Enfortumab vedotin with pembrolizumab for untreated unresectable or metastatic urothelial cancer when platinum-based chemotherapy is suitable

PART 1: For PROJECTOR – contains **no CON** information

Technology appraisal committee C [2nd meeting: 13 May 2025]

Chair: Stephen O'Brien

External assessment group: Southampton Health Technology Assessments Centre

Technical team: Sharlene Ting, Rachel Williams, Lorna Dunning

Company: Astellas

Draft guidance consultation

Preliminary recommendation

Enfortumab vedotin with pembrolizumab **should not be used** for untreated unresectable or metastatic urothelial cancer in adults who can have platinum-based chemotherapy

To help address uncertainty, committee requested data representative of NHS practice and further analyses

- **ToT for avelumab maintenance:** mean ToT and justification for choice of ToT distribution for avelumab, further justification for proportion of people on avelumab maintenance
- **OS of people on standard care treatments:** impact of avelumab maintenance treatment, that is, OS of people on PBC with and without avelumab maintenance treatment

DG consultation responses

- **^Company:** new evidence and analyses using NHS National Disease Registration Service SACT dataset
- **^Merck Sharp & Dohme (manufacturer of pembrolizumab):** provided additional feedback on points such as overestimation of treatment costs for EV+P including use of administration cost codes for pembrolizumab inconsistent with other NICE appraisals (day care setting £392 in ID6332 vs. outpatient setting £208 in TA967, TA997 and TA1017) **[see appendix, slides 18, 19 and 20]**
- **1 web comment:** EV+P is new gold standard for treating metastatic bladder cancer due to high response rates, chance of durable response and good tolerance

^included textual clarification of DG

Abbreviations: DG, draft guidance; EV+P, enfortumab vedotin + pembrolizumab; OS, overall survival; PBC, platinum-based chemotherapy; SACT, Systemic Anti-Cancer Therapy; ToT, time on treatment

Background

RECAP

Urothelial cancer: affects inner lining of bladder (most common, ~90%), urethra, ureter or renal pelvis

- Increases with age (peak 70-90 years), higher incidence in males
- 1 year survival of bladder cancer at diagnosis in England in 2016-20: 64% (stage 3), 29% (stage 4)

Treatment pathway, company positioning and marketing authorisation of enfortumab vedotin (Padcev)

Marketing authorisation: EV in combination with pembrolizumab, is indicated for first-line treatment of adult patients with unresectable or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy

Cisplatin eligible

- Cisplatin + gemcitabine **Avelumab maintenance (TA788)**
- MVAC

Cisplatin ineligible

- Carboplatin + gemcitabine **Avelumab maintenance (TA788)**
- Atezolizumab (PD-L1 ≥5%; TA739)

FIRST LINE

Enfortumab vedotin + pembrolizumab (EV+P)

SECOND LINE

- **PBC rechallenge:** cisplatin / carboplatin + gemcitabine
- Paclitaxel
- Atezolizumab (TA525)

ACM1 committee considerations

- Agree with company's first line positioning of EV+P
- Relevant comparator is PBC (cisplatin/carboplatin + gemcitabine) followed by avelumab maintenance

NICE

Abbreviations: ACM, appraisal committee meeting; EV+P, enfortumab vedotin + pembrolizumab; MVAC, methotrexate, vinblastine, doxorubicin and cisplatin; PBC, platinum-based chemotherapy; PD-L1, Programmed Death-Ligand 1.

EV+P clinical trial evidence

EV-302: ongoing phase 3, multinational, open-label, randomised, controlled trial

- 886 (n=[redacted] UK) adults (≥18 years) with histologically documented unresectable LA or mUC, no prior systemic therapy for LA or mUC, eligible for PBC, had archival tumour tissue for PD-L1 testing, ECOG PS of 0, 1 or 2

ACM1 committee considerations

- EV+P improved PFS and OS compared with PBC
- PBC may not be representative of NHS practice because:
  - time on avelumab maintenance may be longer than seen in NHS (>12 months)
  - it included subsequent therapies not recommended by NICE such as EV monotherapy and P monotherapy (these treatments were more frequent in PBC arm than EV+P arm)
    → OS likely overestimated → affect severity modifier calculation and cost-effectiveness estimates
- Proportion of people on avelumab maintenance in EV-302 (30%) is lower than clinical experts suggest would be seen in NHS (~40% to 47%).
- Overall-survival estimates would be lower in clinical practice if fewer people were to have avelumab than in the trial.

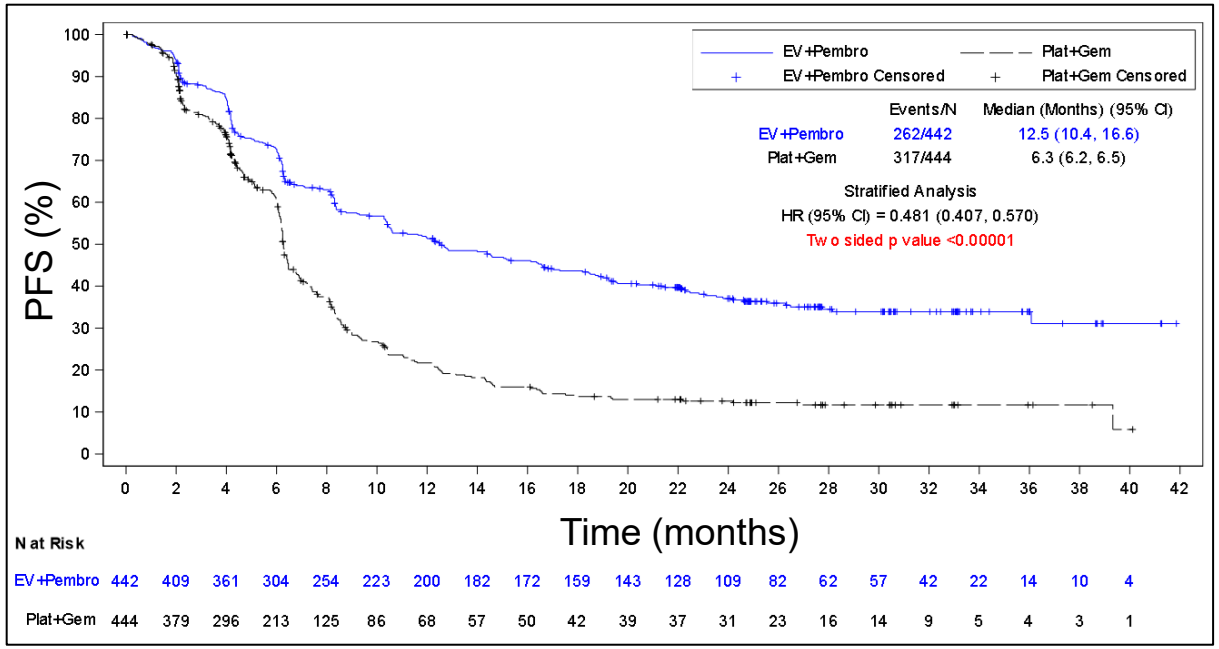
Abbreviations: ACM, appraisal committee meeting; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EV+P, enfortumab vedotin + pembrolizumab; LA, locally advanced; mUC, metastatic urothelial cancer; OS, overall survival; PBC, platinum-based chemotherapy; PD-L1, Programmed Death-Ligand 1; PFS, progression-free survival

EV-302 results – PFS and OS (ITT, Aug 2024 data cut)

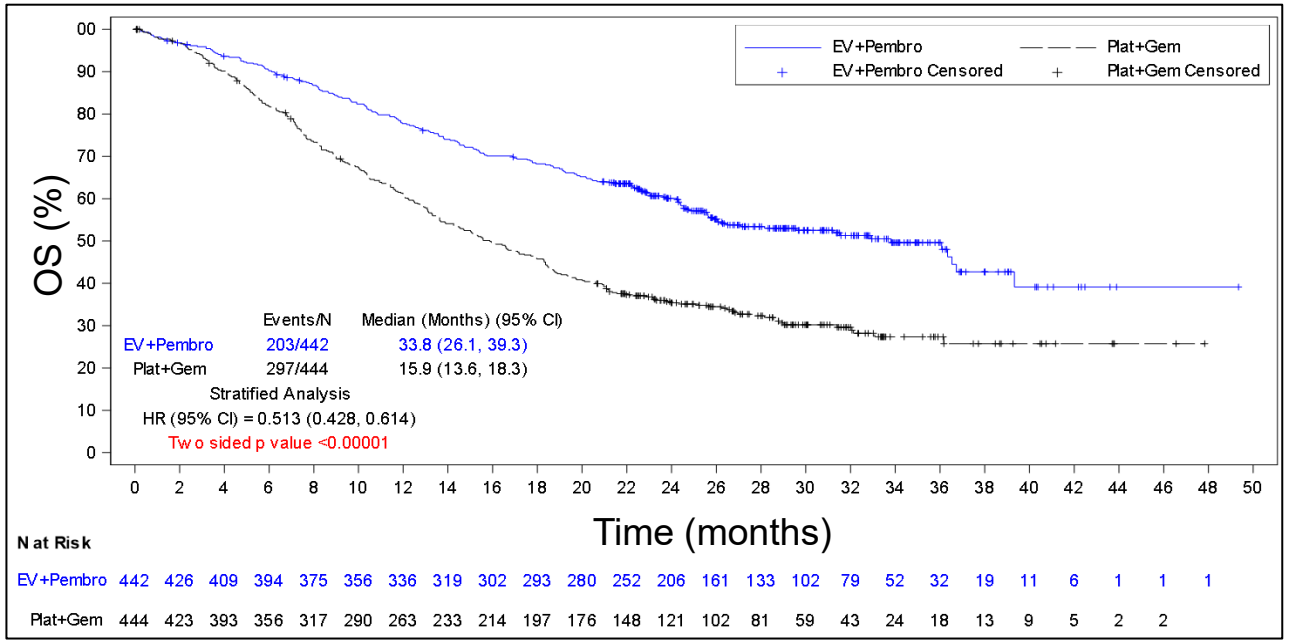
RECAP

EV+P statistically significantly improved PFS and OS compared with PBC

PFS Kaplan-Meier plot



OS Kaplan-Meier plot



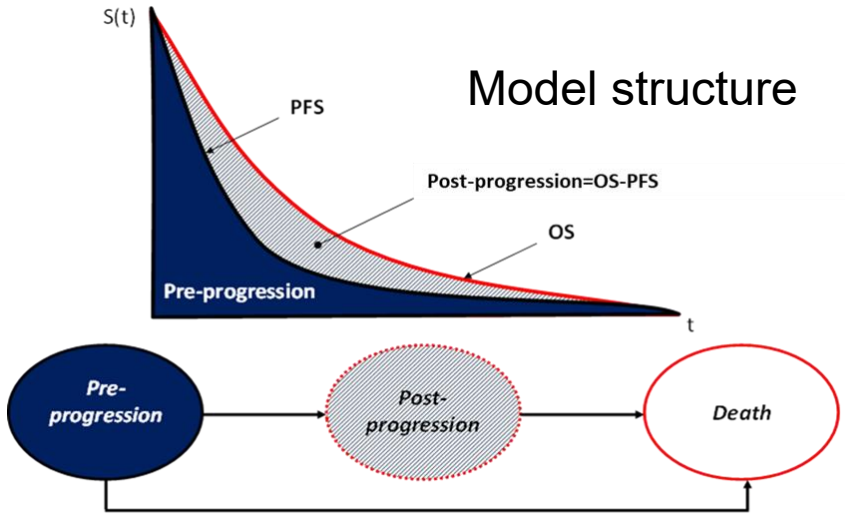
Data cut off: Aug 2024 (ITT)	PFS		OS	
	EV+P (n=442)	PBC (n=444)	EV+P (n=442)	PBC (n=444)
Median in months (95% CI)	12.5 (10.4 – 16.6)	6.3 (6.2 – 6.5)	33.8 (26.1 – 39.3)	15.9 (13.6 – 18.3)
Number of events (%)	262 (59)	317 (71)	203 (46)	297 (67)
HR (95% CI); p value	0.48 (0.41 – 0.57); p<0.00001		0.51 (0.43 – 0.61); p<0.00001	

NICE

Abbreviations: CI, confidence interval; EV+P, enfortumab vedotin + pembrolizumab; HR, hazard ratio; ITT, intention to treat; n, number; OS, overall survival, PBC, platinum-based chemotherapy; PFS, progression free survival

Company's model

RECAP



Model structure

- 3-state partitioned survival model: on-treatment pre-progression (progression-free), post-progression, death
- Lifetime horizon (30 years); 1-week cycle, half-cycle correction; NHS/PSS perspective, 3.5% discounting **from end of year 1**
- **Baseline characteristics**
  - **Full population:** 67.9 years, 77% male, 75.9kg, 1.88m^2 BSA
  - **Cisplatin eligible:** 64.9 years, 79% male, 78.3kg, 1.92m^2 BSA
  - **Cisplatin ineligible:** 71.4 years, 74% male, 73kg, 1.83m^2 BSA

Assumptions	ACM1 committee considerations / preferences
Discounting	EAG's from start of year 1
PFS extrapolation	EAG's log-logistic for both arms
Time on pembrolizumab (see appendix, slide 18)	Company's full KM curve to be correctly implemented
PF utilities (see appendix, slide 19)	EAG's approach. EV+P: treatment independent [redacted]. PBC: treatment dependent first 6 months [redacted], then [redacted]
ICER threshold	Around £30,000 per QALY gained
Treatment waning (see appendix, slide 20)	Difficult to separate waning for EV and P; uncertain

DGC response: Company has provided base case using committee's preferences for these assumptions

- company's presented base case at ACM2 = EAG's base case

Abbreviations: ACM, appraisal committee meeting; BSA, body surface area; EV+P, enfortumab vedotin + pembrolizumab; ICER, incremental cost-effectiveness threshold; KM, Kaplan-Meier; PBC, platinum-based chemotherapy; PFS, progression-free survival; QALY, quality-adjusted life year

New evidence: SACT analyses

Company and NICE provided analyses using SACT dataset (up to July 2024)

Background

- Committee considered EV-302 data from PBC arm may not be representative of NHS practice for standard care
  - Avelumab maintenance: proportion on treatment, mean ToT
  - OS of people on PBC ± avelumab maintenance
- Company and NICE independently did analyses using NDRS SACT data from NHS patients diagnosed with mUC
  - Datasets varied because of differences in selection criteria applied by company and NICE
- NICE shared its analyses with the company who also applied the data in their model and economic analyses

EAG comments (see appendix, slide 21)

- Company's and NICE's selection criteria were generally similar except that the company:
  - included Stage 4 (metastatic) only and multiple tumours (bladder, renal pelvis, ureter) at diagnosis
  - placed time restrictions on start of avelumab maintenance (to avoid off label use) and start of PBC

COMPANY (Pooled A+B, n=771; median 71 years, 67% male)

Cohort A (PBC prior to TA788): n=431
1 Apr 2021 to 30 Apr 2022

Cohort B (PBC after TA788): n=340
1 May 2022 to 31 Jul 2024

NICE (Pooled 1+2, n=793; Median 68 years, 71% male)

Cohort 1 (did not have avelumab maintenance): n=642

Cohort 2 (had avelumab maintenance): n=151

EV-302 (PBC arm, n=444; Median 69 years, 76% male)
n=135 (30.4%) had avelumab

Abbreviations: mUC, metastatic urothelial cancer; n, number; NDRS, National Disease Registration Service; OS, overall survival; PBC, platinum-based chemotherapy; SACT, Systemic Anti-Cancer Therapy; ToT, time on treatment

Key issues

Issue	ICER impact
Does the additional evidence provided by SACT reduce the uncertainty in the evidence for avelumab maintenance ToT and OS for standard care in the NHS?	Large 
At ACM1, the committee concluded that the proportion of people on avelumab maintenance from the clinical trial (30%) was plausible and suitable for decision making. Has the committee heard anything to change its view?	Small 
What approach should be used to model time on treatment for avelumab maintenance?	Small 
Should a 1.2 severity weighting be applied to the incremental QALYs?	Large 

Small: <£3000/QALY; Large: >£3000/QALY

Abbreviations: ACM, appraisal committee meeting; ICER, incremental cost-effectiveness ratio; OS, overall survival; QALY, quality-adjusted life years; SACT, Systemic Anti-Cancer Therapy; ToT, time on treatment; ToT, time on treatment

Key issue: Use of avelumab maintenance (EV-302 and SACT)

Proportion of people starting avelumab maintenance

Company submission	ACM1 company and EAG base cases: EV-302	Company SACT analysis	NICE SACT analysis
~21% to 31%^	30% **(committee preferred)**	Cohort B: 68 out of 340 (20%)	Cohort 2: 151 out of 793 (19%)

^based on 3 sources: EVEREST-2 survey of 41 UK physicians (21% to 28%), Company SACT analysis Apr 2023 to Mar 2024 of bladder cancer at any stage at diagnosis (31%), Market data Jun 2024 of ~50 UK clinicians ([redacted])

EAG comments: Altering % on avelumab in model affects total costs only, so EAG prefers to use 30% in its base case and presents scenario using 20% to reflect SACT data.

Time on avelumab maintenance

Background

- Time on avelumab extrapolated from EV-302. Company: Weibull (mean ToT 16.9m), EAG: exponential (mean 13.9m)
- ACM1 clinical experts: time on avelumab maintenance uncertain (available in routine practice <5 years)

Company

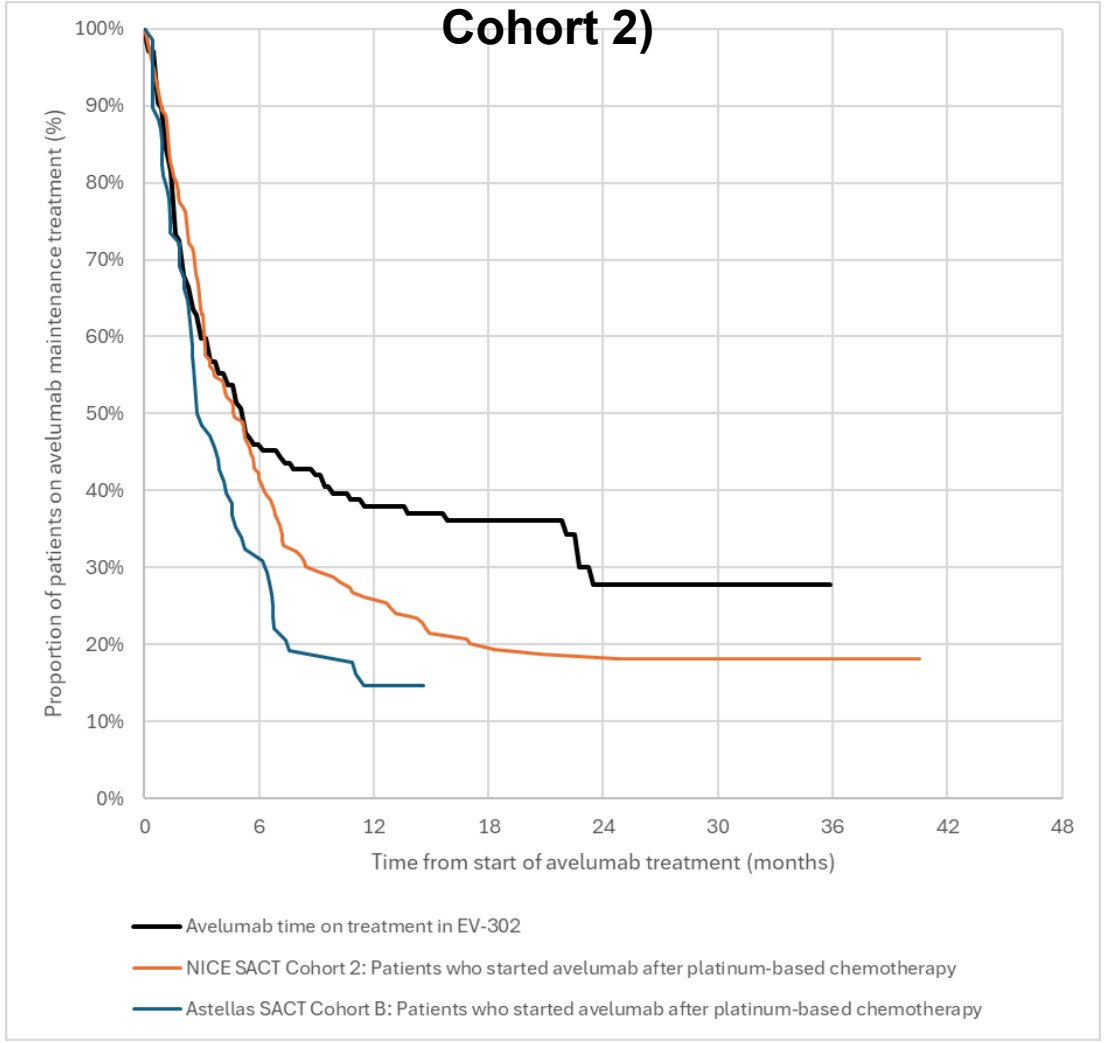
- Provided extrapolations of mean time on avelumab from SACT (company and NICE) – prefer generalised gamma
- People may stay on extended periods of avelumab maintenance and plateaus in EV-302 and NICE SACT Cohort 2 suggest hazards for stopping treatment reduce over time → exponential distribution not appropriate

EAG comments: agree hazards for exponential curve do not predict an avelumab treatment stopping rate that reduces over time, but Weibull overestimates avelumab treatment duration. Exponential produces shortest ToT.

Abbreviations: ACM, appraisal committee meeting; SACT, Systemic Anti-Cancer Therapy; ToT, time on treatment

Time on avelumab maintenance: EV-302 and SACT

Time on avelumab maintenance in EV-302 and SACT datasets (Company Cohort B and NICE Cohort 2)



Proportion estimated to be on avelumab up to 24 months

Cohorts on avelumab maintenance	Time (months)			
	6	12	18	24
EV-302 (PBC arm)	46%	38%	36%	28%
Company SACT Cohort B	32%	15%	n/a	n/a
NICE SACT Cohort 2	42%	26%	19%	18%
Weibull fitted to EV-302 data	56%	41%	32%	26%
Exponential fitted to EV-302 data	65%	43%	28%	18%

Source	Time on avelumab maintenance (months)	
	Mean	Median (95% CI)
Company SACT Cohort B	8.20	2.88 (2.43 – 4.8)
NICE SACT Cohort 2, restricted mean of observed data	11.07	4.7 (3.3 – 5.99)
NICE SACT Cohort 2, company's generalised gamma extrapolation	14.9	4.7 (3.3 – 5.99)
EV-302; Weibull	16.94	[redacted]
EV-302; exponential	13.94	[redacted]

NICE

Abbreviations: CI, confidence interval; KM, Kaplan-Meier; PBC, platinum-based chemotherapy'; SACT, Systemic Anti-Cancer Therapy; ToT, time on treatment

Overall Survival for PBC: EV-302 and SACT

OS for PBC in EV-302 trial is longer than that observed for NHS patients based on SACT data

Clinical experts ACM1: 10-year survival estimates from trial extrapolation (log-logistic) of 5% likely too optimistic
Committee considerations ACM1: choice of OS model impacts the severity weighting and CE estimates

Cohorts	Median, months	Time (months)			
		6	12	24	36
EV-302 PBC arm	15.9	82%	61%	35%	27%
Company SACT Cohort A (before TA788)	11.02	75%	46%	26%	18%
Company SACT Cohort B (after TA788)	10.23	73%	44%	21%	n/a
NICE SACT Cohort 1 (did not have avelumab maintenance)	Pooled 1+2:	64%	35%	18%	13%
NICE SACT Cohort 2 (had avelumab maintenance)	10.1	98%	70%	34%	18%

OS extrapolations of people on PBC in company SACT Pooled cohort A+B

Model	AIC	BIC	Mean, months	Timepoint in years			
				1	2	5	10
Exponential	4592.6	4597.3	17.54	50%	25%	3%	0%
Weibull	4591.0	4600.3	17.11	51%	25%	2%	0%
Log-normal	4738.1	4747.4	28.49	49%	30%	12%	5%
Log-logistic (company preferred)	**4561.7**	**4571.1**	**23.41**	**48%**	**25%**	**8%**	**3%**

NICE

Abbreviations: ACM, appraisal committee meeting; AIC, Akaike information criterion; BIC, Bayesian Information Criterion; CE, cost effectiveness; OS, overall survival; PBC, platinum-based chemotherapy'; SACT, Systemic Anti-Cancer Therapy

Company scenarios using SACT analyses

- Scenario 1: ACM1 EAG base case, but Weibull distribution for time on avelumab maintenance from EV-302
- Scenario 2: replace comparator data from EV-302 with data from Company SACT analyses for OS, proportion of people on avelumab and extrapolation of time on avelumab in PBC using pooled A+B cohort
- Scenario 3: replace comparator data from EV-302 with data from NICE SACT analyses for OS in Cohort 1 (no avelumab)
- Scenario 4: replace comparator data from EV-302 with data from NICE SACT analyses for OS in Cohort 2 (avelumab)

Scenario	ACM1 EAG base case	Scenario 1	Scenario 2	Scenario 3	Scenario 4
% on avelumab (see slide 9)	30%	30%	20%	0%	100%
Time on avelumab maintenance	EV-302: exponential	EV-302: Weibull	Company SACT Pooled cohort A+B: generalised gamma	-	NICE SACT Cohort 2: generalised gamma
PBC OS	EV-302: log-logistic	EV-302: log-logistic	Company SACT Pooled cohort A+B: log-logistic	NICE SACT Cohort 1: log-logistic	NICE SACT Cohort 2: log-logistic

EAG comments

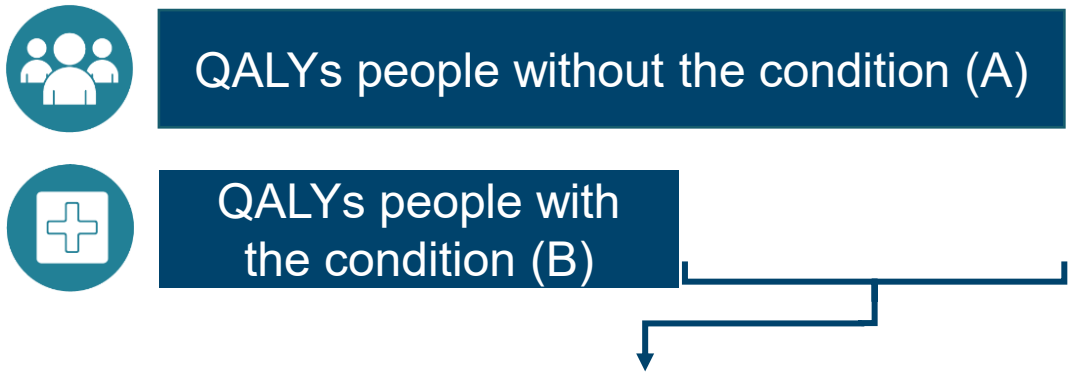
- Altering % on avelumab in model affects total costs of PBC arm but does not affect QALYs gained. Lower % on avelumab would affect OS

Does the additional evidence provided by SACT reduce the uncertainty in the evidence for avelumab maintenance ToT and OS for standard care in the NHS?

Abbreviations: ACM, appraisal committee meeting; OS, overall survival; PBC, platinum-based chemotherapy'; SACT, Systemic Anti-Cancer Therapy; ToT, time on treatment

QALY weightings for severity

Severity modifier calculations and components:



Health lost by people with the condition:

- Absolute shortfall: total = A – B
- Proportional shortfall: fraction = (A – B) / A
- *Note: The QALY weightings for severity are applied based on **whichever of absolute or proportional shortfall implies the greater severity**. If either the proportional or absolute QALY shortfall calculated falls on the cut-off between severity levels, the higher severity level will apply

QALY weight	Absolute shortfall	Proportional shortfall
1	Less than 12	Less than 0.85
X 1.2	12 to 18	0.85 to 0.95
X 1.7	At least 18	At least 0.95

Abbreviations: QALY, quality-adjusted life year

Key issue: Severity modifier

Background

- Company and EAG base case in ACM1 were below severity modifier QALY shortfall cut-off
  - Company provided scenarios using different distributions of EV-302 PBC OS extrapolated data: 5 of 7 curves met the severity modifier threshold of 1.2
- Committee: OS in EV-302 PBC may be overestimated affecting severity modifier calculations → prefer more OS data on PBC +/- avelumab generalisable to NHS

Company

- OS extrapolations using SACT data showed worse median survival for people on standard care in NHS than in EV-302 (**see slide 11**)
- Severity modifier 1.7 in TA on erdafitinib for u/mUC after ≥1 line of treatment suggests 1.2 may apply to 1L EV+P

Scenario	Proportional shortfall	Severity modifier
Corrected base case (EAG and committee's preferred assumptions, exponential distribution for time on avelumab maintenance)	0.84	1.0
Scenario 1: Corrected base case, but Weibull distribution (company preferred) for time on avelumab maintenance	0.84	1.0
Scenario 2: Company SACT Pooled cohorts A+B	0.88	1.2
Scenario 3: NICE SACT Cohort 1 (did not have avelumab maintenance)	0.90	1.2
Scenario 4: NICE SACT Cohort 2 (had avelumab maintenance)	0.87	1.2

Should a x1.2 severity weighting be applied?

Abbreviations: 1L, first line; ACM, appraisal committee meeting; OS, overall survival; PBC, platinum-based chemotherapy'; SACT, Systemic Anti-Cancer Therapy; TA, technology appraisal; u/mUC, unresectable or metastatic urothelial cancer

Summary of cost-effectiveness results

All ICERs are reported in PART 2 because they contain confidential comparator PASes

Summary of corrected base case results

- **Without severity weight**: ICER is **>£30,000/QALY**
- **With severity weight x1.2**: ICER is **>£30,000/QALY**

Results of company scenario analyses 1 to 4 and EAG's scenario analysis using 20% of people on avelumab maintenance:

- **Without severity weight**: all ICERs except for scenario 4 are **>£30,000/QALY**
- **With severity weight x1.2**: all ICERs except for scenario 4 are **>£30,000/QALY**

Abbreviations: PAS, patient access scheme; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year

Other considerations

Equality issues

- From ACM1, committee noted higher incidence of bladder cancer for people from more socioeconomically deprived backgrounds, outcomes may differ based on age and sex and possible unequal access to treatment
    - Committee acknowledged these equality concerns but noted that they could not be addressed in a technology appraisal
- At DG consultation, no new issues raised on equality

Managed access – company did not submit managed access proposal

Criteria for a managed access recommendation. Committee can make a recommendation with managed access if:

- the technology cannot be recommended for use because the evidence is too uncertain
- the technology has the **plausible potential** to be cost effective at the **currently agreed price**
- new evidence that could **sufficiently support the case for recommendation** is expected from ongoing or planned clinical trials, or could be collected from people having the technology in clinical practice
- data could feasibly be collected within a reasonable timeframe (up to a **maximum of 5 years**) without **undue burden**

- Are there any other key uncertainties?
- Are there any equality issues to be considered?
- Are there any uncaptured benefits?

Abbreviations: ACM, appraisal committee meeting; DG, draft guidance

Enfortumab vedotin with pembrolizumab for untreated unresectable or metastatic urothelial cancer when platinum-based chemotherapy is suitable [ID6332]

Supplementary appendix

NICE National Institute for Health and Care Excellence

Other issues raised by MSD: overestimation of treatment costs

ToT for pembrolizumab: delayed dose in KM curve for pembrolizumab may be double counted when 24-month stopping rule is removed

- Full KM curve reaches maturity at 134 weeks (44 Q3W or 22 Q6W treatment cycles costed)
  - ToT cap of 35 administrations for a Q3W regimen or 18 administrations for a Q6W regimen (starting at Week 0 and ending at Week 102), patients who have delayed administrations are costed earlier than actual timing in EV-302 → overestimate proportion of people on pembrolizumab and higher total costs
- Company's administration cost codes for EV+P in combination and monotherapy have not been considered
  - Used currency code SB17Z with service code DCRDN (day case setting, £392) – inconsistent with previous appraisals of pembrolizumab where currency code SB12Z with service code OP (outpatient setting, £208) has been accepted (TA967, TA997 and TA1017)

EAG comments: MSD cost of £208 is negligibly higher than national average unit cost of £204
- Provided 2 scenarios: using MSD cost of £208 only **and** using MSD cost and outpatient costs for all other administration costs (SB12Z £204; SB13Z £506; SB14Z £501; SB15Z £295)

ToT for EV: plausible and alternative approach to modelling ToT for EV suggested by EAG not considered

- EAR: Clinical advice to company suggests that people on EV would halve each year and that no patients would be on treatment by Year 5. Use EV-103 data as supportive evidence to model ToT for EV (generalised gamma)

Should administration costs of pembrolizumab be for outpatient setting at £208 [MSD] (/£204 [EAG]) than day care setting at £392?

Link to Draft guidance consultation
Link to Company's model

Abbreviations: EAR, EAG report; EV+P, enfortumab vedotin + pembrolizumab; KM, Kaplan-Meier; MSD, Merck Sharp & Dohme; OS, overall survival; PBC, platinum-based chemotherapy; Q3W, once every 3 weeks; Q6W, every 6 weeks; ToT, time on treatment

Other issues raised by MSD: PF utility values

Pre-progression utility values according to treatment arm or response are plausible

- Reiterates EV-302 evidence on overall QoL: EV+P had a brief decline at week 3 but returned to normal afterward vs PBC had a steady decline from week 1 to week 17
- Likely company and EAG's pre-progression utility values are underestimated because there are 2 groups: responders to treatment who have high utility and patients with stable disease who have lower utility
- Utilities by response could be undertaken where patients with a complete response or partial response can be classified as a "responder" and those with stable disease as a "non-responder", and their utilities within the PFS health state reported separately. Time to response or progression or death from EV-302 can be modelled to estimate the proportions of PF patients who are non-responders and who are responders. Given that more people on EV+P had a complete response compared to PBC ([redacted] vs [redacted]), this approach would account for some benefits not captured in current QALY calculation

Link to Draft guidance consultation
Link to Company's model

Abbreviations: EV+P, enfortumab vedotin + pembrolizumab; MSD, Merck Sharp & Dohme; PBC. platinum-based chemotherapy; PFS, progression-free survival; QoL, quality of life

Treatment waning and OS extrapolation

Background

- Company and EAG did not include treatment waning in model
- Already accounted for in OS extrapolations (company and EAG preferred log-logistic):
  - hazard rates of log-logistic curves converge over time
  - 5-year follow-up of EV-103 Cohort A (untreated cisplatin-ineligible subgroup) + dose escalation shows sustained plateau in PFS and OS from 3 years
- Committee acknowledged difficulty in separating treatment waning in EV+P → considered uncertain

Company

- Reiterates log-logistic OS extrapolation without additional effect waning is most appropriate given durable response observed in EV-103 and EV-302 (supported by clinical expert feedback)
- States that generalised gamma OS extrapolation is not appropriate

Other considerations (MSD feedback)

- Agrees with company, EAG and clinical experts' views that treatment waning is accounted for in model
- Highlights that no effect waning has been assumed for avelumab maintenance
- Consider generalised gamma should be used to extrapolate OS for PBC and log-logistic for EV+P
  - PBC: if ToT for avelumab maintenance is shorter in NHS than EV-302 and subsequent treatments in EV-302 are not relevant to NHS, OS in NHS is likely shorter
  - Precedent for NICE committees to accept different OS models for each treatment based on clinical plausibility, hazard trends or differing mechanisms of action

Has the committee heard anything to change its views from ACM1?

Link to Draft guidance consultation
Link to Company's model

Abbreviations: EV+P, enfortumab vedotin + pembrolizumab; MSD, Merck Sharp & Dohme; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression-free survival; ToT, time on treatment

SACT datasets: Company and NICE

Characteristic	NICE analysis	Company analysis
Stage of disease	Stage 4 (metastatic) plus either M of 1 (distant metastases) or M status unknown	Stage 4 (metastatic) only
Multiple tumours of interest (bladder, renal pelvis and ureter) diagnosed between 2020 and 2022	Excluded	Included but should a patient have received multiple primary diagnoses of mUC between 2020 and 2022, the first such tumour will be selected.
Avelumab regimens	No restriction	Initiated between one day after the start of the first-line platinum-based regimen and up to 43 weeks from the start of the first-line platinum-based regimen (to avoid off-label use and for other licensed indications)
Platinum based chemotherapy (PBC) treatment date	No restriction	Cohort B started the first platinum-based regimen between 01/05/2022 and 31/07/2024

Link to New evidence: SACT analyses

Abbreviations: SACT, Systemic Anti-Cancer Therapy