SUPPLEMENTARY MATERIAL

**Figure Legends**

**Figure S1.** Model schematic.

Curves provided in this image are hypothetical to illustrate how health state occupancy is determined. OS: overall survival; PD: progressed disease; PF: progression free; PFS: progression-free survival.

**Figure S2.** Parametric survival model extrapolations for OS (avelumab + BSC). BSC: best supportive care; KM: Kaplan-Meier; OS: overall survival.

**Figure S3.** Parametric survival model extrapolations for OS (BSC). BSC: best supportive care; KM: Kaplan-Meier; OS: overall survival.

**Figure S4.** Log-cumulative hazard plot for OS. BSC: best supportive care; OS: overall survival.

**Figure S5.** Standard parametric survival model extrapolations for PFS (avelumab + BSC).BSC: best supportive care; KM: Kaplan-Meier; PFS: progression-free survival.

**Figure S6.** Standard parametric survival model extrapolations for PFS (BSC). BSC: best supportive care; KM: Kaplan-Meier; PFS: progression-free survival.

**Figure S7.** Spline-based parametric survival model extrapolations for PFS (avelumab + BSC).BSC: best supportive care; KM: Kaplan-Meier; PFS: progression-free survival.

Figure S8. Spline-based parametric survival model extrapolations for PFS (BSC). BSC: best supportive care; KM: Kaplan-Meier; PFS: progression-free survival.

Figure S9. Log-cumulative hazard plot for PFS. BSC: best supportive care; PFS: progression-free survival.

**Figure S10.** Extrapolations for TTD (avelumab + BSC). BSC: best supportive care; KM: Kaplan-Meier; TTD: time to treatment discontinuation.

Table S1. Statistical goodness-of-fit scores for OS.

| Model | Avelumab + BSC | | BSC | |
| --- | --- | --- | --- | --- |
| AIC | BIC | AIC | BIC |
| Exponential | 690.99 | 694.84 | 784.62 | 788.48 |
| Generalized gamma | 665.92 | 677.49 | 749.28 | 760.85 |
| Gompertz | 688.87 | 696.59 | 786.36 | 794.08 |
| Log-logistic | 670.66 | 678.38 | 756.55 | 764.26 |
| Log-normal | 664.87 | 672.59 | 750.09 | 757.80 |
| Weibull | 677.76 | 685.47 | 775.16 | 782.87 |
| Values shown in bold represent the lower scores (ie, statistically best-fitting models). AIC: Akaike’s information criteria; BIC: Bayesian information criteria; BSC: best supportive care; OS: overall survival. | | | | |

Table S2. Statistical goodness-of-fit scores for PFS.

| Model | Avelumab + BSC | | BSC | |
| --- | --- | --- | --- | --- |
| AIC | BIC | AIC | BIC |
| INV assessed |  |  |  |  |
| Exponential | 1016.90 | 1020.76 | 936.44 | 940.30 |
| Generalized gamma | 903.47 | 915.04 | 817.12 | 828.69 |
| Gompertz | 981.61 | 989.32 | 907.61 | 915.33 |
| Log-logistic | 964.43 | 972.15 | 822.55 | 830.26 |
| Log-normal | 950.54 | 958.26 | 834.40 | 842.12 |
| Weibull | 1014.15 | 1021.86 | 938.41 | 946.13 |
| 1-knot hazard | 914.96 | 926.53 | 768.86 | 780.43 |
| 1-knot odds | 906.96 | 918.53 | 755.13 | 766.70 |
| 1-knot normal | 899.29 | 910.86 | 797.15 | 808.73 |
| 2-knot hazard | 884.99 | 900.42 | 742.91 | 758.34 |
| 2-knot odds | 884.11 | 899.54 | 745.14 | 760.58 |
| 2-knot normal | 893.73 | 909.17 | 780.83 | 796.26 |
| 3-knot hazard | 879.08 | 898.37 | 707.23 | 726.52 |
| 3-knot odds | 879.89 | 899.18 | **682.25** | 701.54 |
| 3-knot normal | 895.94 | 915.23 | 688.10 | 707.39 |
| BICR assessed |  |  |  |  |
| Exponential | 1005.23 | 1009.09 | 930.79 | 934.65 |
| Generalized gamma | 841.64 | 853.22 | 743.76 | 755.34 |
| Gompertz | 937.21 | 944.93 | 888.59 | 896.31 |
| Log-logistic | 929.00 | 936.71 | 794.70 | 802.41 |
| Log-normal | 918.03 | 925.75 | 809.28 | 817.00 |
| Weibull | 995.02 | 1002.73 | 932.72 | 940.44 |
| 1-knot hazard | 835.01 | 846.58 | 703.36 | 714.94 |
| 1-knot odds | 820.97 | 832.54 | 676.31 | 687.88 |
| 1-knot normal | 818.49 | 830.06 | 698.59 | 710.16 |
| 2-knot hazard | 786.94 | 802.37 | 645.26 | 660.70 |
| 2-knot odds | 787.99 | 803.43 | 657.07 | 672.51 |
| 2-knot normal | 814.61 | 830.04 | 696.77 | 712.20 |
| 3-knot hazard | 785.14 | 804.43 | 610.76 | 630.05 |
| 3-knot odds | 775.59 | 794.88 | **589.38** | **608.67** |
| 3-knot normal | **770.00** | **789.29** | 592.75 | 612.04 |
| Values shown in bold represent the lower scores (ie, statistically best-fitting models). AIC: Akaike’s information criteria; BIC: Bayesian information criteria; BIRC: blinded independent central review; BSC: best supportive care; INV: investigator; PFS: progression-free survival. | | | | |

**Table S1.** Model parameters**.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Input** | **LB** | **UB** | **Distribution** | **Source/justification** |
| Time horizon | 25 years | | Not varied | | Structural assumptions |
| Cycle length | 1 week | | Not varied | |
| Discount rates: costs | 3.50% | | Not varied | |
| Discount rates: QALYs | 3.50% | |
| Discount rates: LYs | 0% | |
| Age, years | 67.500 | 66.81 | 68.19 | Normal | JAVELIN Bladder 100 |
| Proportion male, % | 77 | 74 | 80 | Beta |
| Mean BSA, m2 | 1.87 | 1.40 | 2.331 | Normal |
| Mean weight, kg | 75.1355 | 73.93 | 76.34 | Normal |
| Mean eGFR, mL | 69 | 26.620 | 111.227 | Normal |
| Utilities |  |  |  |  |
| Progression free | 0.772 | 0.760 | 0.785 | Beta |
| Post progression | 0.698 | 0.684 | 0.712 | Beta |
| Total terminal care cost | £4511.83 | £3627.53 | £5396.13 | Normal | Round et al38 |
| Avelumab: 200 mg/10 mL (20 mg per mL) cost per vial | £768.00 | | Not varied | | BNF44 |
| Pembrolizumab subs tx: 100 mg/4 mL (25 mg per mL) cost per vial | £2630.00 | |
| Cisplatin subs tx: 50 mg/50 mL cost per vial | £4.36 | |
| Carboplatin subs tx: 450 mg/45 mL (10 mg per mL) cost per vial | £166.32 | |
| Carboplatin subs tx: 50 mg/5 mL (10 mg per mL) cost per vial | £20.20 | |
| Gemcitabine subs tx: 100 mg/mL cost per vial | £13.09 | |
| Docetaxel subs tx: 80 mg/4 mL (20 mg per mL) cost per vial | £51.00 | |
| Paclitaxel subs tx: 150 mg/25 mL cost per vial | £300.52 | |
| Pemetrexed subs tx: 100 mg powder cost per vial | £150.00 | |
| Admin cost | | | | | |
| Initial infusion (simple) | £183.54 | £147.57 | £219.51 | Normal | NHS reference costs 2018/201937 |
| Complex chemotherapy | £317.73 | £255.45 | £380.00 | Normal |
| RU cost |  |  |  |  |
| Consultant-led oncologist follow-up visit | £194.17 | £156.11 | £232.23 | Normal |
| Non-consultant–led oncologist follow-up visit | £147.38 | £118.49 | £176.26 | Normal |
| Health home visitor | £28.00 | £22.51 | £33.49 | Normal | PSSRU 201936 |
| Community nurse specialist visit | £84.00 | £67.54 | £100.46 | Normal |
| Dietician | £35.00 | £28.14 | £41.86 | Normal |
| GP home consultation | £156.00 | £125.42 | £186.58 | Normal |
| Urologist (consultant) | £104.92 | £84.36 | £125.48 | Normal | NHS reference costs 2018/201937 |
| District nurse | £84.00 | £67.54 | £100.46 | Normal | PSSRU 201936 |
| RU frequency | | | | | |
| PFS avel + BSC | | | | | |
| Oncologist (consultant) | 0.88 | 0.70 | 1.05 | Normal | Clinical validation |
| Clinical nurse specialista | 0.62 | 0.49 | 0.74 | Normal |
| Dietician | 0.06 | 0.05 | 0.08 | Normal |
| GP consultation | 0.26 | 0.21 | 0.31 | Normal |
| Urologist | 0.07 | 0.06 | 0.09 | Normal |
| District nurse | 0.27 | 0.21 | 0.32 | Normal |
| PFS BSC |  |  |  |  |
| Oncologist (consultant) | 0.88 | 0.70 | 1.05 | Normal |
| Clinical nurse specialista | 0.62 | 0.49 | 0.74 | Normal |
| Dietician | 0.06 | 0.05 | 0.08 | Normal |
| GP consultation | 0.26 | 0.21 | 0.31 | Normal |
| Urologist | 0.07 | 0.06 | 0.09 | Normal |
| District nurse | 0.27 | 0.21 | 0.32 | Normal |
| PPS avel + BSC | | | | |
| Oncologist (consultant) | 0.93 | 0.75 | 1.18 | Normal |
| Clinical nurse specialist a | 1.00 | 0.80 | 1.20 | Normal |
| Dietician | 0.16 | 0.13 | 0.20 | Normal |
| GP consultation | 0.72 | 0.58 | 0.87 | Normal |
| Urologist | 0.04 | 0.04 | 0.05 | Normal |
| District nurse | 0.96 | 0.78 | 1.15 | Normal |
| PPS BSC | | | | |
| Oncologist (consultant) | 0.93 | 0.75 | 1.12 | Normal |
| Clinical nurse specialista | 1.00 | 0.80 | 1.20 | Normal |
| Dietician | 0.16 | 0.13 | 0.20 | Normal |
| GP consultation | 0.72 | 0.58 | 0.87 | Normal |
| Urologist | 0.04 | 0.04 | 0.05 | Normal |
| District nurse | 0.96 | 0.78 | 1.15 | Normal |
| AE cost | | | | |  |
| Fatigue | £3518.70 | £2829.04 | £4208.35 | Normal | NHS reference costs 2018/201937 |
| Vomiting | £176.99 | £142.30 | £211.68 | Normal |
| Urinary tract infection | £1454.75 | £1169.62 | £1739.87 | Normal |
| Anemia | £1477.37 | £1187.81 | £1766.93 | Normal |
| Lipase increased | £194.17 | £156.11 | £232.23 | Normal |
| Amylase increased | £194.17 | £156.11 | £232.23 | Normal |
| Back pain | £377.42 | £303.45 | £451.40 | Normal |
| Immune-mediated hepatitis | £499.01 | £401.20 | £596.81 | Normal |
| Immune-mediated rash | £404.26 | £325.03 | £483.50 | Normal |
| Asthenia (assumed same as fatigue) | £3518.70 | £2829.04 | £4208.35 | Normal |
| Hematuria (assumed same as UTI) | £1454.75 | £1169.62 | £1739.87 | Normal |
| Avel + BSC: AE % events, % | | | | | |
| Fatigue | 1.70 | 0.64 | 3.37 | Beta | JAVELIN Bladder 100 |
| Vomiting | 1.20 | 0.32 | 2.53 | Beta | JAVELIN Bladder 100 |
| Urinary tract infection | 4.40 | 2.47 | 6.75 | Beta | JAVELIN Bladder 100 |
| Anemia | 3.80 | 2.03 | 6.03 | Beta | JAVELIN Bladder 100 |
| Lipase increased | 2.90 | 1.41 | 4.92 | Beta | JAVELIN Bladder 100 |
| Amylase increased | 2.00 | 0.82 | 3.77 | Beta | JAVELIN Bladder 100 |
| Back pain | 1.20 | 0.32 | 2.53 | Beta | JAVELIN Bladder 100 |
| Immune-mediated hepatitis | 1.50 | 0.47 | 2.96 | Beta | JAVELIN Bladder 100 |
| Immune-mediated rash | 1.50 | 0.47 | 2.96 | Beta | JAVELIN Bladder 100 |
| Asthenia (assumed same as fatigue) | 0.00 | 0.00 | 0.73 | Beta | JAVELIN Bladder 100 |
| Hematuria (assumed same as UTI) | 1.70 | 0.64 | 3.37 | Beta | JAVELIN Bladder 100 |
| BSC: AE % events, % | | | | | |
| Fatigue | 0.60 | 0.07 | 1.59 | Beta | JAVELIN Bladder 100 |
| Vomiting  **AE events %:**  Where event rates are 0%, 0.5 is added to the Alpha value in the uncertainty parameters so that a non-zero value can be obtained in sensitivity analysis. This is to address that the parameter is not fixed at 0 and there is a risk of patients experiencing that event. | 0.60 | 0.07 | 1.59 | Beta | JAVELIN Bladder 100 |
| Urinary tract infection | 2.60 | 1.19 | 4.47 | Beta | JAVELIN Bladder 100 |
| Anemia | 2.90 | 1.38 | 4.84 | Beta | JAVELIN Bladder 100 |
| Lipase increased | 0.00 | 0.00 | 0.72 | Beta | JAVELIN Bladder 100 |
| Amylase increased | 0.00 | 0.0 | 0.72 | Beta | JAVELIN Bladder 100 |
| Back pain | 2.30 | 0.99 | 4.09 | Beta | JAVELIN Bladder 100 |
| Immune-mediated hepatitis | 0.00 | 0.00 | 0.72 | Beta | JAVELIN Bladder 100 |
| Immune-mediated rash | 0.00 | 0.00 | 0.72 | Beta | JAVELIN Bladder 100 |
| Asthenia (assumed same as fatigue) | 1.20 | 0.31 | 2.49 | Beta | JAVELIN Bladder 100 |
| Hematuria (assumed same as UTI) | 1.40 | 0.47 | 2.91 | Beta | JAVELIN Bladder 100 |
| AE disutility | | | | | |
| Fatigue | −0.07 | −0.04 | −0.11 | Beta | Nafees et al 200826 |
| Vomiting | −0.05 | −0.02 | −0.08 | Beta | Nafees et al 200826 |
| Urinary tract infection | −0.01 | −0.01 | −0.01 | Beta | Sullivan and Ghushchyan27 |
| Anemia | −0.09 | −0.05 | −0.13 | Beta | Beusterien et al 201028 |
| Lipase increased | −0.09 | −0.07 | −0.11 | Beta | Assumed equal to anemia TA58129 |
| Amylase increased | −0.09 | −0.07 | −0.11 | Beta | Assumed equal to anemia |
| Back pain | −0.05 | −0.05 | −0.05 | Beta | Sullivan and Ghushchyan 200627 |
| Immune-mediated hepatitis | −0.06 | −0.06 | −0.06 | Beta | Sullivan and Ghushchyan 200627 |
| Immune-mediated rash | −0.03 | −0.01 | −0.06 | Beta | Nafees et al 200826 |
| Asthenia | −0.07 | −0.04 | −0.11 | Beta | Assumed equal to fatigue |
| Hematuria | −0.01 | −0.01 | −0.01 | Beta | Assumed equal to UTI |
| AE disutility duration | | | | | |
| Fatigue | 108.01 | 86.84 | 129.18 | Normal | TA58129 |
| Vomiting | 19.46 | 15.65 | 23.27 | Normal | TA58129 |
| Urinary tract infection | 14.00 | 11.26 | 16.74 | Normal | Assumption |
| Anemia | 28.00 | 22.51 | 33.49 | Normal | TA58129 |
| Lipase increased | 28.00 | 22.51 | 33.49 | Normal | TA58129 |
| Amylase increased | 28.00 | 22.51 | 33.49 | Normal | Assumed same as lipase increase |
| Back pain | 17.00 | 13.67 | 20.33 | Normal | TA37830,b |
| Immune-mediated hepatitis | 32.90 | 26.45 | 39.35 | Normal | Gauci et al. 201831 |
| Immune-mediated rash | 84.00 | 67.54 | 100.45 | Normal | TA58129 |
| Asthenia | 108.01 | 86.84 | 129.18 | Normal | Assumed equal to fatigue |
| Hematuria | 14.00 | 11.26 | 16.74 | Normal | Assumed equal to UTI |

admin: administration; AE: adverse event; avel: avelumab; BNF: British National Formulary; BSA: body surface area; BSC: best supportive care; eGFR: estimated glomerular filtration rate; GP: general practitioner; NHS: National Health Service; LB: lower bound; LY: life-year; PFS: progression-free survival; PPS: post-progression survival; PSSRU: Personal Social Services Research Unit; QALY: quality-adjusted life-year; RU: resource use; subs: subsequent; TA: technology appraisal; tx: treatment; UB: upper bound; UTI: urinary tract infection.   
a Assumed same as community nurse specialist; b Same as abdominal pain taken from TA306.