Potential for Polio Antiviral Drugs

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Polio Endgame

- Current tools for control, eradication & post-eradication are the same:

  OPV (mOPV) vaccines
  IPV vaccine(s)

- Are these sufficient?
- Can they be improved or supplemented?

- Additional tool: polio antiviral drugs

Another Tool: Polio Antiviral Drugs

NRC workshop Nov05; Report Feb06

Purpose: Explore role of antivirals in control, eradication & post-eradication of polio

Conclusion: There is a role. Recommended that antiviral drugs be developed ASAP

Rationale: Another tool increases flexibility
Address iVDPV
Supplement, complement vaccines
Enhance response effectiveness

How might a polio antiviral be used?

First, Appreciate the Attributes
of an Antiviral

Expected Attributes of an Antiviral

- Easily administered Oral tablet, liquid, food bar
- Fast acting - Within hours
  - Therapeutically to rapidly reduce virus load & excretion; treat CNS infection
  - Prophylactically to immediately protect close contacts; contain virus spread
- Effective irrespective of immune status
- Readily stockpiled Manufacturing, stable, storage
- Rapidly deployable No special shipping conditions

How might a polio antiviral be used?

- Cure chronic poliovirus excretors
- Component of outbreak response
  (control, eradication or post-eradication)
  - Treat infected subjects
  - Prevent / minimize infection of contacts
  - Containment of OPV response ± IPV
  - Alternative to OPV: 1° response ± IPV
- Situation dependent

How feasible is it to develop polio antiviral drugs?

Very feasible!

3 decades of picornavirus antiviral R&D

Several excellent starting points

Potential Poliovirus Antiviral Leads

Select Compounds

Viral Target	Example	Development Stage
Unknown	Ribavirin	Approved (RSV, HCV)
Polymerase	2'-*C*-Me-Cy	Phase 2 (HCV)
2C	MRL 1237	Preclinical (entero)
3A	Enviroxime	Phase 2 nasal/oral (rhino)
3C Protease	Rupintrivir	Phase 2 nasal (rhino)
	Compound 1	Phase 1 oral (rhino)
Capsid	Pleconaril	Phase 3 oral (rhino)
	V-073	Preclinical (entero)

Potential Poliovirus Antiviral Leads

Activity against 3 Serotypes *

Viral Target	Example	Activity (μM)		
		PV1	PV2	PV3
Unknown	Ribavirin	57	64	55
Polymerase	2'-*C*-Me-Cy	15	29	3.9
2C	MRL 1237	5.3	4.6	3.8
3A	Enviroxime	0.20	0.06	0.04
3C Protease	Rupintrivir	0.02	0.04	0.01
	Compound 1	0.26	0.31	0.06
Capsid	Pleconaril	10	1.1	0.22
	V-073	0.02	0.05	0.02

* Unpublished data: Armando DePalma & Johan Neyts, Rega Institute
Steve Oberste & Mark Pallansch, CDC

How long will it take & how much will it cost to develop?

Depends on the starting point of the program

Research lead : 4-6 yrs & $8-12M to IND

Preclinical candidate : < 2 yrs & $5-6M to IND

Clinical time & costs : 3-6 yrs & $20-$60M

Polio Antiviral Drugs
Summary

1. Polio antivirals represent another tool
2. Antiviral attributes portend multiple applications; adjunct to vaccines
3. Polio antiviral development has high probability of success
4. Development in a relevant timeframe
5. Relatively modest financial commitment