A NOVEL APPROACH TO ADJUST FOR THE IMPACT ON SURVIVAL RESULTING FROM PATIENT CROSS-OVER FROM CONTROL TO EXPERIMENTAL TREATMENT IN CLINICAL TRIALS

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OBJECTIVE: Clinical trials are often the best source of efficacy data for economic evaluations of medical interventions. However, their reliability can be compromised when patients cross-over from control to experimental treatment. In two trials evaluating lenalidomide (Len) plus high-dose dexamethasone (Dex) vs Dex alone (MM-009/010) in patients with multiple myeloma (MM), 47% of patients in the Dex alone group were switched to Len +/- Dex at disease progression or following study unblinding. Given the significant efficacy benefits of Len + Dex over Dex alone, the trial data will overestimate the survival with Dex alone biasing the results.

METHODS: External data from the UK Medical Research Council (MRC) MM-IV, V, VI, and VIII trials enrolled between 1980 and 1997 were used to derive an equation reflecting survival without lenalidomide, including prognostic variables to enable adjustment for differences between the MRC and MM-009/010 trials. Applying the MRC equation to the MM-009/010 Dex patient characteristics yielded expected median survival time without cross-over to Len +/- Dex. This was used to calibrate the economic model for the Dex alone group by correcting the scale parameter of the underlying Weibull survival equation, estimated from MM-009/010, assuming the shape parameter remained the same.

RESULTS: Of 873 MRC patients, 826 died. Exponential survival fit the data, with age, MM performance status, M-protein level, and female gender identified as significant predictors of survival. Applying the probability of being normal or overweight and the estimated costs to the distribution of CMR factors resulted in an estimated incremental survival of 14.9 months (95% CI: 12.3–18.0) (compared to 31 months for MM-009/010 Dex patient characteristics, this yielded a median survival of 35.1 months). Compared to MRC MM-IV, M-protein level, and female gender identified as significant predictors of survival.

CONCLUSION: The trial data will overestimate the survival with Dex alone biasing the results. Applying the probability of normal or overweight and the estimated costs to the distribution of CMR factors resulted in an estimated incremental survival of 14.9 months (95% CI: 12.3–18.0) (compared to 31 months for MM-009/010 Dex patient characteristics, this yielded a median survival of 35.1 months).

PROJECTED COST OF CARDIOMETABOLIC RISK FACTORS IN COMMERCIALLY INSURED NORMAL AND OVERWEIGHT PRIMARY CARE PATIENTS

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OBJECTIVE: To determine the economic impact of increased prevalence of cardiometabolic risk (CMR) factors including high blood pressure (BP), loss of glycemic control (DB), high triglycerides (TG) and decreased high density lipoproteins (HDL) in commercially insured overweight patients. Body Mass Index (BMI) > 27 kg/m2 compared to normal weight (BMI < 27 kg/m2).

METHODS: Patients 18–65 years old were identified from an electronic medical record database (EMR) with CMR factors designated by prescription orders or ICD-9 codes and grouped into normal or overweight categories. Similar patients with CMR factors were identified in Medstat MarketScan® administrative claims database using a multivariate two-part regression model, costs from this database were estimated for CMR factors. Probabilities of being normal or overweight from the EMR database were applied to the estimated costs to obtain per patient total annual medical costs for CMR factors stratified by normal and overweight groups.

RESULTS: A total of 75,578 patients with CMR factors were identified in the EMR database. Normal patients were distributed as follows: BP, 23% vs. 77%; DB, 19% vs. 81%; TG, 5% vs. 73%; HDL, 37% vs. 63%; any 2 CMR factors, 13% vs. 87%; any 3 CMR factors, 9% vs. 91%; and all 4 CMR factors, 6% vs. 94%. Estimated costs from the claims database were: high BP, $1630; DB, $1748; high TG’s, $638; low HDL, $1474; and $2606, $2801, $3191 for 2, 3, and 4 CMR factors, respectively. Applying the probability of normal or overweight and the estimated costs to the distribution of CMR factors resulted in an estimated annual cost of $25,000.