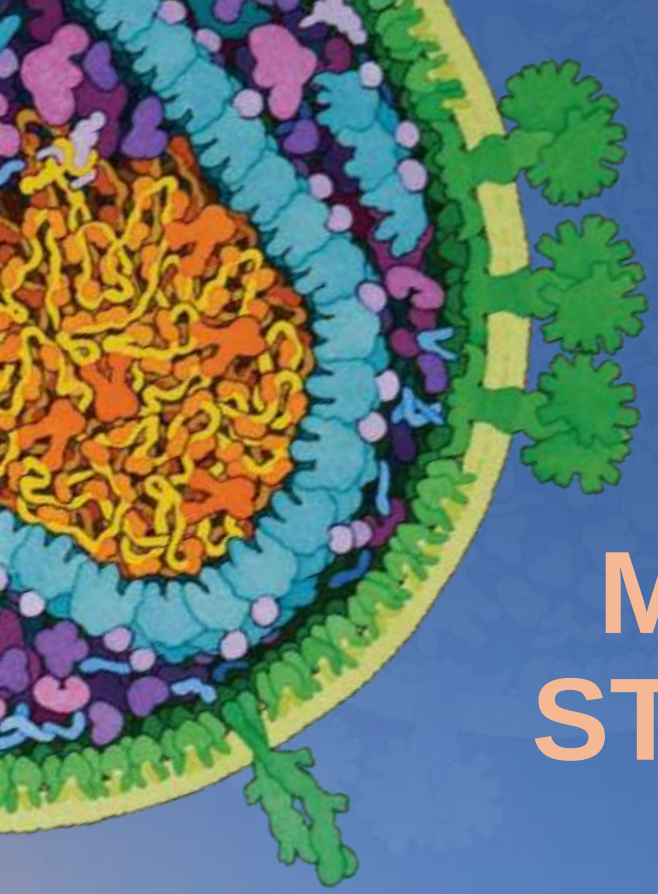

SCIENCE SPOTLIGHT™

MULTICENTER, OPEN-LABELED STUDY OF AVIFAVIR IN PATIENTS WITH COVID-19

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Disclosure: Nothing to disclose

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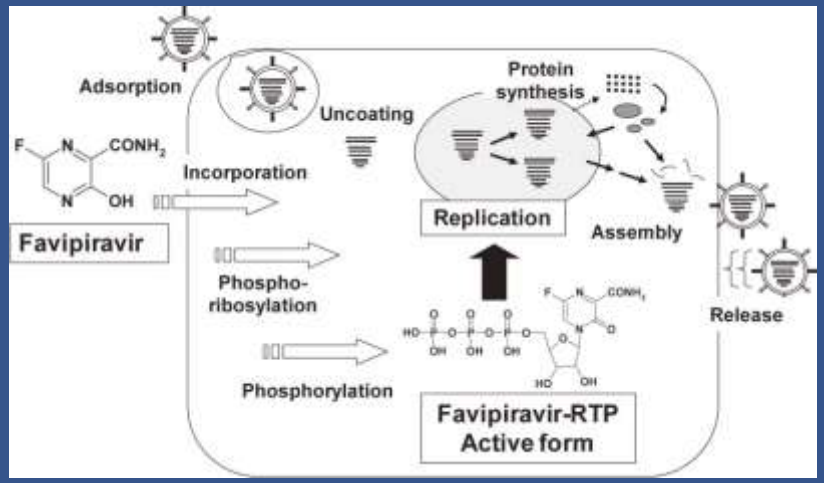
Avifavir® (favipiravir 200 mg oral tablet): An approved antiviral treatment for COVID-19

- Avifavir® is an oral tablet formulation of favipiravir, a broad spectrum inhibitor of viral RNA polymerases including that of SARS-CoV-2 virus.
- It is approved for treatment of COVID-19 in Russia and several other countries in Latin America and Asia.
- Initially, used in hospital setting
  - Since October 2020, the label expanded to include outpatient use.
- Favorable benefit/risk profile in clinical practice:
  - Substantial exposure to the drug in post-approval setting
    - From April through June 30, 2020, total drug exposure across approved countries was estimated at 63,046 individuals
    - From June 30 to Dec 31 – at over 1,000,000 individuals
  - Well tolerated , no new or unexpected safety concerns



Furuta et al. Proc Jpn Acad Ser B 2017; 93

- This study summarizes the outcomes of a retrospective analysis of the initial post-approval clinical effectiveness of Avifavir® vs. Standard of Care (SOC) in Russia (May-June 2020)
  - The effectiveness of post-approval AVIFAVIR therapy was shown consistent with observations made in clinical trials conducted to date.

Study Design and Demographics

Design

- Data were obtained from the Unified national (Russian) information system in the field of healthcare
  - 940 hospitalized patients: 470 each in AVIFAVIR and SOC group
  - Time to viral clearance and clinical improvement as indicators of drug's effectiveness

Treatments:

- Avifavir® dosed for 10 days, using body weight as a cut-off:
  - <75 kg: 1600 mg BID on Day 1, then 600 mg BID on Days 2 to 10.
  - > 75 kg: 1800 mg BID on Day 1, then 800 mg BID on Days 2 to 10
  - Average treatment duration and extent of exposure:

Statistics	Duration of administration (days)	Total received dose (mg)
Mean±CO	9.2±3.8	6199.3±5690.8
Median (Q1-Q3)	10 (7-11)	4000 (2400-9600)

- Backbone SOC included antibiotics and medications for symptoms relief, i.e., antipyretics, anti-tussics, etc.

Patients:

- Comparative demographics at baseline
- Males and females, 18 years of age and older
- Hypertension as a most common co-morbidity
- Hospitalization within 10 days of confirmed infection with SARS-CoV-2
- Majority of patients moderately ill

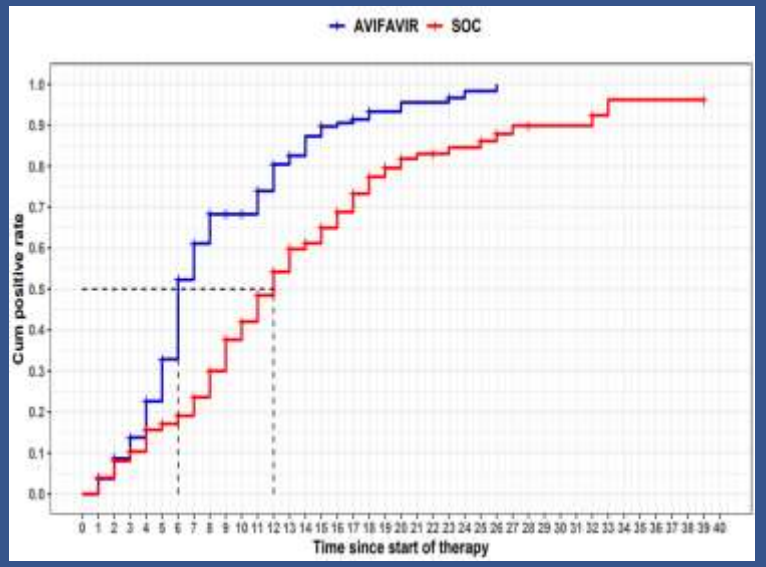
Parameter	AVIFAVIR N=470	Standard of Care N=470	p-value
Age	54.9±17.5*	55.5±19.3*	0.579**
17-44 years old	129 (27.4%)	102 (21.7%)	
45-59 years old	148 (31.5%)	127 (27.0%)	
≥ 60 years old	192 (40.9%)	220 (46.8%)	
Sex			
Female	246 (52.3%)	265 (56.4%)	0.213***
Male	224 (47.7%)	205 (43.6%)	
Duration from onset of symptoms	4.9±2.5	4.7±2.8	0.078**
SpO2, %	94.5±4.8	94.3±6.6	0.731**
≥95	315 (67.0%)	303 (64.5%)	
<95	155 (33.0%)	167 (35.5%)	
Disease severity			
Satisfactory	98 (20.9%)	91 (19.4%)	0.828**
Moderately severe	280 (59.6%)	284 (60.4%)	
Severe	86 (18.3%)	86 (18.3%)	
Extremely severe	6 (1.3%)	9 (1.9%)	

*Mean ± SD ** Student t-test ***χ^2 criterion

AVIFAVIR® in COVID-19 Patients vs. SOC: Efficacy

Viral clearance

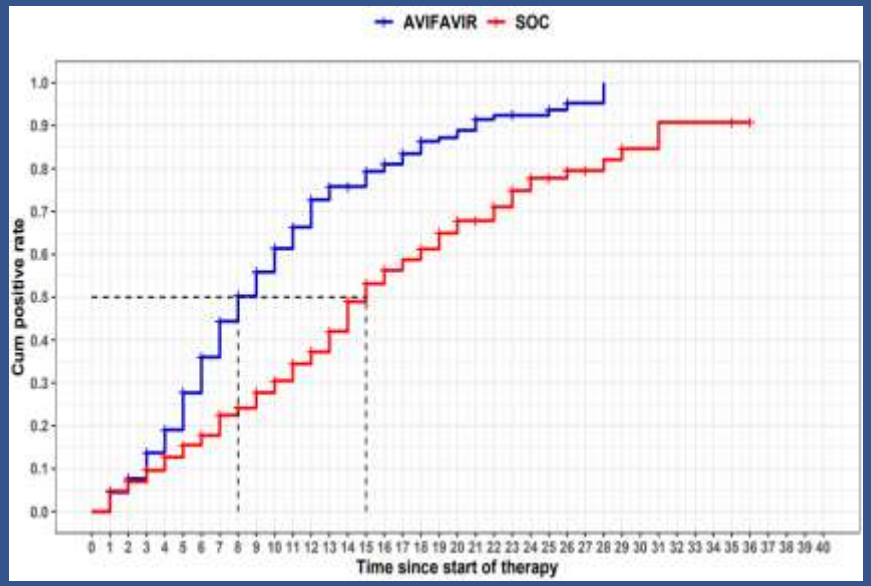
The median time to virus elimination in the AVIFAVIR and SOC groups was 6 and 12 days, respectively (p<0.001).



Treatment group	N	AUC	Median (IQR)	95% CI
AVIFAVIR	322	8.8 (0.4)	6.0 (5.0-12.0)	6.0-7.0
SOC	329	13.6 (0.7)	12.0 (8.0-18.0)	11.0-13.0
p-value (log-rank test)	<0.001			

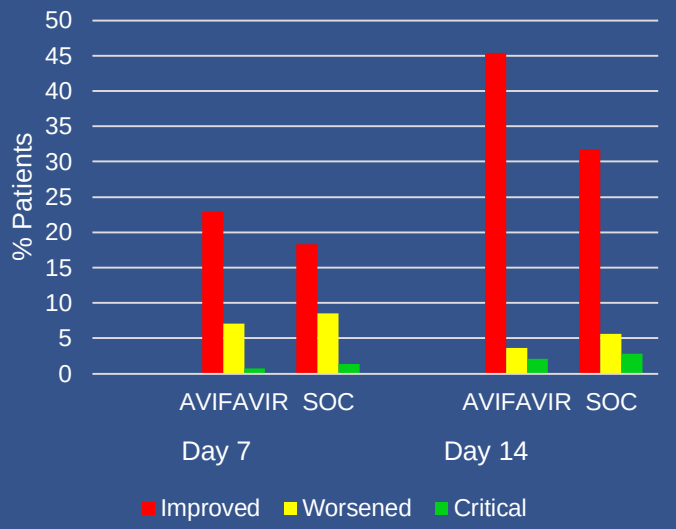
Clinical Improvement

The median time to clinical improvement in the AVIFAVIR and SOC groups was 8 and 15 days, respectively (p <0.001).



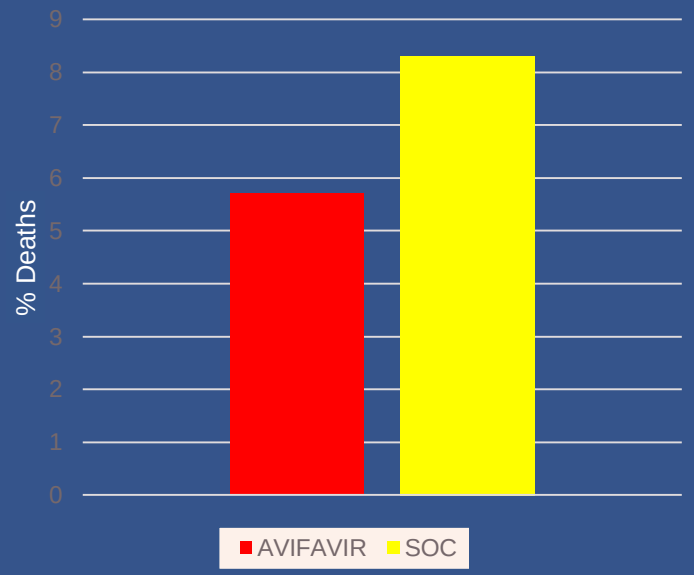
Treatment group	N	AUC	Median (IQR)	95% CI
AVIFAVIR	289	10.3 (0.4)	8.0 (5.0-13.0)	8.0-10.0
SOC	335	16.3 (0.7)	15.0 (9.0-24.0)	14.0-17.0
p-value (log-rank test)	<0.001			

Significantly greater number of patients with clinical improvement in AVIFAVIR vs. SOC group, at 7 days (p=0.0248) and 14 days (p<0.001) of treatment initiation.



AVIFAVIR® in COVID-19 Patients vs. SOC: Safety

Reduced Mortality Rate



Disease outome	AVIFAVIR N=470	Standard of care N=470
Death	27 (5.7%)	39 (8.3%)

Well tolerated, no new or unexpected ADRs

Data Source:	Number of ADRs identified during the reporting period				Total
	Serious		Not serious		
	Sus-pected	Un-expected	Sus-pected	Un-expected	
Healthcare professionals	0	0	0	0	0
Consumers	0	0	0	0	0
Public authorities in healthcare	14	2	18	0	34
Literature data	0	0	0	0	0
Total	0	0	0	0	34

To mitigate the risk of reproductive toxicity, patients are required to sign an informed consent acknowledging the reproductive risk* and consent to practicing reliable contraception for 3 months after the cessation of dosing.

**as posted in the drug label; reporting period April,23 - October,31, 2020*

Conclusions

- The ratio between the **expected benefits** and the **possible risks** of medical use of AVIFAVIR® remains positive

- AVIFAVIR showed early a statistically significant differentiation compared to Standard of care:
  - Faster virological response
  - Shorter time to clinical symptoms
  - Reduced mortality rates

- The obtained results support the importance of an early initiation of antiviral therapies, such as AVIFAVIR, for the treatment success in COVID-19 patients

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