HTA17

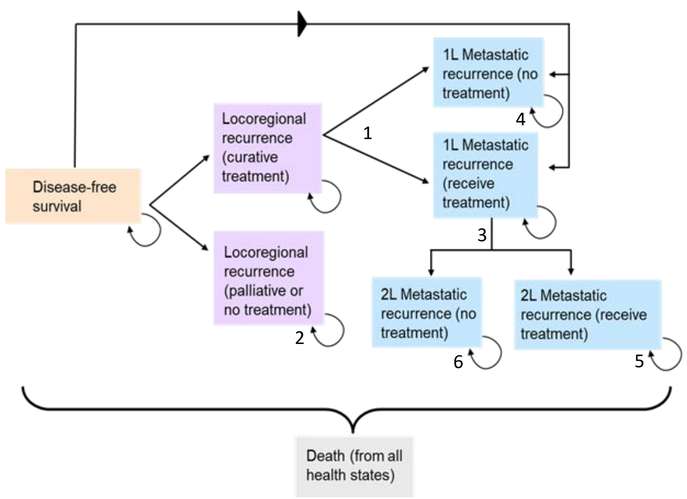
# The Cost-Effectiveness of Adjuvant Atezolizumab for the Treatment of Stage II-IIIA, PD-L1 TC ≥ 50%, NSCLC: A Comparison of Methods for Modelling Health State Transitions following Disease-Free Survival

**Jovanoski N[1], Yip C.Y[2]**
[1]F. Hoffmann-La Roche, Basel, Switzerland
[2]Roche Products Ltd., Welwyn Garden City, United Kingdom

## Background

The cost-effectiveness analysis (CEA) studies the cost-effectiveness of atezolizumab versus chemotherapy as adjuvant treatment for stage II-IIIA, PD-L1 TC ≥ 50%, non-small cell lung cancer (NSCLC) following complete resection [a].

**Figure 1. Model Structure**




The CEA uses the literature and past NICE appraisals (see Table 1) to inform the transition probabilities of the progressive health states numbered in Figure 1.

**Table 1. Data Sources to Inform Transition Probabilities**

| Transition | Source |
|---|---|
| 1 | Digitised data - Nakamichi et al. (2017)[1] |
| 2 | Digitised data - Kruser et al. (2014)[2] |
| 3 | Internal trial data - NCT02366143 (IMpower150)[3] |
| 4 | Digitised data - Wong et al. (2016)[4] |
| 5 | Internal trial data – NCT02008227 (OAK)[5] |
| 6 | Digitised data - Wong et al. (2016)[4] |

The CEA assumes that transitions across the progressive health state are time-invariant, informing them with the results from parametric survival analyses (i.e. assuming that the outcomes follow an exponential distribution).

## Objectives and Methods

Statistical indicators (i.e. Akaike and Bayesian Information Criterion) show that allowing the transitions to be time-variant may be more appropriate. However, given that patients in the CEA continually transition out of the disease-free survival (DFS) health state into the progressive health states, allowing further transitions to be time-variant requires the inclusion of tunnel states that drastically increase the complexity, with questionable added value.

Using time-invariant transition probabilities has been critiqued on the grounds that it may lead to bias in the modelling of overall survival (OS) and consequently other results (NICE Appraisal TA823[7]). Thus, we updated the CEM to allow all transition probabilities to be time-variant to investigate the impact that this would have on the final results with the use of tunnel states.

As improvements in DFS appears to be the main driver of the results, it is unclear if this change will lead to a significant change in the results.

## Results

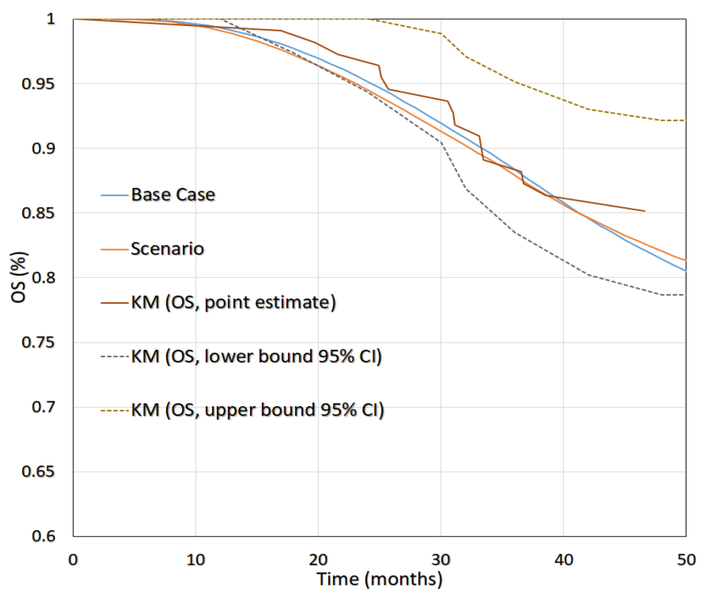
The CEA uses the Akaike and Bayesian Information Criterion to decide what models should be used to inform the transition probabilities in the scenario where we allow them to be time-variant. Table 2 shows the different models used across the different scenarios.

**Table 2. Transition Probabilities**

| Transition | Base Case | Scenario |
|---|---|---|
| 1 | Exponential | Gen. Gamma |
| 2 | Exponential | Gompertz |
| 3 | Exponential | Log-Logistic |
| 4 | Exponential | Gen. Gamma |
| 5 | Exponential | Log-Logistic |
| 6 | Exponential | Gen. Gamma |

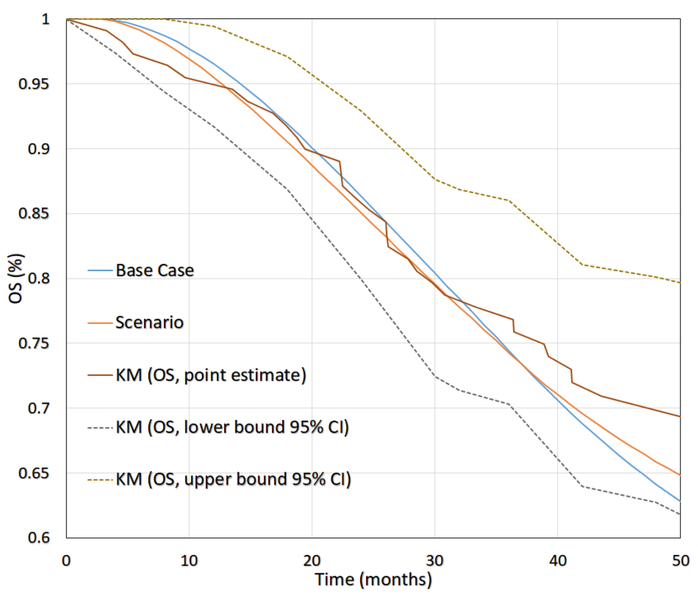
Figures 2 and 3 show that the use of time-variant (scenario) versus time-invariant (base case) transition probabilities to inform the progressive health states results in a marginally different modelled OS that falls within the 95% confidence interval (CI) of the Kaplan-Meier OS (IMpower010 clinical trial[6]). Moreover, Table 3 shows that the incremental cost-effectiveness ratio (ICER) increase by 8% - which is in line with our expectation this alternative approach would not impact decision-making.

**Figure 2. Modelled and Observed OS (Atezolizumab Arm)**




CI: confidence interval; KM: Kaplan-Meier; OS: overall survival

**Figure 3. Modelled and Observed OS (Best Supportive Care Arm)**




CI: confidence interval; KM: Kaplan-Meier; OS: overall survival

**Table 3. Deterministic Results for Base Case and Scenario**

| Interventions | Base Case | | | | Scenario | | | |
|---|---|---|---|---|---|---|---|---|
| | Quality-Adjusted Life Years | | | | | | | |
| | DFS | LR | 1LM | 2LM | DFS | LR | 1LM | 2LM |
| ATZ | 7.829 | 0.094 | 0.195 | 0.040 | 7.829 | 0.165 | 0.233 | 0.044 |
| BSC | 5.535 | 0.155 | 0.384 | 0.065 | 5.535 | 0.278 | 0.473 | 0.072 |
| Diff. | 2.294 | -0.061 | -0.189 | -0.025 | 2.294 | -0.113 | -0.240 | -0.028 |
| | Costs | | | | | | | |
| ATZ | 60, 772 | 1, 153 | 12, 501 | 3, 261 | 60, 772 | 1, 380 | 12, 128 | 3, 641 |
| BSC | 4, 953 | 1, 882 | 32, 393 | 4, 817 | 4, 953 | 2, 272 | 31, 023 | 5, 286 |
| Diff. | 55, 818 | -728 | -19, 892 | -1, 556 | 55, 818 | -892 | -18, 895 | -1, 645 |
| ICER | 16, 390 | | | | 17, 715 | | | |

ATZ: atezolizumab; BSC: best supportive care; DFS: disease-free survival; ICER: incremental cost-effectiveness ratio; LR: locoregional recurrence; 1LM: first-line metastatic; 2LM: second-line metastatic

## Conclusion

The CEA shows that the use of time-variant or time-invariant transition probabilities to model the progressive health states results in only a small change to the modelled OS and the ICER. Moreover, the change in the ICER is not sufficient enough to render the use of atezolizumab as adjuvant treatment for stage II-IIIA, PD-L1 TC ≥ 50%, NSCLC not cost-effective at an ICER threshold of £30,000.

Overall, the use of a more simple model that restricts the progressive health state transitions to being time-invariant appears appropriate, given the limited value of the more complicated approach presented here. Similar checks may assist the development of CEM's with similar decision problems in determining whether the use of time-variant transition probabilities would provide added value to the analysis.

**References**
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2) Kruser TJ, McCabe BP, Mehta MP, Khuntia D, Campbell TC, Geye HM, et al. Reirradiation for locoregionally recurrent lung cancer: outcomes in small cell and non-small cell lung carcinoma. Am J Clin Oncol. 2014;37(1):70-6.
3) A Study of Atezolizumab in Combination With Carboplatin Plus (+) Paclitaxel With or Without Bevacizumab Compared With Carboplatin+Paclitaxel+Bevacizumab in Participants With Stage IV Non-Squamous Non-Small Cell Lung Cancer (NSCLC) (IMpower150). https://classic.clinicaltrials.gov/ct2/show/NCT02366143
4) Wong ML, McMurry TL, Stukenborg GJ, Francescatti AB, Amato-Martz C, Schumacher JR, et al. Impact of age and comorbidity on treatment of non-small cell lung cancer recurrence following complete resection: A nationally representative cohort study. Lung cancer (Amsterdam, Netherlands). 2016;102:108-17.
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**Footnotes**
a) Staging as per the Union Internationale Contre le Cancer and American Joint Committee on Cancer staging system (7th edition).

**Disclosures**
All authors are employed by F. Hoffmann-La Roche Ltd and Roche Products Ltd.

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