



Nov.23, 2015

HPV vaccination associated with neuro-immunopathic syndrome (HANS)

Kusuki Nishioka, MD

Professor of Medicine,
Director, Institute of Medical Science,
Tokyo Medical University



Relations with our HPV vaccine adverse reaction from when? Why not?

Nov 23, 2015

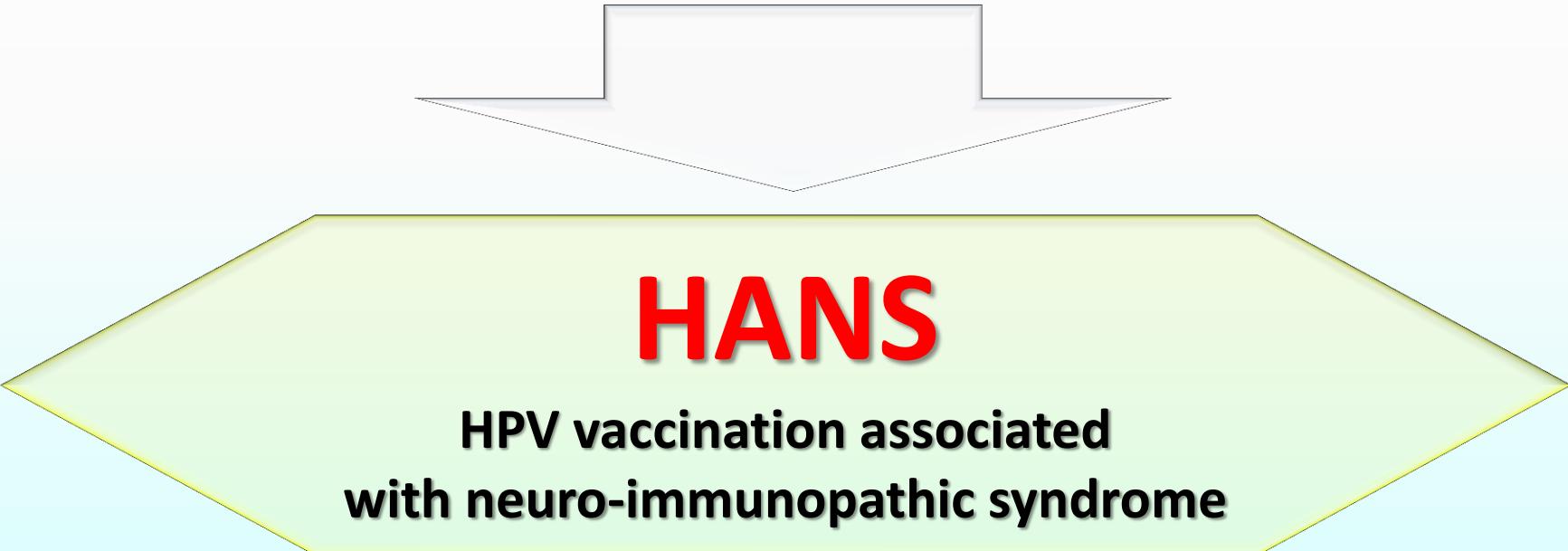
November 2013	Patients like to introduce consultation with fibromyalgia specialist foreign to juvenile fibromyalgia (JFM) has increased
March 2014	<p>It was found that there is a HPV vaccination history in juvenile fibromyalgia patients like 20 people</p> <p>The patients are in addition to the extensive pain had developed symptoms of a variety of central nervous</p>
May 2015	Japan Medical Research Foundation HANS Project Team start

— Study contents —

- A Start a study group by expert researchers
- B Start a medical consultation
- C A study of protocol design and the global common protocol
- D Analysis of vaccination age-adverse reaction onset age, time of onset, living area and clinical symptoms
- E Pathological analysis of basic study
- F Construction of medical care network for patients relief
- G Promotion of model hospital expansion of patient relief in the community



A new syndrome with clinical features of subacute and multilayered manner after HPV vaccination



HANS

**HPV vaccination associated
with neuro-immunopathic syndrome**



Proposed Preliminary Diagnostic Criteria for The Diagnosis of “HANS”

-According to Clinical Symptoms with HANS Patients-

Nov.23, 2015

Major Criteria : Vaccination of human papillomavirus (HPV)

- No abnormality of physical / psychological condition before vaccination of human papillomavirus
 - Wide spread pain
 - Arthralgia and/or arthritis
 - Chronic fatigue, Central nervous system disorder
 - Neurological manifestations
(especially associated demyelination, narcolepsy)
 - Memory impairment
- The appearance of “typical clinical manifestations”

Minor Criteria

- Amenorrhea,
- Vagus nerve disease
- Spinal fluid abnormality
- Involvement of an autoimmune disease (i.e. MS, SSc)



Number of Multilayered Symptoms in 104 Cases with HANS

No. 28 2015

2015/11/2
N=201

2015年後期
JUL～NOV, 2015

49

2015年前期
JAN～JUN, 2015

64

2014年後期
JUL～DEC, 2014

52

2014年前期
JAN～JUN, 2014

34

May-2014 HPV Vaccination Project Term

2013年

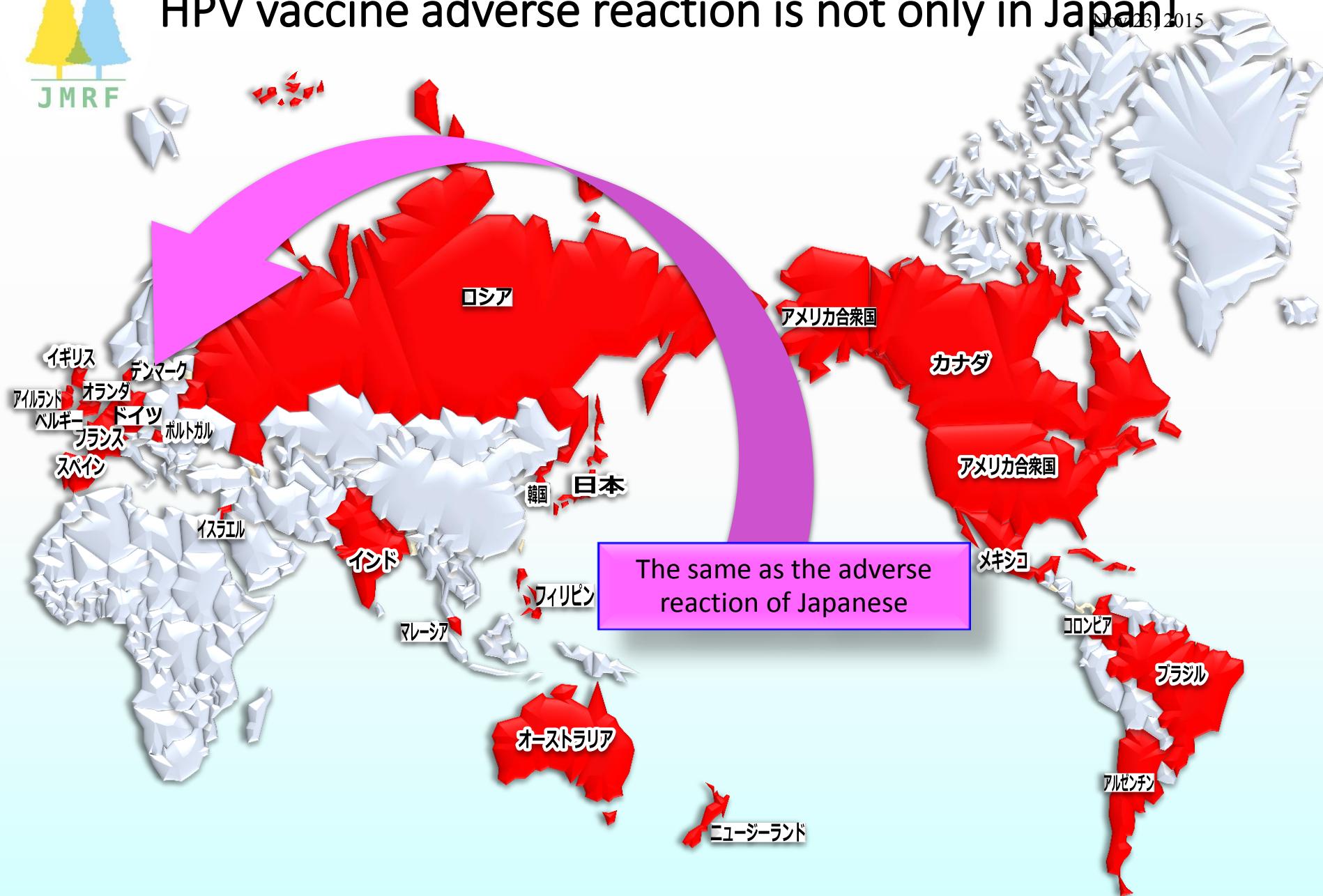
2

0 10 20 30 40 50 60 70 人



HPV vaccine adverse reaction is not only in Japan!

2015/06/23





Global incidence of HPV vaccine adverse reaction

Nov.23, 2015

	DK	GB	AU	US	FR	JP
Adverse reaction	Number of cases	1,730	8,243	3,530	25,176	2,092
	Number of reactions	11,529	19,359	8,815	ND	5,850
Vaccination	Number of doses	1,635,768	ND	9,000,000	67,719,000	5,240,000
	Number of people	630,000 ^b	ND	3,460,000	26,050,000	2,020,000
Vaccination / 1,000 adverse reaction number of cases		2.7	ND	1.0	1.0	1.3

* : PMDA+ MHLW data

a : ANSM : Estimated from described, b : Estimate value = Doses per 2.6

DK: [DHMA](#), Drug Analysis Print : Data lock 2015/7/31

GB: [MHRA](#), Case Series Drug Analysis Print : Data lock 2015/6/5

AU: [TGA](#), DAEN (Database of Adverse Event Notifications) : Data lock 2015/4/16

US: [CDC](#), MMWR(Morbidity and Mortality Weekly Report), Recommendations and Reports 63(5) : 2014/8/29

FR: [ANSM](#), Suivi National **Gardasil®**, 3^{ème} rapport Vaccin contre le papillomavirus human : 2014/2/18

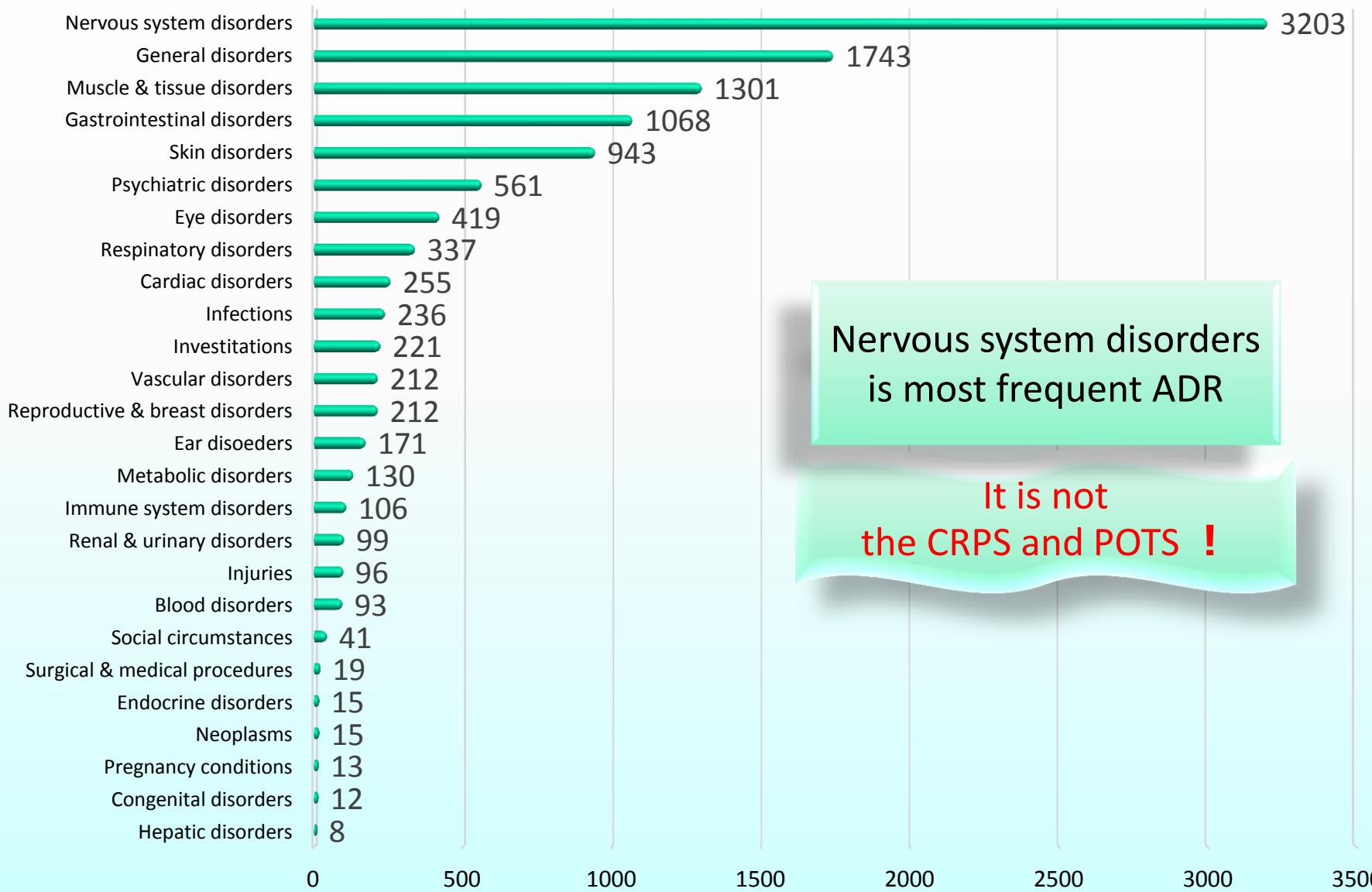
JP: [PMDA](#) Adverse Reaction Database : Data lock 2015/3/31

[MHLW](#), 10th Examination Meeting for Adverse Reaction of Immunization and Vaccine Subcommittee of MHLW Health Sciences Council, data No.1-8 (Data lock 2014/3) : 2014/7/4

Analysis of 11,529 clinical symptoms associated in Danish 1,730 cases with adverse reactions after HPV vaccination

Nov 23, 2015

Report of Adverse reaction by Drug Analysis Print 31. JUL. 2015



Nervous system disorders
is most frequent ADR

It is not
the CRPS and POTS !



Regional distribution of patient 201 cases who received medical consultation

2015/11/2
Nov.23, 2015
N=201

Medical consultation start of the
HPV vaccine adverse reaction
from May 2014



不明
8名

ドイツ
1名



山形県
1名

新潟県
4名

長野県
2名

石川県
2名

京都府
5名

大阪府
12名

滋賀県
2名

愛知県
12名

静岡県
3名

奈良県
4名

三重県
6名

和歌山県
2名

山梨県
2名

神奈川県
23名

東京都
39名

埼玉県
12名

千葉県
14名

群馬県
4名

栃木県
4名

茨城県
3名

福島県
3名

宮城県
3名

福島県
3名

Vaccination age and adverse reaction age at onset of the 104 cases of patients who are diagnosed with HANS

2015/11/2
N=104

1st vaccination age **11～25 years** **14.3 ± 2.3**

adverse reaction age **12～25 years** **15.3 ± 2.5**

contact age **13～27 years** **17.6 ± 2.5**

1st vaccination age

<12 years 20

13～15 years 63

16～18 years 16

>19 years 5



104 analysis of the overlapping symptoms of 4,455 clinical symptoms associated with the example of HANS

Nov.23, 2015

2015.11.2



101-110

91-100

81-90

71-80

61-70

51-60

41-50

31-40

21-30

11-20

1-10

1

1

4

5

7

18

18

17

18

10

5

Overlapping symptoms 4,455

Mean 42.2 ± 20.4

Max 107

Minimum 4

0 2 4 6 8 10 12 14 16 18 20 n

N=104

Characteristic of time-series change of symptoms in HANS patients

Nov.23, 2015

Locomotive disorders

(Gait disturbance)

→Wheelchair,

Bedridden

Consecutive involuntary movement
of whole body

HPV vaccination



Fatigue, Sluggishness,
Malaise

Widespread pain,
Numbness

Brainstem
abnormality

Autonomic nerve system disorders

The symptoms
gradually became
multilayered as time
from vaccination
increased, and their
severity varied from
day to day

Consciousness disorders

Recent memory
impairment,
Epileptic seizure

3 years after HPV vaccination

1st stage

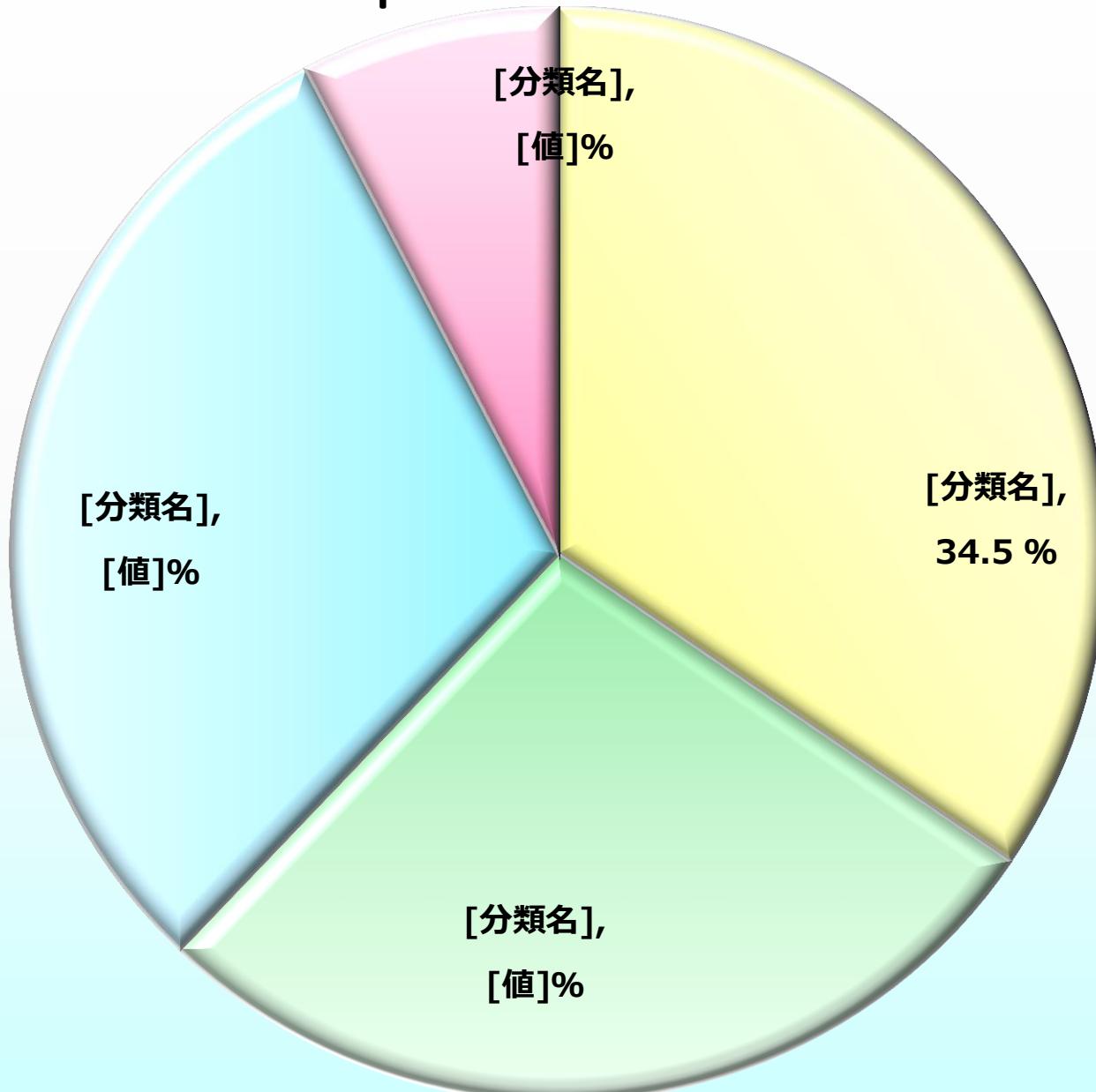
2nd stage

3rd stage

Symptomatic another adverse reaction incidence of HANS patient 104 cases

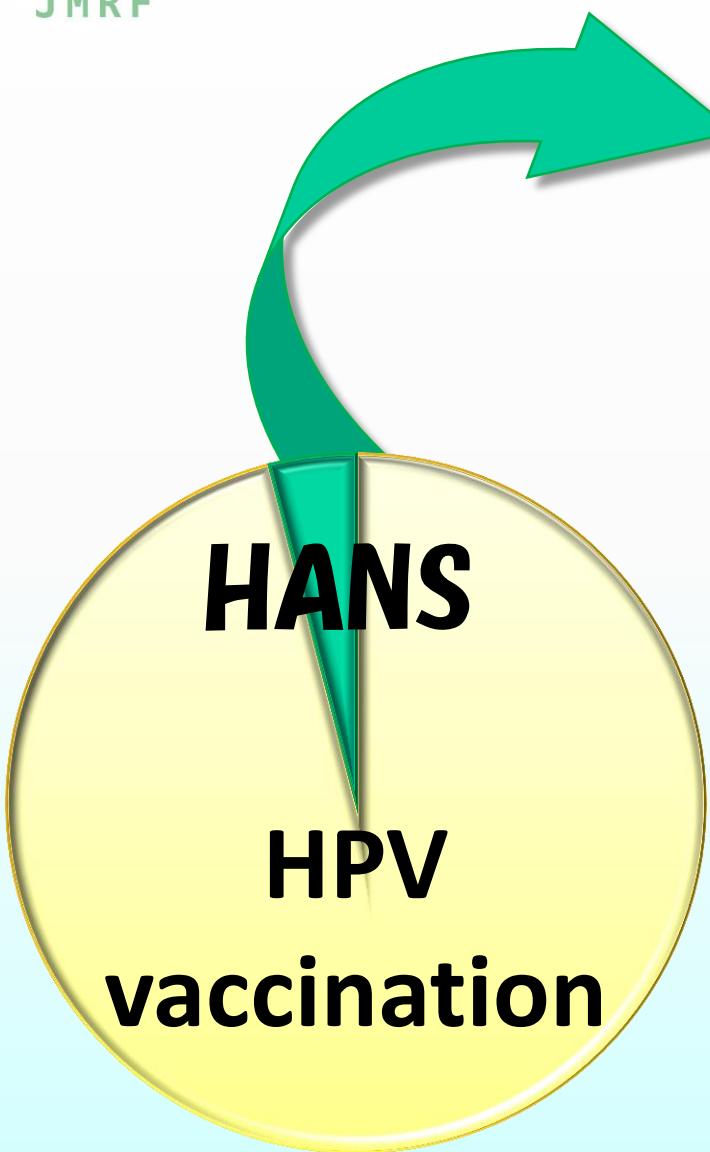
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2015/11/2現在
N=104



Classification of clinical symptom

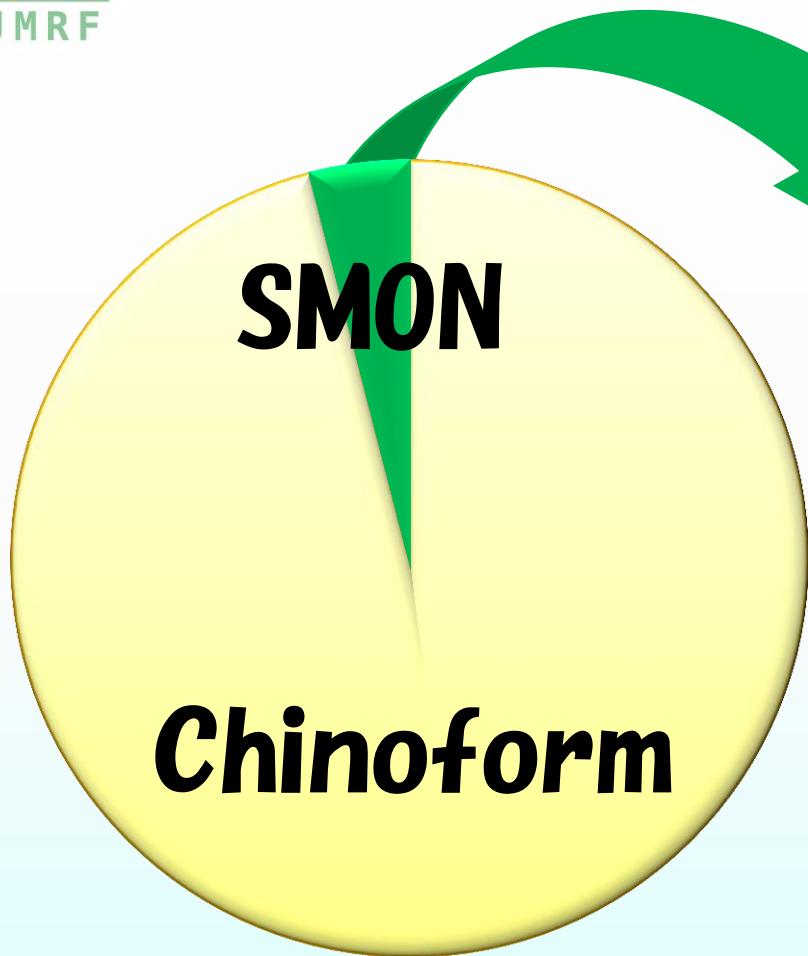
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pain in extremity, widespread pain, photosensitivity reaction, hyperesthesia, acoustic hyperesthesia, hypersomnia, severe menstrual pain	Sensory system disorders
irritable bowel syndrome, bulimia, hyperventilation, asthma, fever, hypothermia, hyperhidrosis, circadian rhythm disorder (sleep disorder), orthostatic syncope, menstruation irregularity, narcolepsy,	Autonomic nerve and endocrine system disorders
posture abnormal, dysstasia, gate disturbance, involuntary movement, convulsion	Locomotor system disorders
apathy, fatigue, irritability, visual hallucination, auditory hallucination, delusion, abusive speech, refusal to attend school, panic attack, prosopagnosia, dyscalculia, poor concentration, decline in academic performance	Cognitive dysfunction and emotional disorders

SMON : The drug induced damage affair

Nov.25, 2015



onset in dysesthesia

dysesthesia of bilaterality

Locomotor system disorders

pyramidal sign

visual disorder of bilaterality

brain inflammation

psychiatric symptom

bladder and rectal disturbance

nervous system • sensory system •
locomotor system , etc

1950

Symptom finding

1958

The first case was reported from Wakayama Medical University

1964

The proposal the SMON (Prof. Tsubaki • Prof. Toyokura, et al.)