

**Supplementary Table. Comparison of therapeutic modalities against EV-A71.**

	PMID	Modality	Viral RNA reduction (%)	Viral plaque reduction	Accessible tissues	Target specificity <i>in vivo</i>	Therapeutic window
<b>Sim et al., 2005</b>	16083932	siRNA	77.5 (in vitro)	~1 log PFU	RD cells	Protein kinase R not activated	N.A.
<b>Tan et al., 2007</b>	17712333	siRNA	100	-	Intestinal	IFN not activated	24hr post EV-A71
<b>Tan et al., 2018</b>	29175128	Chloroquine	-	2 log PFU/ml	Muscles	-	Daily doses over 7 days
<b>Cao et al., 2011</b>	21641277	Immunoglobulin	-	-	-	-	-
<b>Jia et al., 2017</b>	28422137	Immunoglobulin	-	-	-	-	24hr post EV-A71
<b>Sun et al., 2016</b>	27623347	Adenoviral IFN	-	1 log PFU/ml	Muscle	-	12hr post EV-A71
<b>Sun et al., 2020</b>	32424333	Sofosbuvir nucleotide analog	-	0.7 log PFU/ml	Muscle	-	5 doses over 4 days
<b>Gunaseelan et al., 2019</b>	31666401	Prunin	-	4 - 5 log PFU/ml	Muscle	-	Daily doses over 7 days
<b>Tan et al., 2021</b>	33958691	Protein inhibition drugs in combination	-	-	Muscle	-	Daily over 6 days
<b>Fan et al., 2021</b>	34555337	Viral suppressor of RNAi (VSR)-targeting peptides	Approximately 90-99%	-	Muscle, brain, lung	-	2hr post EV-A71, twice a day over 7 days
<b>This study</b>	-	AAV-CRISPR-CasRx	99.9	4 – 5 log PFU/ml	Muscle, brain	No off-target in whole human transcriptome	24hr post EV-A71

“-“, not tested or not shown