CLASSIFICATION AND REGRESSION TREES HELP IN DEVELOPING EMBEDDED EVIDENCE- AND CONSENSUS-BASED GUIDELINES

OBJECTIVES: Clinical evidence on the best therapies for patients with Myelodysplastic Syndromes (MDS) is incomplete; however, expert opinion is subjective, therefore we aimed at imbricating evidence- and experience-based knowledge as to provide complete and high-level information to the clinicians dealing with MDS.

METHODS: A systematic review of literature was performed and evidence was graded according to the Scottish Intercollegiate Guideline Network. For 4 specific interventions (chemotherapy, HLA typing, allogeneic bone marrow transplantation, wait-and-see) evidence gaps were completed through direct elicitation of both clinical experience and transposed evidence from 10 panelists. One hundred and two scenarios were built and the panelists were asked to score from 1 to 9 the appropriateness of each therapy in each scenario (RAND method). Appropriateness was inferred from the characteristics of the scenario (age; IPSS risk class; ECOG score of performance status; anemia; cytogenetics) with the technique of Classification and Regression Trees (CRTs) and a treatment algorithm was thus systematically built. ANOVA helped measuring the variability. RESULTS: Age ($F = 572.2$) and performance status ($F = 5.010$) were significantly related with the appropriateness of HLA typing and explained 85% of the variability; the root CRT split patients according to cutoff ages of 55 and 60 years. The appropriateness of transplantation also depended on age ($F = 409.1$) and performance status ($F = 23.63$). Indeed, the first split made by the CRT was based on cutoff ages of 40 and 55 years; further splits were based on the risk class: patients with INT-2/high risk had higher median appropriateness scores than INT-1/low risk patients, however, anemia and age modulated the appropriateness in INT-1 and low-risk classes. Age ($F = 39.4$), performance status ($F = 27.8$) and risk class ($F = 65.5$) explained 79% of the variability in chemotherapy appropriateness: the CRT first splitted patients based upon IPSS risk class and then upon age (>$65$ yrs). CONCLUSIONS: Guidelines can be based on both evidence and consensus of experts since CRTs are a suitable method for inferring treatment algorithms.

HEALTH STATE VALUATIONS IN SUMMARY MEASURES OF POPULATION HEALTH

OBJECTIVES: A health state valuation constitutes a scalar index of the level of health associated with a particular state on a meaningful cardinal scale anchored by perfect health and death. To date, there have been limited empirical data on health state valuations collected from representative sample surveys. WHO has embarked on measurement of health state valuations as a key component of its commitment to routine monitoring and reporting on the health levels of its Member States. METHODS: Household surveys were conducted in representative population samples in ten countries: China, Colombia, Egypt, Georgia, Indonesia, India, Mexico, Nigeria, Slovakia and Turkey. Individuals were presented with 10 health states described by brief labels and asked to describe each state using standardized questions on six health domains, to rank order the conditions, and to provide valuations of the states using a visual analogue scale (VAS). In parallel studies among highly educated respondents in each site, multi-method exercises were conducted in order to examine methods for adjusting VAS scores to correct for scale distortions. RESULTS: A total of 345,757 valuations were obtained from 32,781 respondents. For any given state, there was substantial variation in the descriptions along the six domains. There was considerable agreement in the mean VAS scores across countries, with most Pearson’s correlation coefficients greater than 0.8 and an intraclass correlation coefficient of 0.745. A large proportion of the cross-national variation in VAS scores was related to differences in the health state descriptions for each condition. CONCLUSIONS: It is feasible to collect information on health state valuations in general population surveys in diverse settings using VAS. New data collection tools and analytical methods can improve the cross-population comparability of data on health measurement and valuation. Further work is needed to examine variation in health state values both.

ECONOMIC STUDY OF MALNUTRITION IN ELDERLY PATIENTS LIVING IN THE COMMUNITY: USE OF PROPENSITY SCORE TO ANALYZE OBSERVATIONAL DATA

OBJECTIVE: To assess the cost of malnutrition and related comorbidities among elderly patients living in the community and determine the value of nutritional support. METHODS: Observational, prospective, longitudinal, cohort study with a 12 months follow-up, with 90 general practitioners in France. Two groups of doctors were selected based on historical prescribing practice: one with frequent (FNS) and one with limited (LNS) use of nutritional support. Three hundred seventy-eight elderly patients aged over 70 living in the community, either at home or in institutions, at risk of malnutrition or with established malnutrition. The observational design was preferred over the randomized option because it would not have been ethical to ask doctors to refrain from providing nutritional support when this was their normal practice. To adjust for baseline differences between
groups, costs were analyzed using a propensity score model. Confidence intervals were estimated using bootstrap methods. **RESULTS:** Population in the two groups was balanced for age, gender, weight and body mass index. The groups differed significantly in terms of housing status ($p < 0.05$) and nutritional status ($p < 0.001$). Adjusted costs per patient of hospital care (€531), nursing care (€145) and other medical care were significantly reduced in the FNS group as compared to the LNS group, with cost savings of €723 (90% CI: €1,444 to €43). Including oral supplementation costs, the total cost savings per patient attributable to nutrition support were €195 (90% CI: €929 to +€478). **CONCLUSION:** Appropriate nutrition diagnosis and support may contribute to reduce the costs of health care. Propensity score models are a valuable framework for the analysis of cost data, when it is not possible to conduct randomized studies.

**ARTHРИTIS & OSTEOPOROSIS—Economic Outcomes**

**PAR 1**

**PHARMACOECONOMIC ANALYSIS OF THE TREATMENT WITH LEFLUNOMIDE-METHOTREXATE OR INFILXIMAB-METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS RESISTANT TO METHOTREXATE**

Rubio Terrés C, Romero F, Burrell A, Domínguez-Gil A

1Aventis Pharma S.A, Madrid, Spain; 2Aventis, Bridgewater, Nj, USA; 3Hospital Universitario, Salamanca, Spain

**OBJECTIVE:** To compare the efficiency of leflunomide-methotrexate or infliximab-methotrexate in patients with rheumatoid arthritis resistant to methotrexate. **METHODS:** Cost-minimization pharmacoeconomic model that compared treatments administered at the recommended doses and regimens during a 12-month period. Use of resources and unit costs were estimated from Spanish sources. Simple univariate sensitivity analysis was made of the base case. **RESULTS:** In two randomized, placebo-controlled clinical trials available, the ACR20 and ACR50 response rates at 6 months were 46.2% and 25.4%, respectively, with leflunomide-methotrexate and 50.0% and 27.0%, respectively, with infliximab-methotrexate (2P = 0.57 and 2P = 0.82). The estimated cost per patient of annual treatment with leflunomide-methotrexate or infliximab-methotrexate is €2,823 versus €11,489, respectively (incremental cost of €8,666). Sensitivity analysis confirmed the robustness of the base case, with incremental costs of infliximab-methotrexate ranging from €7,500 to €9,500. In order to equalize the costs per patient of these alternatives, the cost of acquisition of a package of Infliximab would have to decrease from the present €637.59 to a hypothetical cost of €33.10. **CONCLUSIONS:** The cost per patient of twelve months of treatment with the combination of infliximab-methotrexate is greater than that of leflunomide-methotrexate, due mainly to the higher acquisition cost of Infliximab.

**PAR 2**

**THE COST-EFFECTIVENESS ANALYSIS OF CELECOXIB AND NSAIDS WITH GASTROPROTECTIVE AGENTS FOR TREATMENT OF RHEUMATOID ARTHRITIS IN UKRAINE**

Zaliska O

Lviv Medical University, Lviv, Ukraine

**OBJECTIVES:** To examine the sick rate of rheumatoid arthritis in Ukraine in 1996 to 2001. Celecoxib is a new COX-2-inhibitor drug. Randomized controlled clinical trials—RCCTs showed, that celecoxib is safer than non-steroidal anti-inflammatory drugs (NSAIDs). To analyse direct medical costs for treatment celecoxib vs NSAIDs with gastroprotective agents in patients with rheumatoid arthritis from the perspective of public health care in Ukraine. **METHODS:** A decision tree model in Ukraine based on the use of clinical data from literature. Eight RCCTs showed a significantly higher incidence of ulcer—the 6-month rates of ulcer were 5.89% for NSAIDs vs 1.64% for celecoxib, and for NSAID plus proton-pump inhibitor (PPI)—1.94%. Only direct costs associated with three alternatives: celecoxib; NSAID only; NSAID plus PPI (six months) were analysed. All prices are expressed in Ukrainian hryvnas (UAH). The incremental cost-effectiveness ratio was determined. **RESULTS:** The sick rate of rheumatoid arthritis from 1996 to 2001 was increased 8.6% per year in Ukraine. The direct costs of celebrex and NSAID only were comparable 905,4 UAH vs 897,5 (1USD = 5,2 UAH), but the NSAID plus PPI was significantly more costly 1216,1 UAH per one patient. The incremental cost-effectiveness ratio for celecoxib was 1,86 UAH; NSAID plus PPI—80,6 UAH per 1% of ulcer reduction. The total cost of 100 patients treated with celecoxib was 90540 UAH than NSAIDs plus PPI was 95822 UAH. The threshold analysis suggests that celecoxib would be the dominant therapy if its cost was to decrease by 58%. **CONCLUSIONS:** The treatment with Celecoxib is more effective and safe than NSAID only, and to be cost-effective than NSAID plus PPI in Ukraine.

**PAR 3**

**VARIATION IN RESOURCE UTILIZATION AND TREATMENT COSTS FOR RHEUMATOID ARTHRITIS (RA) ACROSS 5 COUNTRIES IN AN ADALIMUMAB (D2E7) CLINICAL TRIAL**


1University Hospital Nijmegen, Nijmegen, Netherlands; 2Institute for Medical Outcome Research, Lorrach, Germany; 3Abbott Laboratories UK Ltd, Maidenhead, Berkshire, United Kingdom; 4Abbott GmbH & Co. KG, Ludwigshafen, Germany; 5Abbott Laboratories, Chicago, IL, USA

The sick rate of rheumatoid arthritis from 1996 to 2001 was increased 8.6% per year in Ukraine. The direct costs of celebrex and NSAID only were comparable 905,4 UAH vs 897,5 (1USD = 5,2 UAH), but the NSAID plus PPI was significantly more costly 1216,1 UAH per one patient. The incremental cost-effectiveness ratio for celecoxib was 1,86 UAH; NSAID plus PPI—80,6 UAH per 1% of ulcer reduction. The total cost of 100 patients treated with celecoxib was 90540 UAH than NSAIDs plus PPI was 95822 UAH. The threshold analysis suggests that celecoxib would be the dominant therapy if its cost was to decrease by 58%. **CONCLUSIONS:** The treatment with Celecoxib is more effective and safe than NSAID only, and to be cost-effective than NSAID plus PPI in Ukraine.