

GROG et recherche : Virologie

Bruno Lina

Hospices Civils de Lyon, CNR des virus influenza (LYON), F69677, Bron
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Liens d'intérêts :

Argene, AstraZeneca, BioCryst, BMS, BioMérieux, GSK, Novartis, Roche, Sanofi-Pasteur, SP-MSD, Conseil scientifique du GEIG, membre de ESWI

GROG et recherche : Virologie

- Les Vigies des réseaux GROG travaillent en lien étroit avec les CNR
- Le tissu des médecins vigies est une force pour la surveillance et donc pour la recherche
- Ils font des prélèvements analysés par les laboratoires à de multiples fins :
 - Études épidémiologiques
 - Analyses virologiques plus ou moins complexes
 - Évaluation de kits diagnostiques
 - Essais cliniques
- Ces données s'intègrent dans les données de surveillance Européenne (EISS puis EISN) et OMS (Flunet et GISN)

Quelques exemples de
coopération :
épidémiologie et diagnostic

Surveillance of Community-Acquired Viral Infections Due to Respiratory Viruses in Rhone-Alpes (France) during Winter 1994 to 1995

BRUNO LINA,^{1*} MARTINE VALETTE,¹ SOPHIE FORAY,¹ JACQUES LUCIANI,² JEAN STAGNARA,² DARRYL M. SEE,¹ AND MICHELE AYMARD¹

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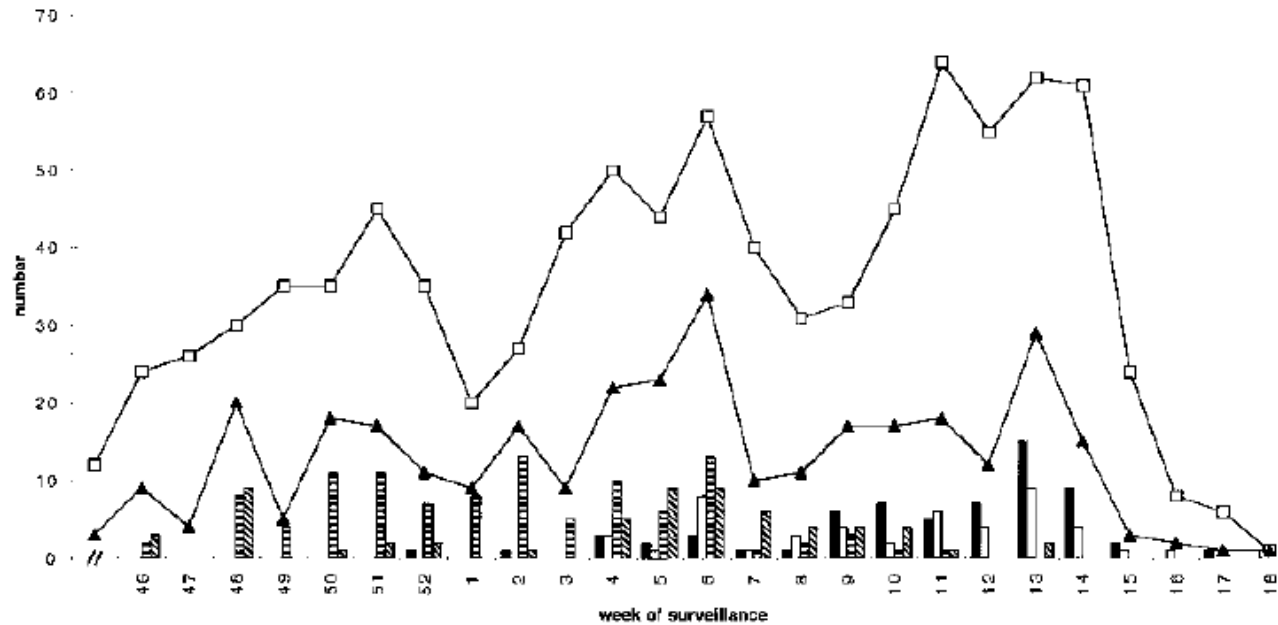


FIG. 1. Seasonal distributions of all specimens collected (□) and positive samples (▲) (lines) and seasonal distributions of individual viruses (bars) [■, influenza virus A; □, influenza virus B; ▨, RSV; ▩, coronavirus]. The surveillance period began on week 38 of 1994 and concluded on week 18 of 1995.

Surveillance of Community-Acquired Viral Infections Due to Respiratory Viruses in Rhone-Alpes (France) during Winter 1994 to 1995

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 DARRYL M. SEE,¹ AND MICHELE AYMARD¹

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 Médecine Lyon Grange Blanche,¹ and Réseau de Surveillance Groupe Régional d'Observation de la Grippe,
 Laboratoire de Virologie, Domaine Rockefeller,² 69373 Lyon Cedex 08, France*

TABLE 3. Percentage of clinical symptoms observed in 340 patients from whose nasal swabs respiratory viral agents were recovered^a

Clinical observation	% patients infected with the following virus (no. of strains isolated):					
	Influenzavirus A (64)	Influenzavirus B (47)	RSV (108)	Adenovirus (22)	Rhinovirus (35)	Coronavirus (64)
Respiratory symptoms						
Clear nasal secretion	79.7	87.2	76.9	72.7	71.4	67.2
Purulent nasal secretion	7.8	10.6	12	9	20	20.3
Cough	93.7 ^b	89.4 ^b	82.4	59.1	77.1	71.9
Physical findings						
Temp not determined	4.7	8.5	15.7	4.5	17.2	21.9
Temp <38.5°C	6.3	2.1	18.5	0	11.4	18.7
Temp between 38.5 and 39.5°C	45.3	53.2	40.7	18.2	51.4	34.4
Temp >39.5°C	43.7	36.2	25	77.3 ^c	20	25
Pharyngitis	61	68.1	42.6	59.1	65.7	60.9
Otitis	12.5	19.1	31.5	18.2	14.3	17.2
Bronchiolitis	1.5	2.1	44.5 ^c	9	8.6	12.5
General symptoms						
Emesis	10.1	4.2	12	9	5.7	10.9
Diarrhea	1.5	2.1	8.3	0	2.8	4.7
Abdominal pain	17.2	12.7	6.5	22.7	14.3	15.6
Myalgia	64.1	65.9	13.9	31.8	57.1	64.2
Asthenia	70.3	68.1	21.3	22.7	62.8	70.3
Headache	67.2	74.5	15.7	45.4	54.3	58.8

^a Data for patients from whom three enteroviruses and five parainfluenza viruses were recovered during the study are not included here.

^b Statistically significant ($P < 0.01$).

^c Statistically significant ($P < 0.001$).

Comparison of Two Nested PCR, Cell Culture, and Antigen Detection for the Diagnosis of Upper Respiratory Tract Infections due to Influenza Viruses

Clémence Magnard, Martine Valette, Michèle Aymard, and Bruno Lina*

Laboratoire de Virologie, Centre National de Référence pour la Grippe (France-Sud), Domaine Rockefeller, Lyon, France

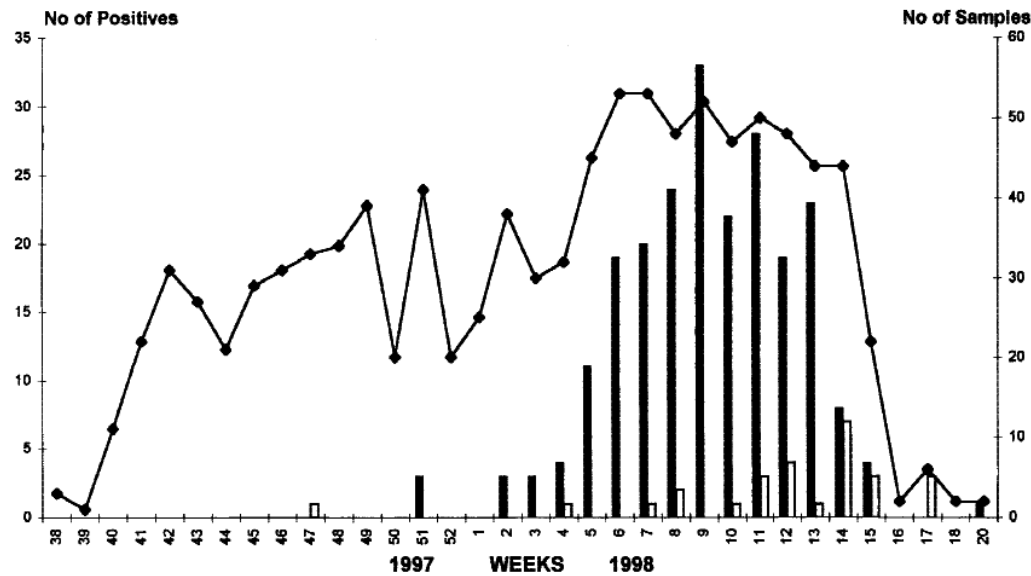


Fig. 1. Result of the influenza surveillance during winter 1997-1998. The surveillance was carried out using influenza detection by IC-ELISA and cell culture. No, number; FLU A, influenza A; FLU B, influenza B.

Comparison of Two Nested PCR, Cell Culture, and Antigen Detection for the Diagnosis of Upper Respiratory Tract Infections due to Influenza Viruses

Clémence Magnard, Martine Valette, Michèle Aymard, and Bruno Lina*

Laboratoire de Virologie, Centre National de Référence pour la Grippe (France-Sud), Domaine Rockefeller, Lyon, France

TABLE I. Comparison of Influenza Detection or Culture on Nasal Swab Specimens Using Four Different Assays

Influenza type	IC-ELISA	Culture	IC-ELISA + Culture	PCR1	PCR2	At least one positive test
A H1N1	0	2	2	2	2	2
A H3N2	38	73	77	84*	74	88*
B	2	2	3	4*	/	5*
Total (%) of positive specimens	40 (26%)	77 (50,6%)	82 (53,6%)	88 (57,1%)	76 (50%)	93 (60,4%)

/, not performed; *, including two A H3N2 and B mixed infections.

TABLE II. Comparison of Sensitivities of Four Tests on Calibrated Viral Suspensions*

Influenza type	Techniques			
	IC-ELISA	Culture	PCR1	PCR2
A H1N1/Beijing 262/95	3,300	30	0.2	2
A H3N2/Sydney 5/97	5,000	45	3	3
B/Harbin 7/94	5,000	45	3	

*Values are in TICD₅₀/μl. Results were adjusted to the volume required for each test. IC-ELISA, immunocapture-ELISA assay; culture was done on MDCK cells and checked at day 4; PCR1 and PCR2 procedures are described in the text.

One hundred fifty-four samples collected during the peak of the influenza epidemic recorded during winter of 1997–1998 in the south of France were processed for influenza detection using antigen detection (ELISA-immunocapture assay), two different nested RT-PCR assays (targeting M and HA genes), and cell culture. Among 154 samples, 93 (60.4%) were positive for influenza detection. Forty specimens (26%) were positive by ELISA, 77 (50%) by culture, 88 (57.1%) using the multiplex HA-PCR and 76 (49.4%) using the M-PCR. Multiplex HA-PCR was thus the most sensitive test. The PCR assay offers an alternative to culture for influenza detection.

Résistance aux antiviraux

Surveillance des résistances aux antiviraux



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Antiviral Research 68 (2005) 43–48



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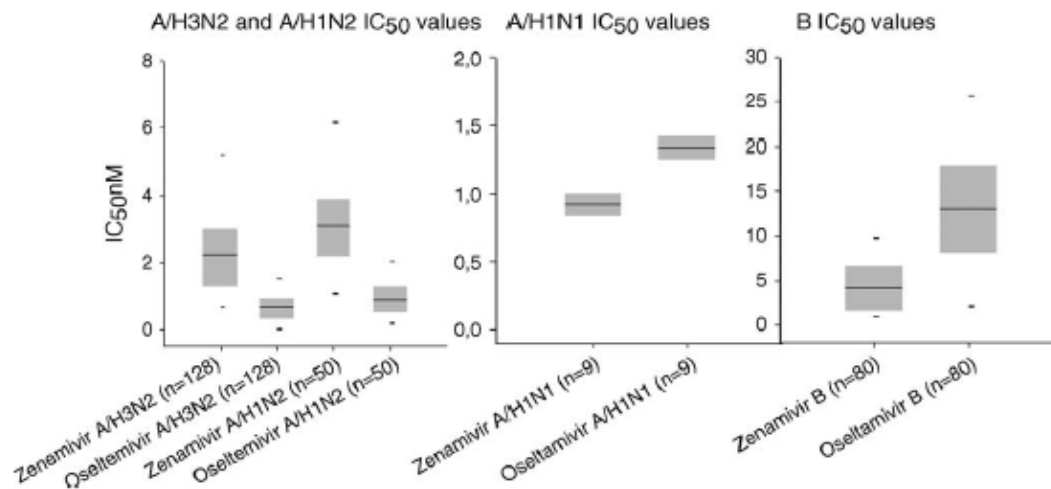
Short communication

Sensitivity of influenza viruses to zanamivir and oseltamivir: A study performed on viruses circulating in France prior to the introduction of neuraminidase inhibitors in clinical practice

O. Ferraris*, N. Kessler, B. Lina

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Surveillance des résistances aux antiviraux

Réseau VIRGIL



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Journal of Clinical Virology 41 (2008) 25–28



www.elsevier.com/locate/jcv

Detection of human influenza A (H1N1) and B strains with reduced sensitivity to neuraminidase inhibitors

Vanessa Escuret^{a,*}, Emilie Frobert^a, Maude Bouscambert-Duchamp^a, Murielle Sabatier^a,
Isidore Grog^c, Martine Valette^b, Bruno Lina^{a,b}, Florence Morfin^a, Olivier Ferraris^a

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Received 19 October 2007; accepted 19 October 2007

Surveillance des résistances aux antiviraux

Réseau VIRGIL

RESEARCH

Oseltamivir-Resistant Influenza Virus A (H1N1), Europe, 2007–08 Season

Adam Meijer, Angie Lackenby, Olav Hungnes, Bruno Lina, Sylvie van der Werf, Brunhilde Schweiger, Matthias Opp, John Paget, Jan van de Kasstele, Alan Hay, and Maria Zambon, on behalf of the European Influenza Surveillance Scheme¹

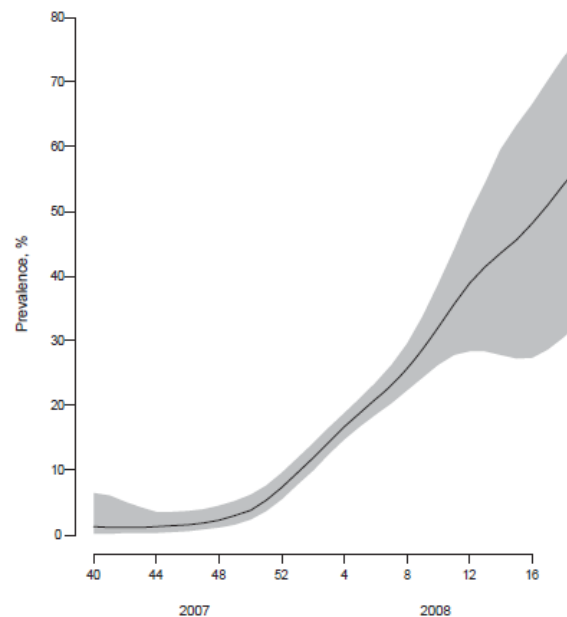
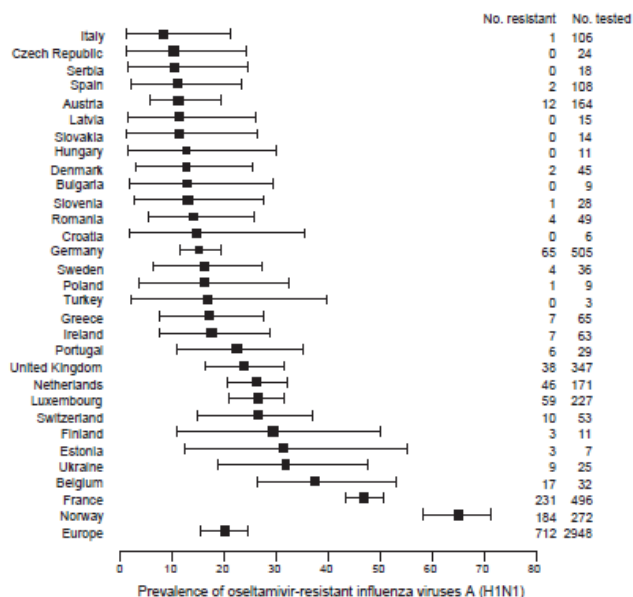
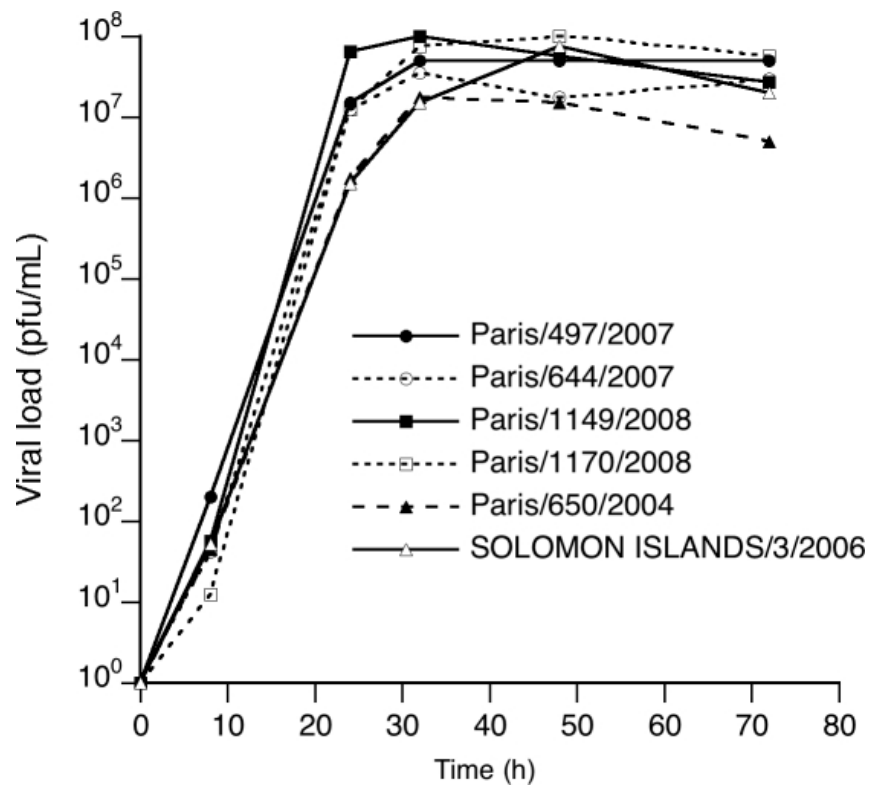
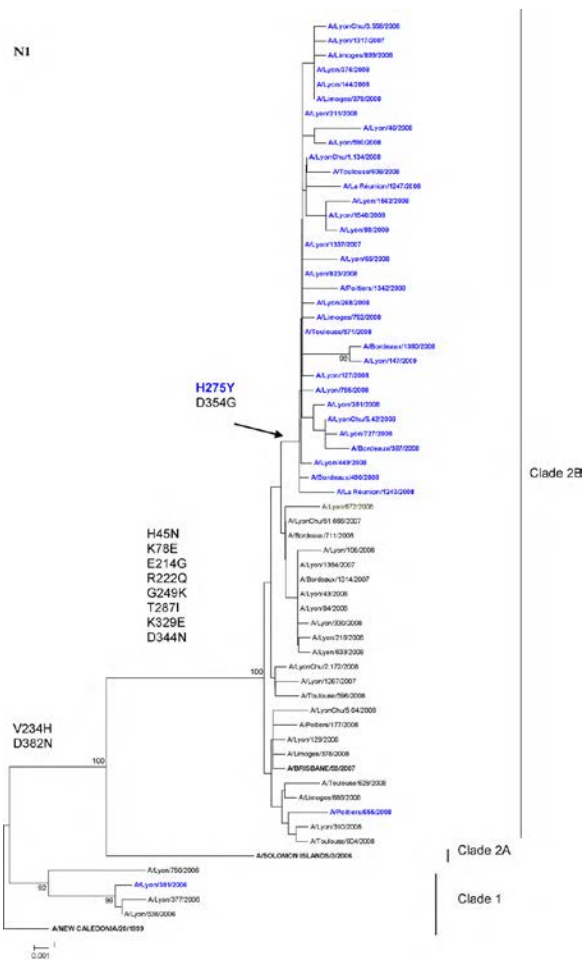


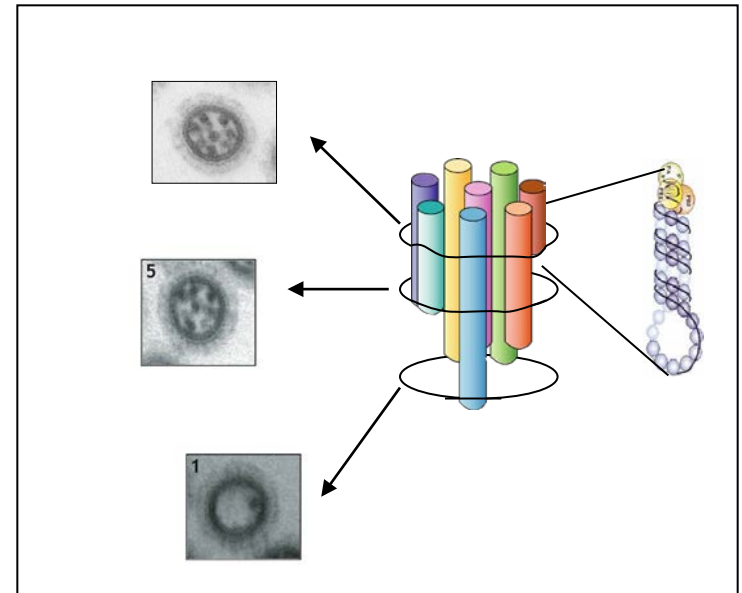
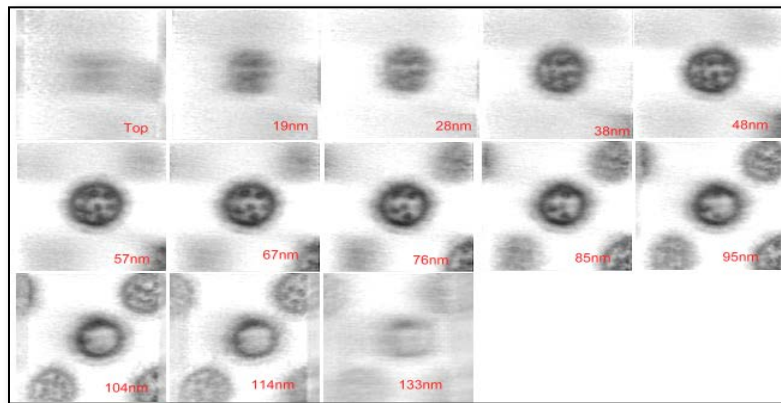
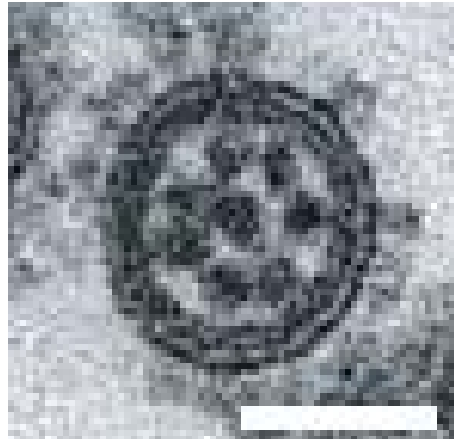
Figure 5. Weighted average prevalence of oseltamivir-resistant influenza viruses A (H1N1), Europe, winter 2007–08. The light gray region indicates the 95% confidence interval.

Surveillance des résistances aux antiviraux

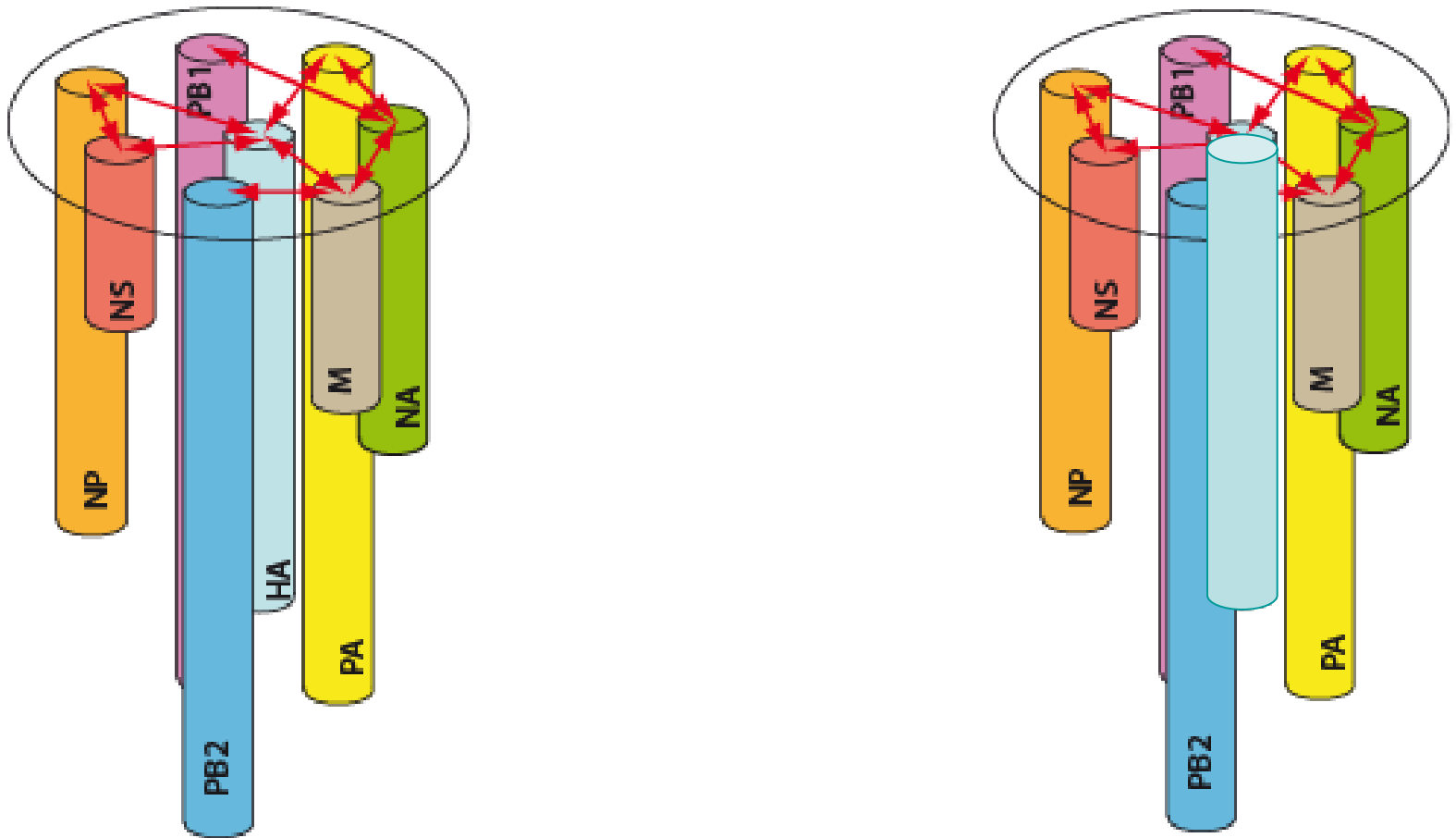


Etude des virus grippaux

Influenza type A : organisation interne



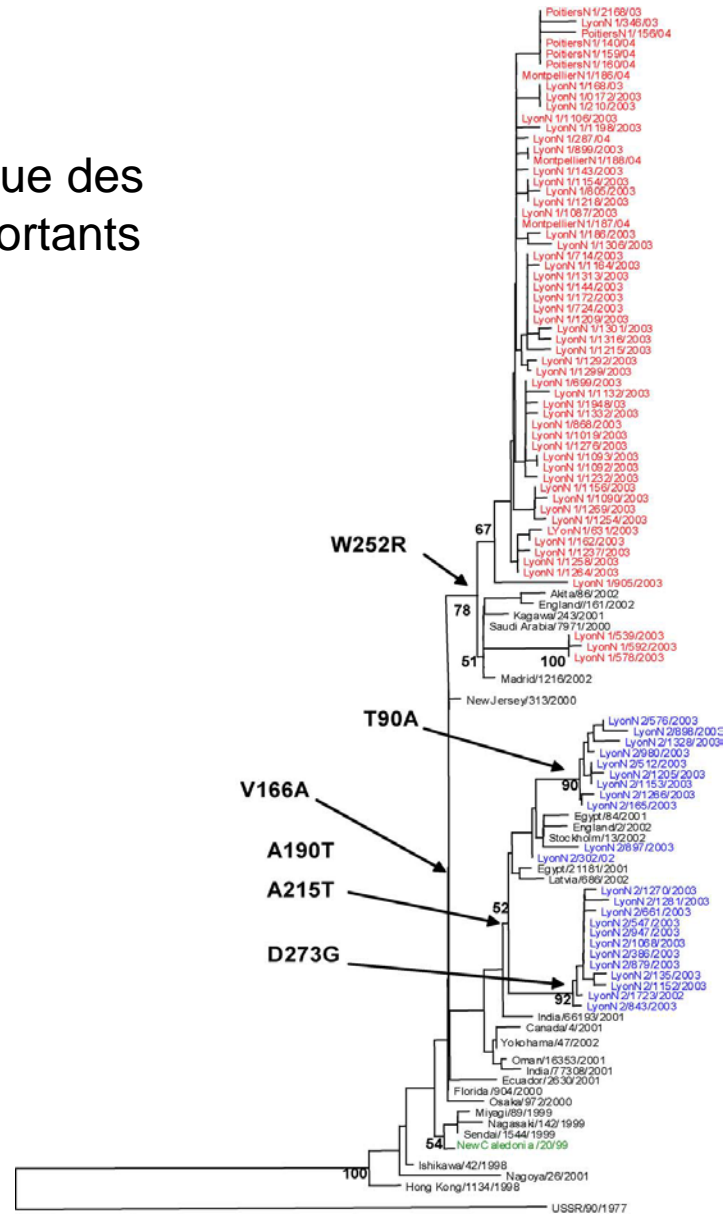
Virus « bizarres » : apparition du virus A(H1N2)



Réassortiment génétique : introduction du gène Ha

Virus « bizarres » : A(H1N2)

- Évolution génétique et antigénique des Ha des virus H1N1 et des réassortants H1N2



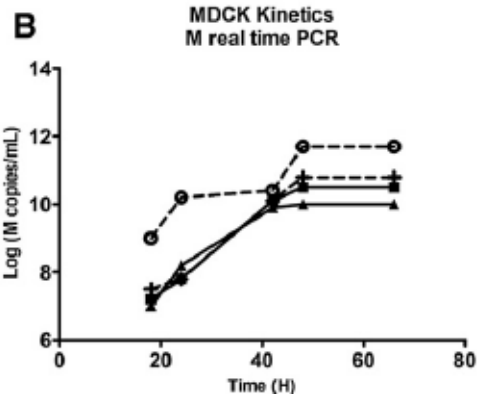
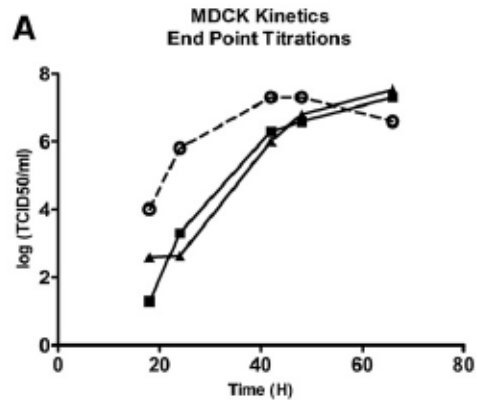
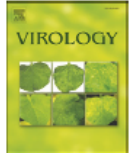
Virus « bizarres » : virus sans Neuraminidase



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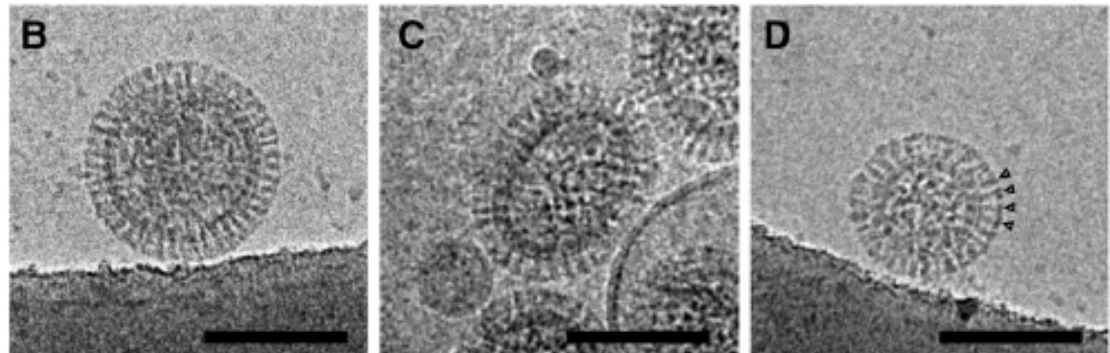
Virology

journal homepage: www.elsevier.com/locate/yviro



In vitro characterization of naturally occurring influenza H3NA₂ viruses lacking the NA gene segment: Toward a new mechanism of viral resistance?

V. Moules^{a,*}, O. Ferraris^{a,1}, O. Terrier^a, E. Giudice^b, M. Yver^a, J.P. Rolland^b, M. Bouscambert-Duchamp^{a,c}, C. Bergeron^a, M. Ottmann^a, E. Fournier^d, A. Traversier^a, C. Boule^e, A. Rivoire^e, Y. Lin^f, A. Hay^f, M. Valette^{a,c}, R. Marquet^d, M. Rosa-Calatrava^a, N. Naffakh^g, G. Schoehn^{h,i}, D. Thomas^b, B. Lina^{a,c}



Virus Pandémique H1N1

RESEARCH ARTICLES

Highly heterogeneous temperature sensitivity of 2009 pandemic influenza A(H1N1) viral isolates, northern France

I Pelletier^{1,2}, D Rousset^{3,4,5,6}, V Enouf^{3,4,5,6}, GROG⁷, F Colbère-Garapin^{1,2}, S van der Werf^{3,4,5,6}, N Naffakh (nadia.naffakh@pasteur.fr)^{3,4,5}

1. Institut Pasteur, Unité de Biologie des Virus Entériques, Département de Virologie, Paris, France
2. INSERM U994 (French National Institute of Health and Medical Research) Paris, France
3. Institut Pasteur, Unité de Génétique Moléculaire des virus à ARN, Département de Virologie, Paris, France
4. CNRS URA3015 (French National Centre for Scientific Research), Paris, France
5. Université Paris Diderot, Sorbonne Paris Cité, Unité de Génétique Moléculaire des virus à ARN, Paris, France
6. Institut Pasteur, Centre National de Référence des virus influenzae (Région Nord), Paris, France
7. Groupes Régionaux d'Observation de la Grippe, Open Rome, Paris, France

Virus Pandémique H1N1

TABLE 1

Origin and characteristics of 2009 pandemic influenza A(H1N1) viral isolates from mild and severe influenza cases, northern France, 24 September–16 December 2009 (weeks 39–51) (n=23)

Viral isolate ^a	Sample type	Week of sampling	Type of patient ^a	Age of patient (years)	Disease severity	Additional information	Haemagglutinin residue 222 ^c	Neuraminidase residue 275 ^c
20097639	Nasal and pharyngeal	51	Outpatient	40	Mild	NA	E	H
20097214	Nasal and pharyngeal	49	Outpatient	47	Mild	NA	D	Y
20096074	Nasal and pharyngeal	45	Outpatient	16	Mild	NA	D	H
20095771	Nasal and pharyngeal	44	Outpatient	24	Mild	NA	D	H
20095509	Nasal and pharyngeal	42	Outpatient	45	Mild	NA	D	H
20095501	Nasal and pharyngeal	43	Outpatient	8	Mild	NA	D	H
20095383	Nasal and pharyngeal	42	Outpatient	29	Mild	NA	D	H
20095016	Nasal and pharyngeal	41	Outpatient	14	Mild	NA	D	H
20097391	Nasal and pharyngeal	49	Inpatient	44	Severe	Deceased	D	H
20097367	Nasal and pharyngeal	48	Inpatient	26	Severe	NA	D	H
20097155	Nasal and pharyngeal	48	Inpatient	2.5	Severe	NA	D	H
20097097 ^a	Lung	49	Inpatient	6	Severe	Deceased	D	H
20097101 ^a	Brain	49	Inpatient	6	Severe	Deceased	G ^a	H
20096934	Nasal and pharyngeal	47	Inpatient	63	Severe	Haemopathy	D	H
20095911	Nasal and pharyngeal	43	Inpatient	10	Severe	Chronic respiratory insufficiency	D	H
20096365	Nasal	45	Inpatient	55	Severe	Chronic obstructive bronchopneumopathy	E	H
20094517	Nasal and pharyngeal	39	Inpatient	20	Severe	NA	D	H
20094518	Nasal and pharyngeal	39	Inpatient	45	Severe	NA	E	H
20094785	Nasal and pharyngeal	40	Inpatient	29	Severe	NA	E	H
20096928	Nasal and pharyngeal	45	Inpatient	22	Severe	Acute respiratory distress syndrome	D	H
20097105	Lung	48	Inpatient	46	Severe	Deceased	G	H
20097208	Nasal and pharyngeal	48	Inpatient	51	Severe	Deceased	D	H
20097388	Nasal and pharyngeal	49	Outpatient	39	Severe	Deceased (at home)	D	H

NA: not available.

^a 2009X.XXX stands for A/Paris/XXXX/2009.

^b Samples from outpatients are from the Groupes Régionaux d'Observation de la Grippe (GROG), the national network of sentinel general practitioners and paediatricians and from the Réseau National des Laboratoires (RENAL), a network of hospital laboratories.

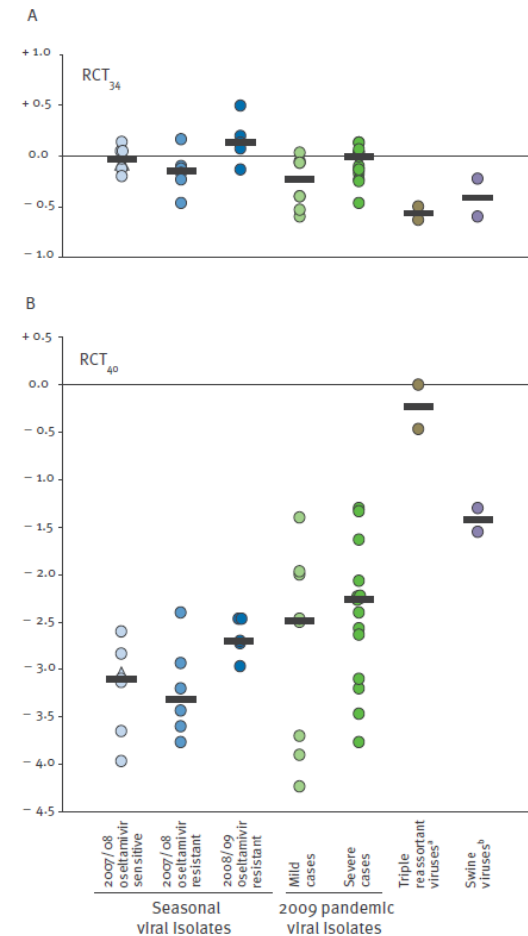
^c Sequence information refers to the viruses isolated after one passage in Madin-Darby canine kidney (MDCK) cells.

^d Viruses 20097097 and 20097101 were isolated from the lung and brain, respectively, of the same patient.

^e The sequence of the virus present in the original specimen was also determined, and a D was found at residue 222 of the haemagglutinin.

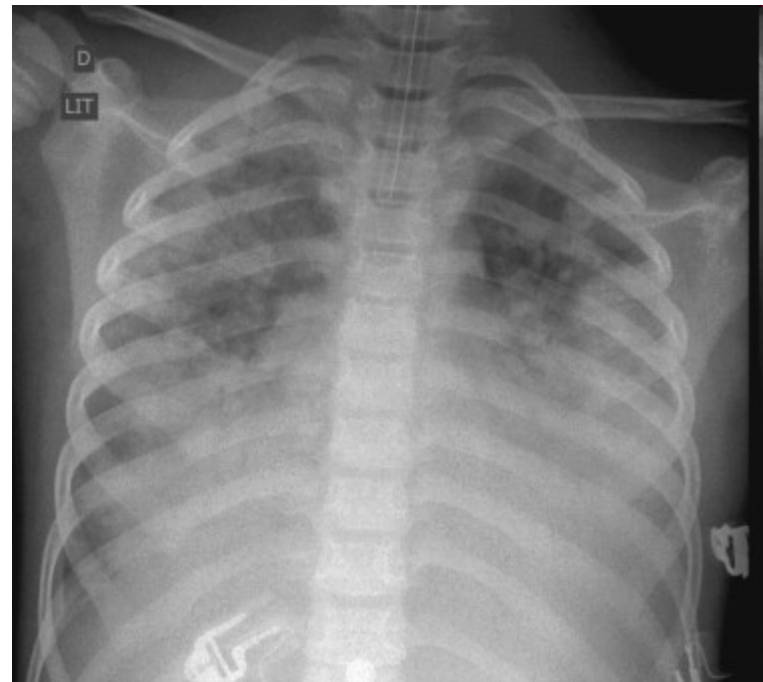
FIGURE

Reproductive capacity of 2009 pandemic influenza A(H1N1) viral isolates (n=23) and 2007/08 and 2008/09 seasonal influenza A(H1N1) viral isolates (n=18) at 34 °C and 40 °C, relative to 37 °C, northern France

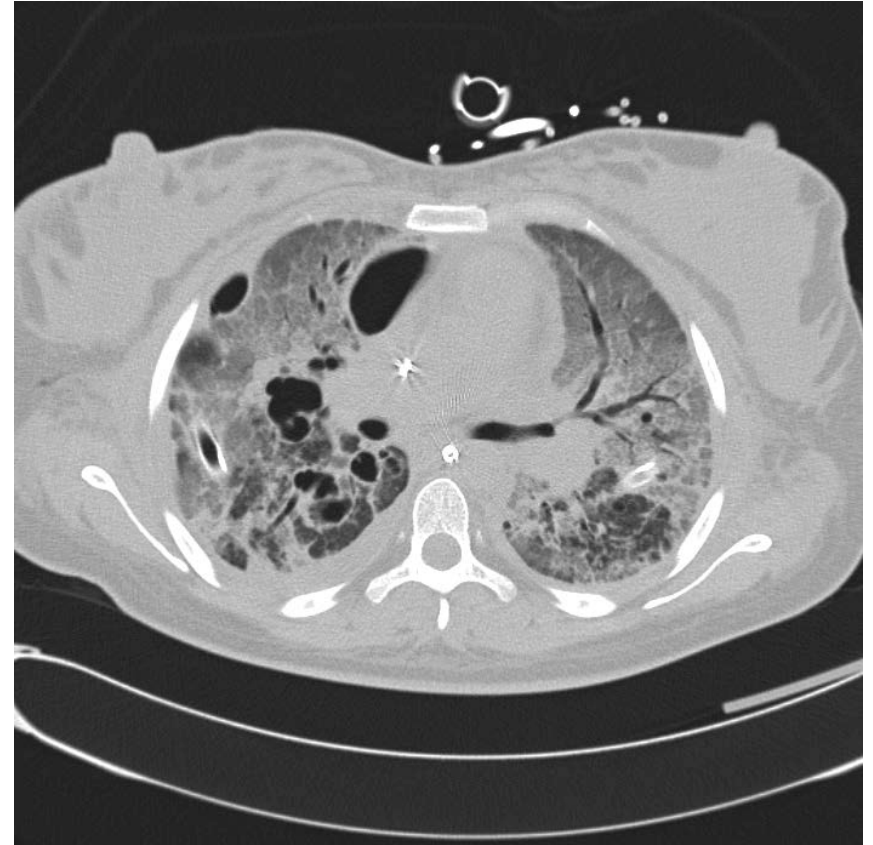
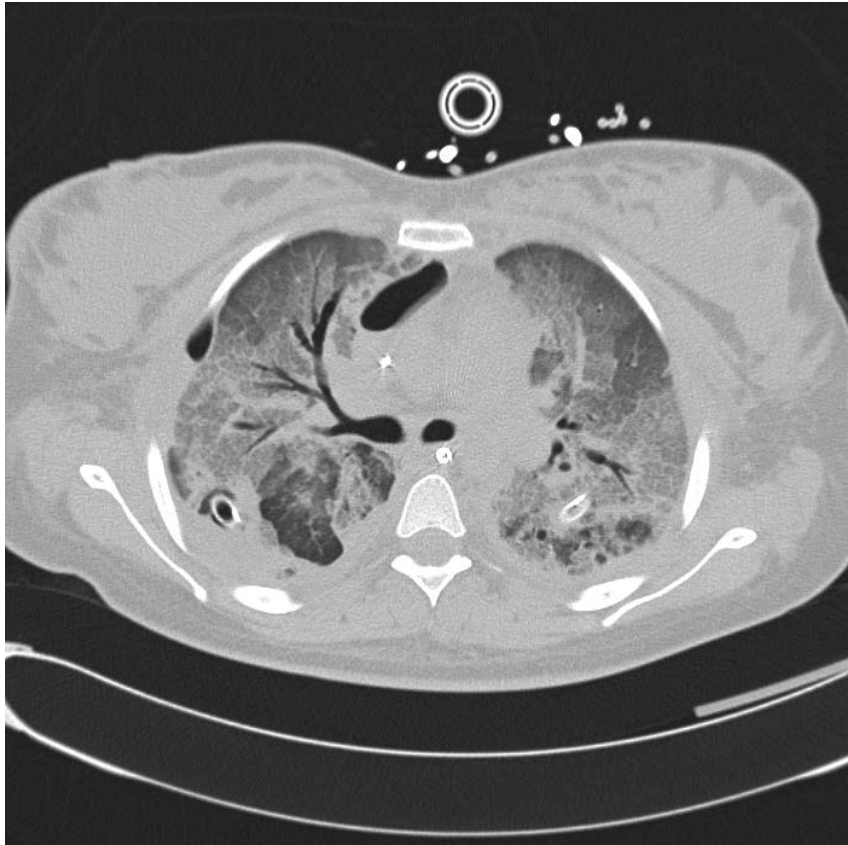


Clinique descriptive de cas

Cas cliniques (pneumonie nécrosante H1N1-Strepto A)



Cas cliniques (SDRA H1N1 et mutant D222G)



Essais cliniques antiviraux

Essais cliniques

OPEN ACCESS Freely available online

PLoS MEDICINE

Efficacy of Oseltamivir-Zanamivir Combination Compared to Each Monotherapy for Seasonal Influenza: A Randomized Placebo-Controlled Trial

Xavier Duval^{1,2,3}, Sylvie van der Werf^{4,5,6}, Thierry Blanchon^{7,8}, Anne Mosnier⁹, Maude Bouscambert-Duchamp^{10,11}, Annick Tibi^{12,13}, Vincent Enouf⁴, Cécile Charlois-Ou¹⁴, Corine Vincent^{2,3,15}, Laurent Andreoletti^{16,17}, Florence Tubach^{2,3,18}, Bruno Lina^{10,11}, France Mentré^{2,3,15}, Catherine Leport^{14,19*}, and the Bivir Study Group[†]

BIVIR

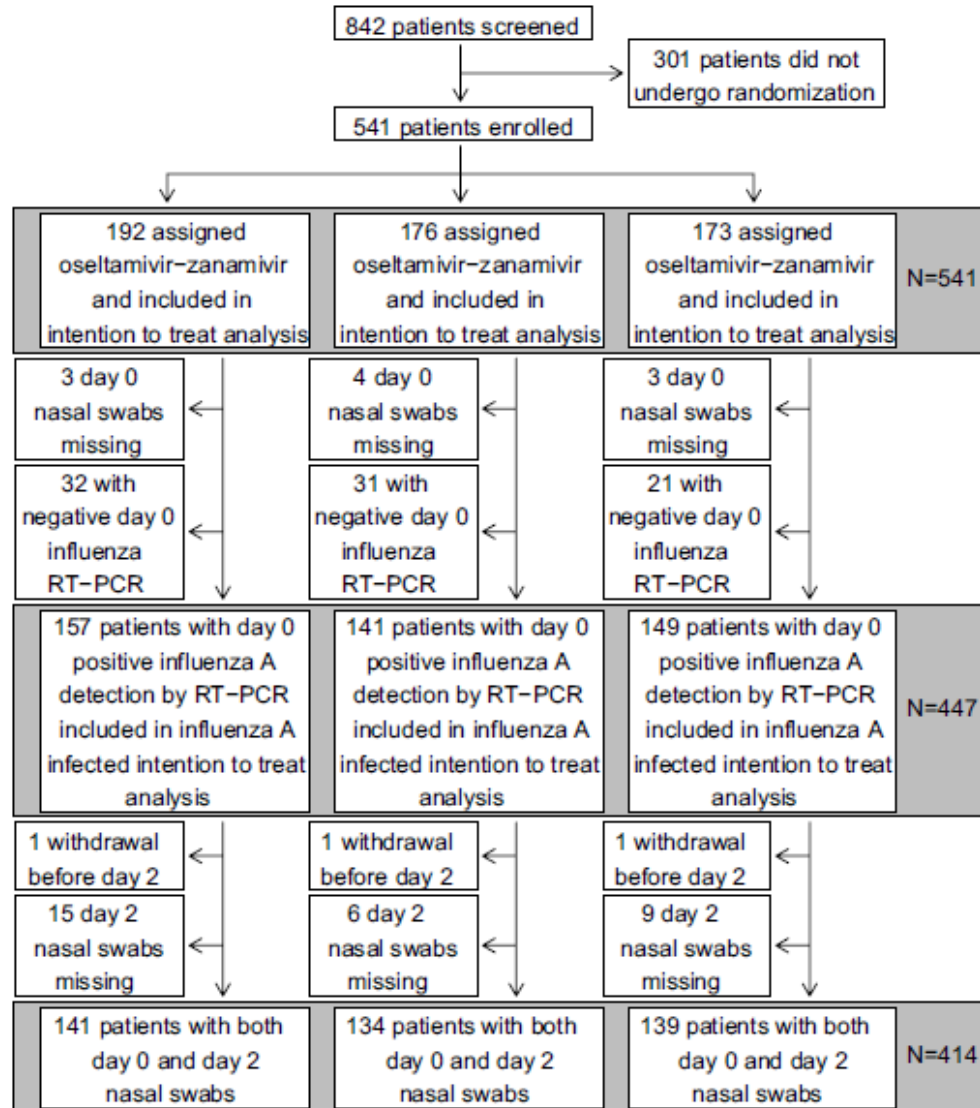
COMBINA

Oseltamivir-zanamivir or oseltamivir-amantadine combination therapies compared to oseltamivir monotherapy in the treatment of the A(H1N1)pdm09 virus

running title: Oseltamivir alone or in combination?

Vanessa Escuret^a, Catherine Cornu^c, Florent Boutitie^d, Vincent Enouf^b, Anne Mosnier^g, Maude Bouscambert-Duchamp^a, Ségolène Gaillard^c, Xavier Duval^e, Thierry Blanchon^h, Catherine Leport^f, François Gueyffier^c, Sylvie Van Der Werf^b and Bruno Lina^a

Essais cliniques (bivir)



Essais cliniques (bivir)

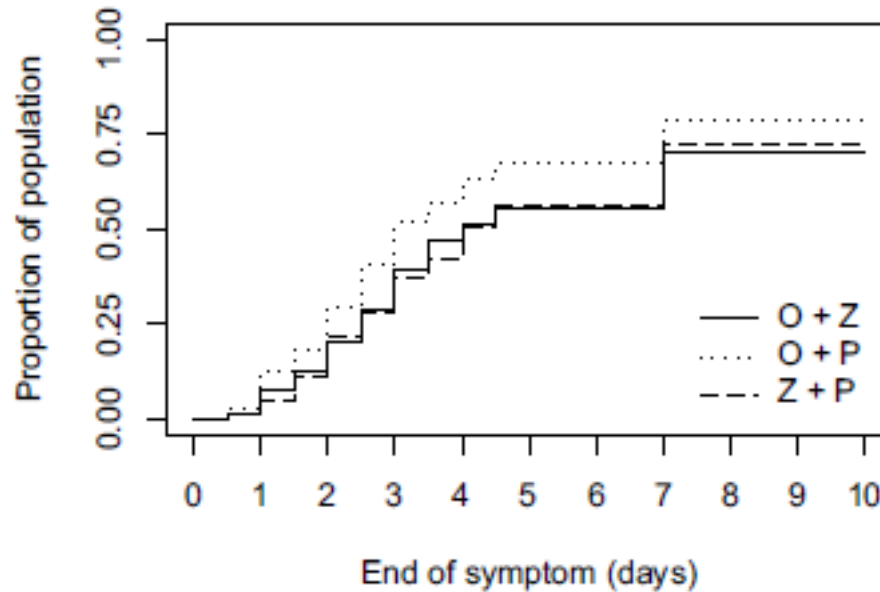
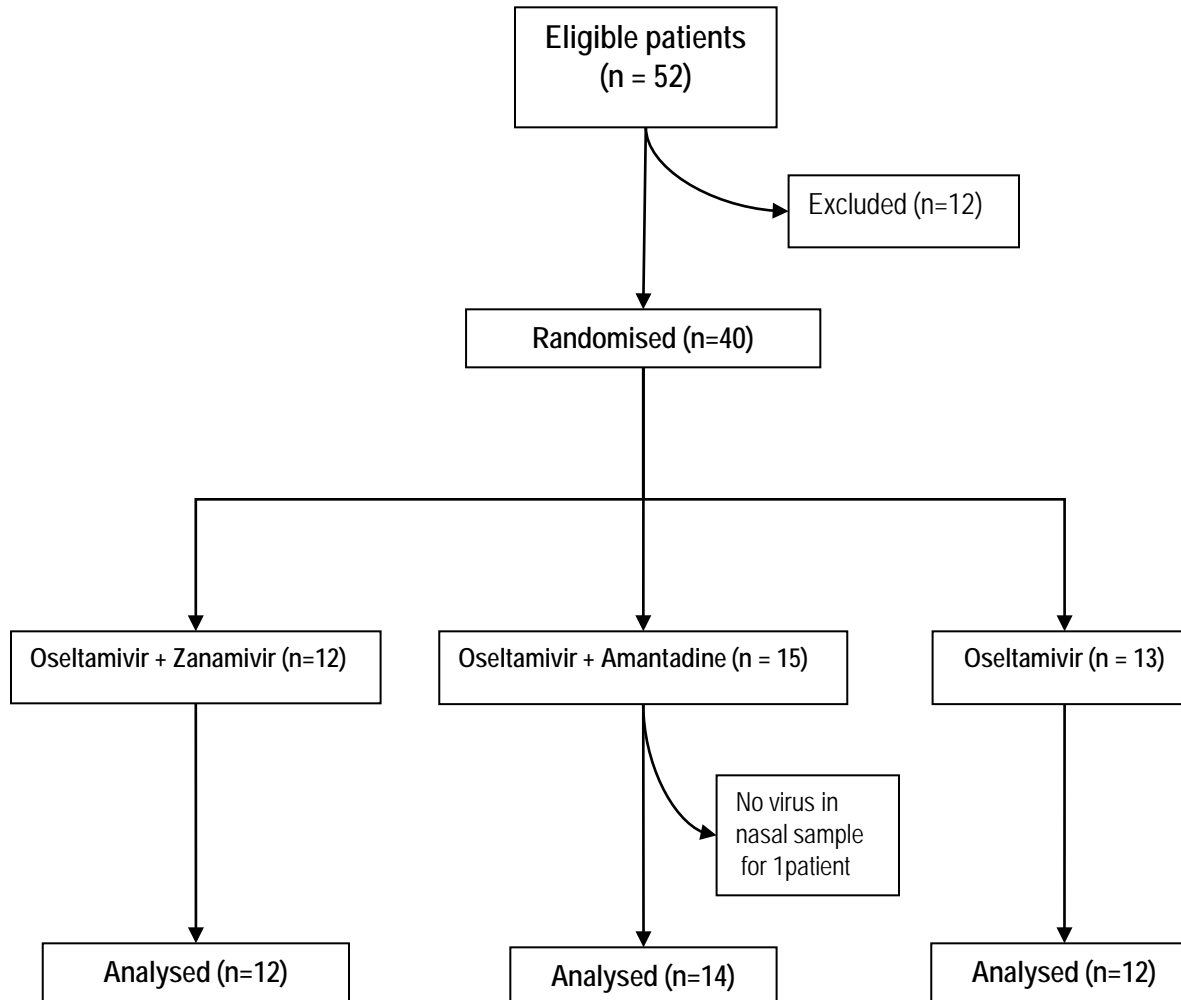
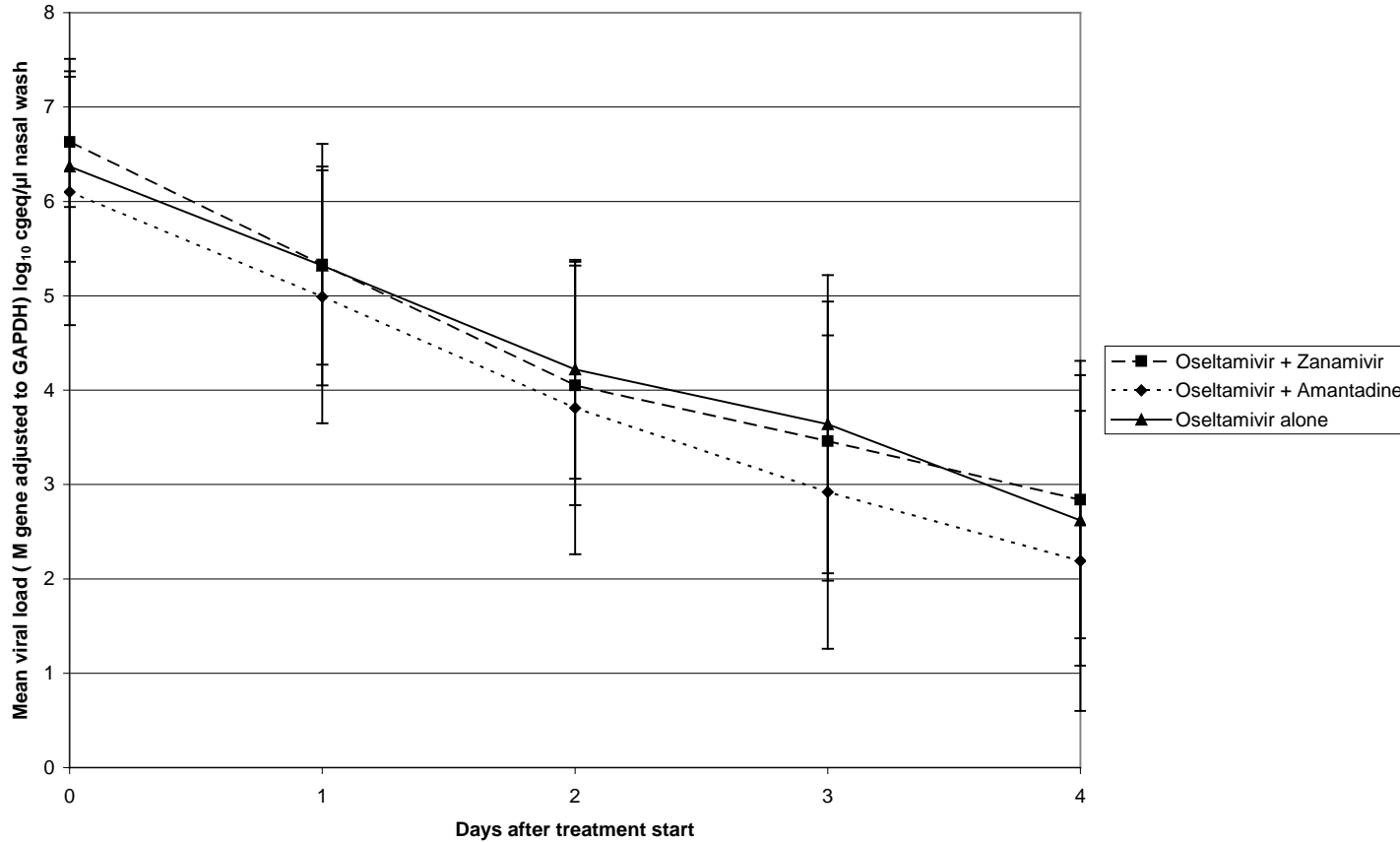


Figure 2. Proportion of the 447 influenza A-infected patients with alleviation of symptoms when treated with combined oseltamivir-zanamivir (plain line), oseltamivir plus placebo (dotted line), or zanamivir plus placebo (dashed line). Log-rank test for oseltamivir-zanamivir versus oseltamivir-placebo: $p=0.025$ and for oseltamivir-zanamivir versus zanamivir-placebo: $p=0.036$. Alleviation of symptoms defined by the presence of no symptoms of nasal stuffiness, sore throat, cough, muscle aches, tiredness-fatigue, feverishness, and headache or only mild ones, for at least 24 h.
doi:10.1371/journal.pmed.1000362g002

Essais cliniques (combina)



Essais cliniques (combina)



	(O+Z)	(O+A)	(O)	(O+Z) versus (O)	(O+A) versus (O)
Estimated Slope	0.96 (0.12)	1.00 (0.11)	0.94 (0.12)	0.90	0.68

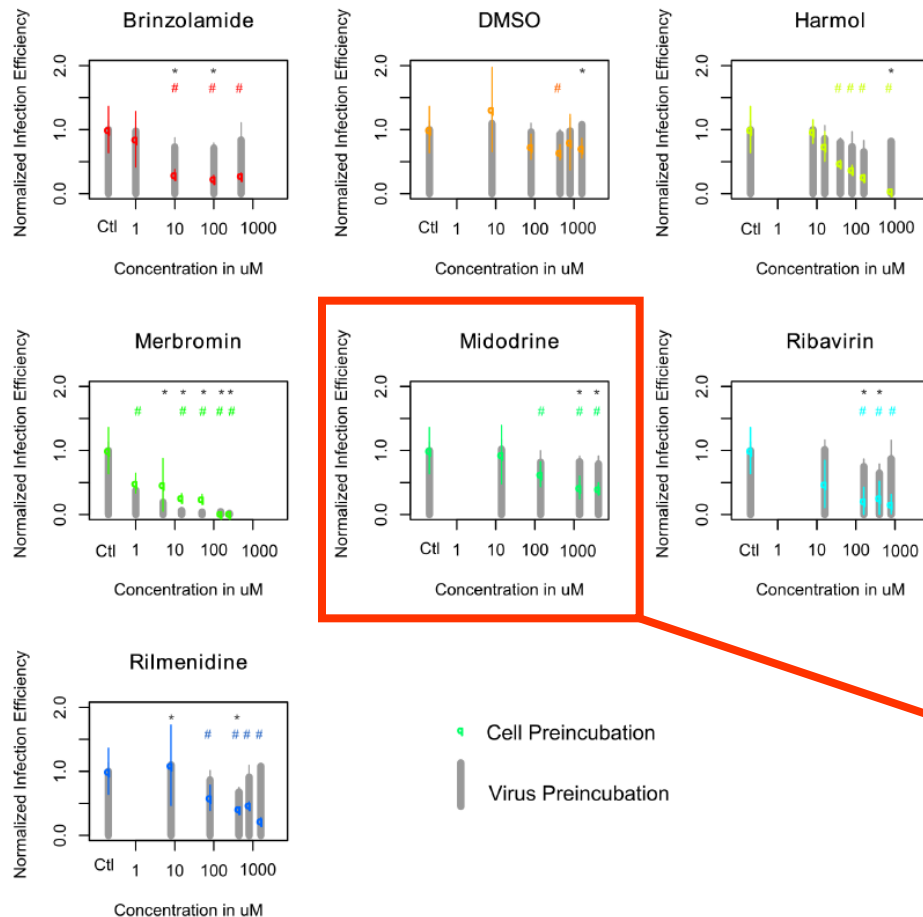
Essais clinique (recherche translationnelle)

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PLoS one

Gene Expression Signature-Based Screening Identifies New Broadly Effective Influenza A Antivirals

Laurence Josset^{1,2*}, Julien Textoris^{3,4,5}, Béatrice Loriod³, Olivier Ferraris¹, Vincent Moules¹, Bruno Lina^{1,2}, Catherine N'Guyen³, Jean-Jacques Diaz⁴, Manuel Rosa-Calatrava^{1*}



flumed

Au total

- Les CNR et le virologues associés à la surveillance de la grippe remercient vivement les médecins Vigies pour leur participation à la surveillance de la grippe, et pour l'envoi régulier de prélèvements aux laboratoires
- Les médecins Vigies sont priés de continuer....