



Diploma in Pharmaceutical Medicine Examination

Part 2

10 October 2024 - Critical Appraisal Paper

Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis by Ytterberg et al
N Engl J Med 2022 Jan 27;386(4):316-326. doi: 10.1056/NEJMoa2109927

Question 1

Why did the United States Food and Drug Administration (FDA) require this study? (2 marks)

Question 2

What was the hypothesis? (1 mark)

Question 3

List 6 design characteristics of the study. (3 marks)

Question 4

- a) Why was this study open label? (1 mark)
- b) What would be the alternative option to allow double-blinding? (1 mark)

Question 5

- a) What were the co-primary endpoints in this study? (1 mark)
- b) What is a co-primary endpoint and what special consideration is required for the statistical analysis? (3 marks)



Question 6

- a) What is a composite endpoint? (1 mark)
- b) Provide one benefit with the use of composite endpoints. (1 mark)
- c) Provide one limitation associated with the use of composite endpoints. (1 mark)

Question 7

- a) Why was it important to enrich the patient population for cardiovascular (CV) risk. (2 marks)
- b) What were the CVS risk factors included in the paper? (3 marks)

Question 8

Which external bodies/groups oversaw the trial and what were their respective functions? (2 marks)

Question 9

What is meant by external adjudication and why is this important? (1 mark)

Question 10

What is censoring and why is the censoring time different for the major adverse cardiovascular events (MACE) and cancer endpoints? (3 marks)

Question 11

How is a number needed to harm calculated and interpreted? (2 marks)

Question 12

- a) What is the null hypothesis for a non-inferiority study? (1 mark)
- b) Comment on why a non-inferiority study was an appropriate choice here. (1 mark)



Question 13

Explain the implications of 3 of the limitations listed for this study. (3 marks)

Question 14

Write a summary of the major adverse cardiovascular events (MACE) results using lay-language (plain English) to inform trial participants of the study outcomes/results. (5 marks)

Question 15

- a) How might the data presented in this paper alter the risk benefit assessment for using tofacitinib? (2 marks)
- b) Which patients would these conclusions not include? (1 mark)

Question 16

- a) What impact did the safety monitoring committee specifically have on this trial? (1 mark)
- b) List four reasons a study trial protocol might include interim analyses. (4 marks)

Question 17

What might be the next steps for the pharmaceutical company after analysing the data from this study and seeing the results? (2 marks)

Question 18

Name 2 alternative trial design that could have been used for this post-authorisation safety study (PASS) study? (2 marks)