol (OR=1.23; 95%CrI: 0.72-2.29); all not statistically significant. Similarly, the odds of clinical remission were greater with certolizumab pegol than with vedolizumab (OR=0.91; 95%CrI: 0.48-1.60) and infliximab (OR=1.18; 95%CrI: 0.68-1.92); all not statistically significant. Certolizumab pegol had the highest probability of serious infections (0.053%) followed by vedolizumab (0.022%), infliximab (0.010%), and adalimumab (0.008%). Vedolizumab had the highest probability of serious adverse events (19%) followed by certolizumab pegol (10%), infliximab (10%), and adalimumab (7%). **CONCLUSIONS:** We did not find any statistically significant differences between biologics in clinical remission, serious infections, and serious adverse events, which highlights the importance for comparative effectiveness research (CER) in this area. CER will be able to guide clinical and formulary decision-makers in selecting biologics with high value for CD.