

Preliminary summary on oseltamivir-resistant H1N1 virus: The Netherlands

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Over the 2007-2008 influenza season in the northern hemisphere influenza, a total of 140 A(H1N1) viruses were tested for oseltamivir resistance (H274Y and/or IC50 for oseltamivir >100 nM) in the Netherlands, of which 42 (30.0%) were found to be resistant (Table 1).

Data includes specimens collected up to 28 April 2008. Testing of further specimens is on-going and figures are subject to change.

Table 1: Trend resistant A(H1N1) viruses by month the specimens were collected*

Month of sampling	Sept 07	Oct 07	Nov 07	Dec 07	Jan 08	Feb 08	Mar 08
No. of H1N1 isolates tested	0	1	2	7	50	71	9
No. (%) of viruses resistant to oseltamivir	n/a	0 (0%)	0 (0%)	1 (14.3%)	12 (24%)	27 (38%)	2 (22.2%)

* part of the data was derived by direct sequencing of PCR positive clinical specimens

IMPORTANT

With the exception of the demography data, the dataset is not complete. It is anticipated that tracking of patient history and follow-up will continue for a further two months. Therefore, the data presented below should not be over interpreted.

Specimen collection sites:

Of the total viruses collected, 41 A(H1N1) viruses for which oseltamivir sensitivity is known were derived from specimens collected in a sentinel network of general practitioners, monitoring influenza-like illness (ILI) incidence from a sample of patients presenting with ILI or acute respiratory illness (ARI) and analysed at the NIC location RIVM, Bilthoven. Of these 41 viruses, 10 (24.4%) were found to be resistant.

The remaining 99 A(H1N1) viruses collected, for which oseltamivir sensitivity is known, were isolated at hospital laboratories and peripheral laboratories and were sent to the National Influenza Centre at the Erasmus Medical Centre, Rotterdam for further characterization. The source of the viruses – outpatient patient, hospitalized patient or patient in institution (e.g. nursing home) – is currently under investigation. Of these 99 viruses, 32 viruses (32.3%) were resistant.

There was no significant difference in the proportion of resistant viruses collected from each source ($p=0.35$ with chi square test).

Geographical distribution:

Preliminary data from the 41 viruses collected from the sentinel network showed a higher proportion of resistance in the western provinces of the country (Noord-Holland and Zuid-Holland) 9/19 (47.4%) compared to the rest of the Netherlands 1/22 (4.5%) ($p=0.001$ with chi square test). The geographical distribution of viruses from the non-sentinel system is under investigation.

Demography:

Specimens have been collected from both adults and children. Median age in years and inter-quartile range of patients with resistant and sensitive A(H1N1) viruses is shown in table 2. There were no significant statistical differences in age distribution between patients with resistant viruses and patients with sensitive viruses.

Table 2. Median age in years (inter-quartile range) of patient with oseltamivir resistant and sensitive A(H1N1) viruses.

Source	Median age patient (inter-quartile range)	
	Resistant virus	Sensitive virus
Sentinel	16.1 (8.4 – 34.0)	26.2 (12.3 – 37.0)
Non-sentinel	0.8 (0.3 – 22.3)	0.8 (0.4 – 6.6)
Total	1.0 (0.3 – 24.6)	4.1 (0.5 – 24.1)

There were no significant statistical differences in gender distribution between patients with resistant and sensitive A(H1N1) viruses (data not shown).

Oseltamivir use:

For the sentinel patients data on oseltamivir use was available for all 41 patients sampled. None of the sentinel patients (41) or their household contacts (40) reported the use of oseltamivir in the two weeks prior to the date of specimen collection.

For the non-sentinel patients, data on oseltamivir use was available for 15 patients (further data are currently being collected). None of the non-sentinel patients reported the use of oseltamivir in the two weeks prior to the date of specimen collection. Household contacts of one patient with an oseltamivir sensitive A(H1N1) virus had used oseltamivir in the two weeks prior to the date of specimen collection.

Vaccination history:

For the sentinel patients data about vaccination history was available for all 41 patients with an A(H1N1) virus. One of the sentinel patients was reported to have been vaccinated with the vaccine for the 2007/2008 season and was infected with oseltamivir sensitive A(H1N1) virus.

Two of the non-sentinel patients were reported to have been vaccinated with the vaccine for the 2007/2008 season. Both were infected with oseltamivir sensitive A(H1N1) virus.

Clinical features:

Clinical data was available for 29 sentinel patients and 15 non-sentinel patients with A(H1N1) virus infection (further data are currently being collected).

Among sentinel patients with a resistant A(H1N1) virus, 1 of 7 patients (14.3%) reported complications and among patients with a sensitive A(H1N1) virus, 2 of 22 (9.1%) reported complications. Among non-sentinel patients with a resistant A(H1N1) virus 2 of 6 patients (33.3%) reported complications and among patients with a sensitive A(H1N1) virus, 3 of 8 (37.5%) reported complications. Complications mentioned were for example: pneumonia, otitis media and sinusitis. The percentages of clinical complications between patients with a sensitive virus or resistant virus were not significantly different for sentinel as distinct from non-sentinel patients.

None of the sentinel patients was hospitalized. Of the non-sentinel patients 3 of 7 (43%) patients with a resistant virus and 4 of the 8 (50%) patients with a sensitive virus were hospitalized.

None of the 29 sentinel and 15 non-sentinel patients died within 4 weeks after the first day of illness.

Special underlying conditions:

Data for sentinel and non-sentinel patients are currently being collected.

Other findings:

Information is currently being collected.

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