# Venetoclax and azacitidine for younger acute myeloid leukemia patients independent of fitness for intensive chemotherapy

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Supplemental Table 1: Baseline clinical and genetic features of the eight study subjects and 16 matched controls with monocytic disease features

| Subject/ Control* | Sex | Age | Baseline Blasts (%) | KMT2A | Mutational Profile | ELN† Risk Group(7) | Molecular Prognostic Risk Signature(4) | Best Response | Salvage Therapy and Response |
|---|---|---|---|---|---|---|---|---|---|
| Subject 1 | F | 22 | 70 | Y | NRAS | N/A | Intermediate | CR | N/A |
| Subject 2 | M | 36 | 42 | N | IDH2, ASXL1, NRAS, PTPN11, SMC1A | N/A | Intermediate | CR | N/A |
| Subject 3 | M | 33 | 50 | Y | FLT3 TKD, NRAS, ETV6, U2AF1, KRAS, NF1 | N/A | Intermediate | No Response | 7+3 with FLT3 inhibitor; CR |
| Subject 4 | F | 42 | 82 | Y | KRAS, NF1 | N/A | Intermediate | No Response | 7+3; no response |
| Subject 5 | M | 54 | 70 | N | TP53 | N/A | Lower | CR | N/A |
| Subject 6 | M | 56 | 90 | Y | NONE | N/A | Higher | No Response | No further therapy |
| Subject 7 | M | 22 | 28 | N | SF3B1, RUNX1 | N/A | Higher | CR | N/A |
| Subject 8 | M | 38 | 95 | N | NRAS, NF1, ASXL1 | N/A | Intermediate | No Response | 7+3; CRi |
| Control 1 | F | 25 | 78 | Y | EZH2, PML | Adverse | N/A | CR | N/A |
| Control 2 | M | 19 | 90 | Y | ASXL1 | Adverse | N/A | CR | N/A |
| Control 3 | M | 28 | 100 | Y | KRAS, RUNX1 | Adverse | N/A | CRi | N/A |
| Control 4 | F | 31 | 50 | N | NRAS, RUNX1 | Adverse | N/A | CRi | N/A |
| Control 5 | M | 28 | 80 | Y | NONE | Adverse | N/A | CRi | N/A |
| Control 6 | F | 43 | 30 | N | NOT DONE | Adverse | N/A | No Response | GCLAC; no response |
| Control 7 | F | 46 | 33 | Y | NONE | Adverse | N/A | CR | N/A |
| Control 8 | M | 47 | 80 | Y | IDH2, RUNX1, DNMT3A | Adverse | N/A | No Response | Azacitidine + venetoclax; CRi |
| Control 9 | F | 55 | 80 | N | NOT DONE | Adverse | N/A | MLFS | N/A |
| Control 10 | M | 57 | 30 | N | U2AF1, PTPN11, TET2, ASXL1 | Adverse | N/A | No Response | No further therapy |
| Control 11 | M | 56 | 80 | N | NOT DONE | Adverse | N/A | CR | N/A |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Control 12 | M | 48 | 80 | N | NOT DONE | Adverse | N/A | CR | N/A |
| Control 13 | F | 54 | 62 | N | PTPN11, U2AF1 | Intermediate | N/A | CR | N/A |
| Control 14 | F | 56 | 55 | N | NONE | Adverse | N/A | No Response | Menin inhibitor; CRi |
| Control 15 | F | 55 | 45 | N | DNMT3A, NRAS, TP53 | Adverse | N/A | No Response | No further therapy |
| Control 16 | F | 30 | 49 | Y | KRAS | Intermediate | N/A | No Response | Decitabine; no response |

*Subjects were study participants and received venetoclax + azacitidine; controls were treated with intensive chemotherapy regimens

†European Leukemia Network

CR=complete remission

CRi=complete remission with incomplete recovery of blood counts

MLFS=morphologic leukemia free state

GLCAC=GCSF+clofarabine+cytarabine

Supplemental Table 2: Response rates for study subjects stratified by the 4-gene molecular prognostic risk signature(4)

| | Overall Response Rate | Complete Remission | Complete Remission with Incomplete Recovery of Blood Counts | Morphologic Leukemia Free State | No Response |
|---|---|---|---|---|---|
| Higher Benefit (N=23) | 18/23 (78%) | 13/23 (57%) | 2 (9%) | 3 (13%) | 5 (22%) |
| Intermediate Benefit (N=9) | 5/9 (56%) | 5/9 (56%) | 0 | 0 | 4/9 (44%) |
| Lower Benefit (N=4) | 2/4 (50%) | 1/4 (25%) | 0 | 1/4 (25%) | 2/4 (50%) |

**Supplemental Figure Legends**

Supplemental Figure 1: Response duration in study subgroups. A)Median duration of response (inclusive of complete remission, complete remission with incomplete recovery of blood counts and morphologic leukemia free state) in study subjects. B)Median duration of complete remission in study subjects. C)Median duration of response in controls. D)Median duration of complete remission in controls.

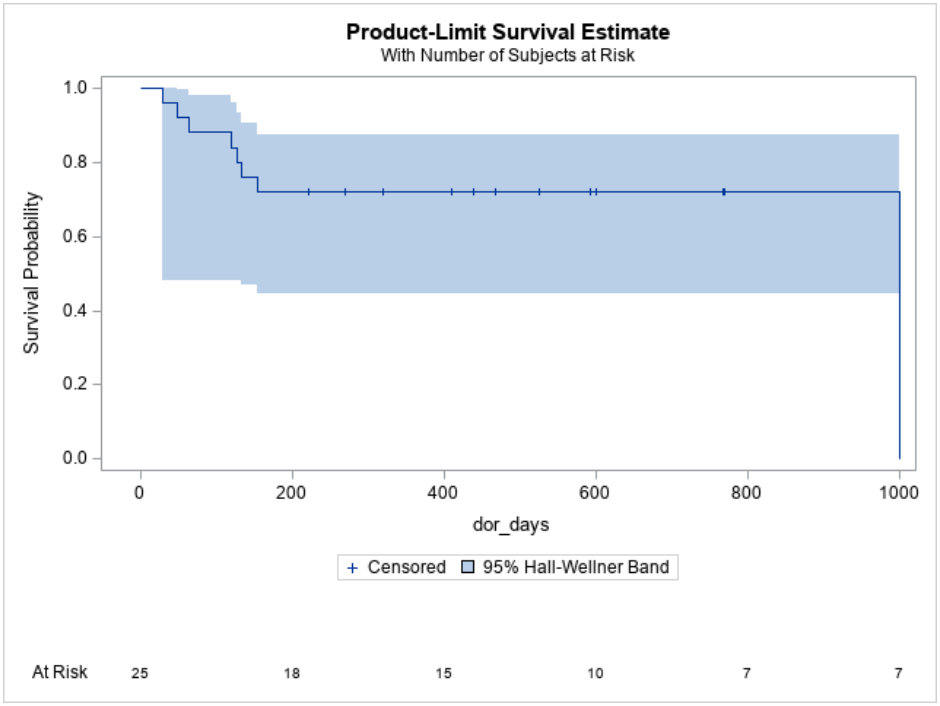
Supplemental Figure 2: Subjects with myelodysplasia-related changes: A)Median duration of response and B)Median overall survival

Supplemental Figure 3: Subjects with monocytic acute myeloid leukemia: A)Median duration of response and B)Median overall survival

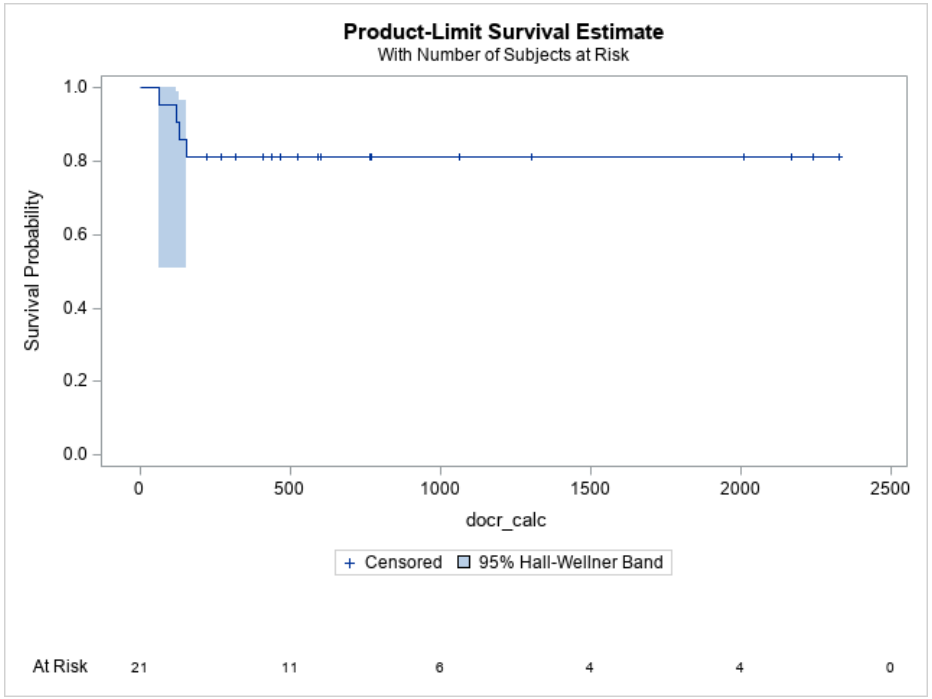
Supplemental Figure 4: Study subjects compared with matched historical controls who received intensive chemotherapy: A)Overall survival and B) progression free survival

# Suppl Figure 1

A




B

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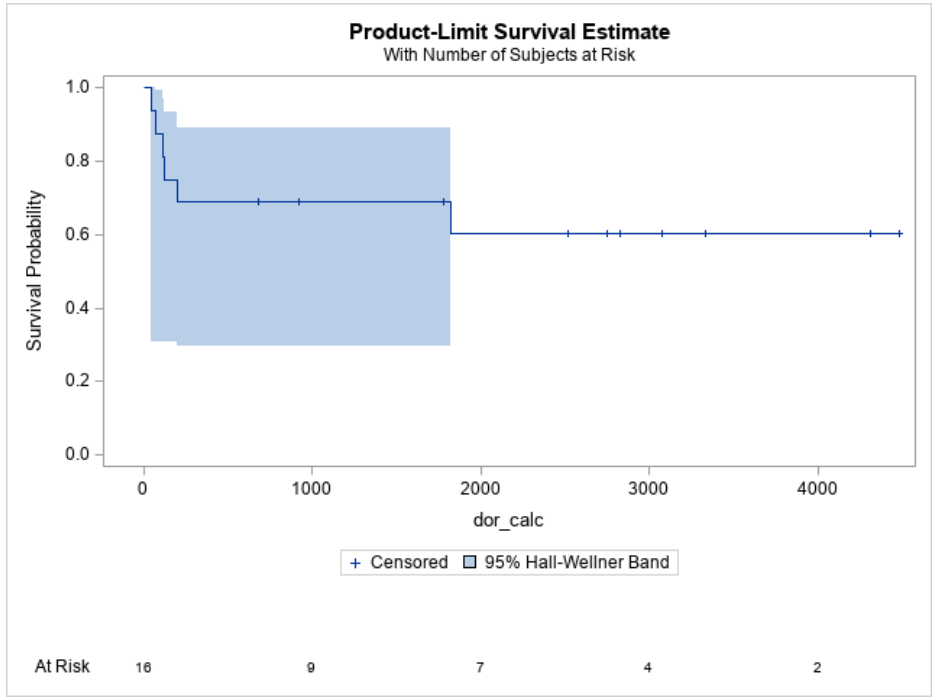


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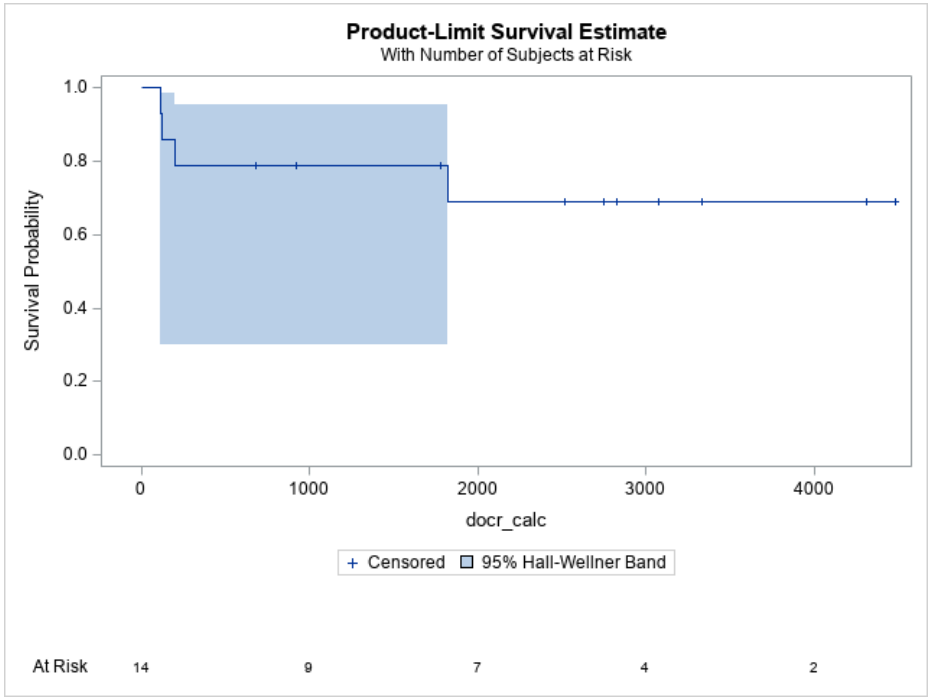
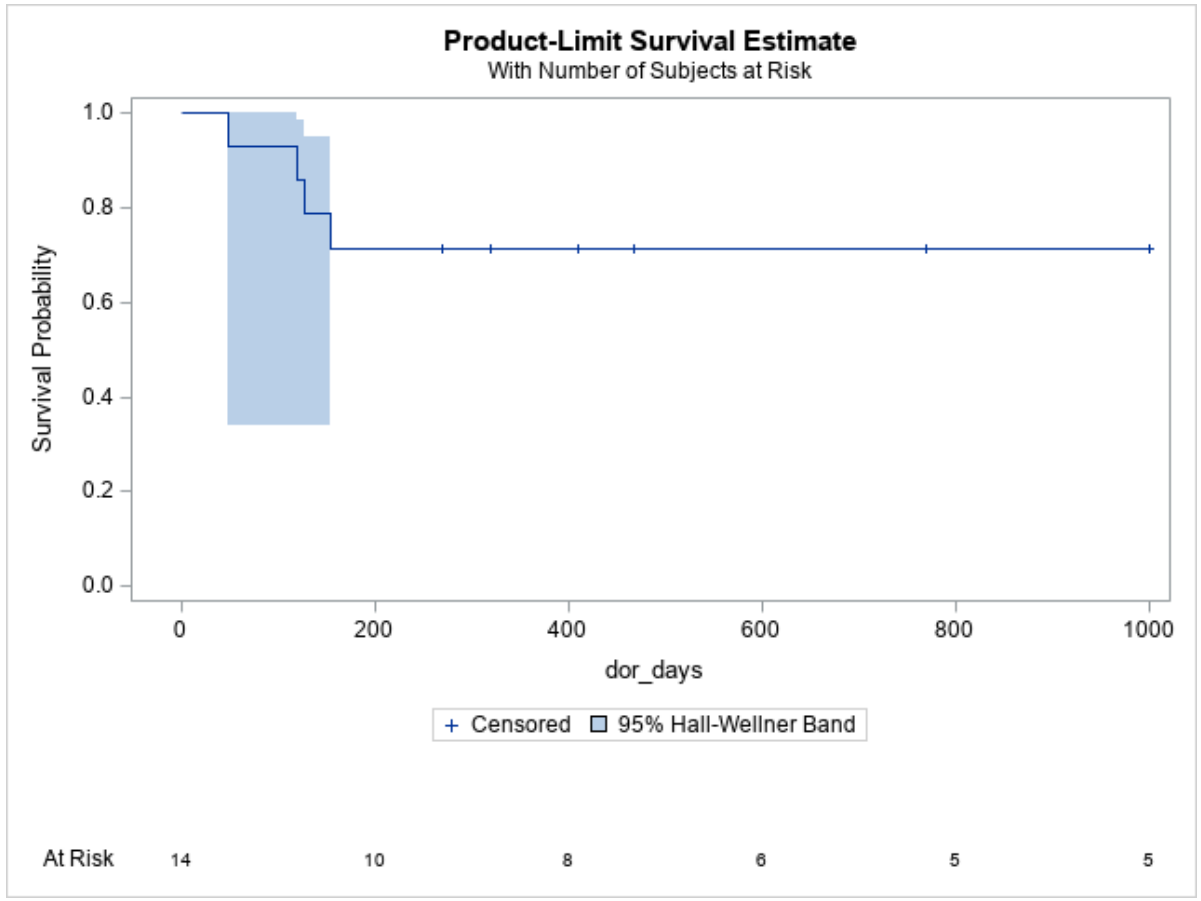


# Supplemental Figure 2

A

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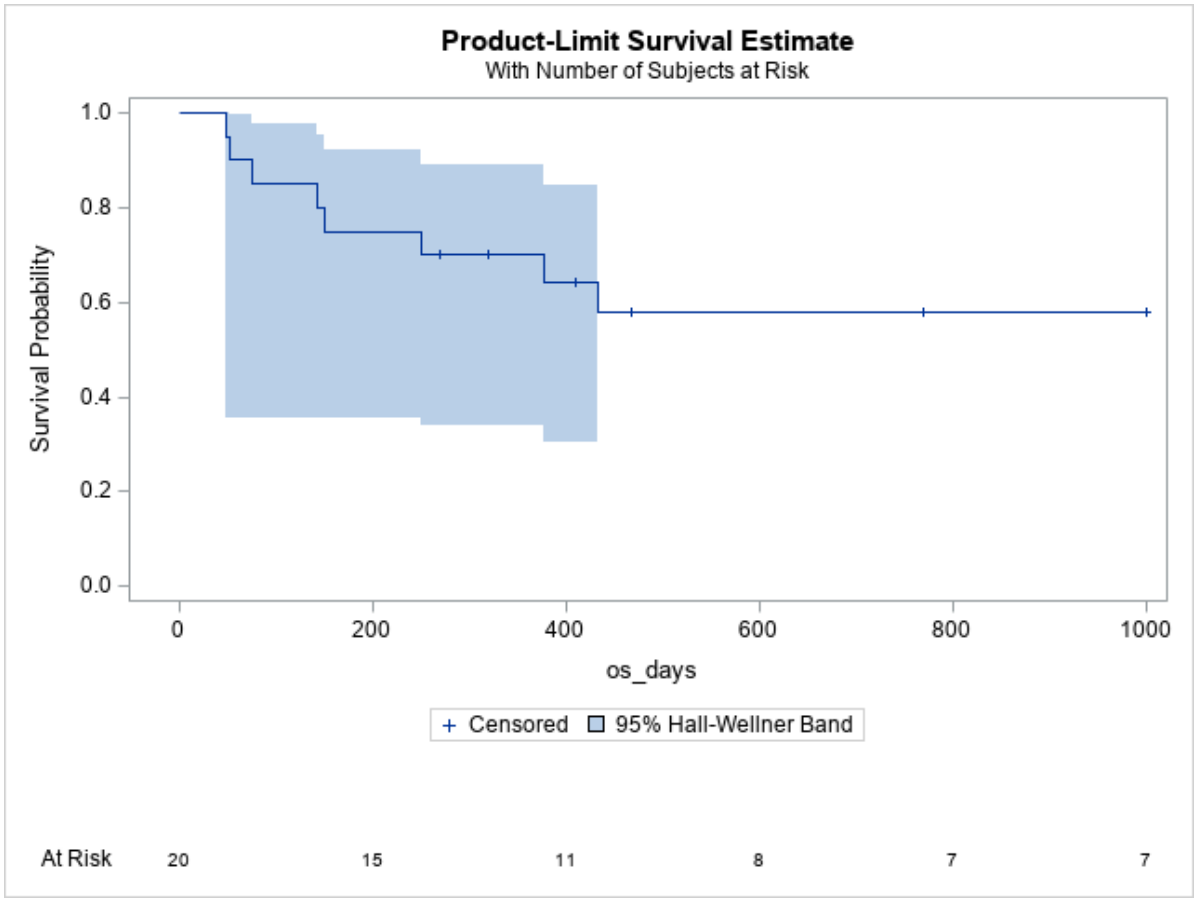
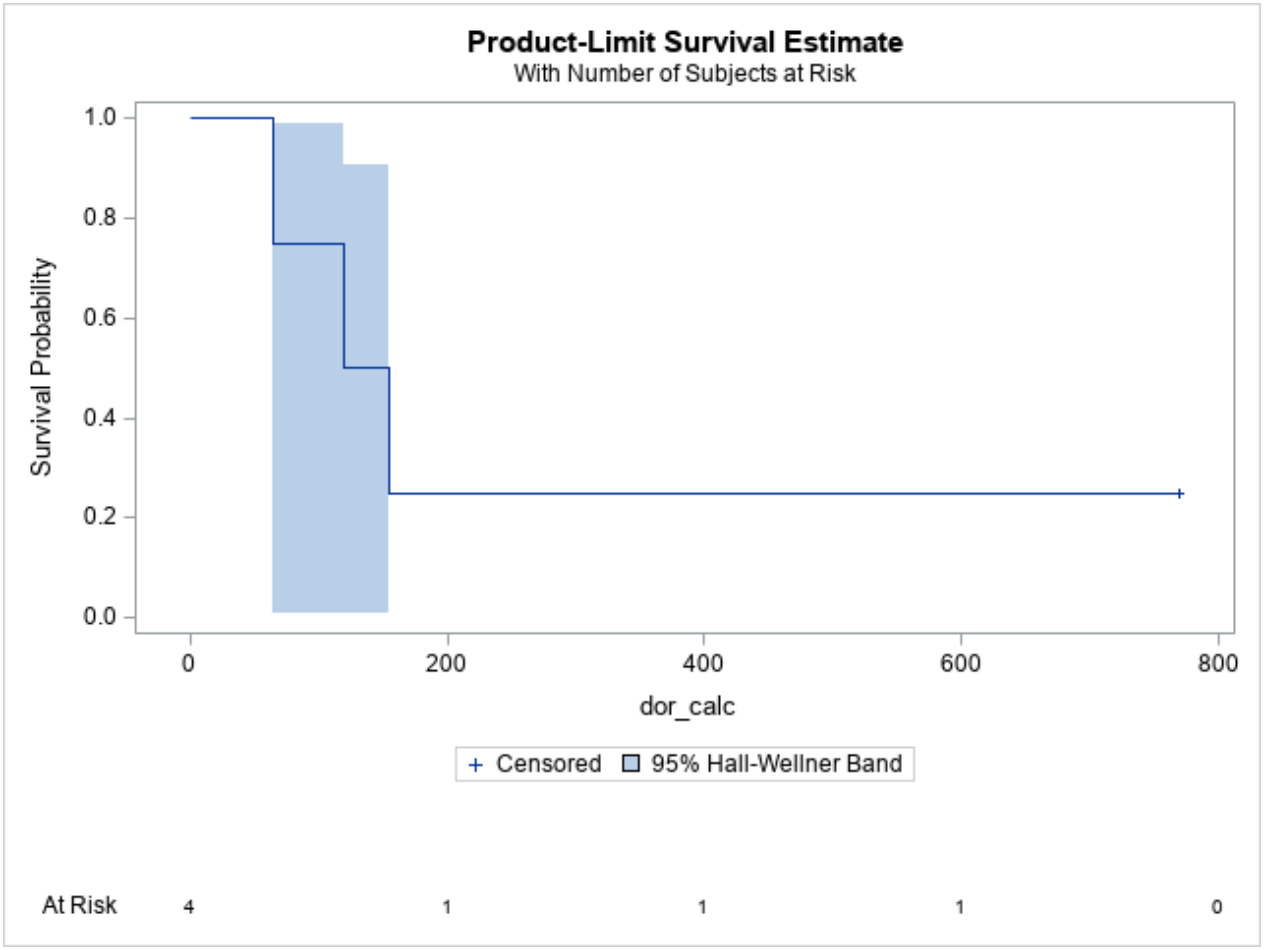


# Supplemental Figure 3

A

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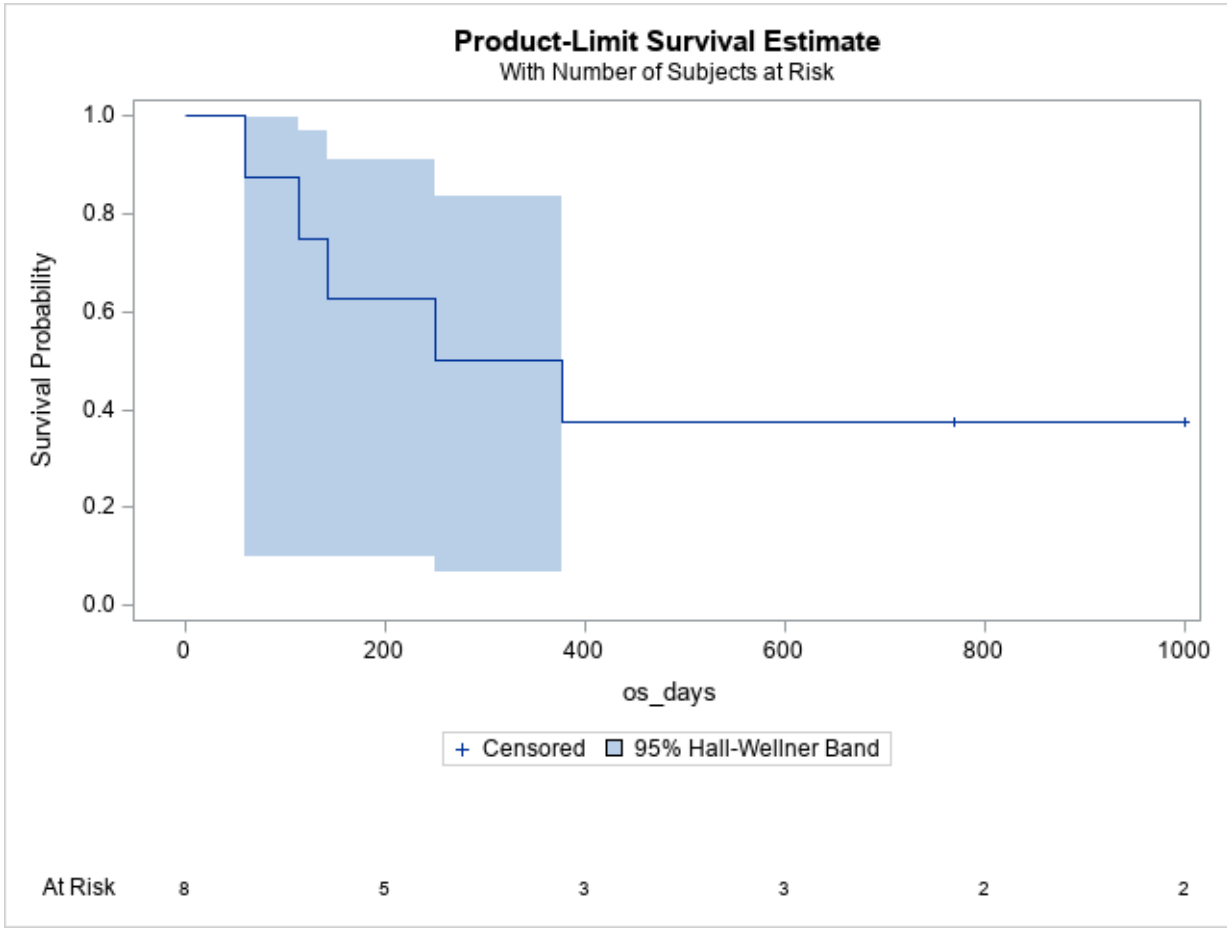
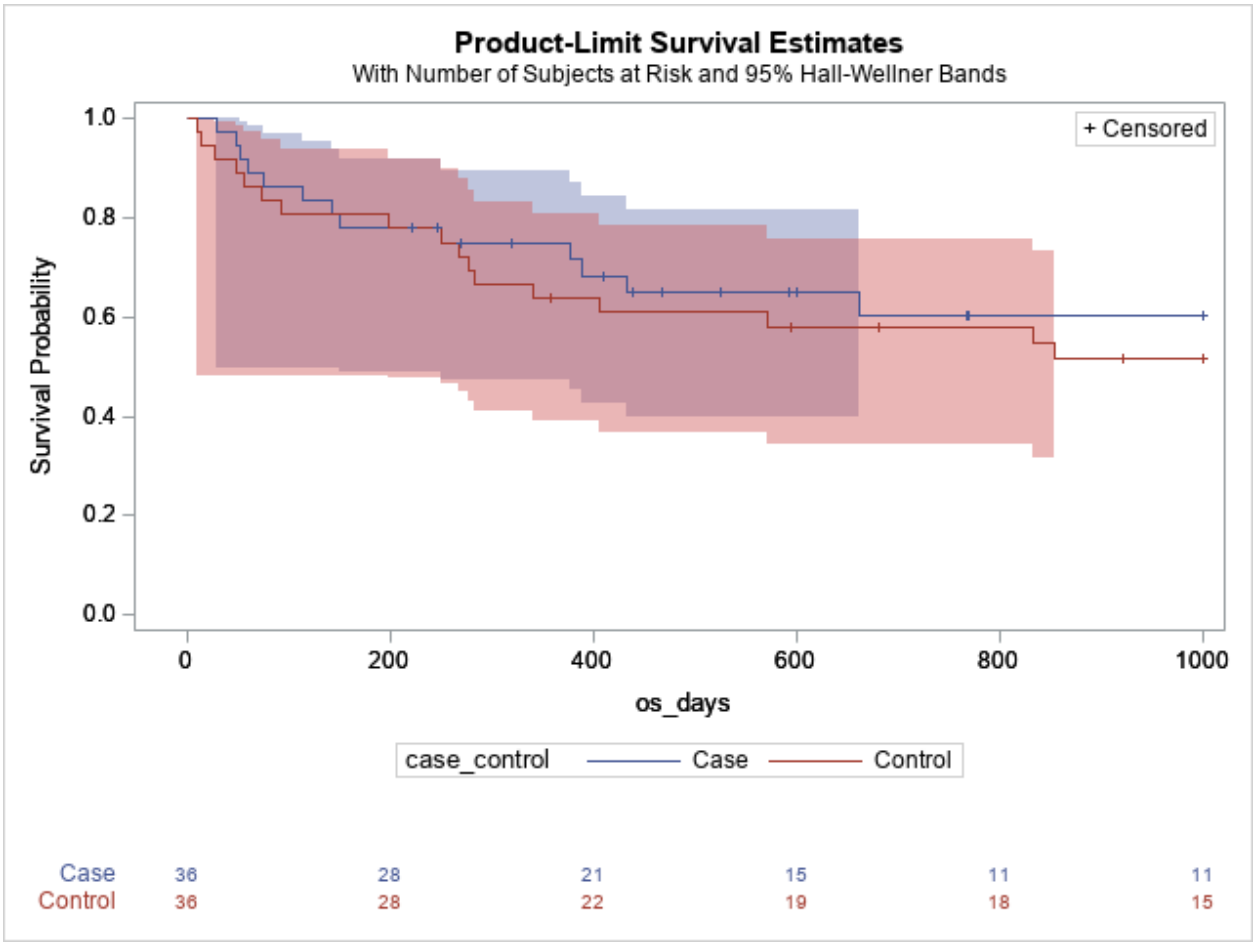


# Supplemental Figure 4

A)




B)