AN EVALUATION OF STATISTICAL METHODS USED TO ANALYSE PATIENT-REPORTED OUTCOMES (PRO) DATA IN PUBLISHED METASTATIC CANCER STUDIES

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OBJECTIVES: As metastatic cancers are generally incurable, treatment goal is to control the cancer and relieve symptoms with minimal side effects, making patient-reported outcomes (PRO) of particular interest in addition to traditional clinical outcomes. The objective of this literature review was to explore and evaluate the PRO data analyses reported in published metastatic cancer studies. METHODS: The literature search was conducted on Medline and Embase databases (1999-2009). Two types of statistical methods were used: the association of PRO scores and clinical outcomes, and the assessment of treatment benefit in terms of PROs. General keywords related to the tumour site and PROs, and key-words specific to each type of analysis were defined. A total of 931 different abstracts were reviewed by one statistician, among which 47 were finally selected for in-depth review. RESULTS: The relation-ship between PRO scores and clinical outcomes was mainly analysed with Cox models, since clinical endpoint was generally survival. When analyses did not involve survival, the association between PRO and clinical outcomes and the use of PRO scores as time-related predictors were analysed with various descriptive non-parametric and parametric statistical methods, depending on parameters like study objectives, design, PRO endpoints used and sample size. Only a few studies discussed the clinical meaningfulness of results alongside statistical significance.

CONCLUSIONS: While a clear consistency was found in the statistical method for the analysis of the link between PRO scores and survival measures, a large heterogeneity of statistical methodologies was observed for other types of PRO analysis. In most studies, the method was appropriate from a statistical perspective but not adapted to the specific nature of PRO data, including under-use of clinically meaningful interpretation of statistical results and absence of specific PRO approaches such as cumulative distribution curves.

USING A WEIBULL PARAMETRIC MODEL FOR FAILURE-TIME DATA TO ASSESS PROGRESSION-FREE SURVIVAL AS A SURROGATE ENDPOINT FOR OVERALL SURVIVAL IN A TRIAL OF PATIENTS WITH METASTATIC RENAL CELL CARCINOMA

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OBJECTIVES: Among surrogate endpoints for overall survival (OS) in oncology trials, progression-free survival (PFS) is increasingly taking the lead. Although there have been some empirical investigations on inter-dependence of OS and PFS, considerable increase of SH between 2007-2010. Furthermore, the increase of SH correlated with the shift towards more stringent goals for metabolic control by official guidelines (currently HbA1c ≤ 6.5%) and implementation of electronic health records. OBJECTIVES: To evaluate the nationwide incidence of SH during the index-treatment period and non-dramatic increase of 87.5% in the frequency of SH (495 events in 2007-2010 versus 264 events in 1997-2000). There was no change in the distribution of SH within the different causes, which suggests that the increase is due to an increase in pre-diabetes and type 2 diabetes patients and an increase in number of SH events. Generalized linear model and logistic regression model were used to compare PPS and proportion of MPR between the two groups, respectively.

CONCLUSIONS: The 761 patients in the hypoglycemia group were matched with 761 patients from the control group of 43,500 patients. As to the index drug, MPR was slightly higher in the hypoglycemia group (0.66 vs. 0.63; p = 0.009), but proportion of MPR ≤ 80% did not significantly differ between the groups (hypoglycemia: 38.44% versus control: 36.06%; p = 0.3387), controlling for the covariates. Also no differences in MPR and proportion of MPR ≥ 80% to overall antihyperglycemics were found between the groups. CONCLUSIONS: It appears that there is little impact of the hypoglycemic event during treatment on the MPR statistics in this population.

CONSIDERABLY INCREASING INCIDENCE OF SEVERE HYPOGLYCEMIA 2007-2010 VERSUS 1997-2000 – A GERMAN LONGITUDINAL POPULATION-BASED STUDY

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OBJECTIVES: In a prospective population-based study covering a German region with 200,000 inhabitants, the incidence of severe hypoglycemia (SH) and clinical characteristics of the corresponding patients were longitudinally compared over two four-year periods between 1997-2000 versus 2007-2010. METHODS: Blood glucose testing was systematically performed in every emergency patient irrespective of the presenting condition, either already prehospitality at the scene of the emergency or immediately after the arrival at the emergency department, respectively. SH was defined as a symptomatic event requiring treatment with intravenous glucose and was confirmed by a blood glucose measurement of <50 mg/dl. RESULTS: Warranting identical methodological conditions, our study revealed a drastic increase of 87.5% in the frequency of SH (46% events in 2007-2010 versus 264 events in 1997-2000). There was no change in the distribution of SH within the different types of diabetes. The incidence of SH between 1997-2000 versus 2007-2010 increased considerably from 11.5 to 27.7 in patients with T2DM and from 18.5 to 33.4 in patients with T1DM. We observed a clear shift from predominantly monotherapy to combination therapy as indicated by lower HbA1c values in increasingly multimorbid subjects. Especially hypoglycemic subjects with T2DM were characterized by a geriatric and multimorbid state (mean age >75 years) receiving additional medical treatment of 3.3 drugs on average versus 2.7 drugs for patients suffering from 3.6 versus 4.4 comorbid diseases with an increase in renal insufficiency from 54% to 76% (relative p-values <0.001). CONCLUSIONS: The nationwide growing incidence of diabetes might have substantially contributed to the considerable increase of SH between 2007-2010. Furthermore, the increase of SH correlated with the shift towards more stringent goals for metabolic control by official German guidelines (currently HbA1c ≤ 6.5%) and the implementation of Electronic Health Records.