Survival Analysis

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1 Sample Size

The $ln(HR)$ follows a normal distribution, we use this to calculate the sample size.

$$ln(\hat{\Delta}) \sim N(ln(\Delta), \left(\frac{1}{d_1} + \frac{1}{d_2}\right))$$

$$\left(\frac{1}{d_1} + \frac{1}{d_2})\right)^{-1} = \left[\frac{(z_{\alpha/2} + z_\beta)^2}{(ln\Delta_0)^2}\right]$$

If hazard ratio set at 2.1, then

$$\left(\frac{1}{d_1} + \frac{1}{d_2})\right)^{-1} = \left[\frac{(1.96 + 0.58)^2}{(ln2.1)^2}\right] = 11.7$$

$$\frac{1}{d_1} + \frac{1}{d_2} = \frac{1}{11.7} = 0.085$$

$$d_1 = d_2 = 23.44$$

Assume the overall event and censored rate is 20%, then the sample size is $48/0.2 = 240$. If overall event rate (including censoring) is 18%, then the sample size is $48/0.18 = 266$.

1.1 Non-inferiority margin Hazard ratio $\Delta_0 = 2.1$

The assumption is that control group (C) event rate 10% and treatment group (T) event rate 20% at 6 months. Assume survival function is an exponential distribution:

$$S_t(t) = exp(-\lambda_1 t), \qquad t = 0.5, S_t = 0.8, -\lambda_1 = ln(0.8)/0.5$$

$$S_c(t) = exp(-\lambda_2 t), \qquad t = 0.5, S_c = 0.9, -\lambda_2 = ln(0.9)/0.5$$

$$\Delta_0 = \frac{\lambda_1}{\lambda_2} = \frac{ln(0.8)}{ln(0.9)} = 2.117$$

1.2 Hazard ratio actual = 0.55

The control group survival 76.8% and treatment group survival 86.2% at 6 months. Assume survival function is an exponential distribution:

$$
\begin{aligned}
S_t(t) &= exp(-\lambda_1 t), \qquad t = 0.5, S_t = 0.862, -\lambda_1 = ln(0.862)/0.5 \\
S_c(t) &= exp(-\lambda_2 t), \qquad t = 0.5, S_c = 0.768, -\lambda_2 = ln(0.768)/0.5
\end{aligned}
$$

$$
\begin{aligned}
HR = \frac{\lambda_1}{\lambda_2} \\
&= \frac{ln(0.862)}{ln(0.768)} = 0.56
\end{aligned}
$$