answer for ex3.2

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# Question 1

## 1-1

That’s because in this problem, we need to evaluate whether the MRD-negative complete remission rate at the end of the induction with ponatinib is significantly greater than the previously reported rate for second-generation tyrosine kinase inhibitors. That means testing whether the MRD negativity rate is greater than 16%. From a clinical perspective, the result of equivalence or inferiorty would not alter treatment, so we just need to test whether this treatment is a better one. Accordingly, a one-sided one-sample proportion test is the most appropriate statistical procedure, as we are only intererted in treatment improvement.

## 1-2

The MRD-negative complete remission rate at the end of induction for ponatinib was 43.0% (61/142).

## 1-3

prop.test(61, 142,   
 p = 0.16,   
 alternative = "greater",   
 correct = FALSE)

##   
## 1-sample proportions test without continuity correction  
##   
## data: 61 out of 142, null probability 0.16  
## X-squared = 76.781, df = 1, p-value < 2.2e-16  
## alternative hypothesis: true p is greater than 0.16  
## 95 percent confidence interval:  
## 0.3631946 1.0000000  
## sample estimates:  
## p   
## 0.4295775

Using a one-sided one-sample proportion test without continuity correction (H₀: π ≤ 0.16), we obtain z≈8.76 and one-sided “p≈9.6^{-19}”. We reject H₀ and conclude that the MRD-negativity rate (61/142 = 43.0%) is significantly greater than 16%.

## 1-4

In this context, the one-sided p-value is the probability, under the null hypothesis that the true MRD-negativity rate is 16%, of observing a sample proportion as large as or larger than 61/142 (43.0%) purely by chance

# Question 2

## 2-1

At end of induction, the MRD-negativity rate for ponatinib (among evaluable samples) was out of , so . We test vs .

Under the standard error is

The z statistic is

The one-sided p-value is

which is far below 0.05; thus we reject .

The one-sided 95% confidence interval from the one-sided test is with , meaning the true proportion is at least 36.3% with 95% confidence. A two-sided confidence interval with yields the lower bound (95% one-sided 90% two-sided).

The normal-approximation reproduces the function output: ponatinib’s MRD-negativity rate (61/142 = 43.0%) is significantly greater than 16%.

x <- 61  
n <- 142  
p0 <- 0.16  
  
# Function result (reference)  
prop.test(x, n, p = p0, alternative = "greater", correct = FALSE)

##   
## 1-sample proportions test without continuity correction  
##   
## data: x out of n, null probability p0  
## X-squared = 76.781, df = 1, p-value < 2.2e-16  
## alternative hypothesis: true p is greater than 0.16  
## 95 percent confidence interval:  
## 0.3631946 1.0000000  
## sample estimates:  
## p   
## 0.4295775

# Hand calculation with normal approximation  
phat <- x / n  
se0 <- sqrt(p0 \* (1 - p0) / n)  
z <- (phat - p0) / se0  
p\_one <- 1 - pnorm(z)  
c(phat = phat, z = z, p\_one\_sided = p\_one)

## phat z p\_one\_sided   
## 0.4295775 8.7625018 0.0000000

“p” = 0.4296, z” “, one-sided p”^{-19}“. These match the direction and magnitude of prop.test (extremely small p), confirming the function’s output.

## 2-2

# One-sided 95% lower confidence bound (since alternative="greater")  
x <- 61  
n <- 142  
p0 <- 0.16  
  
ci\_one <- prop.test(x, n, p = p0, alternative = "greater", correct = FALSE)$conf.int  
ci\_one # returns [lower, 1]

## [1] 0.3631946 1.0000000  
## attr(,"conf.level")  
## [1] 0.95

# Two-sided CI with conf.level = 0.90 → same lower bound as the 95% one-sided CI  
ci\_two <- prop.test(x, n, conf.level = 0.90, correct = FALSE)$conf.int  
ci\_two # [lower, upper]; lower ≈ ci\_one[1]

## [1] 0.3631946 0.4985937  
## attr(,"conf.level")  
## [1] 0.9

The one-sided 95% CI reports only a lower bound (about 0.363): with 95% confidence, the true MRD-negativity rate is at least ~36%. Setting a two-sided CI to 90% reproduces the same lower bound (because 95% one-sided ↔ 90% two-sided).

# Question 3

Using raw data (first-generation TKI) allows for individual-level analysis, consistent outcome definitions, and control of confounders, but may be limited by smaller sample size and representativeness.

Using summary results from the literature (second-generation TKI) provides a quick, often larger comparison group, but risks inconsistencies in measurement, selection bias, and lack of confounder adjustment. These differences may introduce biases such as selection bias, information bias, confounding, and temporal bias.

# Question 4

## 4-1

It makes more sense to perform a two-sided test, because we are interested in whether the imatinib MRD-negativity rate is different from 16% (the historical benchmark for second-generation TKIs). Both higher and lower values would matter in assessing whether imatinib is an appropriate control.

## 4-2

prop.test(15, 68, p = 0.16,  
 alternative = "two.sided")

##   
## 1-sample proportions test with continuity correction  
##   
## data: 15 out of 68, null probability 0.16  
## X-squared = 1.4339, df = 1, p-value = 0.2311  
## alternative hypothesis: true p is not equal to 0.16  
## 95 percent confidence interval:  
## 0.1326222 0.3405789  
## sample estimates:  
## p   
## 0.2205882

• Observed proportion: p = 15/68 = 0.221 (22.1%) • Null value: 0.16 • Test statistic: z • Two-sided p-value ≈ 0.17

Interpretation: Since p ≈ 0.17 is much larger than 0.05, we do not reject H₀. The imatinib MRD-negativity rate (22.1%) is not significantly different from the historical 16%. This suggests that imatinib can be considered an appropriate control consistent with earlier-generation drugs.

# Question 5

## 5-1

The total sample size for this test is n = 13, and the observed sample proportion is p = 6/13 .

## 5-2

dbinom(0:13, 13, 0.25) # probability distribution for X=0,…,13

## [1] 2.375726e-02 1.029481e-01 2.058963e-01 2.516510e-01 2.097092e-01  
## [6] 1.258255e-01 5.592245e-02 1.864082e-02 4.660204e-03 8.630008e-04  
## [11] 1.150668e-04 1.046062e-05 5.811453e-07 1.490116e-08

sum(dbinom(0:13, 13, 0.25)) # should equal 1

## [1] 1

The distribution gives the probabilities of 0–13 events when X Binomial(13,0.25). The sum of probabilities is 1, confirming it is a valid probability distribution.

## 5-3

sum(dbinom(c(0, 6:13), 13, 0.25))

## [1] 0.1039699

By summing the probabilities of outcomes as or more extreme than 6, the two-sided p-value is ≈ 0.104.

## 5-4

binom.test(6, 13, p = 0.25)

##   
## Exact binomial test  
##   
## data: 6 and 13  
## number of successes = 6, number of trials = 13, p-value = 0.104  
## alternative hypothesis: true probability of success is not equal to 0.25  
## 95 percent confidence interval:  
## 0.1922324 0.7486545  
## sample estimates:  
## probability of success   
## 0.4615385

The exact binomial test gives a two-sided p-value = 0.104, a 95% confidence interval of approximately (0.192, 0.749), and a sample estimate of p̂ = 0.462. This matches the manual calculation above.