**Supplemental online material**

**Table S1. Rates of grade ≥3 adverse events per treatment arm and cost per adverse event**

|  |  |  |  |
| --- | --- | --- | --- |
| **Adverse Eventsa** | **Kd70 QW (%)** | **Kd27 BIW (%)** | **Costs per Episode ($)b** |
| Blood and Lymphatic System Disorders |  |  |  |
| Neutropenia | 5.88 | 6.81 | 9,233 |
| Anemia | 17.65 | 17.87 | 6,161 |
| Thrombocytopenia | 7.14 | 6.81 | 5,394 |
| Vascular Disorders |  |  |  |
| Hypertension | 5.46 | 5.11 | 2,639 |
| Thrombo-Embolic Eventc | 2.10 | 1.28 | 9,867c |
| General Disorders and Administration Site Conditions |  |  |  |
| Fatigue | 4.62 | 2.13 | 2,190 |
| Infections and Infestations | 22.69 | 19.57 | 1,281 |
| Infection | 2.10 | 0.85 | 1,281 |
| Bronchitis | 0.84 | 2.13 | 1,230 |
| Pneumonia | 10.08 | 6.81 | 1,648 |
| Sepsis | 2.52 | 1.28 | 13,099 |
| Septic Shock | 2.10 | 0.43 | 41,492 |
| Upper Respiratory Tract Infection | 0.84 | 2.13 | 1,281 |
| Renal and Urinary Disorders |  |  |  |
| Acute Kidney Injury | 3.36 | 3.40 | 14,545 |
| Eye Disorders |  |  |  |
| Cataract | 2.94 | 2.55 | 1,313 |
| Investigations |  |  |  |
| Neutrophil Count Decreased | 2.94 | 0.43 | 9,233 |
| Platelet Count Decreased | 4.20 | 5.11 | 5,394 |
| Metabolism and Nutrition Disorders |  |  |  |
| Hypercalcemia | 1.26 | 2.55 | 7,871 |
| Hyperglycemia | 1.68 | 2.13 | 4,313 |
| Hypokalemia | 2.52 | 1.28 | 3,963 |
| Tumor Lysis Syndrome | 2.94 | 0.85 | 83,302 |
| Neoplasms benign, malignant and unspecified (including cysts and polyps) |  |  |  |
| Plasma Cell Myeloma | 1.68 | 3.40 | 0 |
| Nervous system disorders |  |  |  |
| Syncope | 2.10 | 0.43 | 7,415 |
| Kd70 QW: once weekly carfilzomib 70 mg/m2 and dexamethasone; Kd27 BIW: twice weekly carfilzomib 27mg/m2 and dexamethasone a Percentages and costs are before per cycle adjustments.b Costs for adverse events were from Policy Analysis Inc. (2015), inflated to September 2018. c Calculated as a weighted average of the costs for ‘Deep vein thrombosis’ and for ‘Pulmonary embolism’ in the source. |

**Table S2. Relative frequency of subsequent treatments and cost per cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Relative frequency (%)** | **Drug acquisition cost per cycle ($)** | **Administration cost per cycle ($)** | **Adverse event cost per cycle ($)** |
| Carfilzomib + lenalidomide + dexamethasone | 6.2% | 24,218 | 584 | 299 |
| Carfilzomib + pomalidomide + dexamethasone | 8.8% | 26,153 | 567 | 1,564 |
| Carfilzomib + cyclophosphamide + dexamethasone | 7.7% | 9,943 | 584 | 299 |
| Daratumumab + lenalidomide + dexamethasone | 21.7% | 24,209 | 361 | 773 |
| Daratumumab + bortezomib + dexamethasone | 10.0% | 18.934 | 918 | 993 |
| Daratumumab + pomalidomide + dexamethasone | 28.3% | 36,769 | 776 | 4,177 |
| Daratumumab | 10.8% | 17,721 | 678 | 749 |
| Elotuzumab + lenalidomide + dexamethasone | 2.7% | 25,256 | 335 | 1,098 |
| Ixazomib + lenalidomide + dexamethasone | 2.3% | 24,587 | 0 | 322 |
| Pomalidomide + bortezomib + dexamethasone | 1.5% | 21,290 | 327 | 1,289 |

**Table S3.** **Akaike and Bayesian Information Criterion values for fitted survival models to Kd70 QW and Kd27 BIW, progression-free survival**

|  |  |  |
| --- | --- | --- |
|   | Kd70 QW | Kd27 BIW |
| AIC | BIC | AIC | BIC |
| Weibull | 946.9 | 953.8 | 1008.6 | 1015.6 |
| Loglogistic | 946.4 | 953.4 | 1002.2 | 1009.1 |
| Exponential | 944.9 | 948.4 | 1007.0 | 1010.5 |
| Gompertz | 946.9 | 953.8 | 1008.4 | 1015.4 |
| Gen.Gamma | 945.6 | 956.0 | 1001.8 | 1012.3 |
| Lognormal | 943.8 | 950.8 | 999.9 | 1006.8 |

AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion; Kd70 QW: once weekly carfilzomib 70 mg/m2 and dexamethasone; Kd27 BIW: twice weekly carfilzomib 27 mg/m2 and dexamethasone.

**Table S4. Akaike and Bayesian Information Criterion values for fitted survival models to Kd70 QW and Kd27 BIW, overall survival**

|  |  |  |
| --- | --- | --- |
|   | Kd70 QW | Kd27 BIW |
| AIC | BIC | AIC | BIC |
| Weibull | 564.0 | 571.0 | 633.1 | 640.1 |
| Loglogistic | 563.4 | 570.4 | 632.5 | 639.4 |
| Exponential | 562.4 | 565.8 | 631.4 | 634.8 |
| Gompertz | 563.3 | 570.2 | 633.4 | 640.3 |
| Gen.Gamma | 563.8 | 574.2 | 634.4 | 644.8 |
| Lognormal | 561.8 | 568.8 | 633.1 | 640.1 |

AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion; Kd70 QW: once weekly carfilzomib 70 mg/m2 and dexamethasone; Kd27 BIW: twice weekly carfilzomib 27 mg/m2 and dexamethasone.

**Figure S1. Proportional hazards diagnostic plots**

Panel 1. Progression-free survival: log cumulative hazard plot (time in log scale)



― Kd70 QW

― Kd27 BIW

Kd70 QW: once weekly carfilzomib 70 mg/m2 and dexamethasone; Kd27 BIW: twice weekly carfilzomib 27 mg/m2 and dexamethasone.

Panel 2. Progression-free survival: log cumulative hazard plot (time in real scale)



― Kd70 QW

― Kd27 BIW

Kd70 QW: once weekly carfilzomib 70 mg/m2 and dexamethasone; Kd27 BIW: twice weekly carfilzomib 27 mg/m2 and dexamethasone.

Panel 3. Overall survival: log cumulative hazard plot (time in log scale)



― Kd70 QW

― Kd27 BIW

Kd70 QW: once weekly carfilzomib 70 mg/m2 and dexamethasone; Kd27 BIW: twice weekly carfilzomib 27 mg/m2 and dexamethasone.

Panel 4. Overall survival: log cumulative hazard plot (time in real scale)



― Kd70 QW

― Kd27 BIW

Kd70 QW: once weekly carfilzomib 70 mg/m2 and dexamethasone; Kd27 BIW: twice weekly carfilzomib 27 mg/m2 and dexamethasone.