***Meta-analysis of time-to-event data***

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1. For the trial of Gemcitabine in combination with Oxaliplatin for pancreatic cancer (Louvet et al 2005), please complete the following as far as possible for the outcome ‘Overall Survival’ and ‘Progression Free Survival’.
2. *Overall survival*

|  |  |  |
| --- | --- | --- |
| **Data to extract** | **Research Arm** | **Control Arm** |
| Name of intervention | **GEM OX** | **GEM** |
| Randomisation ratio (e.g. 1:1) | 1 | 1 |
| Number randomised | 163 | 163 |
| Number analysed | 157 (163 ITT) | 156 (163 ITT) |
| Observed events | 133 (PP analysis set) | 136 (PP analysis set) |
| Logrank expected events |  |  |
| Logrank Variance (V) |  | |
| Logrank observed minus expected events (O-E) |  | |
| HR, CI (with level e.g. 95%) or standard error or variance (specify method e.g. Cox model) | ITT: Cox unadjusted  1.18 95% (0.94 to 1.51)  PP: Cox unadjusted  1.20 95% (0.95 to 1.54) | |
| Test statistic, 2-sided p-value and name of test (e.g. logrank) | ITT: logrank test p=0.15  PP: logrank test p=0.13 | |
| Advantage to research or control? | Research = GEM OX (HR>1 indicates adv to Research in this trial so need to specify the opposite of this in the spreadsheet) | |
| Actuarial or Kaplan Meier curves presented | Kaplan Meier – Figure 2 but PP population only | |
| Numbers at risk reported? | No | |
| Follow-up details (minimum and maximum) | Min = 9 months, Max = 33 months  Estimated from median follow-up=21 months and accrual period = 24 months  Fmin= median - 1/2\*(accrual)  Fmax= median + 1/2\*(accrual) | |

***Survival curve estimates if available***

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Time units (e.g. days, months etc): | | | | months | | | | | | | |
|  | | | **Timepoint** | | | | | | | | | |
| **0** | **1.5** | | **3** | **6** | **9** | **12** | **18** | **24** | **30** |
| Survival | | Research | 1.0 | 0.95 | | 0.85 | 0.70 | 0.48 | 0.38 | 0.15 | 0.12 | 0.08 |
| probabilityπ | | Control | 1.0 | 0.96 | | 0.85 | 0.61 | 0.39 | 0.30 | 0.13 | 0.08 | 0.06 |
| Numbers | | Research |  |  | |  |  |  |  |  |  |  |
| at riskπ (if available) | | Control |  |  | |  |  |  |  |  |  |  |

π Extract data at each timepoint

1. *Progression-free survival*

|  |  |  |
| --- | --- | --- |
| **Data to extract** | **Research Arm** | **Control Arm** |
| Name of intervention | **GEM OX** | **GEM** |
| Randomisation ratio (e.g. 1:1) | 1 | 1 |
| Number randomised | 163 | 163 |
| Number analysed | 157 | 156 |
| Observed events |  |  |
| Logrank expected events |  |  |
| Logrank Variance (V) |  | |
| Logrank observed minus expected events (O-E) |  | |
| HR, CI (with level e.g. 95%) or standard error or variance (specify method e.g. Cox model) | PP: Cox unadjusted  1.29 95% (1.01 to 1.69) | |
| Test statistic, 2-sided p-value and name of test (e.g. logrank) | PP: logrank test p=0.04 | |
| Advantage to research or control? | Research = GEM OX (HR>1 indicates adv to Research in this trial so need to specify the opposite of this in the spreadsheet) | |
| Actuarial or Kaplan Meier curves presented | Kaplan Meier – Figure 1 but PP population only | |
| Numbers at risk reported? | No | |
| Follow-up details (minimum and maximum) | Min = 9 months, Max = 33 months  Estimated from median follow-up=21 months and accrual period = 24 months  Fmin= median - 1/2\*(accrual)  Fmax= median + 1/2\*(accrual) | |

***Survival curve estimates if available***

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Time units (e.g. days, months etc): | | | | months | | | | | | | |
|  | | | **Timepoint** | | | | | | | | | |
| **0** | **1.5** | | **3** | **6** | **9** | **12** | **18** | **22** |  |
| Survival | | Research | 1.0 | 0.93 | | 0.68 | 0.55 | 0.27 | 0.20 | 0.08 | 0.08 |  |
| probabilityπ | | Control | 1.0 | 0.90 | | 0.58 | 0.37 | 0.20 | 0.14 | 0.10 | 0.06 |  |
| Numbers | | Research |  |  | |  |  |  |  |  |  |  |
| at riskπ (if available) | | Control |  |  | |  |  |  |  |  |  |  |

π Extract data at each timepoint

1. Enter all data extracted in part 1 into the excel spreadsheet available as supplementary material from the link <https://static-content.springer.com/esm/art%3A10.1186%2F1745-6215-8-16/MediaObjects/13063_2006_188_MOESM1_ESM.xls>
2. Record the calculated estimates of log(HR) and SE(logHR) obtained

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Method** | **Comments** | **Output taken from output\_information tab of excel spreadsheet** | | |
| **logHR** | **SE(logHR)** | **HR(CI)** |
| 1. **Overall survival** | | | | |
| Cox model HR with CI  (1) | HR and 95% CI from the output sheet may differ slightly to the actual input values due to rounding error | ITT: 0.17  PP: 0.18 | ITT: 0.12  PP: 0.12 | 1.18(0.93 – 1.50)  1.20(0.94 – 1.53) |
| Logrank p-value with observed events **(2)** | ITT not estimable as no events given | PP: 0.18 | PP: 0.12 | 1.20(0.95 – 1.53) |
| Kaplan Meier Curve  **(3)** | ITT not estimable as only PP curves given. Note that the spreadsheet calculation based on curves (calculation method 10) assumes that HR<1 indicates advantage to Research **THEREFORE THE ACTUAL OUTPUT HERE NEEDS TO BE REVERSED**  (i.e. logHR=0.13 SE(logHR)=0.1  HR(95%CI) (1.14(0.94 – 1.38)) | PP: -0.13 | PP: 0.10 | 0.88(0.72 – 1.07) |
| 1. **Progression-free**   **survival** | | | | |
| Cox model HR with CI **(1)** |  | 0.25 | 0.13 | 1.29(1.00 – 1.66) |
| Logrank p-value with observed events **(2)** |  |  |  |  |
| Kaplan Meier Curve **(3)** | Note that the spreadsheet calculation based on curves (calculation method 10) assumes that HR<1 indicates advantage to Research **THEREFORE THE ACTUAL OUTPUT HERE NEEDS TO BE REVERSED**  (i.e. logHR=0.15 SE(logHR)=0.1  HR(95% CI): 1.16(0.96 – 1.41) | -0.15 | 0.10 | 0.86(0.70 – 1.04) |