**Comparison of Cost-effectiveness results using APEX trial's full data set and 1-prior line of therapy data only**

In the following section, we present the results comparing two sets of data used in calculating reduction in overall survival associated with Velcade while applying stopping rules and VRS for Initial M-protein criteria.

Two sets of results presented in the table below clearly demonstrate that using either the full database or 1-prior line of therapy only to calculate overall survival reduction has negligible impact on cost-effectiveness results. Detailed calculations and results are provided in the attached excel spreadsheet.

1. Incremental costs are lower < £200 in 1-prior therapy sample than total APEX sample.
2. Incremental. QALY is < 0.3 months lower in 1-prior therapy sample than total APEX sample.
3. Cost-effectiveness (CE) differs by < £700 between 1-prior therapy sample and total APEX sample.
4. Applying the VRS rule to either 3 or 4 cycle stopping rule lowers costs without affecting OS and both are below £30,000.
5. Costs are lower with 4-cycle stopping rule than 3-cycle rule while incremental QALY is higher.
6. Therefore, 4-cyle stopping rule with VRS scenario dominants other scenarios in higher inc. OS and lower costs.

**Table: Summary of Cost-Effectiveness Results based on M-protein Initial criteria With CR+PR+MR***

| **APEX Full data set (CR+PR+MR)** | | | |
|---|---|---|---|
| **M-Protein Initial** | **Inc. Cost** | **Inc. QALY months** | **ICER (PSA)** |
| 3-cycle stopping Rule | £21,733 | 8.2 | £31,994 (£27,406-£40,977) |
| 3-cycle stopping Rule + VRS | £19,177 | 8.2 | £28,231 (£24,275-£35,903) |
| 4-cycle stopping Rule | £22,570 | 8.4 | £32,316 (£28,709-£40,790) |
| 4-cycle stopping Rule + VRS | £19,145 | 8.4 | £27,417 (£23,269-£35,039) |
| **APEX 1-prior line of therapy only (CR+PR+MR)** | | | |

| **M-Protein Initial** | **Inc. Cost** | **Inc. QALY months** | **ICER (PSA)** |
|---|---|---|---|
| 3-cycle stopping Rule | £21,576 | 7.9 | £32,669 (£28,257-£41,559) |
| 3-cycle stopping Rule + VRS | £19,020 | 7.9 | £28,799 (£24,634-£37,282) |
| 4-cycle stopping Rule | £22,410 | 8.2 | £32,991 (£28,951-£41,855) |
| 4-cycle stopping Rule + VRS | £18,986 | 8.2 | £27,950 (£24,024-£35,513) |

[*] *Scenarios that use a CP+PR definition of response within the VRS are not included as they are outside of the terms of the proposed VRS scheme.*