



Medicines That Make a Difference[®]

Nezulcitinib (TD-0903) Phase 2 Top-line Results

Inhaled lung-selective pan-JAK inhibitor to treat:

Acute lung injury due to COVID-19

June 21, 2021

Forward-looking statements

Under the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, the company cautions investors that any forward-looking statements or projections made by the company are subject to risks and uncertainties that may cause actual results to differ materially from the forward-looking statements or projections.

Examples of forward-looking statements in this presentation may include the Company's goals, designs, strategies, plans and objectives, the Company's regulatory strategies and timing of clinical studies (including the data therefrom), the potential characteristics, benefits and mechanisms of action of the Company's product and product candidates, the potential that the Company's research programs will progress product candidates into the clinic, the Company's expectations for product candidates through development, the Company's expectations regarding its allocation of resources, potential regulatory approval and commercialization (including their differentiation from other products or potential products), product sales or profit share revenue and the Company's expectations for its expenses, excluding share-based compensation and other financial results.

The company's forward-looking statements are based on the estimates and assumptions of management as of the date of this presentation and are subject to risks and uncertainties that may cause the actual results to be materially different than those projected, such as risks related to the impacts on the COVID-19 global pandemic on our business, additional future analysis of the data resulting from our clinical trial(s), delays or difficulties in commencing, enrolling or completing clinical studies, the potential that results from clinical or non-clinical studies indicate the Company's compounds or product candidates are unsafe or ineffective, risks that product candidates do not obtain approval from regulatory authorities, the feasibility of undertaking future clinical trials for our product candidates based on policies and feedback from regulatory authorities, dependence on third parties to conduct clinical studies, delays or failure to achieve and maintain regulatory approvals for product candidates, risks of collaborating with or relying on third parties to discover, develop, manufacture and commercialize products, and risks associated with establishing and maintaining sales, marketing and distribution capabilities with appropriate technical expertise and supporting infrastructure, disagreements with Innoviva, Inc. and TRC LLC, the uncertainty of arbitration and litigation and the possibility that an arbitration award or litigation result could be adverse to the Company.

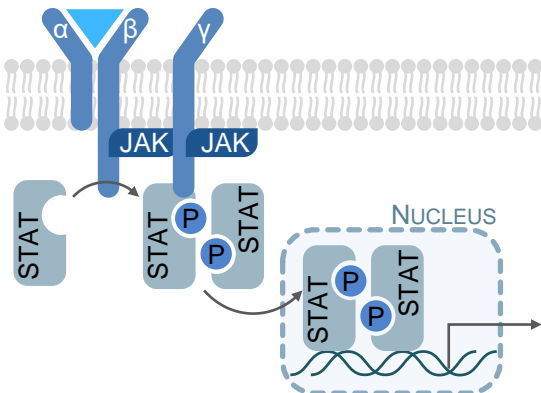
Other risks affecting Theravance Biopharma are in the company's Form 10-Q filed with the SEC on May 6, 2021, and other periodic reports filed with the SEC.

Nezulcitinib: an inhaled, lung-selective pan-JAK inhibitor in development

Broadly inhibits the pulmonary inflammatory cascade caused by viral infection

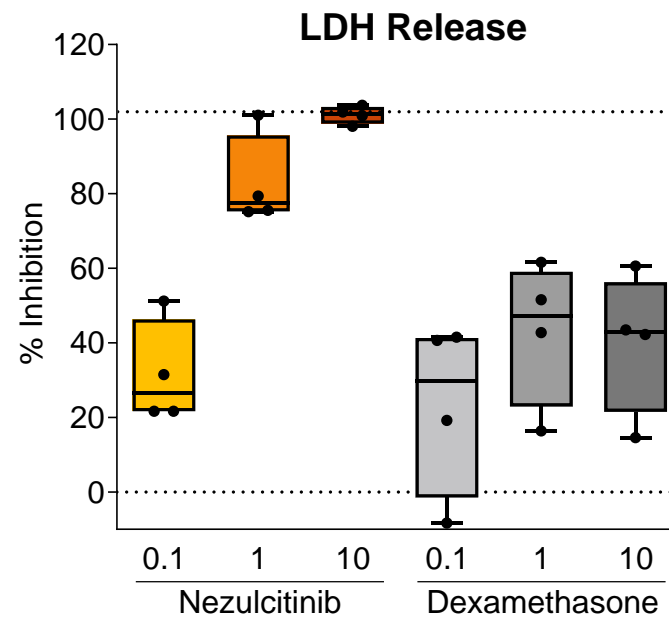
Potential therapeutic benefit via three activities:

Potent pan-JAK inhibition

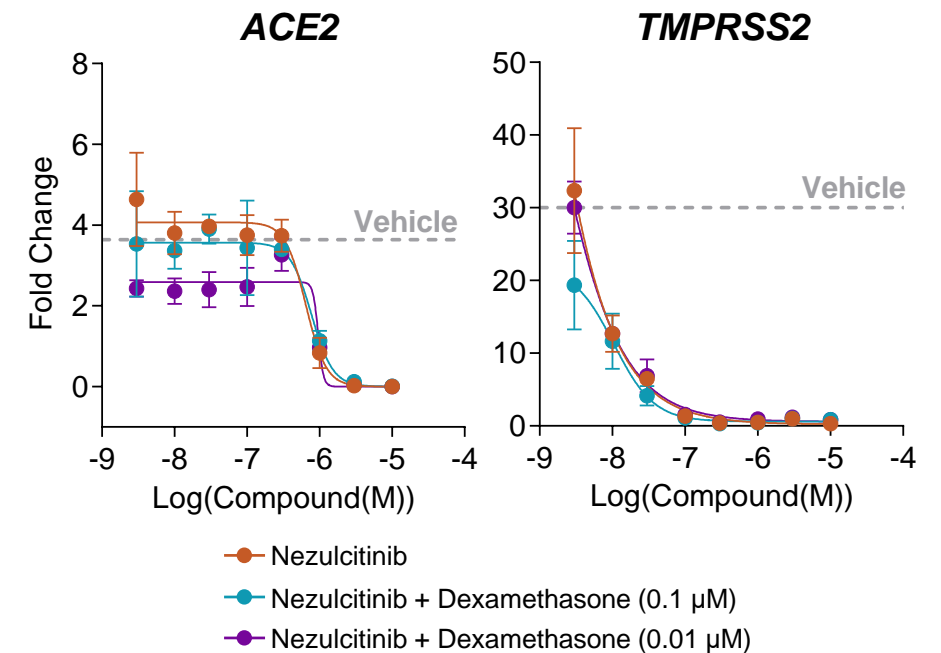


- Suppresses release of key inflammatory markers associated with COVID-19 from epithelial and immune cells (IFN γ , IL-6, IP-10, MCP-1, GM-CSF)

Protection against virus-induced cell death



Prevention of cell entry, limiting virus dissemination in lung



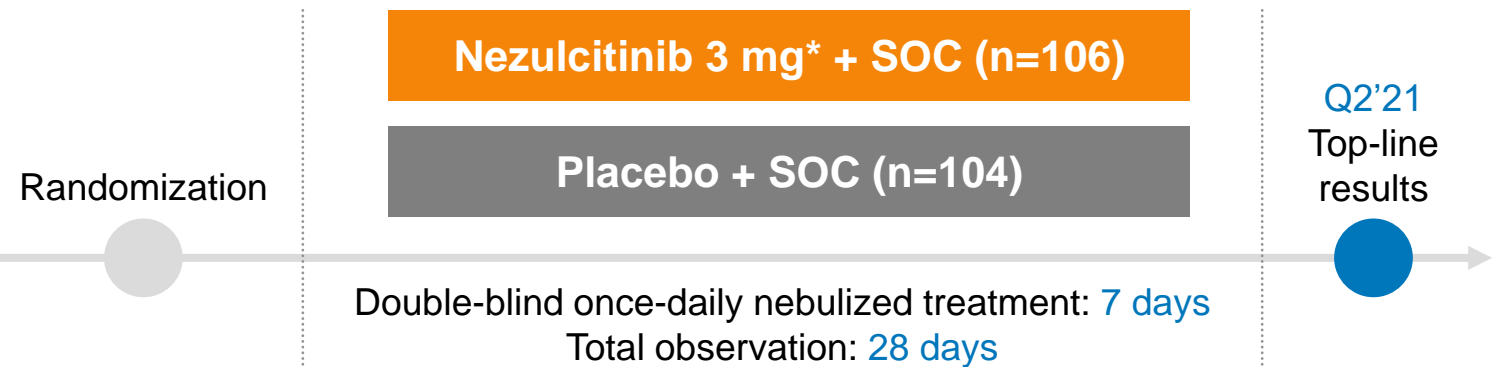
Our goal: nezulcitinib to be the first inhaled treatment to broadly interrupt viral-induced activation and restore immune system balance in the lung

Nezulcitinib: randomized, double-blind, placebo-controlled Ph 2 study in hospitalized patients with severe COVID-19 with impaired oxygenation

Part 2 Study 0188

Key inclusion criteria: Hospitalized patients aged 18–80 y requiring supplemental oxygen to maintain >90% saturation (not requiring IMV) with positive SARS-CoV-2 test <72 h prior to randomization and symptom onset >2–14 d prior to hospitalization

Countries: SA, EUR, UK, USA



Nezulcitinib Phase 2 COVID-19 trial summary

▶ Efficacy outcomes, n=210 (ITT)

- **Primary:** No statistically significant difference between nezulcitinib and placebo for RFDs from randomization through Day 28
- **Secondary:** No difference in change from baseline at Day 7 in SaO₂/FiO₂ ratio, proportion of patients in each category of the 8-point Clinical Status scale, and proportion of patients alive and respiratory failure-free at Day 28
- A favorable trend in improvement for nezulcitinib when compared to placebo for 28-day all-cause mortality and time to recovery

▶ Post-hoc analyses for baseline CRP, n=201

- CRP <150 mg/L (n=171): Nezulcitinib showed improvement in time to recovery and 28-day all-cause mortality
- CRP ≥150 mg/L (n=30): No differences between groups

▶ Nezulcitinib was well-tolerated when administered once-daily for up to seven days

▶ Plasma exposure was low, consistent with expectations for a lung-selective medicine

Summary of patient disposition

(Randomized population)

n (%)	Nezulcitinib n=106	Placebo n=104	Total n=210
Patients randomized and treated with study drug	103 (100%)	102 (100%)	205 (100%)
Patients completed study	92 (89.3%)	89 (87.3%)	181 (88.3%)
Patients discontinued from study	11 (10.7%)	13 (12.7%)	24 (11.7%)
Reasons for withdrawal			
Adverse event	8 (7.8%)	13 (12.7%)	21 (10.2%)
Lost to follow-up	1 (1.0%)	0	1 (0.5%)
Withdrawal by patients	2 (1.9%)	0	2 (1.0%)

*24 patients discontinued early from the study: 21 for AEs (19 leading to death), 2 by patient's choice, and 1 was lost to follow-up after being discharged to a different hospital.

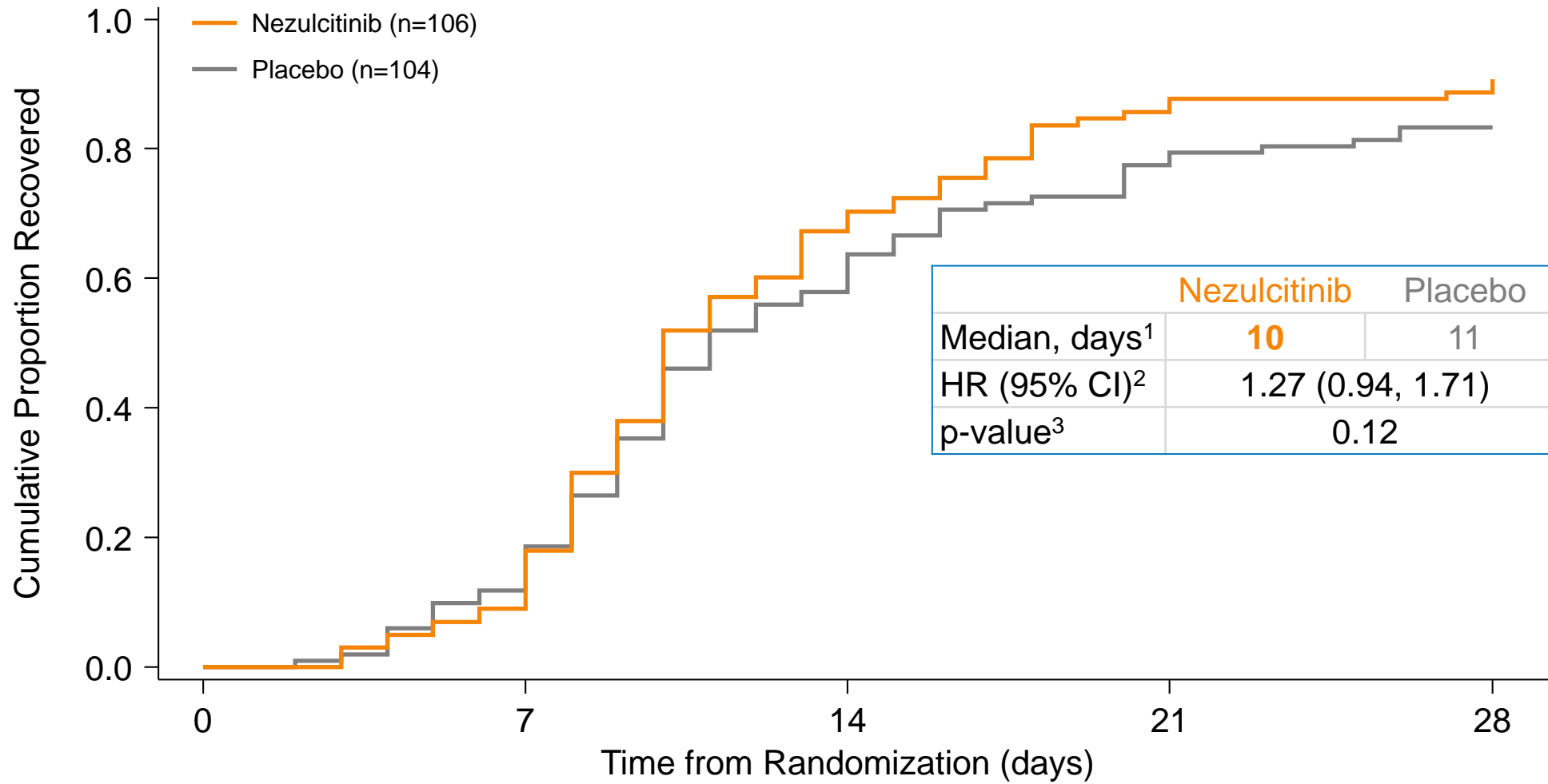
Baseline demographics and clinical characteristics

	Nezulcitinib n=106	Placebo n=104
Mean age, years \pm SD	58.3 \pm 12.42	58.1 \pm 12.54
Male, n (%)	65 (61.3%)	63 (60.6%)
White, n (%)	104 (98.1%)	102 (98.1%)
Mean BMI, kg/m ² \pm SD	30.10 \pm 3.71	30.10 \pm 4.12
Number of comorbidities, %		
1	23.6%	24.0%
\geq 2	46.2%	45.2%
Overall corticosteroids, %	98.1%	100%
Dexamethasone, %	91.3%	91.2%
Remdesivir, n (%)	12 (11.7%)	7 (6.9%)
Mean oxygen, L/min \pm SD	7.33 \pm 7.24	6.73 \pm 2.73
Mean CRP, mg/L \pm SD	75.26 \pm 72.21	70.54 \pm 70.13
CS 5: n=169 (80%)*	n=87	n=82
CS 6: n=39 (19%)*	n=18	n=21

Respiratory failure-free days from randomization to day 28 (ITT)

RFD	Nezulcitinib n=106	Placebo n=104
n	100	102
Median, days (Q1, Q3)	21.0 (17.5, 23.0)	21.0 (15.0, 23.0)
Mean, days (SD)	18.5 (7.57)	17.4 (8.63)
Common odds ratio (95% CI)	1.14 (0.71, 1.85)	
p-value	0.61	

Nezulcitinib showed a trend of improvement in time to recovery compared to placebo (ITT)



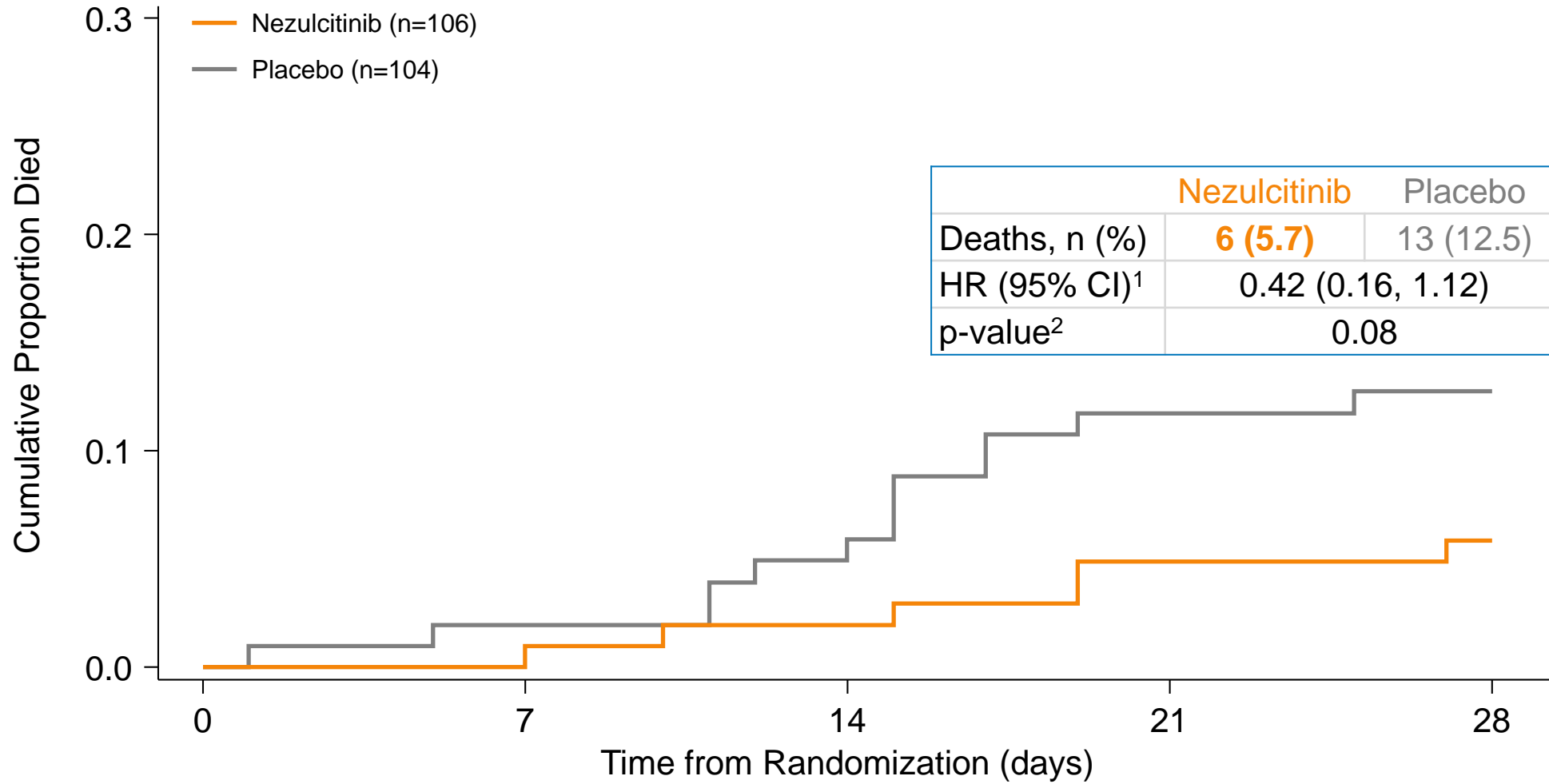
1. Kaplan-Meier estimates.

2. Hazard ratio (nezulcitinib vs placebo) and 95% CI calculated from Cox proportional hazards model adjusting for baseline age strata (≤ 60 vs > 60 years).

3. Stratified log-rank p-value stratified by baseline age strata (≤ 60 vs > 60 years) comparing distribution of nezulcitinib vs placebo.

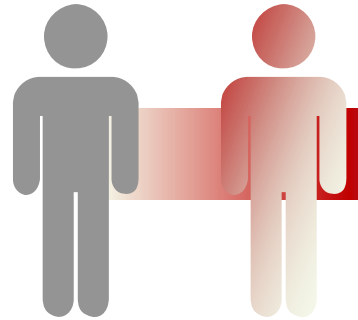
CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat. Time to recovery defined as elapsed time (in days) from baseline to first date with a score of 1, 2, or 3 on the 8-point clinical status scale through Day 28.

Nezulcitinib showed a trend of improvement in 28-day all-cause mortality rate and time to mortality (ITT)



CRP and patients hospitalized with COVID-19

Normal CRP
<10 mg/L



~85% severe COVID-19

CRP elevation

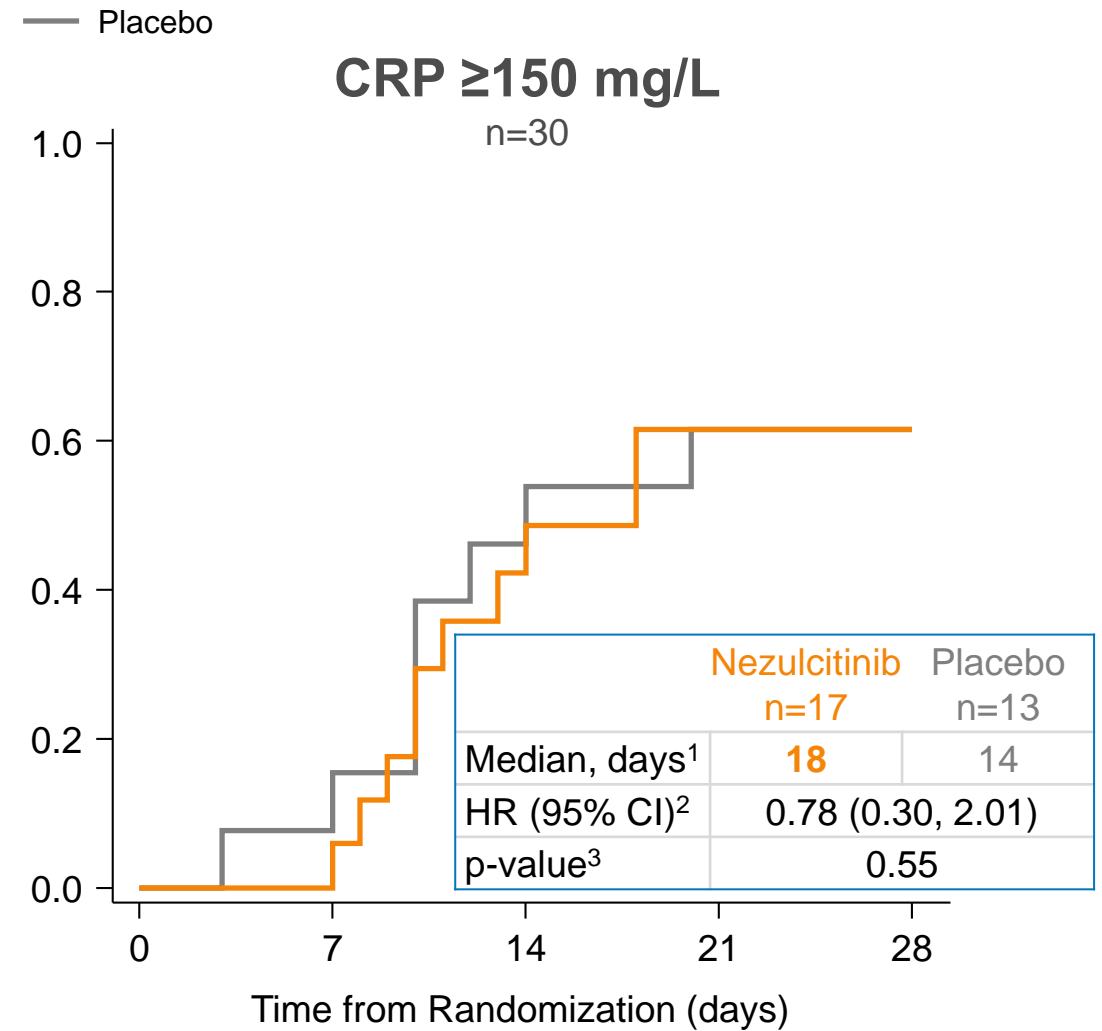
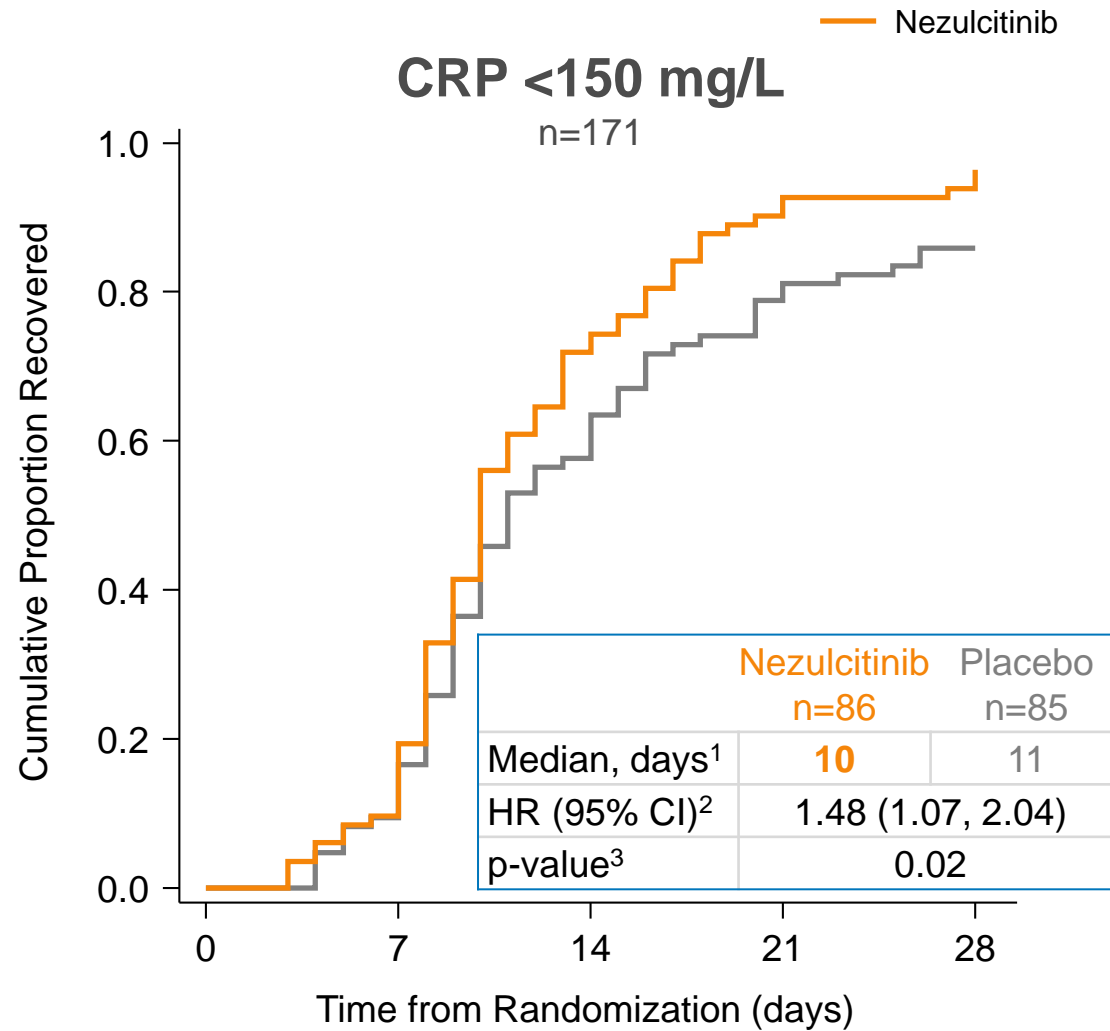


CRP stable



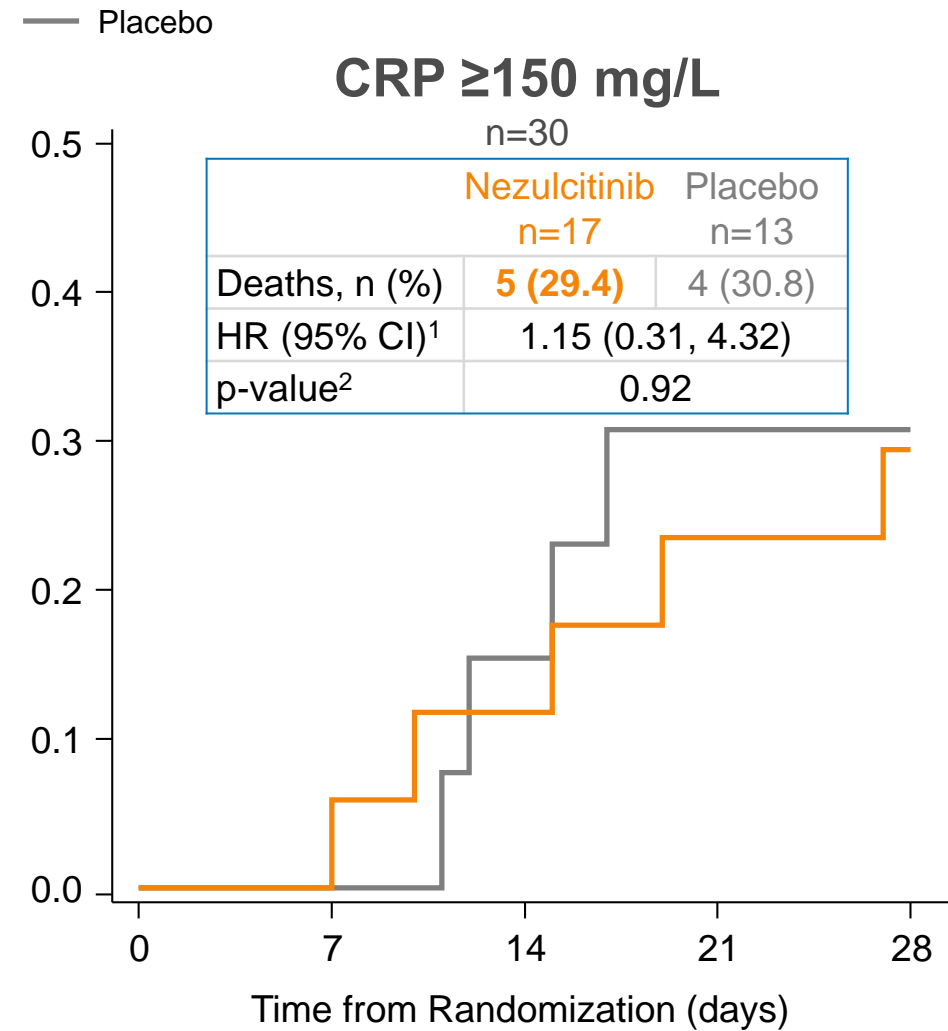
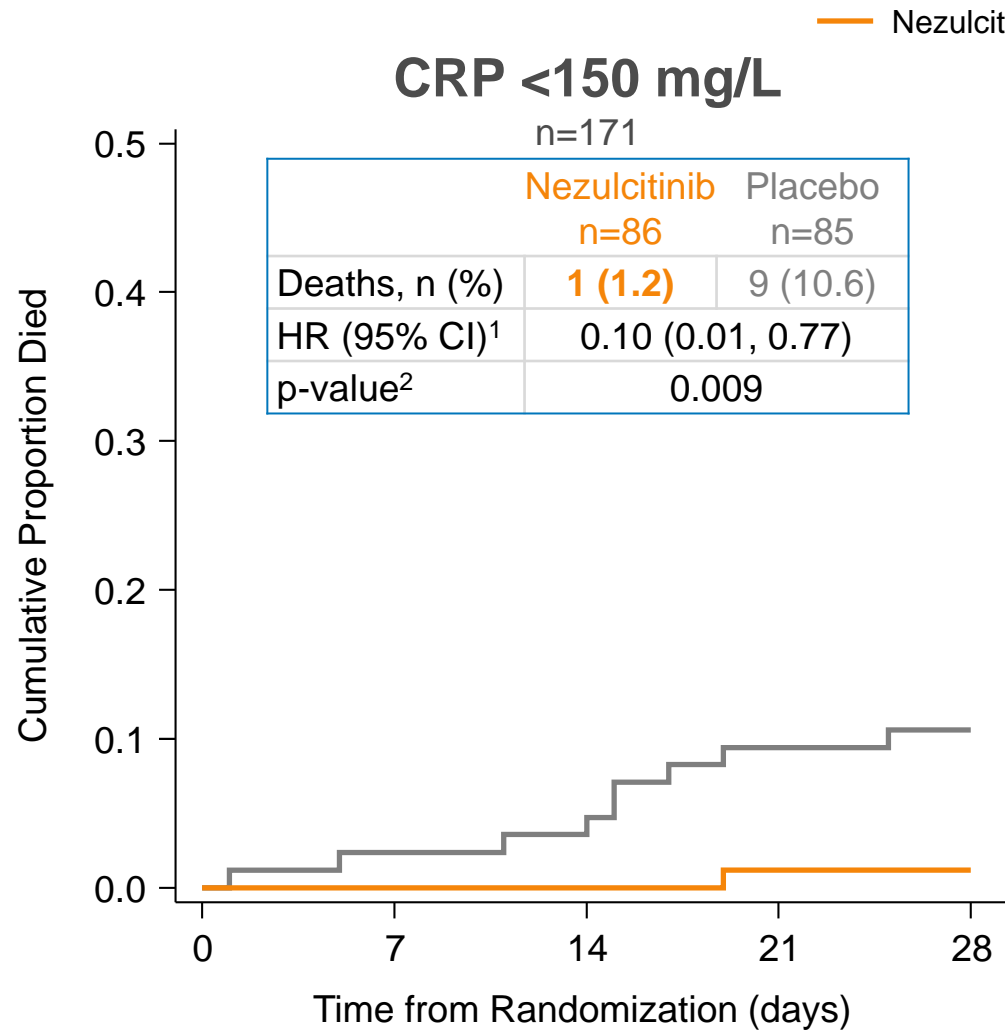
Potential for classification of COVID-ALI endotypes

Nezulcitinib: improvement in time to recovery compared to placebo in patients with baseline CRP <150 mg/L



1. Kaplan-Meier estimates.
 2. Hazard ratio (nezulcitinib vs placebo) and 95% CI calculated from Cox proportional hazards model adjusting for baseline age strata (≤60 vs >60 years).
 3. Stratified log-rank p-value stratified by baseline age strata (≤60 vs >60 years) comparing distribution of nezulcitinib vs placebo.
 CI, confidence interval; CRP, C-Reactive protein; HR, hazard ratio.

Nezulcitinib: improvement in 28-day all-cause mortality rate and time to mortality compared to placebo in patients with baseline CRP <150 mg/L



1. Hazard ratio (nezulcitinib vs placebo) and 95% CI calculated from Cox proportional hazards model adjusting for baseline age strata (≤60 vs >60 years).
2. Unstratified log-rank p-value comparing distribution of nezulcitinib vs placebo.
CI, confidence interval; CRP, C-Reactive protein; HR, hazard ratio.

Executive summary of safety results

	Nezulcitinib n=103	Placebo n=102
Adverse events	34.0%	41.2%
Serious adverse events	9.7%	15.7%
Liver abnormalities or disease	9.7%	7.8%
Serious infections	1.0%	2.0%
Venous thromboembolism	0	4.9%

- ▶ Nezulcitinib was well tolerated when administered once-daily for up to seven days

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Thank You