Presentation #92

Obeldesivir Reduced SARS-CoV-2 Infectious Titers in the BIRCH Phase 3 Clinical Trial

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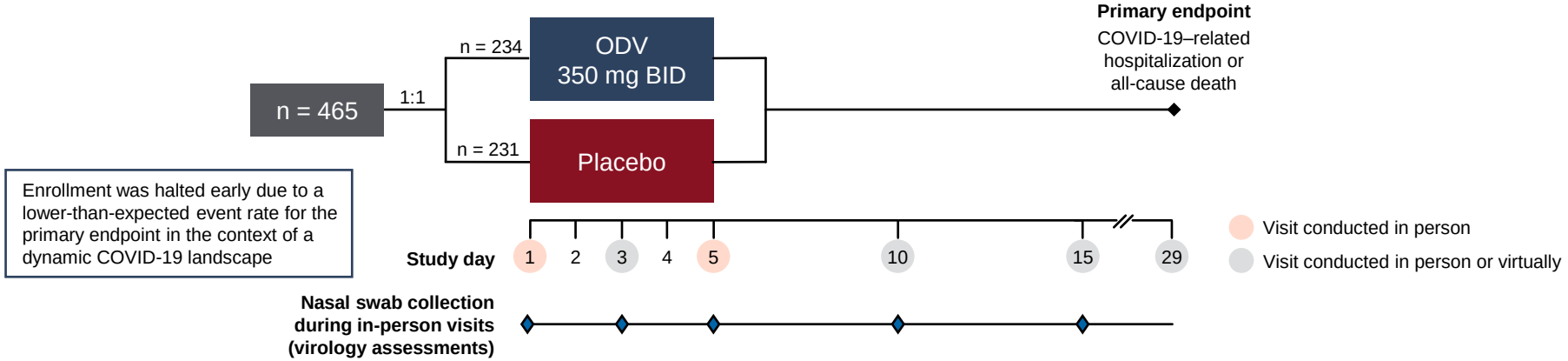
Author Disclosures

Lauren Rodriguez, **Yiannis Koullias**, **Afsaneh Mozaffarian**, **Kim Etchevers**, **Shuguang Chen**, **Robert H Hyland**, **Joe Llewellyn**, **Romas Geleziunas**, and **Charlotte Hedskog** are employees of and may own stock in Gilead Sciences, Inc. **Anca Streinu-Cercel** received grant or research support and honoraria from Gilead Sciences, Inc. **Antonella Castagna** served as an advisor or consultant for Bristol Myers Squibb, Gilead Sciences, Inc., Janssen, Merck Sharp & Dohme, and ViiV Healthcare. **Juan Maria Gonzalez Del Castillo**, **Leon F Fouche**, and **Shan-Chwen Chang** have no conflicts to report.

The BIRCH Study

A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of ODV for the Treatment of COVID-19 in Participants With Risk Factors for Severe Disease



COVID-19–related hospitalization or all-cause death, n (%)[a]

ODV (n = 211)	0
Placebo (n = 207)	1 (0.5)

Key secondary and exploratory endpoints

- Change from baseline in SARS-CoV-2 viral RNA copy number
- Change from baseline in SARS-CoV-2 infectious viral titer
- Proportion of participants with negative infectious viral titer

[a]Analysis set included participants who were randomized, received ≥1 dose of study drug, and were SARS-CoV-2 positive at baseline as confirmed by RT-PCR at the central laboratory.

BID, twice daily; **ODV**, obeldesivir; **RT-PCR**, reverse transcriptase–polymerase chain reaction.

Full results of the BIRCH study are reported in Poster P-2026

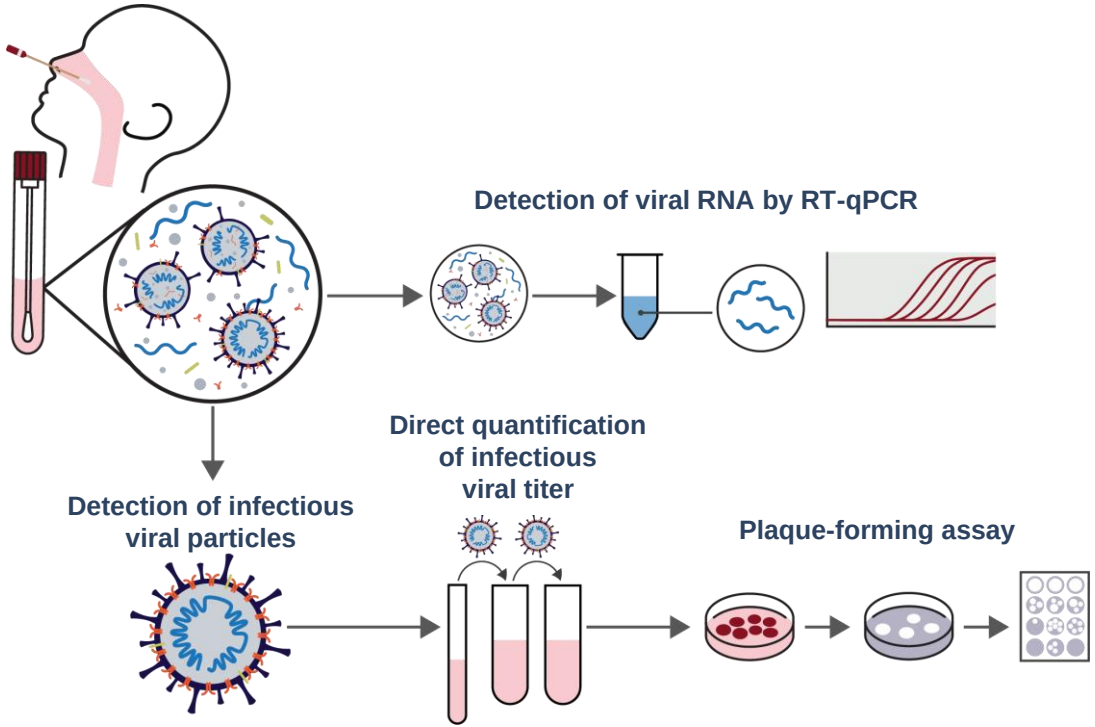
BIRCH Baseline Characteristics

Full Analysis Positive Set[a]

	ODV (n = 211)	Placebo (n = 207)	Total (n = 418)
Age, years, median (range)	57 (20-89)	55 (18-87)	56 (18-89)
Randomization stratum: duration of symptoms, n (%)			
≤3 days	162 (77)	164 (79)	326 (78)
COVID-19 vaccination status, n (%)			
Ever	124 (59)	119 (57)	243 (58)
Duration of COVID-19 symptoms, days, mean (SD)	3 (1)	2 (1)	2 (<1)
SARS-CoV-2 antibody serostatus, n (%)[b]			
Overall positive	192 (91)	191 (92)	383 (92)
SARS-CoV-2 viral RNA copy number, n	204	203	407
Log_{10} copies/mL, mean (SD)[c]	6.4 (1.4)	6.4 (1.4)	6.4 (1.4)
$\geq 10^6$ copies/mL, n (%)	137 (67)	130 (64)	267 (66)

[a]Full analysis positive set included all participants who were randomized, received ≥1 dose of study drug, and had central laboratory–positive SARS-CoV-2 RT-PCR at baseline.
[b]Serostatus was defined as positive when anti-spike antibody or anti-nucleocapsid antibody was positive and was defined as negative when both were negative. Serostatus percentages do not include those with missing values.
[c]Result of "No SARS-CoV-2 detected" was imputed as 746.5 copies/mL (2.87 log_{10} copies/mL); "<2228 copies/mL" was imputed as 1114 copies/mL (3.05 log_{10} copies/mL).
ODV, obeldesivir; **RT-PCR**, reverse transcriptase–polymerase chain reaction.

SARS-CoV-2 Viral RNA Copy Number Versus Infectious Viral Titer



RNA copy number (RT-qPCR):
detects total viral RNA, including residual (noninfectious) viral RNA[1]

Infectious titer (plaque-forming assay):
detects replication-competent (infectious) virus

Plaque-forming assay

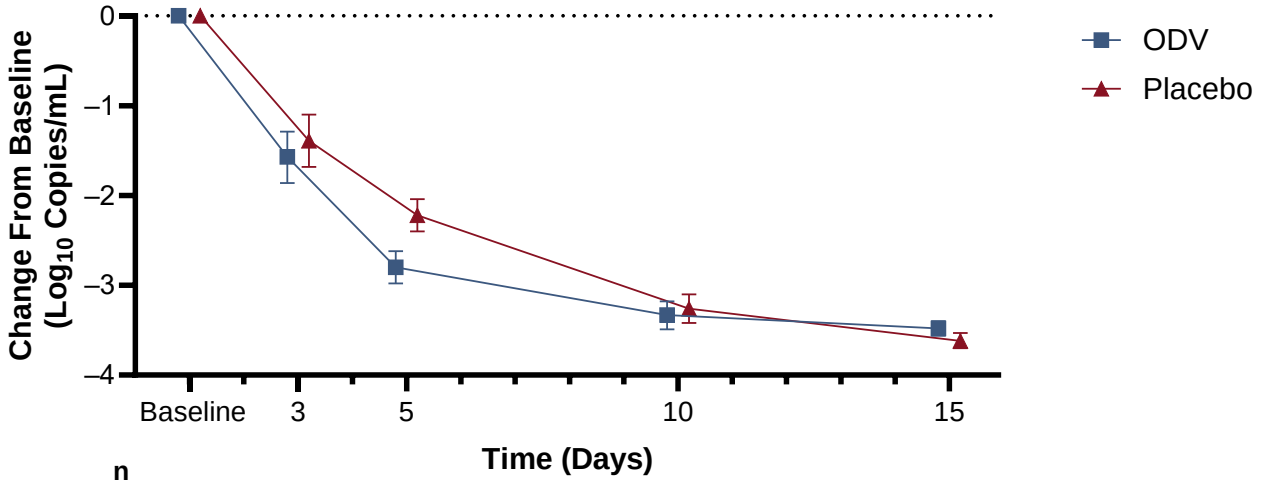
- Inoculation of Vero E6 cells with nasal swab sample serial dilutions
- Incubation for 96 hours with a carboxymethylcellulose overlay
- Staining of cell monolayer
- Quantification of PFU

ODV, obeldesivir; **PFU**, plaque-forming unit; **RT-qPCR**, reverse transcriptase–quantitative polymerase chain reaction.

1. Puhach O, et al. *Nat Rev Microbiol*. 2023;21(3):147-161.

Change From Baseline in SARS-CoV-2 Nasal Swab Viral RNA Copy Number

Virology Analysis Set[a]



n					
ODV	193	101	175	115	121
Placebo	192	98	179	107	112
Treatment difference vs placebo					
LS mean		–0.19	–0.58	–0.07	0.14
SE		0.21	0.13	0.11	0.05
Nominal *P* value		0.368	**<0.001**	0.499	0.011

Similar results in sub-analysis of participants with baseline viral RNA copy number
- $<10^6$ copies/mL
- $\geq 10^6$ copies/mL

[a]Virology analysis set included participants who were randomized, received ≥1 dose of study drug, and had a baseline SARS-CoV-2 viral RNA copy number ≥LLOQ.
Data are plotted as LS mean ± 95% CI. LS mean (SE), 95% CI, and *P* value were from MMRM with baseline viral RNA copy number and randomization strata as covariates.
LLOQ, lower limit of quantitation; **LS**, least squares; **MMRM**, mixed-effects model repeated measures; **ODV**, obeldesivir.

Nasal Swab SARS-CoV-2 Infectious Viral Titer Assessment

Virology analysis set[a]

Testing criteria

Viral RNA copy number ≥10^6 copies/mL at any visit

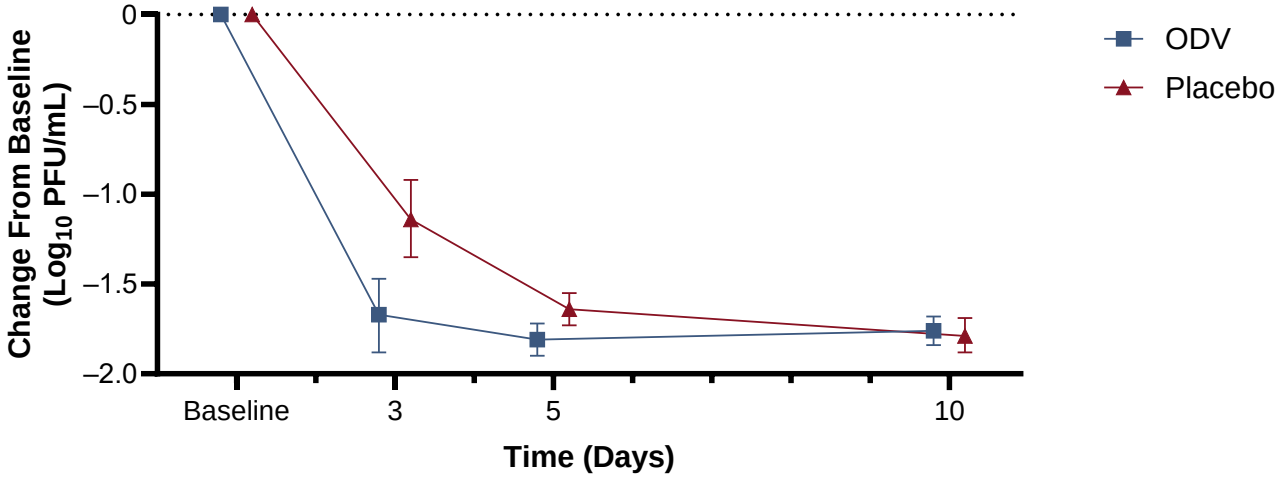
Participants with ≥200 PFU/mL at baseline had additional testing on Day 3 or Day 5, independent of viral RNA copy number

If Day 3 or Day 5 samples were available, the Day 10 sample was also tested, if available

[a]Virology analysis set included participants who were randomized, received ≥1 dose of study drug, and had a baseline SARS-CoV-2 viral RNA copy number ≥LLOQ.
LLOQ, lower limit of quantification; **PFU**, plaque-forming unit.

Change From Baseline in SARS-CoV-2 Infectious Viral Titer

Virology Analysis Set[a]



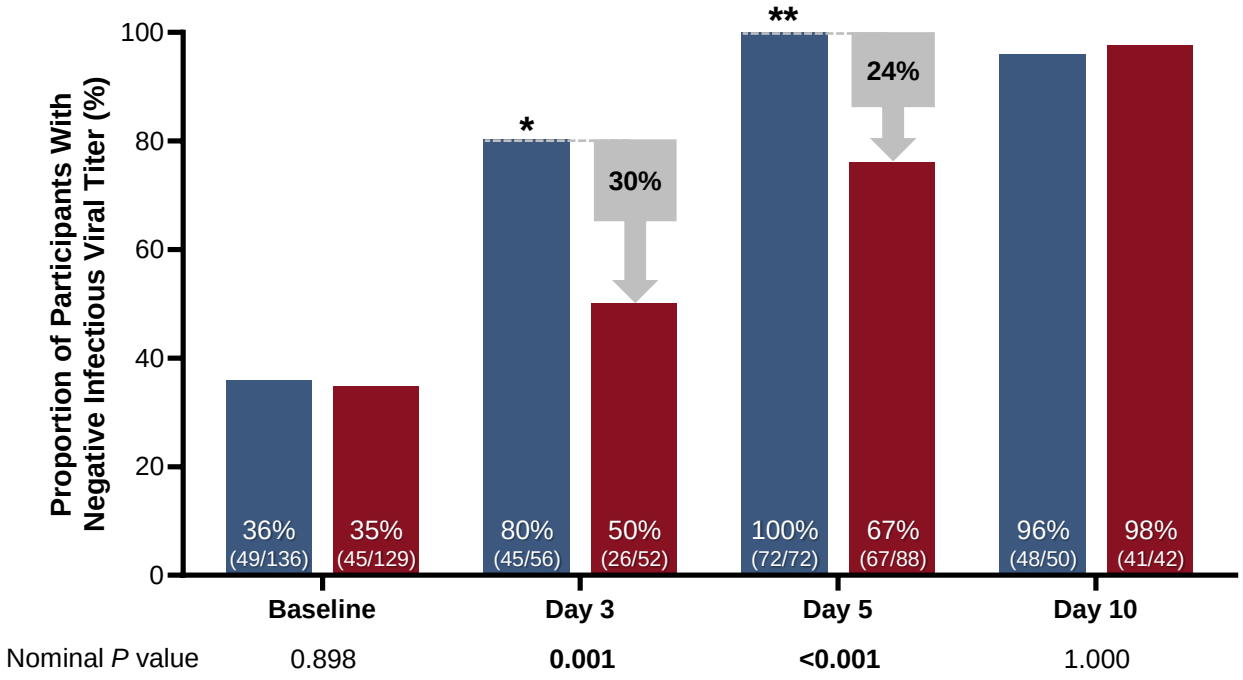
n	Baseline	Day 3	Day 5	Day 10
ODV	136	54	70	49
Placebo	129	50	81	42
Treatment difference vs placebo				
LS mean		–0.54	–0.17	0.03
SE		0.15	0.05	0.05
Nominal *P* value		**<0.001**	**0.001**	0.605

Similar results in sub-analysis of participants with baseline infectious viral titer ≥200 PFU/mL and tested on Day 3 or Day 5

[a]Virology analysis set included participants who were randomized, received ≥1 dose of study drug, and had a baseline SARS-CoV-2 viral RNA copy number ≥LLOQ. Data are plotted as LS mean ± 95% CI. LS mean (SE), 95% CI, and *P* value were from MMRM with baseline infectious viral titer and stratification factors as covariates. Only 1 participant had a result at Day 15, which was excluded from this analysis.
LLOQ, lower limit of quantitation; **LS,** least squares**; MMRM,** mixed-effects model repeated measures**; ODV**, obeldesivir; **PFU**, plaque-forming unit.

Participants With Negative SARS-CoV-2 Infectious Viral Titer

Virology Analysis Set[a]



Similar results in sub-analysis of participants with baseline infectious viral titer ≥200 PFU/mL and tested on Day 3 or Day 5

[a]Virology analysis set included participants who were randomized into the study, received ≥1 dose of study drug, and had a baseline SARS-CoV-2 viral RNA copy number ≥LLOQ.
* nominal *P* <0.01. ** nominal *P* <0.001. *P* value was from the Fisher's exact test. Baseline was the last available value recorded on or prior to the first dosing date of study drug.
LLOQ, lower limit of quantitation; **ODV**, obeldesivir; **PFU**, plaque-forming unit.

Conclusions

- ODV reduced SARS-CoV-2 nasal swab viral RNA copy number compared to placebo on Day 5
- ODV reduced SARS-CoV-2 nasal swab infectious viral titer compared to placebo on Days 3 and 5
- ODV increased the proportion of participants with negative SARS-CoV-2 nasal swab infectious viral titer compared to placebo on Days 3 and 5
- Overall, ODV treatment reduced nasal swab viral RNA copy number and infectious titer, demonstrating its ability to inhibit SARS-CoV-2 replication in adults with risk factors for developing severe COVID-19

Visit our poster presentation for more results from the BIRCH study

Title: Obeldesivir for the Treatment of COVID-19 in People With Risk Factors for Progression to Severe Disease: The BIRCH Study
Poster Session: COVID-19: Treatment
Date: Saturday, October 19
Time: 12:15 to 1:30 pm
Location: Hall J & K
Poster: P-2026
Presenter: Anca Streinu-Cercel

ODV, obeldesivir.

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