

Supplementary Information

Journal: Pharmacoeconomics Open

Title: Artificial intelligence to automate network meta-analyses: Four case studies to evaluate the potential application of large language models

Authors: Tim Reason¹, Emma Benbow¹, Julia Langham¹, Andy Gimblett¹, Sven L. Klijn², Bill Malcolm³

¹ Estima Scientific, London, United Kingdom; ² Bristol Myers Squibb, Princeton, NJ, USA; ³ Bristol Myers Squibb, Uxbridge, UK

Corresponding author: Tim Reason, Estima Scientific, London, United Kingdom, tim.reason@estima-sci.com

Declarations

Funding: This study was supported by Bristol Myers Squibb.

Conflicts of Interest: Tim Reason, Emma Benbow, Julia Langham, and Andy Gimblett are consultants at Estima Scientific and have worked on behalf of Bill Malcolm and Sven L. Klijn, who are employees and shareholders of Bristol Myers Squibb.

SUPPLEMENTARY TABLE S1. Case Study 1 - Studies and publications available for Case Study 1 - clinical response in patients with moderate to severe hidradenitis suppurativa.

Study	Treatment	N	Proportion of patients with clinical response
PIONEER I [1]	Placebo	154	26.0%
	Adalimumab 40 mg weekly	153	41.8%
PIONEER II [1]	Placebo	163	27.6%
	Adalimumab 40 mg weekly	163	58.9%
SUNSHINE [2]	Placebo	180	34%
	Secukinumab 300 mg every 2 weeks	181	45%
	Secukinumab 300 mg every 4 weeks	180	42%
SUNRISE [2]	Placebo	183	31%
	Secukinumab 300 mg every 2 weeks	180	42%
	Secukinumab 300 mg every 4 weeks	180	46%
BE HEARD 1 [3]	Placebo	72	28.7%
	Bimekizumab 320 mg every 2 weeks	289	47.8%
	Bimekizumab 320 mg every 4 weeks	144	45.3%
BE HEARD 2 [3]	Placebo	74	32.2%
	Bimekizumab 320 mg every 2 weeks	291	52.0%
	Bimekizumab 320 mg every 4 weeks	144	53.8%

SUPPLEMENTARY TABLE S2. Case Study 2 - Studies and publications available for Case Study 2 - base case analysis of overall survival of patients receiving 2nd line treatment for non-small cell lung cancer.

Study	Reference treatment	N	Active treatment	N	Hazard ratio [95% CI] Active vs. reference
CheckMate017 [4]	Docetaxel 75 mg/m ² every 3 weeks	137	Nivolumab 3 mg/kg every 2 weeks	135	0.59 [0.44, 0.79]
CheckMate057 [5]	Docetaxel 75 mg/m ² every 3 weeks	290	Nivolumab 3 mg/kg every 2 weeks	292	0.73 [96%, 0.59, 0.89]
KEYNOTE-010 [6]	Docetaxel 75 mg/m ² every 3 weeks	343	Pembrolizumab 2 mg/kg every 3 weeks	345	0.73 [0.62, 0.87]
			Pembrolizumab 10 mg/kg every 3 weeks	346	0.59 [0.49, 0.71]
OAK [7]	Docetaxel 75 mg/m ² every 3 weeks	612	Atezolizumab 1200 mg every 3 weeks	613	0.78 [0.68, 0.89]
POPLAR [7]	Docetaxel 75 mg/m ² every 3 weeks	143	Atezolizumab 1200 mg every 3 weeks	144	0.76 [0.58, 1.00]

CI confidence interval.

SUPPLEMENTARY TABLE S3: Case Study 3 - Studies and publications available for Case Study 3 - sensitivity analysis of overall survival of patients receiving 2nd line treatment for non-small cell lung cancer.

Study	Reference treatment	N	Active treatment	N	Hazard ratio [95% CI] Active vs. reference
CheckMate017 [4]	Docetaxel 75 mg/m ² every 3 weeks	137	Nivolumab 3 mg/kg every 2 weeks	135	0.59 [0.44, 0.79]
CheckMate057 [5]	Docetaxel 75 mg/m ² every 3 weeks	290	Nivolumab 3 mg/kg every 2 weeks	292	0.73 [96%, 0.59, 0.89]
KEYNOTE-010 [6]	Docetaxel 75 mg/m ² every 3 weeks	343	Pembrolizumab 2 mg/kg every 3 weeks	345	0.73 [0.62, 0.87]
			Pembrolizumab 10 mg/kg every 3 weeks	346	0.59 [0.49, 0.71]
OAK [7]	Docetaxel 75 mg/m ² every 3 weeks	612	Atezolizumab 1200 mg every 3 weeks	613	0.78 [0.68, 0.89]
POPLAR [7]	Docetaxel 75 mg/m ² every 3 weeks	143	Atezolizumab 1200 mg every 3 weeks	144	0.76 [0.58, 1.00]
CheckMate078 [8]	Docetaxel 75 mg/m ² every 3 weeks	166	Nivolumab 3 mg/kg every 2 weeks	338	0.68 [97.7%, 0.52, 0.9]
I4T-JE-JVCG [9]	Placebo plus docetaxel 60 mg/m ² every 3 weeks	81	Ramucirumab 10 mg/kg plus docetaxel 60 mg/m ² every 3 weeks	76	0.86 [0.56, 1.32]
REVEL [10]	Placebo plus docetaxel 75 mg/m ² every 3 weeks	625	Ramucirumab 10 mg/kg plus docetaxel 75 mg/m ² every 3 weeks	628	0.86 [0.75, 0.98]
LUME-Lung 1 [11]	Docetaxel 75 mg/m ² every 3 weeks	659	Nintedanib plus docetaxel 75 mg/m ² every 3 weeks	655	0.94 [0.83, 1.05]
GFPC 05-06 [12]	Pemetrexed 500 mg/m ² every 3 weeks	75	Docetaxel 75 mg/m ² every 3 weeks	75	1.17 [0.831, 1.64]
H3E-MC- JMID [13]	Docetaxel 75 mg/m ² every 3 weeks	392	Pemetrexed 500 mg/m ² every 3 weeks	390	0.99 [0.84, 1.17]
JMEI [14]	Docetaxel 75 mg/m ² every 3 weeks	288	Pemetrexed 500 mg/m ² every 3 weeks	283	0.99 [0.82, 1.2]

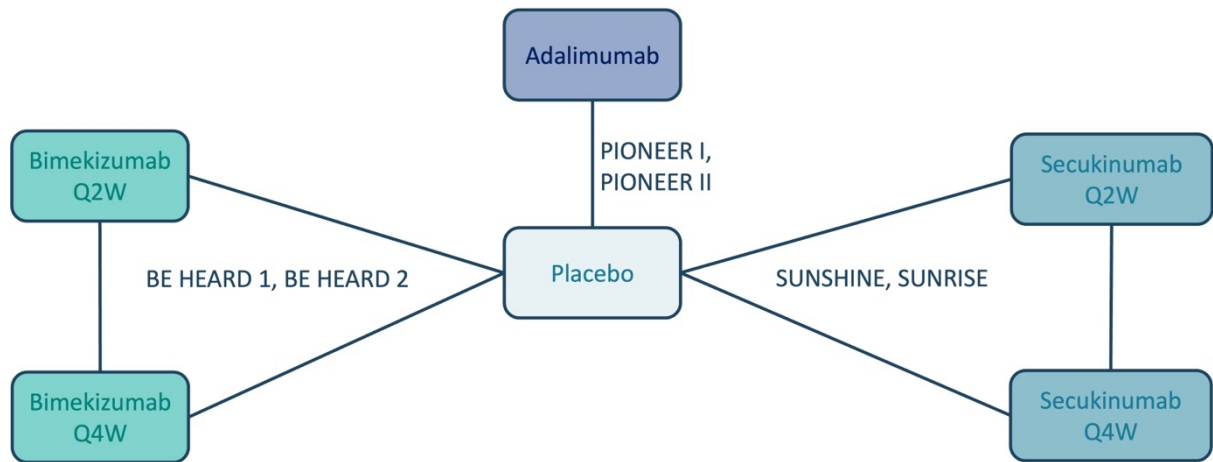
CI confidence interval.

SUPPLEMENTARY TABLE S4: Case Study 4 - Studies and publications available for Case Study 4 - base case analysis of progression-free survival of patients receiving 2nd line treatment for non-small cell lung cancer.

Study	Reference treatment	N	Active treatment	N	Hazard ratio [95% CI] Active vs. reference
CheckMate017 [4]	Docetaxel 75 mg/m ² every 3 weeks	137	Nivolumab 3 mg/kg every 2 weeks	135	0.62 [0.47, 0.81]
CheckMate057 [5]	Docetaxel 75 mg/m ² every 3 weeks	290	Nivolumab 3 mg/kg every 2 weeks	292	0.92 [0.77, 1.11]
KEYNOTE-010 [6]	Docetaxel 75 mg/m ² every 3 weeks	343	Pembrolizumab 2 mg/kg every 3 weeks	345	0.88 [0.74, 1.05]
			Pembrolizumab 10 mg/kg every 3 weeks	346	0.79 [0.66, 0.94]
OAK, ITT850 [15]	Docetaxel 75 mg/m ² every 3 weeks	425	Atezolizumab 1200 mg every 3 weeks	425	0.96 [0.85, 1.08]
OAK, ITT1225 [15]		612		613	0.93 [0.80, 1.08]
POPLAR [16]	Docetaxel 75 mg/m ² every 3 weeks	143	Atezolizumab 1200 mg every 3 weeks	144	0.92 [0.71, 1.20]

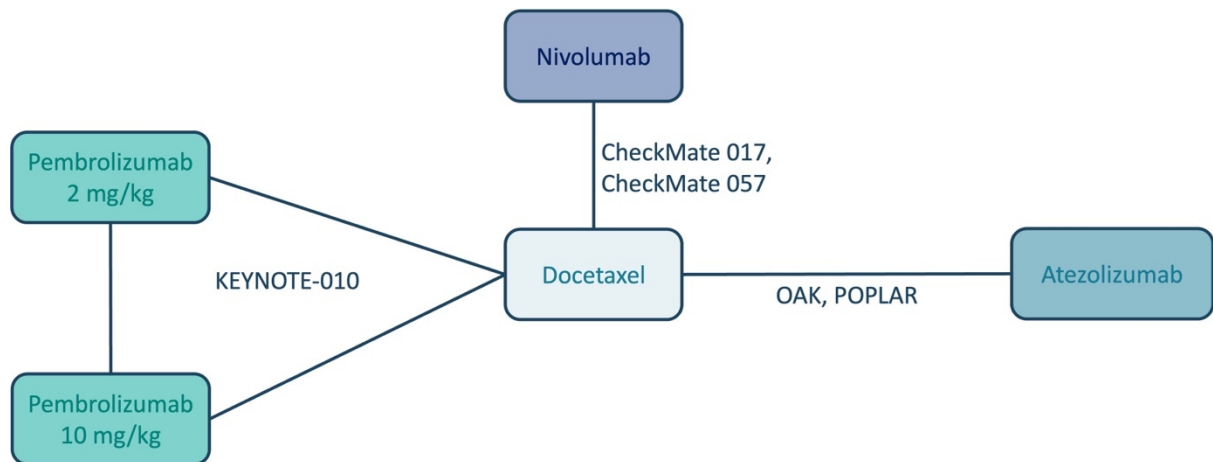
CI confidence interval.

SUPPLEMENTARY FIG. S1. Network diagram for Case Study 1 - clinical response in patients with hidradenitis suppurativa. Treatments are shown in the boxes e.g., adalimumab; the names of the RCTs are shown along the lines e.g., SUNSHINE, SUNRISE.



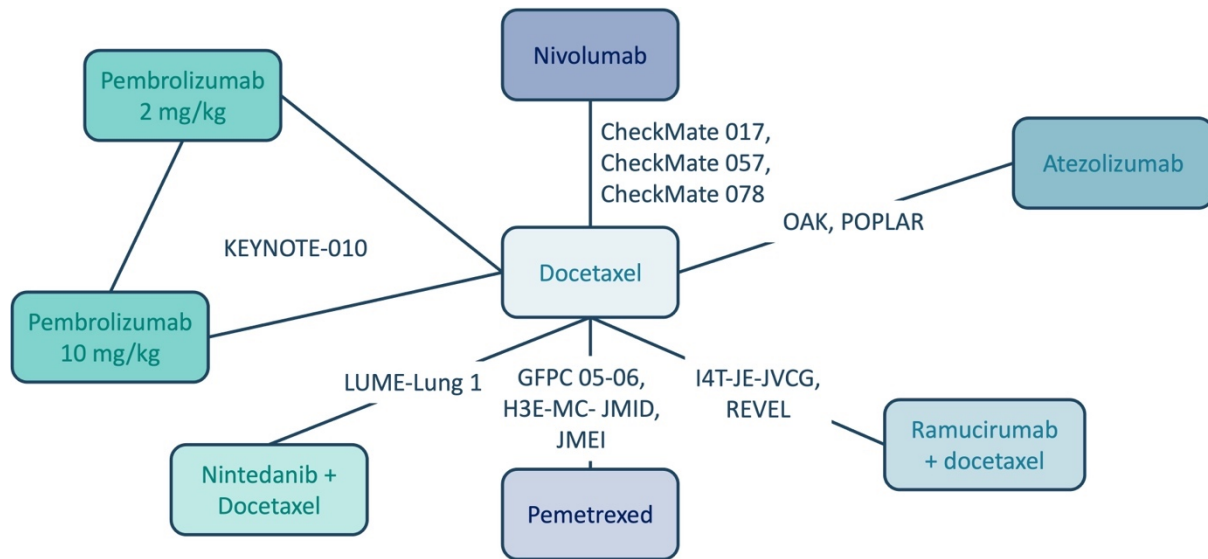
Q2W once every 2 weeks; *Q4W* once every 4 weeks, *RCT* randomised controlled trial

SUPPLEMENTARY FIG. S2. Network diagram for Case Study 2 - OS of patients receiving 2nd line treatment for NSCLC (base case analysis). Treatments are shown in the boxes e.g., nivolumab; the names of the RCTs are shown along the lines e.g., KEYNOTE-010, CheckMate 017.



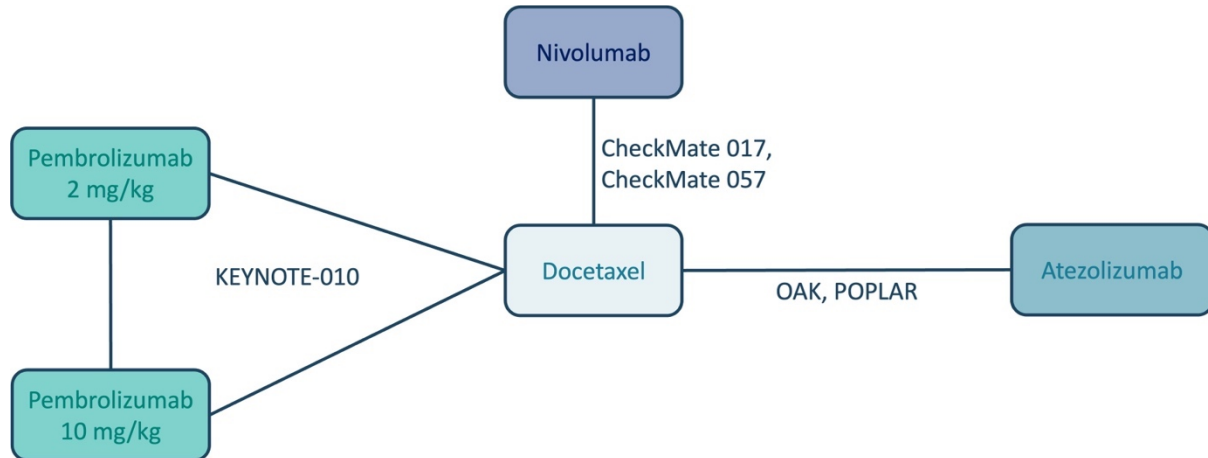
NSCLC non-small cell lung cancer; *OS* overall survival, *RCT* randomised controlled trial

SUPPLEMENTARY FIG. S3. Network diagram for Case Study 3 - OS of patients receiving 2nd line treatment for NSCLC (sensitivity analysis). Treatments are shown in the boxes e.g., nivolumab; the names of the RCTs are shown along the lines e.g., OAK, REVEL.



NSCLC non-small cell lung cancer, OS overall survival, RCT randomised controlled trial

SUPPLEMENTARY FIG. S4. Network diagram for Case Study 4 - PFS of patients receiving 2nd line treatment for NSCLC. Treatments are shown in the boxes e.g., nivolumab; the names of the RCTs are shown along the lines e.g., KEYNOTE-010, CheckMate 017.



NSCLC non-small cell lung cancer, PFS progression-free survival, RCT randomised controlled trial

SUPPLEMENTARY FIG. S5. Example of the development of the overall survival data extraction prompt.

Initial prompt to extract overall survival hazard ratios from text:

Extract the following: the treatment comparison, numbers at risk for each treatment, overall survival hazard ratio (HR) and overall survival hazard ratio confidence intervals and confidence level (e.g., 95%) from this study. Also extract the total trial size, and the randomisation ratio.

This initial prompt resulted in an output from GPT-4 where it would often combine the data for the same treatments for publications where more than one study was reported. The GPT-4 output also often contained data that was not of interest e.g., PFS data when we only wanted OS data and only mentioned data that was found but was unclear whether other required data was available. The format of the returned output was very variable, and it did not consistently record the treatment comparison associated with a hazard ratio, and often missed trial size data. Thus, we added the text shown in bold to the prompt.

First adjustment of prompt to extract overall survival hazard ratios from text:

If there are multiple studies, extract and report from each separately.

Extract data pertaining to overall survival. If something is not in the dataset, mark as not reported.

Extract in the following format: the treatment comparison, numbers at risk for each treatment, overall survival hazard ratio (HR) and overall survival hazard ratio confidence intervals and confidence level (e.g., 95%) from this study. Also extract the treatment comparison used for the hazard ratio e.g., treatment 1 vs. treatment 2, the total trial size (or total number of patients enrolled), and the randomisation ratio.

SUPPLEMENTARY FIG. S6. Example R script for prompt to write R script required for survival analysis.

```
145 library(multinma)
146 library(dplyr)
147
148 parkinsons_contrast <- parkinsons %>% select(studyn, trtn, n, diff, se_diff)
149
150 # Example data
151 #>   studyn trtn    y    se    n  diff se_diff
152 #> 1     1    1 -1.22 0.504  54   NA  0.504
153 #> 2     1    3 -1.53 0.439  95 -0.31  0.668
154 #> 3     2    1 -0.70 0.282 172   NA  0.282
155 #> 4     2    2 -2.40 0.258 173 -1.70  0.382
156 #> 5     3    1 -0.30 0.505  76   NA  0.505
157 #> 6     3    2 -2.60 0.510  71 -2.30  0.718
158
159
160 # Set up data network
161 contr_net <- set_agd_contrast(parkinsons_contrast,
162                               study = studyn,
163                               trt = trtn,
164                               y = diff,
165                               se = se_diff,
166                               sample_size = n)
167
168 # Run analysis
169 contr_fit_FE <- nma(contr_net,
170                    trt_effects = "fixed",
171                    prior_trt = normal(scale = 100))
172
173 print(contr_fit_FE)
174
175 df <- summary(contr_fit_FE)[[1]]
176
177 # Convert the list to a dataframe
178 df <- do.call(data.frame, df)
179
180 print(df)
```

From Parkinson's example provided online [17].

SUPPLEMENTARY FIG. S7: Example R script generated with an LLM (GPT-4) for case study 1.

```
1 library(multinma)
2 library(dplyr)
3
4 # Convert percentage of clinical responses to number of clinical responses
5 convert_to_number <- function(response_percent, total_patients) {
6   round(response_percent * total_patients / 100)
7 }
8
9 # Data
10 data <- data.frame(
11   studyn = c(1, 1, 2, 2, 3, 3, 3, 4, 4, 4),
12   trtn = c(1, 2, 1, 2, 3, 4, 1, 3, 4, 1),
13   trtc = c("Placebo", "ADA Weekly", "Placebo", "ADA Weekly", "Secukinumab 2 weeks", "Secukinumab 4 weeks", "P
14   r = c(convert_to_number(26.0, 154), convert_to_number(41.8, 153), convert_to_number(27.6, 163), convert_to_
15   n = c(154, 153, 163, 163, 181, 180, 180, 180, 180, 183)
16 )
17
18 # Create network
19 network <- set_agd_arm(data,
20   study = studyn,|
21   trt = trtc,
22   r = r,
23   n = n,
24   trt_ref = "Placebo")
25
26 # Fit model
27 fit_FE <- nma(network,
28   trt_effects = "fixed",
29   prior_intercept = normal(scale = 100),
30   prior_trt = normal(scale = 100))
31
32 # Print results
33 print(fit_FE)
34
35 # Summary
36 df <- summary(fit_FE)[[1]]
37
38 # Convert the list to a dataframe
39 df <- do.call(data.frame, df)
40
41 # Filter out mu parameters
42 df <- df %>% filter(!grepl("^mu", parameter))
43
44 # Transform 'row.names' into a column
45 df <- df %>% mutate(rows = row.names(df))
46
47 # Exponentiate the d nodes
48 df <- df %>%
49   mutate_at(vars(mean, `X2.5.`, `X97.5.`), ~ifelse(grepl("^d", rows), exp(.), .))
50
51 print(df)
52
53 # Treatment index
54 # 1: Placebo
55 # 2: ADA Weekly
56 # 3: Secukinumab 2 weeks
57 # 4: Secukinumab 4 weeks
```

SUPPLEMENTARY FIG. S8: Example R script generated by AI for case study 2.

```
1 library(multinma)
2 library(dplyr)
3
4 # Data from the studies
5 data <- data.frame(
6   studyn = c(1, 1, 2, 2, 3, 3, 4, 4, 5, 5, 6, 6),
7   trtn = c(1, 2, 1, 3, 1, 4, 1, 2, 1, 5, 1, 5),
8   n = c(137, 135, 343, 345, 343, 346, 290, 292, 143, 144, 612, 613),
9   HR = c(NA, 0.59, NA, 0.73, NA, 0.59, NA, 0.73, NA, 0.76, NA, 0.78),
10  LCI = c(NA, 0.44, NA, 0.62, NA, 0.49, NA, 0.59, NA, 0.58, NA, 0.68),
11  UCI = c(NA, 0.79, NA, 0.87, NA, 0.71, NA, 0.89, NA, 1.00, NA, 0.89),
12  CI = c(95, 95, 95, 95, 95, 95, 96, 96, 95, 95, 95, 95)
13 )
14
15 # Calculate diff and se_diff
16 data <- data %>%
17   mutate(
18     diff = if_else(is.na(HR), NA_real_, log(HR)),
19     se_diff = if_else(CI == 95, (log(UCI) - log(LCI)) / 3.92,
20                       (log(UCI) - log(LCI)) / (2 * abs(qnorm((100 - CI) / 200))))
21   )
22
23 # Set up data network
24 contr_net <- set_agd_contrast(data,
25                               study = studyn,
26                               trt = trtn,
27                               y = diff,
28                               se = se_diff,
29                               sample_size = n)
30
31 # Run analysis
32 contr_fit_FE <- nma(contr_net,
33                    trt_effects = "fixed",
34                    prior_trt = normal(scale = 100))
35
36 # Print results
37 contr_fit_FE %>%
38   summary() %>%
39   .[[1]] %>%
40   as.data.frame() %>%
41   print()
42
43 # Treatment index
44 treatment_index <- c("1" = "Docetaxel", "2" = "Nivolumab", "3" = "Pembrolizumab 2 mg/kg",
45                     "4" = "Pembrolizumab 10 mg/kg", "5" = "Atezolizumab")
46 print(treatment_index)
```

Note: The CheckMate057 study reported a 96% confidence interval for the overall survival hazard ratio (Table S2). GPT-4 consistently extracted this information and thus it is included in entries 7 and 8 of the “CI” list shown in the example above.

SUPPLEMENTARY FIG. S9: Example small report generated for case study 1.

Introduction

Hidradenitis suppurativa (HS) is a chronic, inflammatory skin disease characterized by recurrent, painful, boil-like lumps (nodules) under the skin. The disease primarily affects areas bearing apocrine sweat glands or sebaceous glands, such as the underarms, under the breasts, inner thighs, groin and buttocks. HS is a debilitating condition that can significantly impact the quality of life of affected individuals, leading to physical discomfort and psychological distress. The disease is estimated to affect approximately 1-4% of the global population, with a higher prevalence in women and individuals of African descent. The economic burden of HS on healthcare systems is substantial, with costs arising from long-term disease management, surgical interventions, and hospitalizations.

Methods

In this study, we conducted a network meta-analysis (NMA) to compare the clinical response of different treatments for HS. The treatments included were Placebo, Adalimumab (ADA) Weekly, Secukinumab every 2 weeks, Secukinumab every 4 weeks, Bimekizumab 320 mg every 2 weeks (Q2W), and Bimekizumab 320 mg every 4 weeks (Q4W).

The NMA was performed using a fixed effects model with a binomial likelihood and logit link. The model was fitted using the multilevel modelling software Stan, with four chains each with 2000 iterations and a warmup of 1000 iterations. The model convergence was assessed using the potential scale reduction factor (Rhat), where a value close to 1 indicates good convergence.

Results

The model converged well with all Rhat values close to 1. The results are presented in the table below as odds ratios (OR), which represent the odds of a clinical response with the treatment compared to the odds of a clinical response with placebo. An OR greater than 1 indicates a higher likelihood of a clinical response with the treatment compared to placebo.

Treatment	Mean OR	SD	2.5% CrI	97.5% CrI
Adalimumab weekly	2.84	0.17	2.06	3.90
Bimekizumab 320 mg Q2W	2.24	0.20	1.52	3.30
Bimekizumab 320 mg Q4W	2.20	0.22	1.44	3.38
Secukinumab 2 weeks	1.61	0.15	1.20	2.16
Secukinumab 4 weeks	1.65	0.15	1.22	2.19

Interpretation

The results suggest that all treatments were significantly more effective than placebo in achieving a clinical response in patients with HS. Adalimumab weekly had the highest mean odds ratio, suggesting it may be the most effective treatment among those included in the analysis. However, the credible intervals for the treatments overlap, indicating that the differences between treatments may not be statistically significant.

SUPPLEMENTARY FIG. S10: Example of the interpretation of the results for case study 2.

Introduction

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for approximately 85% of all lung cancer cases. It is a serious health concern worldwide, with a high disease burden on healthcare systems and patients. The second-line treatment of NSCLC is particularly challenging due to the aggressive nature of the disease and the limited effectiveness of available therapies.

Network meta-analysis (NMA) is a statistical method that allows for the comparison of multiple treatments simultaneously by combining direct and indirect evidence within a network of randomized controlled trials. This method is particularly useful in areas such as NSCLC where numerous treatments are available, and direct comparisons between all treatments are not feasible.

Methods

In this analysis, we conducted a fixed-effects NMA to compare the overall survival of five second-line treatments for NSCLC: Docetaxel, Nivolumab, Pembrolizumab (2 mg/kg and 10 mg/kg), and Atezolizumab. The data were derived from six studies, and the treatment effects were expressed as log hazard ratios. The model was run using the 'multinma' package in R, with Docetaxel set as the reference treatment.

Results

The model converged successfully, as indicated by the potential scale reduction factor (Rhat) values close to 1 for all parameters. The results are presented in the table below, with the treatment effects converted to the natural scale by exponentiation:

Treatment	Mean Hazard Ratio (95% CrI)
Nivolumab	0.68 (0.58, 0.80)
Pembrolizumab 2 mg/kg	0.73 (0.62, 0.86)
Pembrolizumab 10 mg/kg	0.59 (0.49, 0.71)
Atezolizumab	0.78 (0.69, 0.88)

Interpretation

Compared to Docetaxel, all four treatments showed a significantly lower hazard ratio, indicating a survival benefit. Pembrolizumab 10 mg/kg had the greatest survival benefit with a mean hazard ratio of 0.59, followed by Nivolumab (0.68), Pembrolizumab 2 mg/kg (0.73), and Atezolizumab (0.78).

These results suggest that Pembrolizumab 10 mg/kg may be the most effective second-line treatment for NSCLC in terms of overall survival. However, the credible intervals for the hazard ratios overlap, indicating that the differences between treatments may not be statistically significant. Further research is needed to confirm these findings and to consider other important outcomes such as quality of life and adverse events.

Example Prompts Used for Binary Outcome Analysis

Data extraction:

*If there are multiple studies extract and report from each separately. Please extract data pertaining to the clinical response outcome from this text. If something is not in the text, mark as not reported. Extract in the following format: Treatment 1, Treatment 2....Treatment n,
Number of clinical responses 1, Number of clinical responses 2...Number of clinical responses n ,
Number at risk 1, Number at risk 2....Number at risk n,
Total trial size, Randomisation ratio*

R script production:

*Update the shell script with the clinical response data from this text making sure that new studies and treatments are updated correctly in the studyn and trtn columns and new studies and treatments are given unique identifiers where appropriate.
Each study should be given a different number and each treatment should be given a different number.
Before the data for the NMA is created you will need some R code that converts percentage of clinical responses to number of clinical responses; it should be number of clinical responses that goes into the data frame and you should round to the nearest whole number.
Do not allow any non-whole numbers (non-integers) in the r column.
If the number of responses provided is not a whole number, then use the percentage of clinical responses to calculate the number of responses.*

Here is the data: {data}

And here is the shell script:

```
library(multinma)
library(dplyr)

#> studyn trtn trtc r n
#> 1 1 1 Control 3 39
#> 2 1 2 Beta Blocker 3 38
#> 3 2 1 Control 14 116
#> 4 2 2 Beta Blocker 7 114
#> 5 3 1 Control 11 93
#> 6 3 2 Beta Blocker 5 69

blocker_net <- set_agd_arm(blocker,
  study = studyn,
  trt = trtc,
  r = r,
  n = n,
  trt_ref = "Control")
...
```

Report generation and interpretation:

*Please interpret this NMA output pertaining to the clinical outcome response in hidradenitis suppurativa considering the treatment index near the bottom of this R script:
{generated script}*

The NMA output is at the bottom of the R output and the d nodes are odds ratios, with corresponding credible intervals (CrI).

Your interpretation should be in language suitable for a medical journal.

Include an introduction to the disease area Hidradenitis Suppurativa.

You should also give brief methods text about how the analysis was conducted and say whether the model has converged; give me a nice table of results and do not forget to compare the outcome to the reference treatment in the network in your tables and narrative.

In your narrative, please state whether the results are statistically significant or not i.e., the credible interval either lies fully to the right of 1, or fully to the left.

Here are the results: {results from analysis}

Example Prompts Used for Overall Survival Analysis (Time-to-event Outcome)

Prompts for progression-free survival analysis very similar.

Data extraction:

If there are multiple studies extract and report from each separately.

Please extract data pertaining to overall survival. If something is not in the dataset mark as not reported.

Extract in the following format: the treatment comparison,

numbers at risk for each treatment, overall survival hazard ratio (HR) and overall survival hazard ratio confidence intervals and level (e.g., 95%) from this text.

The treatment comparison used for the hazard ratio i.e., treatment 1 vs. treatment 2.

Total trial size (or total number of patients enrolled), Randomisation ratio.

R script production:

Update the shell script with the overall survival data from this text. Each study should be given a different number, and each unique treatment should be given a different number.

One hazard ratio will be reported per treatment comparison. Record both treatments from the treatment comparison in the trtn column. Please ensure the order of the treatment comparison is maintained within the trtn column.

The diff column needs to include a row for each treatment, one row being the reported hazard ratio and the second "NA".

Before the data for the NMA is created you will need some R code that converts the hazard ratio to $\log(\text{hazard ratio})$; it should be the natural log of the hazard ratio that goes into the data frame for diff.

You will also need some R code that converts the confidence intervals to a standard error.

You will need to use the formula

$$\text{sediff} = (\log(\text{UCI}) - \log(\text{LCI})) / (2 * \text{abs}(\text{qnorm}(100 - x) / 200)),$$

where x is the reported confidence interval level.

se_diff should contain an entry for each treatment: "NA" for the reference treatment and the relevant value for the active treatment.

Here is the data:

{data}

And here is the shell script:

```
library(multinma)
```

```
library(dplyr)
```

```
parkinsons_contrast <- parkinsons %>% select(studyn, trtn, n, diff, se_diff)
```

```
# Example data
```

```
#> studyn trtn y se n diff se_diff  
#> 1 1 1 -1.22 0.504 54 NA 0.504  
#> 2 1 3 -1.53 0.439 95 -0.31 0.668  
#> 3 2 1 -0.70 0.282 172 NA 0.282  
#> 4 2 2 -2.40 0.258 173 -1.70 0.382  
#> 5 3 1 -0.30 0.505 76 NA 0.505  
#> 6 3 2 -2.60 0.510 71 -2.30 0.718
```

```
# Set up data network
```

```
contr_net <- set_agd_contrast(parkinsons_contrast,  
                             study = studyn,  
                             trt = trtn,  
                             y = diff,  
                             se = se_diff,  
                             sample_size = n)
```

```
...
```

Report generation and interpretation:

*Please interpret this NMA output pertaining to overall survival in second line non-small cell lung cancer considering the treatment index near the bottom of this R script:
{generated script}*

The NMA results are at the bottom of the R output and are expressed as log hazard ratios with corresponding credible intervals (CrI). Your interpretation should be in language suitable for a medical journal and the results should be converted to the natural scale (they are currently on the log scale) before interpreting by exponentiation.

Please write a short introduction section describing the disease area (2L NSCLC). Please also include a description of NMA in general in your introduction. You should also give brief methods text about how the analysis was conducted and say whether the model has converged; give me a nice table of results and do not forget to compare the outcome to the reference treatment in the network in your tables and narrative.

In your narrative, please state whether the results are statistically significant or not i.e., the credible interval either lies fully to the right of 1, or fully to the left.

Here are the results: {results from analysis}

References

1. Kimball AB, Okun MM, Williams DA, Gottlieb AB, Papp KA, Zouboulis CC, et al. Two Phase 3 Trials of Adalimumab for Hidradenitis Suppurativa. *N Engl J Med*. 2016 Aug 4;375(5):422–34. <https://doi.org/10.1056/NEJMoal504370>
2. Kimball AB, Jemec GBE, Alavi A, Reguiat Z, Gottlieb AB, Bechara FG, et al. Secukinumab in moderate-to-severe hidradenitis suppurativa (SUNSHINE and SUNRISE): week 16 and week 52 results of two identical, multicentre, randomised, placebo-controlled, double-blind phase 3 trials. *The Lancet*. 2023 Mar;401(10378):747–61. [https://doi.org/10.1016/S0140-6736\(23\)00022-3](https://doi.org/10.1016/S0140-6736(23)00022-3)
3. Kimball A, Zouboulis C, Sayed C. Bimekizumab in patients with moderate-to-severe hidradenitis suppurativa: 48-week efficacy and safety from BE HEARD I & II, two phase 3, randomized, double-blind, placebo controlled, multicenter studies. American Academy of Dermatology Annual Meeting; 2023; New Orleans, LA.
4. Brahmer J, Reckamp KL, Baas P, Crinò L, Eberhardt WEE, Poddubskaya E, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non–Small-Cell Lung Cancer. *N Engl J Med*. 2015 Jul 9;373(2):123–35. <https://doi.org/10.1056/NEJMoal504627>
5. Borghaei H, Paz-Ares L, Horn L, Spigel DR, Steins M, Ready NE, et al. Nivolumab versus Docetaxel in Advanced Nonsquamous Non–Small-Cell Lung Cancer. *N Engl J Med*. 2015 Oct 22;373(17):1627–39. <https://doi.org/10.1056/NEJMoal507643>
6. Herbst RS, Baas P, Kim DW, Felip E, Perez-Gracia JL, Han JY, et al. Factors associated with better overall survival (OS) in patients with previously treated, PD-L1–expressing, advanced NSCLC: Multivariate analysis of KEYNOTE-010. *J Clin Oncol*. 2017 May 20;35(15_suppl):9090–9090. https://doi.org/10.1200/JCO.2017.35.15_suppl.9090
7. Mazieres J, Rittmeyer A, Gadgeel S, Hida T, Gandara DR, Cortinovis DL, et al. Atezolizumab Versus Docetaxel in Pretreated Patients With NSCLC: Final Results From the Randomized Phase 2 POPLAR and Phase 3 OAK Clinical Trials. *J Thorac Oncol Off Publ Int Assoc Study Lung Cancer*. 2021 Jan;16(1):140–50. <https://doi.org/10.1016/j.jtho.2020.09.022>
8. Wu YL, Lu S, Cheng Y, Zhou C, Wang J, Mok T, et al. Nivolumab Versus Docetaxel in a Predominantly Chinese Patient Population With Previously Treated Advanced NSCLC: CheckMate 078 Randomized Phase III Clinical Trial. *J Thorac Oncol*. 2019 May;14(5):867–75. <https://doi.org/10.1016/j.jtho.2019.01.006>
9. Yoh K, Hosomi Y, Kasahara K, Yamada K, Takahashi T, Yamamoto N, et al. A randomized, double-blind, phase II study of ramucirumab plus docetaxel vs placebo plus docetaxel in Japanese patients with stage IV non-small cell lung cancer after disease progression on platinum-based therapy. *Lung Cancer*. 2016 Sep;99:186–93. <https://doi.org/10.1016/j.lungcan.2016.07.019>
10. Garon EB, Ciuleanu TE, Arrieta O, Prabhaskar K, Syrigos KN, Goksel T, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): a multicentre, double-blind, randomised phase 3 trial. *The Lancet*. 2014 Aug;384(9944):665–73. [https://doi.org/10.1016/S0140-6736\(14\)60845-X](https://doi.org/10.1016/S0140-6736(14)60845-X)
11. Reck M, Kaiser R, Mellemegaard A, Douillard JY, Orlov S, Krzakowski M, et al. Docetaxel plus nintedanib versus docetaxel plus placebo in patients with previously treated non-small-cell lung cancer (LUME-Lung 1): a phase 3, double-blind, randomised controlled trial. *Lancet Oncol*. 2014 Feb;15(2):143–55. [https://doi.org/10.1016/S1470-2045\(13\)70586-2](https://doi.org/10.1016/S1470-2045(13)70586-2)
12. Vergnenegre A, Corre R, Berard H, Paillot D, Dujon C, Robinet G, et al. Cost-Effectiveness of Second-Line Chemotherapy for Non-small Cell Lung Cancer: An Economic, Randomized, Prospective, Multicenter

- Phase III Trial Comparing Docetaxel and Pemetrexed: The GFPC 05-06 Study. *J Thorac Oncol*. 2011 Jan;6(1):161–8. <https://doi.org/10.1097/JTO.0b013e318200f4c1>
13. Sun Y, Wu YL, Zhou CC, Zhang L, Zhang L, Liu XY, et al. Second-line pemetrexed versus docetaxel in Chinese patients with locally advanced or metastatic non-small cell lung cancer: A randomized, open-label study. *Lung Cancer*. 2013 Feb;79(2):143–50. <https://doi.org/10.1016/j.lungcan.2012.10.015>
 14. Hanna N, Shepherd FA, Fossella FV, Pereira JR, De Marinis F, von Pawel J, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. *J Clin Oncol Off J Am Soc Clin Oncol*. 2004 May 1;22(9):1589–97. <https://doi.org/10.1200/JCO.2004.08.163>
 15. Fehrenbacher L, Von Pawel J, Park K, Rittmeyer A, Gandara DR, Ponce Aix S, et al. Updated Efficacy Analysis Including Secondary Population Results for OAK: A Randomized Phase III Study of Atezolizumab versus Docetaxel in Patients with Previously Treated Advanced Non–Small Cell Lung Cancer. *J Thorac Oncol*. 2018 Aug;13(8):1156–70. <https://doi.org/10.1016/j.jtho.2018.04.039>
 16. Smith DA, Vansteenkiste JF, Fehrenbacher L, Park K, Mazieres J, Rittmeyer A, et al. Updated survival and biomarker analyses of a randomized phase II study of atezolizumab vs docetaxel in 2L/3L NSCLC (POPLAR). *J Clin Oncol*. 2016 May 20;34(15_suppl):9028–9028. https://doi.org/10.1200/JCO.2016.34.15_suppl.9028
 17. Phillipppo DM. multinma: Bayesian Network Meta-Analysis of Individual and Aggregate Data <https://cran.r-project.org/web/packages/multinma/index.html>. Accessed 05 Jan 2024.