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12th June 2015

Dear Janet,

Re. Pembrolizumab for treating unresectable, metastatic melanoma after progression with ipilimumab [ID760]

MSD welcomes the opportunity to answer the additional clarification questions. As requested we have uploaded the new answers to questions B1 – a, B1 – b, B1 – c, B1 – d, B1 – e, B1 – f, B1 – g, B1 – h on the NICE Docs.

Please note that given the short timeframe we have not been able to conduct the RPSFT adjustment for today's deadline. This may be feasible and we are currently investigating how long this will take with our global statisticians. We will get back to you as soon as we have more clarity on this point.

Please also note that the data issues associated with the IPCW adjustment method are unchanged regardless of the analysis. For this reason we have not provided updated results as the former ones still stand.

We have highlighted in turquoise 'commercial in confidence' information. We could not highlight the Kaplan-Meier graphs but would be grateful if you could please also treat them as 'commercial in confidence'.

Should NICE or the ERG require any further clarification we would be more than happy to provide an answer to them.

Kind regards,

[redacted], Head of HTA and OR

Survival Analysis of KN002 PFS and OS Based on Investigator Assessment - for NICE Clarification Question B1

[redacted]

June 11, 2015

The software we used for this analysis is R, whose version is shown below.

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## [1] "R version 3.2.0 (2015-04-16)"
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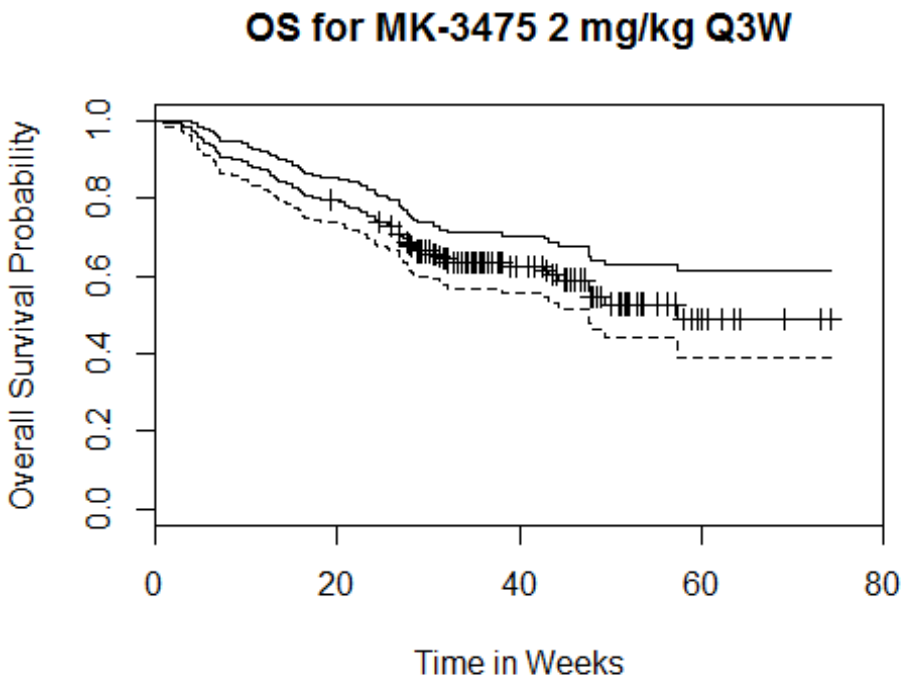
The Pembro 2mg, OS, B1-a

[redacted]

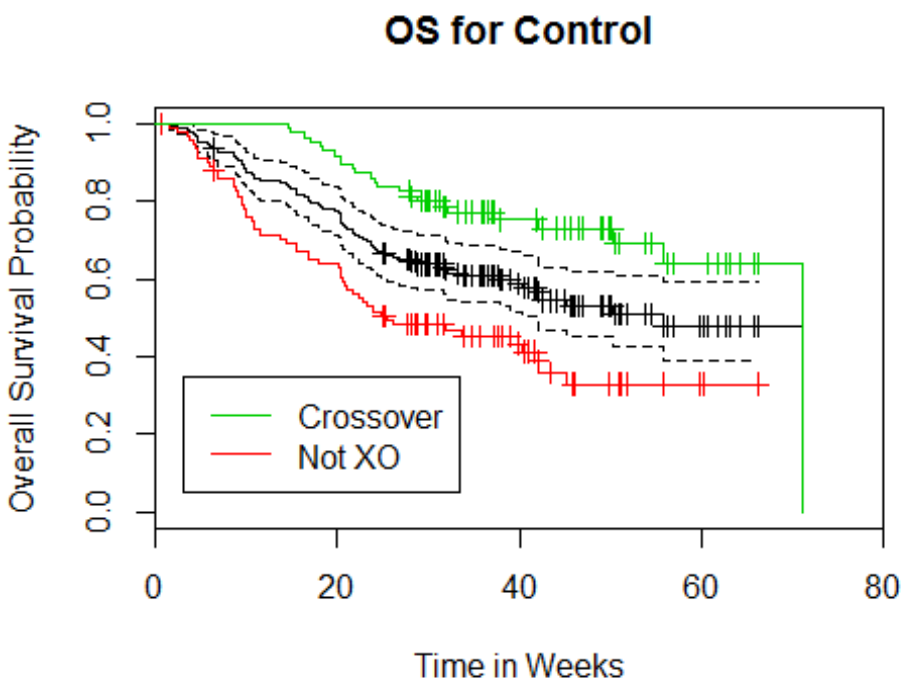


In the table below, to match SAS output, the first column time is "Time in Weeks"; the second one "n.risk" is "Number Left"; the third one "n.event" is "Number Failed" and the last one "std.err" is "Survival Standard Error".

[redacted]

The Control, OS, B1-b

[redacted]



In the table below, to match SAS output, the first column time is "Time in Weeks"; the second one "n.risk" is "Number Left"; the third one "n.event" is "Number Failed" and the last one "std.err" is "Survival Standard Error".

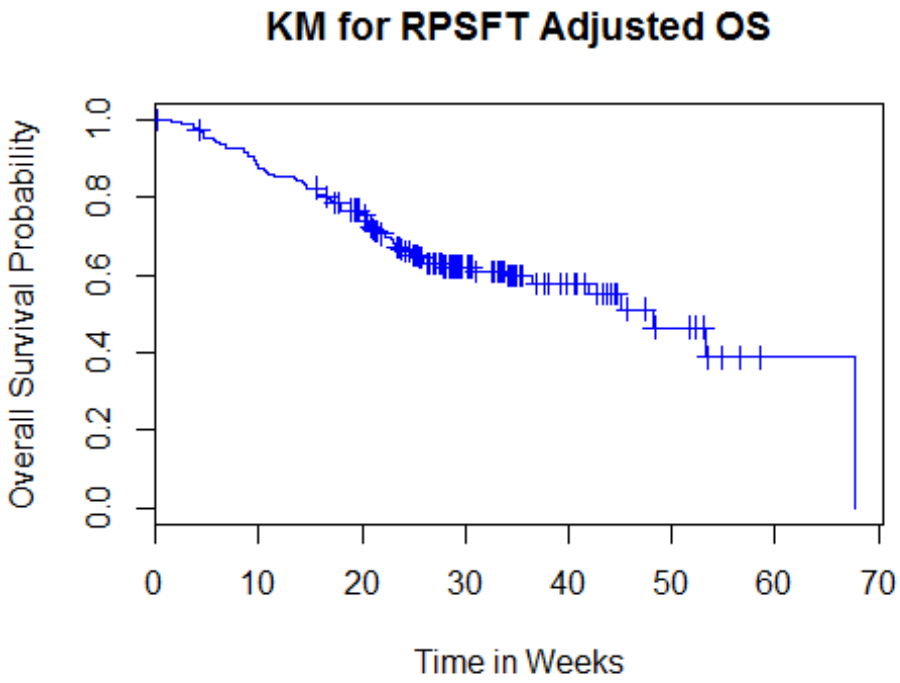
[redacted]

[redacted]

By subgroups, Crossover vs not Crossover,

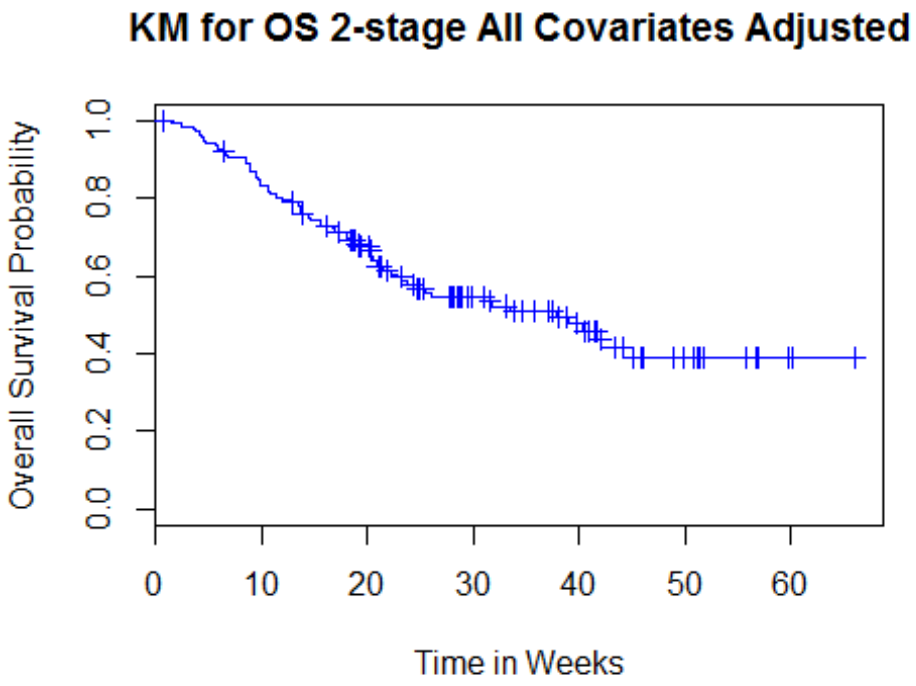
[redacted]

The Control, OS, B1-c



[redacted]

[redacted]



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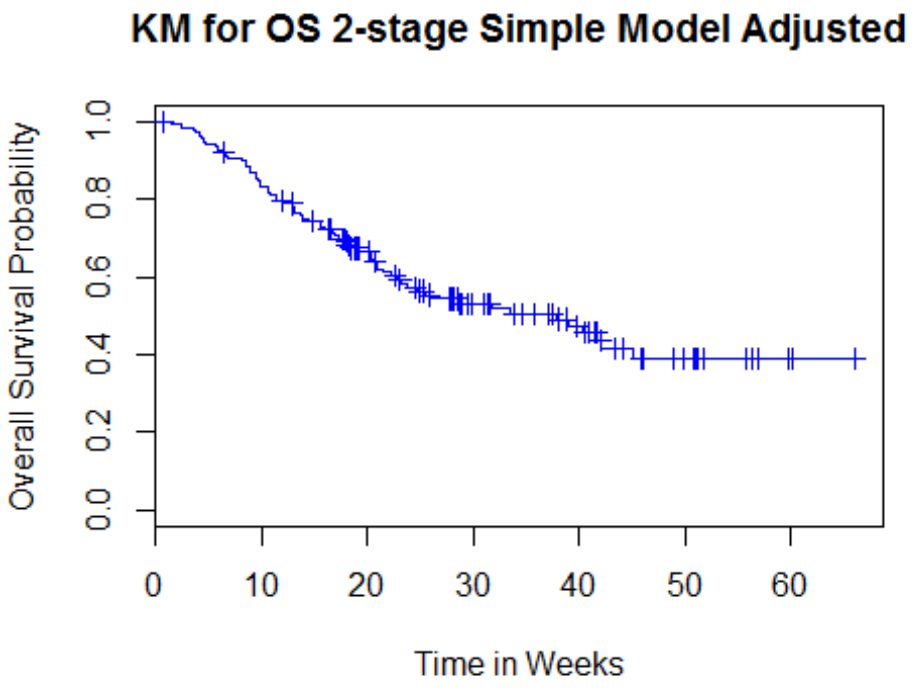
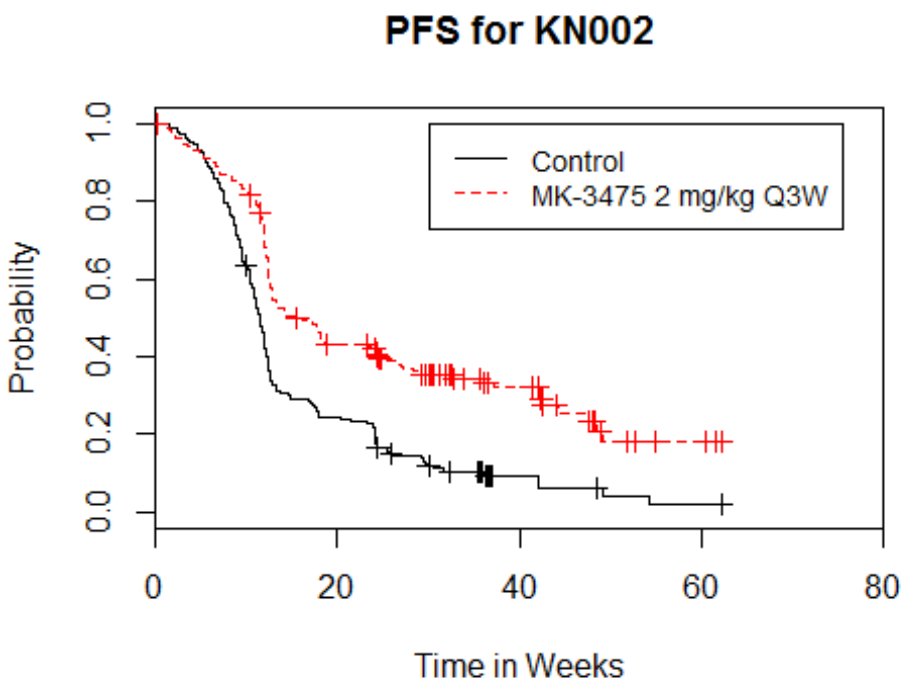

KM for OS 2-stage Simple Model Adjusted
Overall Survival Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
10
20
30
40
50
60
Time in Weeks

[redacted]

IPCW crossover adjustment

Please note that the KM analysis for the adjusted OS using the IPCW method cannot be provided. This method censors patients at the time of the treatment switch and therefore the adjustment is not done at the patient level; additionally, only the adjusted hazard ratio was estimated.

The Control, PFS, B1-d



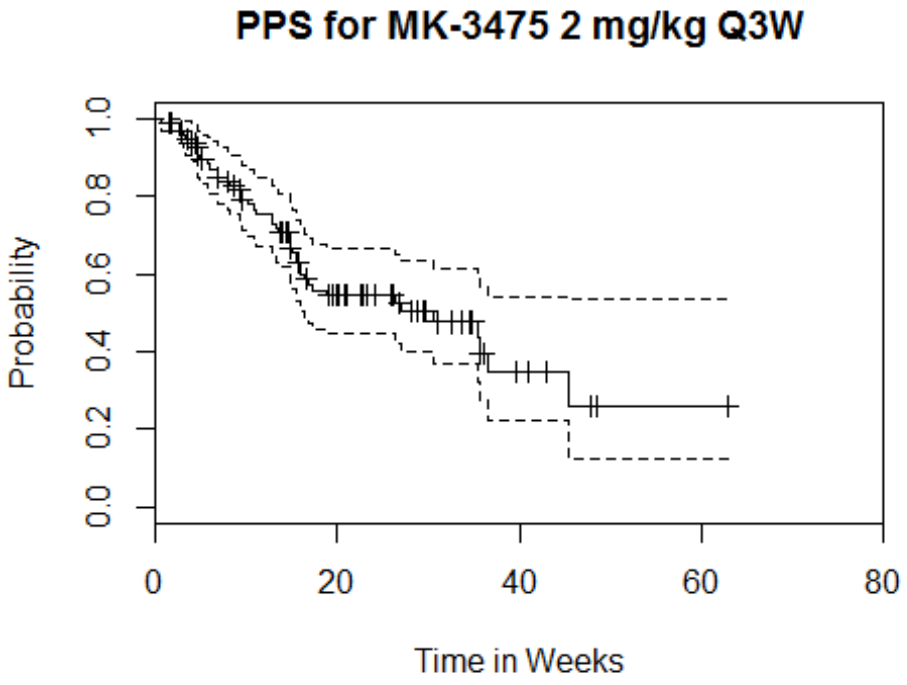
By Treatment group,

[redacted]

[redacted]

The Pembro 2mg, PPS, B1-e

[redacted]

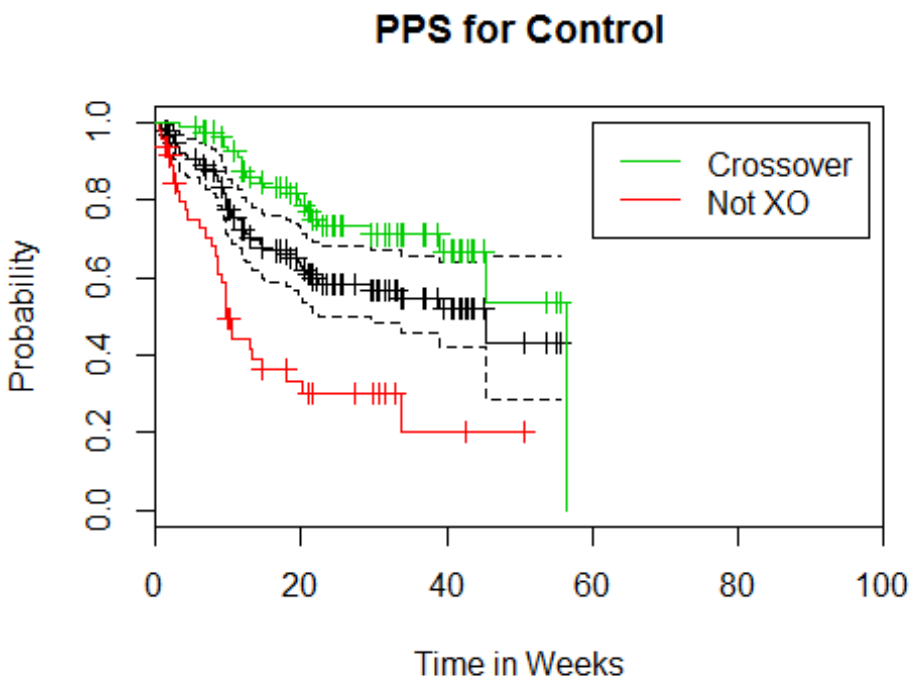


[redacted]

[redacted]

The Control, PPS, B1-f

[redacted]

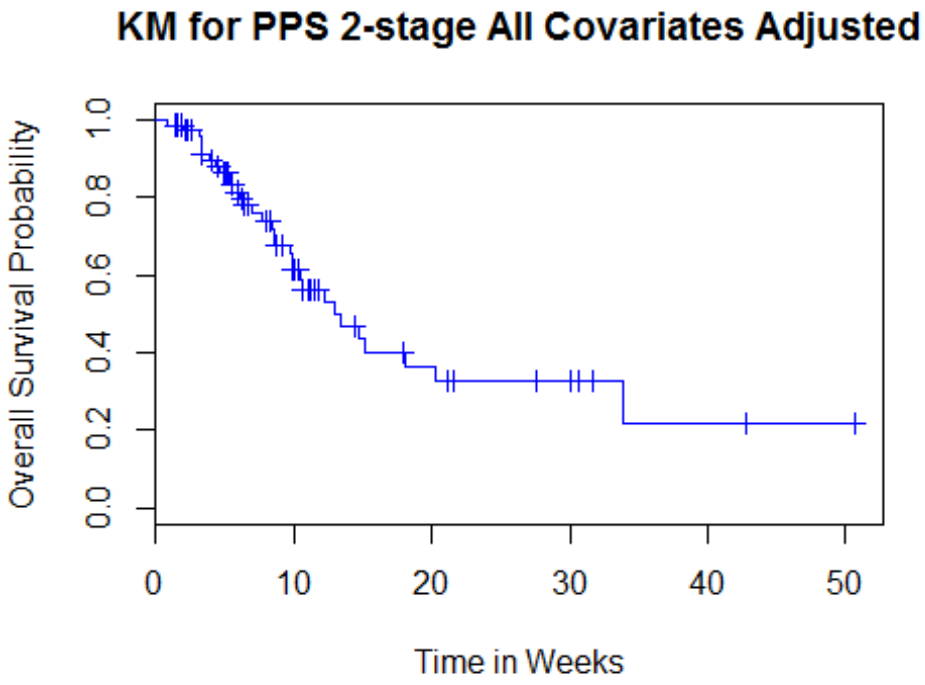

PPS for Control
Probability
0.0
0.2
0.4
0.6
0.8
1.0
0
20
40
60
80
100
Time in Weeks
Crossover
Not XO

[redacted]

By subgroups, Crossover vs not Crossover,

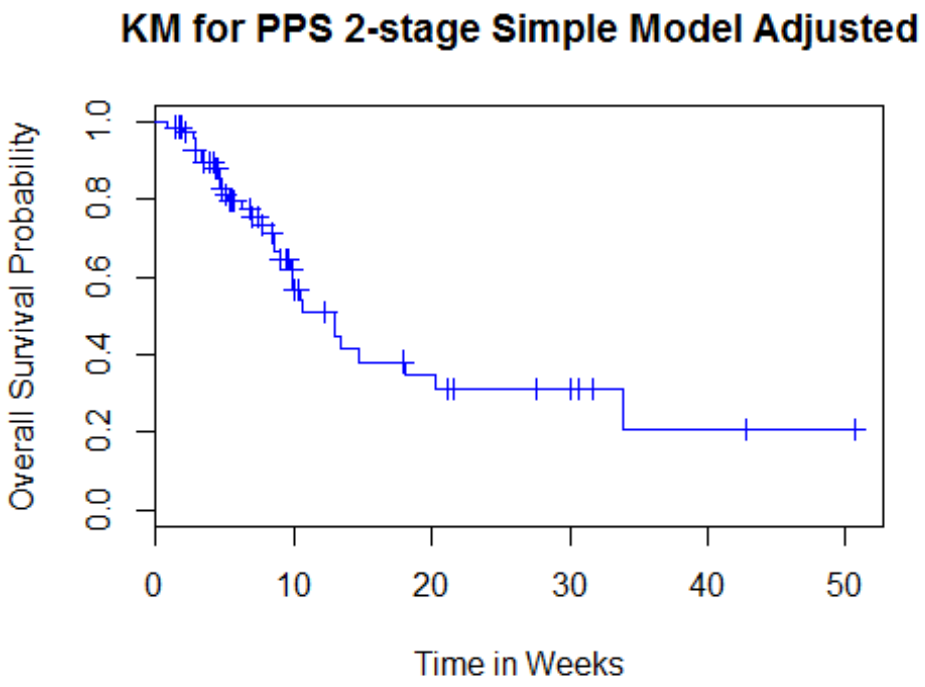
[redacted]

The Control, PPS, B1-g



[redacted]

[redacted]

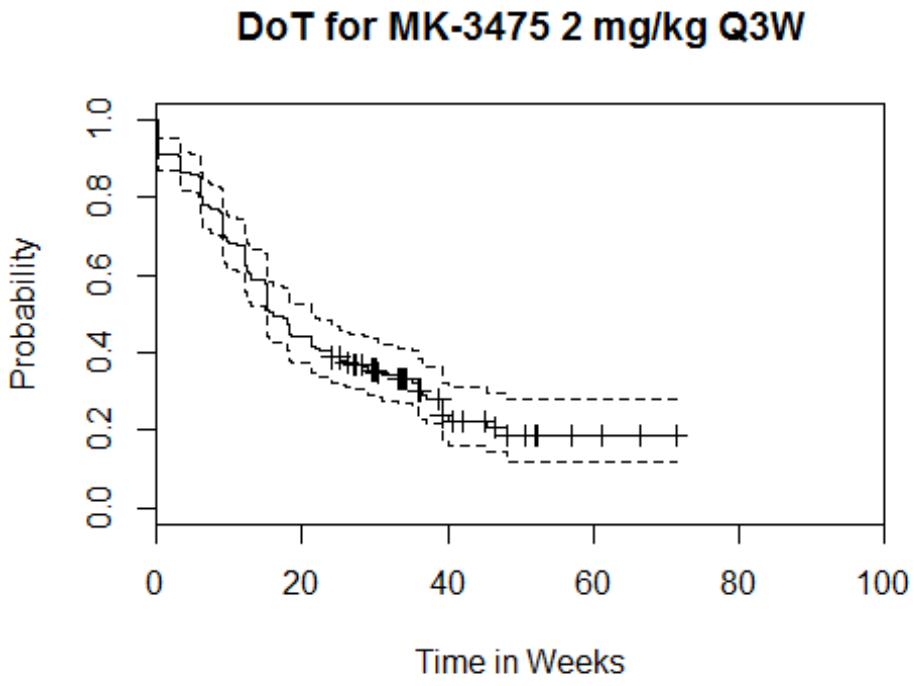


[redacted]

[redacted]

The Q3W, Duration of Treatment, DoT, B1-h

[redacted]



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