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Supplemental Appendix 2
Statistical Analysis Plan

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Study of Co-trimoxazole or Doxycycline and their Impact on Clinical Outcomes Using Pragmatic Design in Idiopathic Pulmonary Fibrosis

Statistical Analysis Plan

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21	Table of Contents	
22	I. Overview	4
23	II. Study Design	4
24	Randomization	4
25	Data Sources	4
26	III. Analysis Population and Missing Data	4
27	IV. General Methodology	5
28	V. Primary Endpoint	5
29	VI. Secondary Endpoints	5
30	VII. Endpoint Descriptions	6
31	Primary Endpoint	6
32	VIII. Secondary Endpoint Descriptions	7
33	Secondary Endpoint #1	7
34	Secondary Endpoint #2	8
35	Secondary Endpoint #3	8
36	Secondary Endpoint #4	9
37	Secondary Endpoint #5	10
38	Secondary Endpoint #6	10
39	Secondary Endpoint #7	11
40	Secondary Endpoint #8	12
41	Secondary Endpoint #9	12
42	Secondary Endpoint #10	13
43	Secondary Endpoint #11	14
44	Secondary Endpoint #12	15
45	Secondary Endpoint #13	15
46	IX. Safety endpoints	16
47	Serious adverse events	16
48	Concomitant Medication	16
49	X. Trial conduct	17
50	Compliance	17
51	Therapy crossover	17
52	XI. Exploratory analyses	17
53	Six minute walk test	17
54	XII. Interim Analyses	18
55	XIII. Subgroup of Interest	18
56	XIV. References	19
57	XV. Tables/Listing/Graph Mock-ups	19

58

59 I. Overview

60 CleanUP-IPF is a randomized, unblinded, multi-center clinical trial of patients with a
61 diagnosis of idiopathic pulmonary fibrosis (IPF). A total of approximately 500 patients
62 will be enrolled in the trial. Eligible patients will be randomized to the following
63 treatment strategies:

- 64 • Standard care
- 65 • Standard care + oral antimicrobial therapy

66
67 Patients randomized to receive antimicrobial therapy will be given co-trimoxazole
68 unless they have an allergy, contraindication to co-trimoxazole, renal insufficiency
69 (GFR < 30 ml), are hyperkalemic (potassium > 5 mEq/L), or are concomitantly taking
70 an angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB),
71 or potassium sparing diuretic in which case they will receive doxycycline.
72

73 II. Study Design

74 **Randomization**

75
76 Eligible patients will be randomized 1:1 to either receive or not receive a prescription
77 drug voucher for oral antimicrobial therapy in the form of one double strength 160mg
78 trimethoprim/800mg sulfamethoxazole (double strength co-trimoxazole) twice daily
79 plus folic acid 5 mg daily OR doxycycline 100mg once daily if weight < 50 kilograms or
80 100mg twice daily if weight > 50 kilograms.

81

82 **Data Sources**

83

84 A database of case report form and biomarker core lab data will be created in
85 eClinicalOS (eCOS), and the data then transferred to SAS for analysis. The randomized
86 treatment assignment will be provided through data collected by the eCOS system.
87

88 III. Analysis Population and Missing Data

89 The primary analysis will be based on intention to treat. All randomized patients will
90 be included in the analysis population for assessing the primary and secondary
91 endpoints. Extensive efforts being made in connection with the clinical sites to ensure
92 data quality and completeness, it is expected that exclusion of patients for any
93 endpoint analysis will be minimal.
94

95 For the primary endpoint patients without any observed non-elective, respiratory
96 hospitalization or all-cause mortality will be censored at their last visit or lung
97 transplantation. For the adjustment variables in the primary model the imputation
98 method will be dictated by the amount of missingness. If all the adjustment variables
99 have a missing data rate of 2% or below (approximately 10 or less out of 500) then a
100 simple imputation method will be implemented. If any one of the adjustment variables
101 has a missing data rate over 2% (approximately more than 10 out of 500) then
102 multiple imputation method will be implemented. For the simple approach categorical

103 adjustment variables will be imputed to the mode and continuous adjustment
 104 variables will be imputed to the median value. For the multiple imputation the full
 105 conditional specification method (FCS) method will be used and assume an arbitrary
 106 missing data pattern [Berglund and Heeringa 2014]. The multiple imputation scenario
 107 (20 planned iterations) will be constructed which includes the treatment group
 108 indicator variable and the adjustment variables planned for the primary model.
 109

110 IV. General Methodology

111 Definition of Statistical Significance: The statistical plan will test non-directional
 112 hypotheses, i.e., all tests will be 2-sided. The level of significance for all efficacy and
 113 safety analyses will be 0.05.

114 Statistical Tests: For situations where one observation per patient is observed, (e.g.
 115 safety comparisons at individual time points), a general analysis convention will be
 116 used unless otherwise specified. For continuous and ordinal variables, treatment
 117 group differences will be tested using the Wilcoxon rank-sum test for two groups and
 118 Kruskal-Wallis one-way analysis of variance for comparisons of more than two groups.
 119 For censored data, like time to event, treatment group differences will be tested using
 120 the log rank test. For discrete variables, treatment group differences will be tested
 121 using the chi-square test. In the situation of low cell counts the treatment group
 122 differences will be tested using Fisher's exact method.

123 Descriptive Statistics: For continuous and ordinal variables the number of
 124 observations, number of missing values, mean, standard deviation, median, twenty-
 125 fifth percentile, and seventy-fifth percentile will be given. For binary (e.g. yes/no),
 126 categorical, and/or ordinal variables a simple count and percent will be provided.
 127 Other statistics may be considered if necessary.

128 Descriptive Plots: Descriptive plots may replace or produced in addition to descriptive
 129 statistics if deemed appropriate. If deemed necessary plots of descriptive statistics
 130 such as spaghetti, mosaic, box, cumulative distribution, and loess curves will be
 131 provided.

132 Study Listings: Study data will be listed by treatment group, visit if applicable, and
 133 patient where appropriate.

134 Software and Validation Procedures: All data presented in interim and final analyses
 135 will be generated and validated under the guidance of the DCRI Clinical Trials
 136 Statistical SOPs.
 137

138 V. Primary Endpoint

139 The primary endpoint of this study will be the comparison of "Standard care + oral
 140 antimicrobial therapy" and "Standard care" for the time to first non-elective,
 141 respiratory hospitalization or all-cause mortality.
 142

143 VI. Secondary Endpoints

144 Secondary goals of this study are to assess differences between treatment groups for
 145 the following:

- 146 1. Time to death from any cause
- 147 2. Time to first non-elective respiratory hospitalization
- 148 3. Time to first non-elective all-cause hospitalization
- 149 4. Total number of non-elective respiratory hospitalizations
- 150 5. Total number of non-elective all-cause hospitalizations

- 151 6. Change in FVC from randomization to 12 months
 152 7. Change in DLCO from randomization to 12 months
 153 8. Total number of respiratory infections
 154 9. Change in UCSD-Shortness of Breath Questionnaire from randomization to 12 months
 155 10. Change in Fatigue Severity Scale score from randomization to 12 months
 156 11. Change in Leicester Cough Questionnaire score from randomization to 12 months
 157 12. Change in EQ-5D score and SF-12 score from randomization to 12 months
 158 13. Change in ICEpop CAPability measure for Older people (ICECAP-O) score from
 159 randomization to 12 months
 160

161 VII. Endpoint Descriptions

162 **Primary Endpoint**

163
 164 Endpoint Description: Time to first non-elective, respiratory hospitalization or all-
 165 cause mortality.
 166

167 Response Variable Definition: Time to first respiratory hospitalization or all-cause
 168 mortality (primary endpoint) will be defined as the time to first observed event
 169 respiratory hospitalization or all-cause mortality. All patients will have some
 170 information regarding mortality and last visit of follow-up. Patients without any
 171 observed respiratory hospitalization or death event at the time of analysis will be
 172 censored at their last visit or lung transplantation. The respiratory hospitalizations
 173 will be reviewed and adjudicated by a clinical events committee (CEC).
 174

175 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
 176 enrollment, use of standard of care medications at enrollment, and choice of
 177 antimicrobial agent prior to randomization. Note that the baseline DLCO and baseline
 178 FVC will be added to regression models using the % predicted versions for all
 179 endpoints.
 180

181 Handling of Dropouts and Missing Data:

182 The censoring mechanism is assumed to be non-informative. Supportive analyses will
 183 be performed to assess the impact of a potential informative censoring.
 184

185 Diagnostic tests: The additional continuous covariates to be used in the primary
 186 analysis model will be assessed for major departures from linearity by inspection of
 187 restricted cubic spline plots. If a departure is observed then a suitable transformation
 188 will be explored. In addition the proportional hazard assumptions will be explored by
 189 inspection of Martingale residuals plots for all model covariates. If a major departure
 190 is observed then the variable will added to the model as a stratification variable.
 191

192 Statistical Tests: The Cox proportional hazards regression model will be used to
 193 estimate outcome differences between the two treatment arms: “Standard care + oral
 194 antimicrobial therapy” and “Standard care”. The outcome is the time to first non-
 195 elective, respiratory hospitalization or all-cause mortality with model terms for
 196 treatment arm, baseline measurement, and covariates. Hazard ratios and 95%
 197 confidence intervals will summarize the differences between treatment arms.
 198

199 Interpretation of Results: For Cox regression models a hazard ratio below 1.00 will
 200 indicate a reduction in events for “Standard care + oral antimicrobial therapy” arm. A

201 hazard ratio above 1.00 will indicate increase in events for “Standard care + oral
202 antimicrobial therapy” arm.

203
204 Alternative Analysis: To explore therapy crossovers an alternative analysis scenario
205 will be constructed. Therapy crossover will be defined as patients assigned “Standard
206 care” and receiving after randomization “oral antimicrobial therapy”. The previous
207 presented primary analysis model will be used and modified. Specifically the
208 response variable definition for the “Standard care” assigned patients (with crossover)
209 will be changed such that the time to event and event indicator variables will be
210 censored at the time of therapy crossover. The same statistical model and
211 interpretation will be used as the primary analysis.

212

213 VIII. Secondary Endpoint Descriptions

214 **Secondary Endpoint #1**

215 Endpoint Description: Time to death from any cause.

216

217 Response Variable Definition: Time to death will be defined as the time to all-cause
218 mortality. All patients will have some information regarding mortality and last visit of
219 follow-up. Patients without any observed death at the time of analysis will be censored
220 at their last visit or lung transplantation.

221

222 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
223 enrollment, use of standard of care medications at enrollment, and choice of
224 antimicrobial agent prior to randomization.

225

226 Handling of Dropouts and Missing Data: The censoring mechanism is assumed to be
227 non-informative. Supportive analyses will be performed to assess the impact of a
228 potential informative censoring.

229

230 Diagnostic tests: The additional continuous covariates to be used in the primary
231 analysis model will be assessed for major departures from linearity by inspection of
232 restricted cubic spline plots. If a departure is observed then a suitable transformation
233 will be explored. In addition the proportional hazard assumptions will be explored by
234 inspection of Martingale residuals plots. If a major departure is observed then the
235 variable will be added to the model as a stratification variable.

236

237 Statistical Tests: The Cox proportional hazards regression model will be used to
238 estimate outcome differences between the two treatment arms: “Standard care + oral
239 antimicrobial therapy” and “Standard care”. The outcome is the time to death from
240 any cause with model terms for treatment arm, baseline measurement, and covariates.
241 Hazard ratios and 95% confidence intervals will summarize the differences between
242 treatment arms.

243

244 Interpretation of Results: For Cox regression models a hazard ratio below 1 will
245 indicate a reduction in events for “Standard care + oral antimicrobial therapy” arm. A
246 hazard ratio above 1.00 will indicate increase in events for “Standard care + oral
247 antimicrobial therapy” arm.

248

249 **Secondary Endpoint #2**

250 Endpoint Description: Time to first non-elective respiratory hospitalization

251
252 Response Variable Definition: Time to first non-elective respiratory hospitalization will
253 be defined as the time to first non-elective respiratory hospitalization. The
254 hospitalizations will be reviewed and adjudicated by a CEC as non-elective respiratory
255 hospitalizations. All patients will have some information regarding mortality and last
256 visit of follow-up. Patients without any observed event at the time of analysis will be
257 censored at their last visit, death, or lung transplantation.

258
259 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
260 enrollment, use of standard of care medications at enrollment, and choice of
261 antimicrobial agent prior to randomization.

262
263 Handling of Dropouts and Missing Data: The censoring mechanism is assumed to be
264 non-informative. Supportive analyses will be performed to assess the impact of a
265 potential informative censoring.

266
267 Diagnostic tests: The additional continuous covariates to be used in the primary
268 analysis model will be assessed for major departures from linearity by inspection of
269 restricted cubic spline plots. If a departure is observed then a suitable transformation
270 will be explored. In addition the proportional hazard assumptions will be explored by
271 inspection of Martingale residuals plots. If a major departure is observed then the
272 variable will added to the model as a stratification variable.

273
274 Statistical Tests: The Cox proportional hazards regression model will be used to
275 estimate outcome differences between the two treatment arms: “Standard care + oral
276 antimicrobial therapy” and “Standard care”. The outcome is the time to first non-
277 elective respiratory hospitalization with model terms for treatment arm, baseline
278 measurement, and covariates. Hazard ratios and 95% confidence intervals will
279 summarize the differences between treatment arms.

280
281 Interpretation of Results: For Cox regression models a hazard ratio below 1.00 will
282 indicate a reduction in events for “Standard care + oral antimicrobial therapy” arm. A
283 hazard ratio above 1.00 will indicate increase in events for “Standard care + oral
284 antimicrobial therapy” arm.

285 **Secondary Endpoint #3**

286 Endpoint Description: Time to first non-elective all-cause hospitalization

287
288
289 Response Variable Definition: Time to first non-elective hospitalization will be defined
290 as the time to first non-elective hospitalization. The hospitalizations will be reviewed
291 and adjudicated by a CEC as non-elective all-cause hospitalizations. All patients will
292 have some information regarding mortality and last visit of follow-up. Patients without
293 any observed event at the time of analysis will be censored at their last visit, death, or
294 lung transplantation.

295
296 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
297 enrollment, use of standard of care medications at enrollment, and choice of
298 antimicrobial agent prior to randomization.

299
 300 Handling of Dropouts and Missing Data: The censoring mechanism is assumed to be
 301 non-informative. Supportive analyses will be performed to assess the impact of a
 302 potential informative censoring.

303
 304 Diagnostic tests: The additional continuous covariates to be used in the primary
 305 analysis model will be assessed for major departures from linearity by inspection of
 306 restricted cubic spline plots. If a departure is observed then a suitable transformation
 307 will be explored. In addition the proportional hazard assumptions will be explored by
 308 inspection of Martingale residuals plots. If a major departure is observed then the
 309 variable will added to the model as a stratification variable.

310
 311 Statistical Tests: The Cox proportional hazards regression model will be used to
 312 estimate outcome differences between the two treatment arms: “Standard care + oral
 313 antimicrobial therapy” and “Standard care”. The outcome is the time to first non-
 314 elective all-cause hospitalization with model terms for treatment arm, baseline
 315 measurement, and covariates. Hazard ratios and 95% confidence intervals will
 316 summarize the differences between treatment arms.

317
 318 Interpretation of Results: For Cox regression models a hazard ratio below 1.00 will
 319 indicate a reduction in events for “Standard care + oral antimicrobial therapy” arm. A
 320 hazard ratio above 1.00 will indicate increase in events for “Standard care + oral
 321 antimicrobial therapy” arm.

322

323 **Secondary Endpoint #4**

324 Endpoint Description: Total number of non-elective respiratory hospitalizations

325

326 Response Variable Definition: The hospitalizations will be reviewed and adjudicated by
 327 a clinical events committee (CEC) as non-elective respiratory hospitalizations.

328

329 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
 330 enrollment, and choice of antimicrobial agent prior to randomization.

331

332 Handling of Dropouts and Missing Data: All patients will have some information
 333 regarding mortality and last visit of follow-up. Lung transplantation will be additional
 334 censoring variable in this analyses. The censoring mechanism is assumed to be non-
 335 informative. Supportive analyses will be performed to assess the impact of a potential
 336 informative censoring.

337

338 Diagnostic tests: The additional continuous covariates to be used in the primary
 339 analysis model will be assessed for major departures from linearity by inspection
 340 scatter plots with LOESS curves. If a departure is observed then a suitable
 341 transformation will be explored. The validity of this model in terms of meeting
 342 modeling assumptions will be assessed via standard modeling diagnostics and
 343 goodness-of-fit measures.

344

345 Statistical Tests: A Poisson regression model will be used to estimate outcome ratio
 346 between the two treatment arms: “Standard care + oral antimicrobial therapy” and
 347 “Standard care”. The outcome is the total number of non-elective respiratory
 348 hospitalizations with model terms for treatment arm, baseline measurement, and

349 covariates. Rates and 95% confidence intervals will summarize the differences
350 between treatment arms.

351
352 Interpretation of Results: For poisson regression models a ratio below 1.00 will
353 indicate a reduction in events for “Standard care + oral antimicrobial therapy” arm. A
354 hazard ratio above 1.00 will indicate increase in events for “Standard care + oral
355 antimicrobial therapy” arm.

356 357 **Secondary Endpoint #5**

358 Endpoint Description: Total number of non-elective all-cause hospitalizations

359
360 Response Variable Definition: The hospitalizations will be reviewed and adjudicated by
361 a CEC as non-elective all-cause hospitalizations.

362
363 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
364 enrollment, use of standard of care medications at enrollment, and choice of
365 antimicrobial agent prior to randomization.

366
367 Handling of Dropouts and Missing Data: All patients will have some information
368 regarding mortality and last visit of follow-up. Lung transplantation will be additional
369 censoring variable in this analyses. The censoring mechanism is assumed to be non-
370 informative. Supportive analyses will be performed to assess the impact of a potential
371 informative censoring.

372
373 Diagnostic tests: The additional continuous covariates to be used in the primary
374 analysis model will be assessed for major departures from linearity by inspection
375 scatter plots with LOESS curves. If a departure is observed then a suitable
376 transformation will be explored. The validity of this model in terms of meeting
377 modeling assumptions will be assessed via standard modeling diagnostics and
378 goodness-of-fit measures.

379
380 Statistical Tests: The Poisson regression model will be used to estimate outcome ratio
381 between the two treatment arms: “Standard care + oral antimicrobial therapy” and
382 “Standard care”. The outcome is the total number of non-elective all-cause
383 hospitalizations with model terms for treatment arm, baseline measurement, and
384 covariates. Rates and 95% confidence intervals will summarize the differences
385 between treatment arms.

386
387 Interpretation of Results: For Poisson regression models a ratio below 1.00 will
388 indicate a reduction in events for “Standard care + oral antimicrobial therapy” arm. A
389 ratio above 1.00 will indicate increase in events for “Standard care + oral antimicrobial
390 therapy” arm.

391 392 **Secondary Endpoint #6**

393 Endpoint Description: Change in FVC (L) from randomization to 12 months

394
395 Response Variable Definition: The FVC data will be collected at baseline and 12
396 months. The change from baseline will be calculated for the 12 month values by
397 subtracting the baseline result.

398

399 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
400 enrollment, use of standard of care medications at enrollment, and choice of
401 antimicrobial agent prior to randomization.

402
403 Handling of Dropouts and Missing Data: All patients will have some information
404 regarding mortality and last visit of follow-up. Lung transplantation will be additional
405 censoring variable in this analyses. The censoring mechanism is assumed to be non-
406 informative. Supportive analyses will be performed to assess the impact of a potential
407 informative censoring.

408
409 Diagnostic tests: The additional continuous covariates to be used in the primary
410 analysis model will be assessed for major departures from linearity by inspection
411 scatter plots with LOESS curves. If a departure is observed then a suitable
412 transformation will be explored. The validity of this model in terms of meeting
413 modeling assumptions will be assessed via standard modeling diagnostics and
414 goodness-of-fit measures.

415
416 Statistical Tests: The linear regression model will be used to estimate outcome
417 differences between the two treatment arms: “Standard care + oral antimicrobial
418 therapy” and “Standard care”. The outcome is the measured result at 12 months with
419 model terms for treatment arm, baseline measurement, and covariates. Descriptive
420 statistics will be calculated at baseline and 12 months by treatment group.

421
422 Interpretation of Results: For linear models a difference below 0.00 will indicate a
423 reduction in score for “Standard care + oral antimicrobial therapy” arm. A difference
424 above 0.00 will indicate increase in score for “Standard care + oral antimicrobial
425 therapy” arm.

426

427 **Secondary Endpoint #7**

428 Endpoint Description: Change in DLCO from randomization to 12 months

429

430 Response Variable Definition: The DLCO data will be collected at baseline and 12
431 months. The change from baseline will be calculated for the 12 month values by
432 subtracting the baseline result.

433

434 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
435 enrollment, use of standard of care medications at enrollment, and choice of
436 antimicrobial agent prior to randomization.

437

438 Handling of Dropouts and Missing Data:

439 All patients will have some information regarding mortality and last visit of follow-up.
440 Lung transplantation will be additional censoring variable in this analyses. The
441 censoring mechanism is assumed to be non-informative. Supportive analyses will be
442 performed to assess the impact of a potential informative censoring.

443

444 Diagnostic tests: The additional continuous covariates to be used in the primary
445 analysis model will be assessed for major departures from linearity by inspection
446 scatter plots with LOESS curves. If a departure is observed then a suitable
447 transformation will be explored. The validity of this model in terms of meeting

448 modeling assumptions will be assessed via standard modeling diagnostics and
449 goodness-of-fit measures.

450

451 Statistical Tests: The linear regression model will be used to estimate outcome
452 differences between the two treatment arms: “Standard care + oral antimicrobial
453 therapy” and “Standard care”. The outcome is the measured result at 12 months with
454 model terms for treatment arm, baseline measurement, and covariates. Descriptive
455 statistics will be calculated at baseline and 12 months by treatment group.

456

457 Interpretation of Results: For linear models a difference below 0.00 will indicate a
458 reduction in score for “Standard care + oral antimicrobial therapy” arm. A difference
459 above 0.00 will indicate increase in score for “Standard care + oral antimicrobial
460 therapy” arm.

461

462 **Secondary Endpoint #8**

463 Endpoint Description: Total number of respiratory infections

464

465 Response Variable Definition: all lower respiratory tract infection(s) treated with
466 antibiotic treatment will be collected in follow-up.

467

468 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
469 enrollment, use of standard of care medications at enrollment, and choice of
470 antimicrobial agent prior to randomization.

471

472 Handling of Dropouts and Missing Data: The censoring mechanism is assumed to be
473 non-informative. Supportive analyses will be performed to assess the impact of a
474 potential informative censoring.

475

476 Diagnostic tests: The additional continuous covariates to be used in the primary
477 analysis model will be assessed for major departures from linearity by inspection
478 scatter plots with LOESS curves. If a departure is observed then a suitable
479 transformation will be explored. The validity of this model in terms of meeting
480 modeling assumptions will be assessed via standard modeling diagnostics and
481 goodness-of-fit measures.

482

483 Statistical Tests: A Poisson regression model will be used to estimate outcome ratio
484 between the two treatment arms: “Standard care + oral antimicrobial therapy” and
485 “Standard care”. The outcome is the total number of respiratory infections with model
486 terms for treatment arm, baseline measurement, and covariates. Rates and 95%
487 confidence intervals will summarize the differences between treatment arms.

488

489 Interpretation of Results: For Poisson regression models a ratio below 1.00 will
490 indicate a reduction in events for “Standard care + oral antimicrobial therapy” arm. A
491 ratio above 1.00 will indicate increase in events for “Standard care + oral antimicrobial
492 therapy” arm.

493

494 **Secondary Endpoint #9**

495 Endpoint Description: Change in UCSD-Shortness of Breath Questionnaire from
496 randomization to 12 months

497

498 Response Variable Definition: The UCSD-Shortness of Breath Questionnaire data will
499 be collected at baseline and 12 months. For the collect questionnaire data the UCSD-
500 Shortness of Breath score will be calculated. The change from baseline will be
501 calculated for the 12 month values by subtracting the baseline result.

502

503 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
504 enrollment, use of standard of care medications at enrollment, and choice of
505 antimicrobial agent prior to randomization.

506

507 Handling of Dropouts and Missing Data:

508 The censoring mechanism is assumed to be non-informative. Supportive analyses will
509 be performed to assess the impact of a potential informative censoring.

510

511 Diagnostic tests: The additional continuous covariates to be used in the primary
512 analysis model will be assessed for major departures from linearity by inspection
513 scatter plots with LOESS curves. If a departure is observed then a suitable
514 transformation will be explored. The validity of this model in terms of meeting
515 modeling assumptions will be assessed via standard modeling diagnostics and
516 goodness-of-fit measures.

517

518 Statistical Tests: The linear regression model will be used to estimate outcome
519 differences between the two treatment arms: “Standard care + oral antimicrobial
520 therapy” and “Standard care”. The outcome is the measured result at 12 months with
521 model terms for treatment arm, baseline measurement, and covariates. Descriptive
522 statistics will be calculated at baseline and 12 months by treatment group.

523

524 Interpretation of Results: For linear models a difference below 0.00 will indicate a
525 reduction in score for “Standard care + oral antimicrobial therapy” arm. A difference
526 above 0.00 will indicate increase in score for “Standard care + oral antimicrobial
527 therapy” arm.

528

529 **Secondary Endpoint #10**

530 Endpoint Description: Change in Fatigue Severity Scale score from randomization to
531 12 months

532

533 Response Variable Definition: The Fatigue Severity Scale Questionnaire data will be
534 collected at baseline and 12 months. For the collect questionnaire data the Fatigue
535 Severity Scale score will be calculated. The change from baseline will be calculated for
536 the 12 month values by subtracting the baseline result.

537

538 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
539 enrollment, use of standard of care medications at enrollment, and choice of
540 antimicrobial agent prior to randomization.

541

542 Handling of Dropouts and Missing Data: The censoring mechanism is assumed to be
543 non-informative. Supportive analyses will be performed to assess the impact of a
544 potential informative censoring.

545

546 Diagnostic tests: The additional continuous covariates to be used in the primary
547 analysis model will be assessed for major departures from linearity by inspection

548 scatter plots with LOESS curves. If a departure is observed then a suitable
549 transformation will be explored. The validity of this model in terms of meeting
550 modeling assumptions will be assessed via standard modeling diagnostics and
551 goodness-of-fit measures.

552
553 Statistical Tests: The linear regression model will be used to estimate outcome
554 differences between the two treatment arms: “Standard care + oral antimicrobial
555 therapy” and “Standard care”. The outcome is the measured result at 12 months with
556 model terms for treatment arm, baseline measurement, and covariates. Descriptive
557 statistics will be calculated at baseline and 12 months by treatment group.

558
559 Interpretation of Results: For linear models a difference below 0.00 will indicate a
560 reduction in score for “Standard care + oral antimicrobial therapy” arm. A difference
561 above 0.00 will indicate increase in score for “Standard care + oral antimicrobial
562 therapy” arm.

563 **Secondary Endpoint #11**

564 Endpoint Description: Change in Leicester Cough Questionnaire score from
565 randomization to 12 months

566
567 Response Variable Definition: The Leicester Cough Questionnaire data will be collected
568 at baseline and 12 months. For the collect questionnaire data the Leicester Cough
569 Questionnaire score will be calculated. The change from baseline will be calculated for
570 the 12 month values by subtracting the baseline result.

571
572 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
573 enrollment, use of standard of care medications at enrollment, and choice of
574 antimicrobial agent prior to randomization.

575
576 Handling of Dropouts and Missing Data:
577 The censoring mechanism is assumed to be non-informative. Supportive analyses will
578 be performed to assess the impact of a potential informative censoring.

579
580 Diagnostic tests: The additional continuous covariates to be used in the primary
581 analysis model will be assessed for major departures from linearity by inspection
582 scatter plots with LOESS curves. If a departure is observed then a suitable
583 transformation will be explored. The validity of this model in terms of meeting
584 modeling assumptions will be assessed via standard modeling diagnostics and
585 goodness-of-fit measures.

586
587 Statistical Tests: The linear regression model will be used to estimate outcome
588 differences between the two treatment arms: “Standard care + oral antimicrobial
589 therapy” and “Standard care”. The outcome is the measured result at 12 months with
590 model terms for treatment arm, baseline measurement, and covariates. Descriptive
591 statistics will be calculated at baseline and 12 months by treatment group.

592
593 Interpretation of Results: For linear models a difference below 0.00 will indicate a
594 reduction in score for “Standard care + oral antimicrobial therapy” arm. A difference
595 above 0.00 will indicate increase in score for “Standard care + oral antimicrobial
596 therapy” arm.

597 **Secondary Endpoint #12**

598 Endpoint Description: Change in EQ-5D score and SF-12 score from randomization to
599 12 months

600
601 Response Variable Definition: The SF-12 questionnaire data will be collected at
602 baseline and 12 months. The EQ-5D questionnaire data will be collected at baseline
603 and 12 months. For the collect questionnaire data the EQ-5D score and SF-12 score
604 will be calculated. The change from baseline will be calculated for the 12 month
605 values by subtracting the baseline result.

606
607 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
608 enrollment, use of standard of care medications at enrollment, and choice of
609 antimicrobial agent prior to randomization.

610
611 Handling of Dropouts and Missing Data:

612 The censoring mechanism is assumed to be non-informative. Supportive analyses will
613 be performed to assess the impact of a potential informative censoring.

614
615 Diagnostic tests: The additional continuous covariates to be used in the primary
616 analysis model will be assessed for major departures from linearity by inspection
617 scatter plots with LOESS curves. If a departure is observed then a suitable
618 transformation will be explored. The validity of this model in terms of meeting
619 modeling assumptions will be assessed via standard modeling diagnostics and
620 goodness-of-fit measures.

621
622 Statistical Tests: The linear regression model will be used to estimate outcome
623 differences between the two treatment arms: “Standard care + oral antimicrobial
624 therapy” and “Standard care”. The outcome is the measured result at 12 months with
625 model terms for treatment arm, baseline measurement, and covariates. Descriptive
626 statistics will be calculated at baseline and 12 months by treatment group.

627
628 Interpretation of Results: For linear models a difference below 0.00 will indicate a
629 reduction in score for “Standard care + oral antimicrobial therapy” arm. A difference
630 above 0.00 will indicate increase in score for “Standard care + oral antimicrobial
631 therapy” arm.

632 **Secondary Endpoint #13**

633 Endpoint Description: Change in ICEpop CAPability measure for Older people
634 (ICECAP-O) score from randomization to 12 months

635
636 Response Variable Definition: The ICECAP-O questionnaire data will be collected at
637 baseline and 12 months. For the collect questionnaire data the ICECAP-O score will
638 be calculated. The change from baseline will be calculated for the 12 month values by
639 subtracting the baseline result.

640
641 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
642 enrollment, use of standard of care medications at enrollment, and choice of
643 antimicrobial agent prior to randomization.

644

645 Handling of Dropouts and Missing Data: The censoring mechanism is assumed to be
646 non-informative. Supportive analyses will be performed to assess the impact of a
647 potential informative censoring.

648
649 Diagnostic tests: The additional continuous covariates to be used in the primary
650 analysis model will be assessed for major departures from linearity by inspection
651 scatter plots with LOESS curves. If a departure is observed then a suitable
652 transformation will be explored. The validity of this model in terms of meeting
653 modeling assumptions will be assessed via standard modeling diagnostics and
654 goodness-of-fit measures.

655
656 Statistical Tests: The linear regression model will be used to estimate outcome
657 differences between the two treatment arms: “Standard care + oral antimicrobial
658 therapy” and “Standard care”. The outcome is the measured result at 12 months with
659 model terms for treatment arm, baseline measurement, and covariates. Descriptive
660 statistics will be calculated at baseline and 12 months by treatment group.

661
662 Interpretation of Results: For linear models a difference below 0.00 will indicate a
663 reduction in score for “Standard care + oral antimicrobial therapy” arm. A difference
664 above 0.00 will indicate increase in score for “Standard care + oral antimicrobial
665 therapy” arm.

666

667 IX. Safety endpoints

668 **Serious adverse events**

669 Endpoint Description: Frequency and types of serious adverse events (SAEs) during
670 the following-up period of the trial.

671

672 Response Variable Definition: SAEs will be identified by the site PI and coded into the
673 MEDRA medical dictionary.

674

675 Statistical Tests: The number of patients with one or more SAEs will be tabulated
676 along with the total number of distinct SAEs. Comparison of the “Standard care + oral
677 antimicrobial therapy” and “Standard care” arms will be done with a chi-square test,
678 i.e. the number of patient with one or more events. Other groupings of SAEs maybe
679 generated as deemed necessary.

680

681 Interpretation of Results: For cases where “Standard care + oral antimicrobial therapy”
682 rate is less than “Standard care” rate will indicate a reduction for “Standard care +
683 oral antimicrobial therapy” arm. For cases where “Standard care + oral antimicrobial
684 therapy” rate is greater than “Standard care” rate will indicate an increase for
685 “Standard care + oral antimicrobial therapy” arm.

686

687 **Concomitant Medication**

688 Endpoint Description: Frequency and types of concomitant medication usage during
689 the following-up period of the trial.

690

691 Response Variable Definition: Concomitant medication will be collected each visit and
692 phone contact with the site.

693

694 Statistical Tests: The number of patients with one or more given concomitant
 695 medication will be tabulated. Shift tables from baseline will be generate also.
 696 Comparison of the “Standard care + oral antimicrobial therapy” and “Standard care”
 697 arms will be done with a chi-square test, i.e. the number of patient with one or more
 698 occurrences. Other groupings of concomitant medication maybe generated as deemed
 699 necessary.

700
 701 Interpretation of Results: For cases where “Standard care + oral antimicrobial therapy”
 702 rate is less than “Standard care” rate will indicate a reduction for “Standard care +
 703 oral antimicrobial therapy” arm. For cases where “Standard care + oral antimicrobial
 704 therapy” rate is greater than “Standard care” rate will indicate an increase for
 705 “Standard care + oral antimicrobial therapy” arm.

706

707 X. Trial conduct

708 **Compliance**

709 Endpoint Description: Rates of therapy distribution and adherence within the
 710 assigned testing strategy: Standard care + oral antimicrobial therapy.

711

712 Response Variable Definition: Data related to the distribution (payment system for
 713 prescriptions called TRIALCARD) of the assigned therapy will be collected during
 714 patient follow-up. Patient response to therapy adherence in weeks prior to contact will
 715 be collect at 6 months intervals

716

717 Statistical Tests: No statistical tests are planned. The rates of therapy distribution
 718 and adherence are to be estimated at 6 and 12 months for the Standard care + oral
 719 antimicrobial therapy assigned patients.

720

721 **Therapy crossover**

722 Endpoint Description: Rates of oral antimicrobial therapy crossover for the “Standard
 723 care” assigned patients.

724

725 Response Variable Definition: Time to first crossover will be defined as the time to first
 726 oral antimicrobial therapy usage in the patients randomized to “Standard care”

727

728 Statistical Tests: No statistical tests are planned. Kaplan-meier event rates will be
 729 calculated at representative intervals for ther standard care therapy assigned patients.
 730 Time to event plots will be generated also. The rates of therapy crossover are to be
 731 estimated at 6 and 12 months for the standard care therapy assigned patients.

732

733 XI. Exploratory analyses

734 **Six minute walk test**

735 Endpoint Description: Change in six minute walk test and pre/post walk Borg
 736 assessment from randomization to 12 months

737

738 Response Variable Definition: The six minute walk test data will be collected at
 739 baseline and 12 months. The change from baseline will be calculated for the 12
 740 month values by subtracting the baseline result.

741

742 Additional Covariates: Age, sex, baseline DLCO, baseline FVC, use of NAC at
 743 enrollment, use of standard of care medications at enrollment, and choice of
 744 antimicrobial agent prior to randomization.

745
 746 Handling of Dropouts and Missing Data: All patients will have some information
 747 regarding mortality and last visit of follow-up. Lung transplantation will be additional
 748 censoring variable in this analyses. The censoring mechanism is assumed to be non-
 749 informative. Supportive analyses will be performed to assess the impact of a potential
 750 informative censoring.

751
 752 Diagnostic tests: The additional continuous covariates to be used in the primary
 753 analysis model will be assessed for major departures from linearity by inspection
 754 scatter plots with LOESS curves. If a departure is observed then a suitable
 755 transformation will be explored. The validity of this model in terms of meeting
 756 modeling assumptions will be assessed via standard modeling diagnostics and
 757 goodness-of-fit measures.

758
 759 Statistical Tests: The linear regression model will be used to estimate outcome
 760 differences between the two treatment arms: “Standard care + oral antimicrobial
 761 therapy” and “Standard care”. The outcome is the measured result at 12 months with
 762 model terms for treatment arm, baseline measurement, and covariates. Descriptive
 763 statistics will be calculated at baseline and 12 months by treatment group.

764
 765 Interpretation of Results: For linear models a difference below 0.00 will indicate a
 766 reduction in score for “Standard care + oral antimicrobial therapy” arm. A difference
 767 above 0.00 will indicate increase in score for “Standard care + oral antimicrobial
 768 therapy” arm.

769

770 XII. Interim Analyses

771 There will be one planned interim review for efficacy. The efficacy review will focus on
 772 the composite endpoint of respiratory hospitalization or all-cause death and should
 773 occur once 300 enrolled subjects have been followed for 12 months. The information
 774 time will be computed by dividing the observed number of primary endpoint events by
 775 the projected number of primary endpoint events. To conserve the overall type I error
 776 rate of 0.05 the O'Brien-Fleming Spending Function will be used to allow for stopping
 777 if large treatment effects are observed while allowing the final significance level to be
 778 conserved at the nominal level (Lan and DeMets 1983).

779

780 XIII. Subgroup of Interest

781 The following subgroups of interest will be based on information available prior to
 782 randomization:

- 783 • Use of standard of care medications at enrollment
- 784 • Antimicrobial therapy determined prior to randomization
- 785 • Use of NAC at enrollment

786 The subgroups of interest will be assess seperately for the primary endpoint within
 787 the framework of cox proportional hazards regression model. The subgroup variable
 788 and subgroup by treatment arm intereaction will be added to the model. If the
 789 interaction is significant then the hazard ratios and 95% confidence intervals will be

790 estimated for the difference in treatment arms for the separate levels of the subgroup
791 variable.

792 The antimicrobial therapy determined prior to randomization is made up to 2 groups:
793 1) Co-trimoxazole and 2) Doxycycline. The baseline and primary/secondary analyses
794 will be repeated for these 2 groups separately.
795

796 XIV. References

797 Berglund, Patricia and Heeringa, Steven. Multiple Imputation of Missing Data Using
798 SAS®. SAS Institute, July 2014, pp83-89.

799 Lan, KK Gordan, Demets, David L, Discrete sequential boundaries for clinical trials,
800 Biometrika Volume 70, Issue 3Pp. 659-663
801

802 XV. Tables/Listing/Graph Mock-ups

803 The tables, listings, and figures shown below are the template versions and may be
804 modified as needed. It is planned that there will be separate sets of tables based on
805 the subgroups of interest listed above.
806

CLEANUP-IPF Study
Final Analysis Table 1.1
Enrollment and Patient Follow-up
Patient Enrollment by Site

Investigational Site	Enrolled
(101) <<Site name>>	N/N (xx.x%)
(102) <<Site name>>	N/N (xx.x%)
(103) <<Site name>>	N/N (xx.x%)
(104) <<Site name>>	N/N (xx.x%)
...	...
(140) <<Site name>>	N/N (xx.x%)
Total	N/N (xx.x%)

CLEANUP-IPF Study
Final Analysis Table 1.2
Enrollment and Patient Follow-up
Completed and Withdrawn Patients

Event	Oral antimicrobial therapy N= N _{NEVAL}	Standard Care N= N _{NEVAL}	All Patients N= N _{NEVAL}	P-Value
Started Study	N	N	N	
Completed	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	
Study Termination due to Death	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	
Withdrawal				
6 Months				x.xxx
# of Events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
12 Months				x.xxx
# of Events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
18 Months				x.xxx
# of Events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
24 Months				x.xxx
# of Events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Reasons for Withdrawal				
Reason #1	N	N	N	
Reason #2	N	N	N	
...	
Reason #X	N	N	N	
Therapy Distribution				
6 Months	N/N (xx.x%)			
12 Months	N/N (xx.x%)			
Therapy adherence (7 Days Prior)				
6 Months	N/N (xx.x%)			

CLEANUP-IPF Study
Final Analysis Table 1.2
Enrollment and Patient Follow-up
Completed and Withdrawn Patients

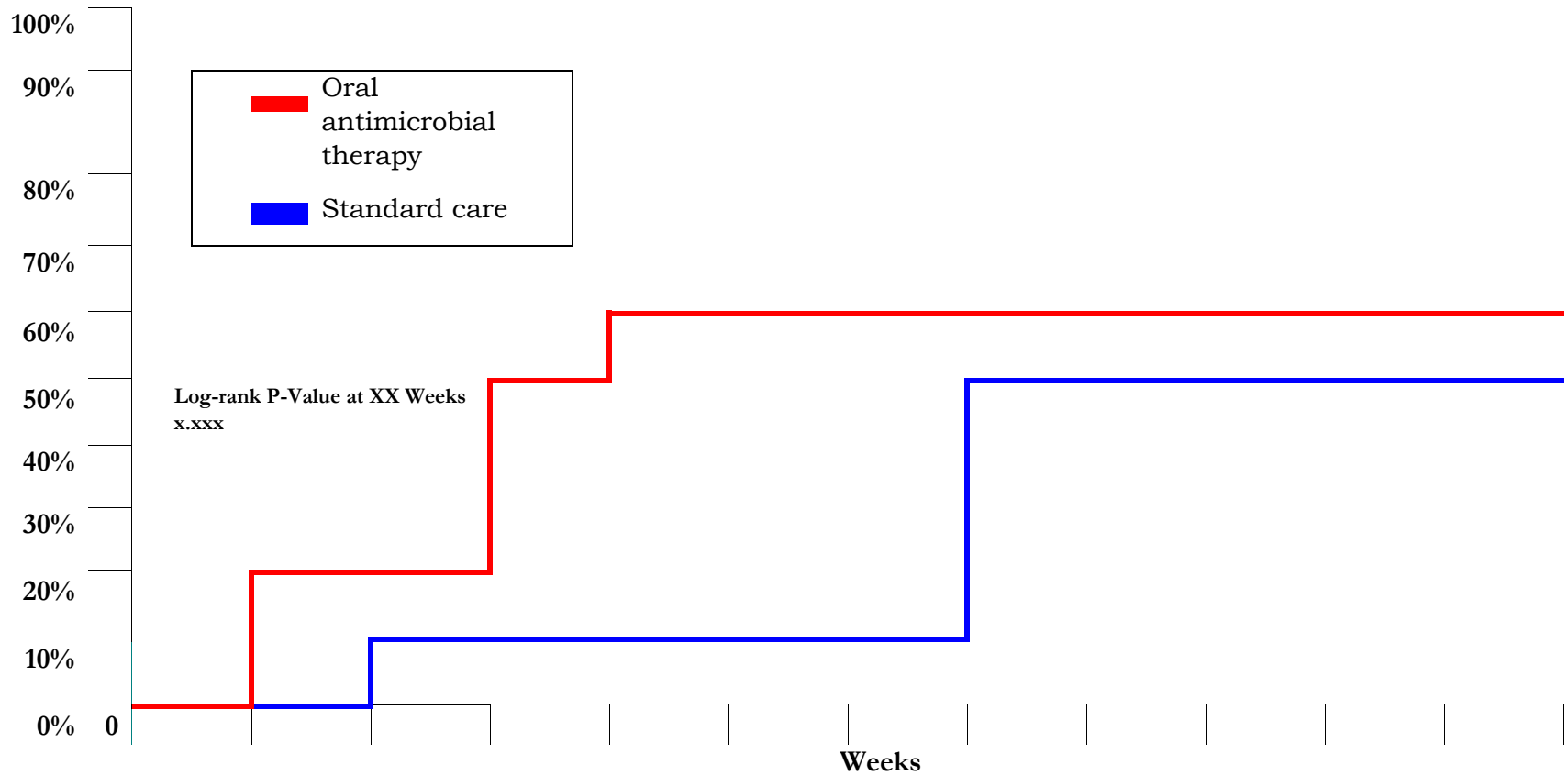
Event	Oral antimicrobial therapy N= N _{EVAL}	Standard Care N= N _{EVAL}	All Patients N= N _{EVAL}	P-Value
12 Months	N/N (xx.x%)			
Therapy crossover				
6 Months				
# of Events/# of Patients	N/N			
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)			
12 Months				
# of Events/# of Patients	N/N			
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)			
18 Months				
# of Events/# of Patients	N/N			
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)			
24 Months				
# of Events/# of Patients	N/N			
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)			

808

809

810

CLEANUP-IPF Study
Final Analysis Graph 1.2.1
Enrollment and Patient Follow-up
Completed and Withdrawn Patients
Withdrawal Rate, Kaplan-Meier Estimates



811
812
813

CLEANUP-IPF Study
Final Analysis Table 2.1
Baseline
Demographic and Risk Factor Summary

Parameter Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N= NEVAL	P-Value
Age (Years)				x.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median (Q1, Q3)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Min, Max	x.xx, x.xx	x.xx, x.xx	x.xx, x.xx	
Female	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Weight (kg)				x.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median (Q1, Q3)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Height (cm)				x.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median (Q1, Q3)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
BMI				x.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median (Q1, Q3)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Ethnicity (Hispanic or Latino)	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Race				
American Indian or Alaska Native	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Asian	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Black or African American	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Native Hawaiian or other Pacific Islander	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
White	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Other	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Minorities ¹	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
BP (systolic)(mmHg)				x.xxx
N	xx	xx	xx	

CLEANUP-IPF Study
Final Analysis Table 2.1
Baseline
Demographic and Risk Factor Summary

Parameter Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N= NEVAL	P-Value
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median (Q1, Q3)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
BP (diastolic)(mmHg)				x.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median (Q1, Q3)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Heart rate (bpm)				x.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median (Q1, Q3)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
SpO2 (%)				x.xxx
N	xx	xx	xx	
Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	
Median (Q1, Q3)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Marital Status				
Single	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Married	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Divorced	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Domestic Partner	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Widowed	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx

1. Any patient whose ethnicity is Hispanic or Latino, or whose race is non-white

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816
817

CLEANUP-IPF Study
Final Analysis Table 2.2
Baseline
Medical History

Parameter	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N= NEVAL	P-Value
Coronary artery disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Acute MI	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Valvular heart disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Congestive Heart failure	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Atrial fibrillation	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Intermittent claudication	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Peripheral vascular disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Cerebrovascular disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Dementia	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Chronic pulmonary disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Connective tissue disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Ulcer disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Mild liver disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Diabetes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Hemiplegia	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Moderate or severe renal disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Diabetes with end organ damage	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Any tumor	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Leukemia	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Lymphoma	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Moderate or severe liver disease	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Metastatic solid tumor	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
AIDS	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Lung cancer	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Other cancer	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Gastroesophageal reflux (GER)	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx

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CLEANUP-IPF Study
Final Analysis Table 2.3
Baseline
Prior Medications

Parameter	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N= NEVAL	P-Value
Proton Pump Inhibitors (PPI)	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
H2 Blockers (H2 Receptor Antagonists)	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Chronic prednisone (>1month)	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Azathioprine	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
N-acetylcysteine (NAC)	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Cotrimoxazole	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Albuterol/ atrovent/ other metered-dose inhaler (MDI)	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Pirfenidone	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx
Nintedanib	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	x.xxx

820

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CLEANUP-IPF Study
Final Analysis Table 2.4
Baseline
6 Minute Walk Test

Parameter Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N=NEVAL	P-Value
Resting SpO2 (%)				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Borg Scale Pre-Walk Rating (0-10 Range)				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Borg Scale Post-Walk Rating (0-10 Range)				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Six Minute Walk Distance (m)				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	

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CLEANUP-IPF Study
Final Analysis Table 3.1
Primary Efficacy
Summary of Events

Event	Oral antimicrobial therapy N= N _{NEVAL}	Standard Care N= N _{NEVAL}	All Patients N= N _{NEVAL}	P-Value
Primary Endpoint	N (xx.x%)	N (xx.x%)	N (xx.x%)	x.xxx
1 st Respiratory hospitalization	N (xx.x%)	N (xx.x%)	N (xx.x%)	
Death	N (xx.x%)	N (xx.x%)	N (xx.x%)	
At 6 Months				x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
At 12 Monthss				x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
At 18 Months				x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
At 24 Months				x.xxx

CLEANUP-IPF Study
Final Analysis Table 3.1
Primary Efficacy
Summary of Events

Event	Oral antimicrobial therapy N= N _{NEVAL}	Standard Care N= N _{NEVAL}	All Patients N= N _{NEVAL}	P-Value
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Mortality				
# of events	N/N	N/N	N/N	
Cause of Death				
Reason #1				
Reason #	N	N	N	
...	
Reason #X	N	N	N	
At 6 Months				
# of events/# of Patients	N/N	N/N	N/N	x.xxx

CLEANUP-IPF Study
Final Analysis Table 3.1
Primary Efficacy
Summary of Events

Event	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N= NEVAL	P-Value
Kaplan-Meier Event Rate (95% CI) At 12 Monthss	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI) At 18 Months	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI) At 24 Months	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Non-elective hospitalization				
Patients with one of more Number per patient	N (xx.x%)	N (xx.x%)	N (xx.x%)	
0	N (xx.x%)	N (xx.x%)	N (xx.x%)	
1	N (xx.x%)	N (xx.x%)	N (xx.x%)	
2	N (xx.x%)	N (xx.x%)	N (xx.x%)	
3	N (xx.x%)	N (xx.x%)	N (xx.x%)	
At 6 Months				x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
At 12 Monthss				x.xxx
# of events/# of Patients	N/N	N/N	N/N	

CLEANUP-IPF Study
Final Analysis Table 3.1
Primary Efficacy
Summary of Events

Event	Oral antimicrobial therapy N= N _{NEVAL}	Standard Care N= N _{NEVAL}	All Patients N= N _{NEVAL}	P-Value
Kaplan-Meier Event Rate (95% CI) At 18 Months	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI) At 24 Months	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Respiratory hospitalization				
Patients with one of more Number per patient	N (xx.x%)	N (xx.x%)	N (xx.x%)	
0	N (xx.x%)	N (xx.x%)	N (xx.x%)	
1	N (xx.x%)	N (xx.x%)	N (xx.x%)	
2	N (xx.x%)	N (xx.x%)	N (xx.x%)	
3	N (xx.x%)	N (xx.x%)	N (xx.x%)	
At 6 Months				x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
At 12 Months				x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
At 18 Months				x.xxx
# of events/# of Patients	N/N	N/N	N/N	

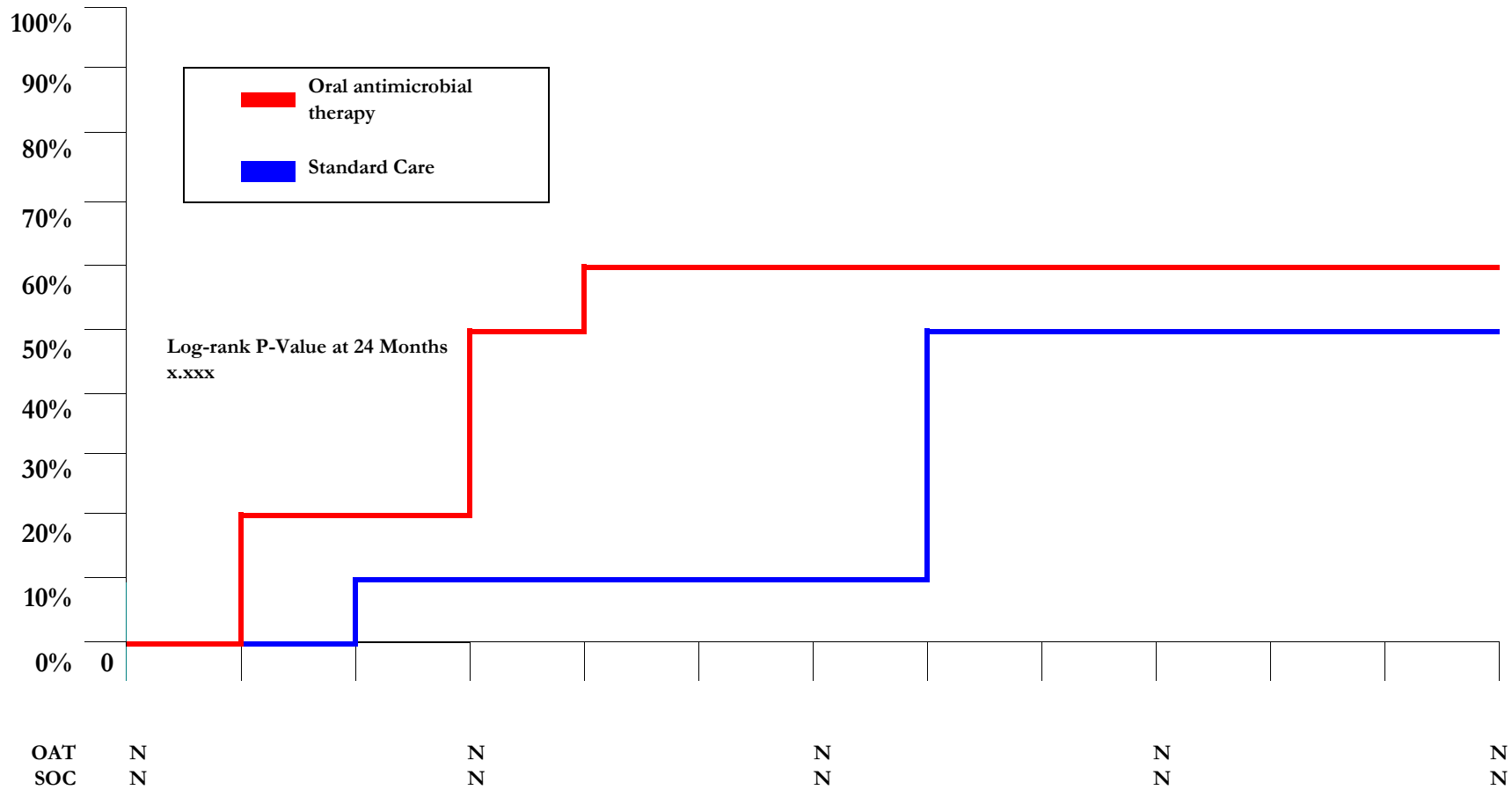
CLEANUP-IPF Study
Final Analysis Table 3.1
Primary Efficacy
Summary of Events

Event	Oral antimicrobial therapy N= N _{EVAL}	Standard Care N= N _{EVAL}	All Patients N= N _{EVAL}	P-Value
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
At 24 Months				x.xxx
# of events/# of Patients	N/N	N/N	N/N	
Kaplan-Meier Event Rate (95% CI)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	
Respiratory infections				
Patients with one of more	N (xx.x%)	N (xx.x%)	N (xx.x%)	
Number per patient				
0	N (xx.x%)	N (xx.x%)	N (xx.x%)	
1	N (xx.x%)	N (xx.x%)	N (xx.x%)	
2	N (xx.x%)	N (xx.x%)	N (xx.x%)	
3	N (xx.x%)	N (xx.x%)	N (xx.x%)	

824

825

CLEANUP-IPF Study
Final Analysis Table 3.1.1
Primary Efficacy
Time to first 1st Respiratory hospitalization or Death
Kaplan-Meier Plot



827	CLEANUP-IPF Study
828	Final Analysis Table 3.1.2
829	Primary Efficacy
830	Time to Death
831	Kaplan-Meier Plot
832	
833	CLEANUP-IPF Study
834	Final Analysis Table 3.1.3
835	Primary Efficacy
836	Time to first 1st Respiratory hospitalization
837	Kaplan-Meier Plot
838	
839	CLEANUP-IPF Study
840	Final Analysis Table 3.1.4
841	Primary Efficacy
842	Time to first 1st Non-elective hospitalization
843	Kaplan-Meier Plot
844	

**CLEANUP-IPF Study
Final Analysis Table 3.2
Primary Efficacy
Model Analysis**

Comparison	Estimate with 95% Confidence Interval	Test Statistic	Nominal P-Value
Time to 1st Respiratory hospitalization or Death			
Hazard ratio of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Time to first 1st Respiratory hospitalization			
Hazard ratio of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Time to first 1st Non-elective hospitalization			
Hazard ratio of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Total Respiratory hospitalizations			
Rate of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	
Rate of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	
Ratio of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Total Non-elective hospitalizations			
Rate of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Rate of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Ratio of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Total Respiratory infections			
Rate of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Rate of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Ratio of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx

845

846

CLEANUP-IPF Study
Final Analysis Table 4.1.1
Secondary Efficacy
FVC and DLCO
Descriptive Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= N_{EVAl}	All Patients N=N_{EVAl}	P-Value
FVC (liters)				
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
FVC % Predicted				
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	

CLEANUP-IPF Study
Final Analysis Table 4.1.1
Secondary Efficacy
FVC and DLCO
Descriptive Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= N_{EVAl}	All Patients N=N_{EVAl}	P-Value
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
DL_{CO} (mL/min/mmHg)				x.xxx
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
DL_{CO} Corrected (mL/min/mmHg)				x.xxx
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	

CLEANUP-IPF Study
Final Analysis Table 4.1.1
Secondary Efficacy
FVC and DLCO
Descriptive Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= N _{EVAl}	All Patients N=N _{EVAl}	P-Value
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
DL_{CO} % Predicted				x.xxx
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	

CLEANUP-IPF Study
Final Analysis Table 4.1.2
Primary Efficacy
FVC and DLCO
Change from Baseline Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= N _{NEVAL}	Standard Care N= N _{NEVAL}	All Patients N=N _{NEVAL}	P-Value
FVC (liters)				
Week 12				
N	xx	xx	xx	x.xxxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				
N	xx	xx	xx	x.xxxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
FVC % Predicted				
Week 12				
N	xx	xx	xx	x.xxxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				
N	xx	xx	xx	x.xxxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
DL_{CO} (mL/min/mmHg)				
Week 12				
N	xx	xx	xx	x.xxxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	

CLEANUP-IPF Study
Final Analysis Table 4.1.2
Primary Efficacy
FVC and DLCO
Change from Baseline Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= N _{EVAL}	All Patients N=N _{EVAL}	P-Value
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
DL_{CO} Corrected (mL/min/mmHg)				
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
DL_{CO} % Predicted				
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	

CLEANUP-IPF Study
Final Analysis Table 4.1.3
Secondary Efficacy
FVC and DLCO
Model Analysis

Comparison	Estimate with 95% Confidence Interval	Test Statistic	Nominal P-Value
FVC (liters)			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
FVC % Predicted			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
DL_{CO} (mL/min/mmHg)			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
DL_{CO} Corrected (mL/min/mmHg)			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx

Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
DL_{CO} % Predicted			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx

CLEANUP-IPF Study
Final Analysis Table 4.2.1
Secondary Efficacy
Quality of Life Measures
Descriptive Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= N _{EQVAL}	All Patients N=N _{EQVAL}	P-Value
UCSD Shortness of Breath				
Questionnaire Total Score (0*-120				
Range)				
Baseline				
N	XX	XX	XX	X.XXX
Mean (SD)	X.XX (XX.X)	X.XX (XX.X)	X.XX (XX.X)	
Median (Q1, Q3)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
12 Months				
N	XX	XX	XX	X.XXX
Mean (SD)	X.XX (XX.X)	X.XX (XX.X)	X.XX (XX.X)	
Median (Q1, Q3)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
24 Months				
N	XX	XX	XX	X.XXX
Mean (SD)	X.XX (XX.X)	X.XX (XX.X)	X.XX (XX.X)	
Median (Q1, Q3)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
EuroQoL Score(0-1* Range)				
EuroQoL Thermometer Response				
(0-100* Range)				
ICECAP-O: Summary Score (0-1*				
Range)				
SF-12 Score				
Fatigue Severity Scale score				
Leicester Cough Questionnaire score				

CLEANUP-IPF Study
Final Analysis Table 4.2.2
Secondary Efficacy
Quality of Life Measures
Change from Baseline Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= N _{EVAl}	All Patients N=N _{EVAl}	P-Value
UCSD Shortness of Breath				
Questionnaire Total Score (0*-120				
Range)				
12 Months				
N	XX	XX	XX	X.XXX
Mean (SD)	X.XX (XX.X)	X.XX (XX.X)	X.XX (XX.X)	
Median (Q1, Q3)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
24 Months				
N	XX	XX	XX	X.XXX
Mean (SD)	X.XX (XX.X)	X.XX (XX.X)	X.XX (XX.X)	
Median (Q1, Q3)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	X.XX (X.XX, X.XX)	
EuroQoL Score(0-1* Range)				
EuroQoL Thermometer Response				
(0-100* Range)				
ICECAP-O: Summary Score (0-1*				
Range)				
SF-12 Score				
Fatigue Severity Scale score				
Leicester Cough Questionnaire score				

851

852

853

**CLEANUP-IPF Study
Final Analysis Table 4.2.3
Secondary Efficacy
Quality of Life Measures
Model Analysis**

Comparison	Estimate with 95% Confidence Interval	Test Statistic	Nominal P-Value
UCSD Shortness of Breath Questionnaire Total Score			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
EuroQoL Thermometer Response			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
ICECAP-O: Summary Score			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
SF-12 Score			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx

Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Fatigue Severity Scale score			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Leicester Cough Questionnaire score			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx

CLEANUP-IPF Study
Final Analysis Table 5.1
Safety
Serious Adverse Events

Body System Event Name	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N= NEVAL	P-Value
Any Body System and Event	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
1 st Body System Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
1 st Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
2 nd Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
...	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
X th Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
2 nd Body System Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
1 st Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
2 nd Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
...	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
X th Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
X th Body System Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
1 st Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
2 nd Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
...	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx
X th Event Name	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	$N_{PAT} (xx.x\%) N_{SAE}$	x.xxx

Summarization format $N_{PAT} (xx.x\%) N_{SAE}$, where N_{PAT} is the number of patient with at least one SAE, $xx.x\% = N_{PAT}$ divided by the total number of randomized patients times 100, and N_{SAE} is the number of SAEs observed

CLEANUP-IPF Study
Final Analysis Table 5.2
Safety
Concomitant Medications Shift Table

Parameter	Baseline Usage	Post-Baseline Usage	Oral antimicrobial therapy N= NEVAL	Standard Care N= N _{NEVAL}	All Patients N= N _{NEVAL}
PPI					
	No	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Overall	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
H2 Blocker					
	No	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Overall	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
Chronic prednisone					
	No	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Overall	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
Azathioprine					
	No	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)

CLEANUP-IPF Study
Final Analysis Table 5.2
Safety
Concomitant Medications Shift Table

Parameter	Baseline Usage	Post-Baseline Usage	Oral antimicrobial therapy N= N _{NEVAL}	Standard Care N= N _{NEVAL}	All Patients N= N _{NEVAL}
NAC	Overall	Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Overall	No	N/N (xx.x%)	N/N (xx.x%)
Cotrimoxazole	Overall	Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Overall	No	N/N (xx.x%)	N/N (xx.x%)
MDI	Overall	Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Overall	No	N/N (xx.x%)	N/N (xx.x%)

CLEANUP-IPF Study
Final Analysis Table 5.2
Safety
Concomitant Medications Shift Table

Parameter	Baseline Usage	Post-Baseline Usage	Oral antimicrobial therapy N= N _{NEVAL}	Standard Care N= N _{NEVAL}	All Patients N= N _{NEVAL}
Pirfenidone		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	No	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Overall	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
Nintedanib		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	No	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
		Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Overall	No	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)
	Yes	N/N (xx.x%)	N/N (xx.x%)	N/N (xx.x%)	

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CLEANUP-IPF Study
Final Analysis Table 6.1.1
Exploratory Endpoint
Six Minute Walk Test
Descriptive Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= N_{EVAL}	All Patients N=N_{EVAL}	P-Value
Resting SpO2 (%)				
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Borg Scale Pre-Walk Rating (0-10 Range)				
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	

CLEANUP-IPF Study
Final Analysis Table 6.1.1
Exploratory Endpoint
Six Minute Walk Test
Descriptive Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= N _{EVAL}	All Patients N=N _{EVAL}	P-Value
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Borg Scale Post-Walk Rating (0-10 Range)				x.xxx
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Six Minute Walk Distance (m)				x.xxx
Baseline				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	

CLEANUP-IPF Study
Final Analysis Table 6.1.1
Exploratory Endpoint
Six Minute Walk Test
Descriptive Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= N_{NEVAL}	Standard Care N= N_{NEVAL}	All Patients N=N_{NEVAL}	P-Value
Median (Q1, Q3) Week 24	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	

CLEANUP-IPF Study
Final Analysis Table 6.1.2
Exploratory Endpoint
Six Minute Walk Test
Change from Baseline Summary

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N=NEVAL	P-Value
Resting SpO2 (%)				
Week 12				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Borg Scale Pre-Walk Rating (0-10 Range)				
Week 12				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Borg Scale Post-Walk Rating (0-10 Range)				
Week 12				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				
N	xx	xx	xx	x.xxx
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	

**CLEANUP-IPF Study
Final Analysis Table 6.1.2
Exploratory Endpoint
Six Minute Walk Test
Change from Baseline Summary**

Parameter Visit Statistic	Oral antimicrobial therapy N= NEVAL	Standard Care N= NEVAL	All Patients N=NEVAL	P-Value
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Six Minute Walk Distance (m)				x.xxx
Week 12				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	
Week 24				x.xxx
N	xx	xx	xx	
Mean (SD)	x.xx (xx.x)	x.xx (xx.x)	x.xx (xx.x)	
Median (Q1, Q3)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	

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**CLEANUP-IPF Study
Final Analysis Table 6.1.3
Exploratory Endpoint
Six Minute Walk Test
Model Analysis**

Comparison	Estimate with 95% Confidence Interval	Test Statistic	Nominal P-Value
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Borg Scale Pre-Walk Rating (0-10 Range)

Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Borg Scale Post-Walk Rating (0-10 Range)			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx
Six Minute Walk Distance (m)			
Slope of Oral antimicrobial therapy	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Slope of Standard Care	xx.xx (xx.xx, xx.xx)	xxx.xx	x.xxx
Difference of Oral antimicrobial therapy vs. Standard Care	xx.xx (xx.xx, xx.xx)	xx.xx	x.xxx

862 Addendum to the CleanUP-IPF Analysis Plan (signed 28NOV2016)

863

864 Fernando J. Martinez, Principal Investigator

865 Imre Noth, Principal Investigator

866 Kevin Anstrom, Principal Investigator

867 Jerry Kirchner, Project Leader

868 Eric Yow, Statistician

869

870 29MAY2020

871

872 On 19DEC2019 the DCC received a memorandum from the Executive Secretary of CleanUP-IPF
873 DSMB regarding the recommendations for investigators of the CleanUP-IPF study following
874 DSMB meeting 18DEC2019 meeting conference call. The recommendations were to terminate the
875 trial and proceed with an orderly study close-out. Study PIs and DCC developed and implemented a
876 plan to complete patient visits and follow-up in March 2020 and database lock by May 2020.

877

878 Beginning in mid-March across the United States stay at home orders were issued due to the
879 COVID19 pandemic. The stay at home orders limited site PIs and coordinators access to medical
880 records and other key patient data. The impact of limited access was the following:

- 881 • Entry of some visit data
- 882 • Responses to database queries
- 883 • Collecting and submitting patients records for endpoint adjudication
- 884 • Collecting and submitting patients records for medical monitor review of serious adverse
885 events and MedDRA coding

886

887 The impact of COVID19 on the data lock and reporting the primary results for publication are the
888 following:

- 889 • Unable to complete all adjudication of primary endpoint components: death and
890 hospitalization
- 891 • Entry of serious adverse events and associated term in database to allow MedDRA system
892 organ class coding

893

894 Given the need to report timely results in the public domain and the unknown end of COVID19
895 pandemic, the deviation of the primary statistical analysis reporting would be as follows:

- 896 • According to the Statistical Analysis Plan (SAP), the primary analysis of the primary
897 endpoint was to be based on CEC adjudicated endpoints. Now, the plan is to use
898 adjudicated results if available. If the CEC adjudicated result is not available then the site
899 reported result would be used for the endpoint.
- 900 • For serious adverse events, the summary of MedDRA system organ class coding was
901 planned for the primary statistical analysis and reporting of results. The serious adverse
902 event analysis would be altered as follows:

- 903 ○ For events with serious adverse event term entry in the database and MedDRA
904 system organ class coding, we will use MedDRA coding.
905 ○ For events without serious adverse event term entry in the database and without
906 MedDRA system organ class coding, the medical monitor would review the available
907 documentation and if reasonable information is available to classify to MedDRA
908 system organ class, then the medical monitor result will be used.
909 ○ For events without serious adverse event term entry in the database, and no
910 MedDRA system organ class coding, and no documentation to support a
911 classification by the medical monitor, then the result will not be coded.
912

913 The primary analysis is based on the final locked dataset and events collected. A sensitivity analysis of the
914 primary results will be constructed to explore possible differences in snapshots or timeframes of the data.
915 The results would be censored at date of the DSMB meeting on 17DEC2019 and again at 01MAR2020
916 (associated with the COVID 19 pandemic) to understand any differences in the data collection affected the
917 results.

918