

Maastricht, The Netherlands, ⁴Netherlands Comprehensive Cancer Organisation, Eindhoven, The Netherlands, ⁵Comprehensive Cancer Centre the Netherlands (IKNL), Enschede, The Netherlands

OBJECTIVES: To evaluate the patterns of metachronous metastases in patients with breast cancer. **METHODS:** Patients diagnosed with non-metastatic (M0) breast cancer at initial diagnosis between 2006-2008 were selected from the Eindhoven Cancer Registry, which is a population-based registry and records data on newly diagnosed cancer patients. By means of active follow-up, additional data on date of diagnosis and localization of metachronous metastases were collected directly from the patient files. Anatomical sites of metastasis were registered according to the International Classification of Diseases for Oncology (ICD-0). Proportions of metachronous metastases between tumour and treatment characteristics were compared using the Chi2 test. A p-value <0.05 was considered significant. **RESULTS:** There were 1,382 patients diagnosed with M0 breast cancer with a mean (\pm SD) age of 60.3 (\pm 13.8) years. Of those, 116 patients (8%) developed metachronous metastases during a median (\pm SD) follow-up of 4.1 (\pm 1.1) years. The mean (\pm SD) age at the time of diagnosis of metachronous metastases was 61.7 (\pm 14.3) years. Diagnosis of metachronous metastases was confirmed by imaging in 76 patients (66%), in 39 patients (34%) by histopathology and 1 patient (1%) based on clinical symptoms. The most frequent metastatic sites affected were bone (29%) and liver (17%). Breast cancer patients who developed metachronous metastases were significantly more often diagnosed with a hormone receptor positive and a HER2-negative tumor, had a poor tumor grade, had a tumor size greater than 2.1 cm, and more often received chemotherapy at initial breast cancer diagnosis. **CONCLUSIONS:** Of the initially M0 breast cancer patients, 8% developed metachronous metastases, of which one-third developed bone metastasis. The risk of developing metachronous metastases varies among different characteristics at initial breast cancer diagnosis. Identifying the patterns of metachronous metastases and characteristics increasing the risk for developing metachronous metastases contributes to tailored follow-up and adequate initial M0 breast cancer treatment.

PCN16

TREATMENT STRATEGIES FOR ELDERLY PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA: A META-ANALYSIS AND INDIRECT TREATMENT COMPARISON

Buchberger M¹, Rochau U², Vukicevic D¹, Willenbacher W³, Siebert U⁴
¹UMIT - University for Health Sciences, Medical Informatics and Technology, Dept. of Public Health & HTA, Hall in Tyrol, Austria, ²UMIT - University for Health Sciences, Medical Informatics and Technology, Dept. of Public Health & HTA/ ONCOTYROL - Center for Personalized Cancer Medicine, Hall in Tyrol/Innsbruck, Austria, ³ONCOTYROL - Center for Personalized Cancer Medicine/Medical University Innsbruck, Innsbruck, Austria, ⁴Department of Health Policy & Management, Harvard Medical School, Institute for Technology Assessment & Department of Radiology, Hall i.T., Austria

OBJECTIVES: Elderly patients with newly diagnosed multiple myeloma (MM) are usually not considered for stem cell transplantation. Treatment alternatives include multidrug regimens combining prednisone (P)/dexamethasone (D), thalidomide (T), bortezomib (V), cyclophosphamide (C), and melphalan (M). Head-to-head comparisons between the different treatments are lacking. We compared the effectiveness of different first-line treatment strategies for patients with MM (age > 65 years) in terms of progression-free survival (PFS) and overall survival (OS). **METHODS:** We performed a systematic literature search in MEDLINE, EMBASE, Cochrane Library and CRD databases. The primary search yielded 2,673 citations. Ten randomized controlled trials (RCT), enrolling a total of 3,782 patients, were included in our meta-analysis and indirect treatment comparisons. We calculated pooled hazard ratios (HR) with 95% confidence intervals (95%CI). **RESULTS:** Meta-analysis of six RCTs comparing MPT vs. MP showed a statistically significant benefit of MPT in PFS (HR 0.75, 95%CI 0.64-0.88) but no statistically significant difference in OS (HR 0.90, 95%CI 0.75-1.08). The indirect comparison of MPT vs. MPV showed a benefit in PFS for MPV (HR 1.41, 95%CI 1.04-1.90) but no OS difference (HR 1.29, 95%CI 0.98-1.70) using MP regimen as the common comparator. There was no difference between MPT vs. CTD, indirectly analyzed with MP as common comparator (PFS: HR 0.91, 95%CI 0.73-1.14; OS: HR 1.01, 95%CI 0.78-1.32). Indirect comparison was also possible for VMPT-VT vs. VTD, both compared to MPV in the original RCTs. VMPT-VT showed a statistically significant benefit in PFS (HR 0.48, 95%CI 0.33-0.71) but no difference in OS (HR 1.04, 95%CI 0.69-1.59) compared to VTD. **CONCLUSIONS:** While some regimens showed improved PFS, there was no evidence for a benefit in OS comparing the different treatment strategies. Combining all treatment strategies based on published data by using a network meta-analysis may help to identify the optimal treatment option.

PCN17

BAYESIAN NETWORK META-ANALYSIS TO ASSESS RELATIVE EFFICACY OF IBRUTINIB VERSUS IDELALISIB+OFATUMUMAB AND PHYSICIAN'S CHOICE IN RELAPSED/REFRACTORY CLL PATIENTS

Diels J¹, van Sanden S²
¹Janssen Research & Development, Beerse, Belgium, ²Janssen EMEA, Beerse, Belgium

OBJECTIVES: To assess the relative efficacy of ibrutinib (IBR), a first-in-class BTK-inhibitor, versus idelalisib+ofatumumab (IDEL+OFA) and physician's choice in relapsed/refractory (R/R) CLL-patients using Bayesian Network Meta-Analysis (NMA). **METHODS:** Three RCTs in R/R CLL-patients were identified with OFA as common treatment arm. IBR (Byrd, 2014) and IDEL+OFA (Jones, 2015) showed improved investigator-assessed PFS (HR=0.13 and 0.27, respectively) and OS (HR=0.39 and 0.74, respectively) versus ofatumumab in R/R CLL-patients. Osterberg (2014) compared PFS (INV) (HR=0.56) and OS (HR=0.72) for OFA to physician's choice (PC), a mix of well-established CLL-treatments, in more severe patients. A Bayesian NMA was conducted in line with NICE guidelines, using a fixed-effect model with non-informative priors. Posterior distributions for the HR were summarized by median values and 95% credible intervals. **RESULTS:** HR for PFS (INV) comparing IBR vs IDEL+OFA and PC were 0.49 ([0.28;0.87],P(HR<1)=99.2%) and 0.07 ([0.04;0.13],P(HR<1)=100%), respectively. HR for OS comparing IBR vs IDEL+OFA and PC were 0.52 ([0.24;1.14],P(HR<1)=94.7%) and 0.28 ([0.13;0.80],P(HR<1)=100%), respec-

tively. **DISCUSSION:** In absence of head-to-head trials, indirect comparisons can provide useful insights to clinicians and reimbursement-decision making on relative efficacy of treatments. The probabilistic interpretation of Bayesian results suits these purposes, allowing probabilistic statements on which treatment is likely to be the most effective. Bayesian probabilities and credible intervals have different interpretation than classical p-values and confidence intervals. Bayesian results fit well in decision modelling, as resulting posterior distributions can serve as priors in probabilistic cost-effectiveness modelling. Assumptions behind NMA to generate unbiased results were considered valid for IBR vs IDEL+OFA-comparisons, as included patient-populations were nearly identical. Estimates versus PC may be conservative, given higher relative treatments effect in more severe patients. **CONCLUSIONS:** In absence of direct evidence, NMA-results suggest improved PFS and OS for IBR compared to IDEL+OFA and to PC in R/R CLL-patients with high certainty, and can serve as input in HTA-decision modelling.

PCN18

ASSESSMENT OF MAJOR MOLECULAR RESPONSE (MMR) AND COMPLETE CYTOGENETIC RESPONSE (CCyR) AS SURROGATE OUTCOMES OF SURVIVAL IN CHRONIC MYELOID LEUKEMIA CHRONIC PHASE (CML-CP) PATIENTS

Kwon H, Park J, Shin M, Shin S
 National Evidence based Health-care Collaborating Agency, Seoul, South Korea

OBJECTIVES: This study aims to investigate the association of the major molecular response (MMR) and complete cytogenetic response (CCyR) as surrogate outcomes with overall survival (OS) and progression free survival (PFS) in chronic phase of chronic myeloid leukemia (CML-CP) patients using evidence from observational or experimental study. **METHODS:** We conducted using existing systematic reviews and meta-analysis to quantify the association between CCyR and/or MMR at 12 months and OS and/or PFS. The overall survival rate or progression free survival rate according to the responders or non-responders of MMR or CCyR at 12 months after the initiation of first-line TKI therapy (imatinib, dasatinib or nilotinib) was extracted by two independent reviewers. A weighted average of the OS and PFS at different yearly intervals was estimated respectively for both the responders and non-responders with assumption of no censoring. The analyses were carried out using R package "metafor". **RESULTS:** Eleven studies provided data on the association between CCyR or MMR and OS or PFS after imatinib treatment however there were no such studies about dasatinib or nilotinib treatment. Patients who experience CCyR following 12 months' TKI therapy have better long-term (7-year) OS and PFS (OS 97.0% vs 82.5; PFS 97.0% vs 69.6%) than patients who are non-responders at 12 months. Patients who experience MMR at 12 months' TKI therapy have better long-term (5-year) OS and PFS (OS 99.4% vs 93.4%; PFS: 89.9% vs 85.3%). **CONCLUSIONS:** This study identified evidence of the association between CCyR and/or MMR and survival among the TKI treated CML-CP patients, and this is based entirely on imatinib treatment studies. The evidence of dasatinib and nilotinib is limited by the amount and quality of data available. Therefore further research is needed whether this relationship between the surrogate outcomes and final outcomes are equally applicable to dasatinib and nilotinib.

PCN19

COMPARISON OF TREATMENT DURATION AMONG TARGETED AGENTS IN RENAL CELL CARCINOMA (RCC)

Feinberg BA¹, Bohr M¹, Drenning J², Garofalo DF¹, Montgomery J²
¹Cardinal Health, Dublin, OH, USA, ²Cardinal Health, Dallas, TX, USA

OBJECTIVES: Conducting comparative effectiveness research among multiple classes of treatments may inform optimal treatment based on the real-world effectiveness. We conducted a retrospective analysis comparing the duration of six leading treatment options in renal cell carcinoma stratified by line of therapy. **METHODS:** Using claims data (MORE2 Registry), patients with renal cell carcinoma who started and completed at least one line of treatment during the study period (January 2012 to February 2014) were identified by ICD9 code 189.0. Line of therapy (LOT) was assigned based on the patient's available treatment history. Analysis was stratified by LOT. Univariate analysis of variance was performed to compare mean durations among treatment options, LOT, and therapeutic class. Multivariate analysis controlling for demographic and treatment characteristics will be presented in the poster. **RESULTS:** Patients received 1240 complete lines of therapy. Mean duration of treatment by line of therapy was as follows: 1st LOT: 4.0 mo (n=599); 2nd LOT: 3.2 mo (n=357); 3rd LOT 3.1 mo (n=284). There was statistically significant difference in mean duration of therapy between the groups of patients by second line regimen (p=0.003). Within the second line patient group the tyrosine kinase inhibitor (TKI) treated patients had greater duration compared to the mammalian target of rapamycin (mTOR) treated patients (3.5 mo vs 2.6 mo, p-value=0.006). However no difference in duration was observed among first (p=0.7239) and third line regimens (p=0.6476). **CONCLUSIONS:** In this study there was statistically significant difference in duration among leading systemic agents used for second-line treatment of RCC where patients were shown to remain on TKI treatment longer than mTOR treatment. Future research should determine if toxicity and costs influence duration in this therapeutic area.

PCN20

EVALUATION OF PATTERNS OF CARE IN RENAL CELL CARCINOMA (RCC): HIGH UNMET NEED PERSISTS

Feinberg BA¹, Bohr M¹, Drenning J², Garofalo DF¹, Montgomery J²
¹Cardinal Health, Dublin, OH, USA, ²Cardinal Health, Dallas, TX, USA

OBJECTIVES: Understanding prescriber perceptions of efficacy and tolerability among available RCC treatments in a real-world population may inform current areas of unmet need and provide context for the adoption of new therapeutics. We conducted a retrospective analysis evaluating the drug utilization patterns and duration of tyrosine kinase inhibitors (TKI) and mammalian target of rapamycin (mTOR) inhibitors in patients with newly diagnosed and relapsed RCC. **METHODS:** Using claims data (MORE2 Registry), patients with RCC who completed at least one