Favorable outcome of patients with Kawasaki disease treated with unified protocol with Cyclosporine A as the third line therapy

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## **Presenter Disclosure Information**

Hiromichi Hamada Favorable outcome of patients with Kawasaki disease treated with unified protocol with Cyclosporine A as the third line therapy

FINANCIAL DISCLOSURE: No relevant financial relationship exists

UNLABELED/UNAPPROVED USES DISCLOSURE: Cyclosporine A

## IVIG non-responders in Japan

26691 KD patients were reported between 2011-2012 (two years) in Japan. Among them, 24346 patients received IVIG, and 4150 (17.0%) did not respond it.

## 4150 / 24346= 17.0%

Nakamura et al: 22nd report of Nationwide study of Kawasaki disease in Japan, 2013

## Cyclosporine A for Kawasaki disease

Raman V, Kim J, Sharkey A, et al. *Pediatr Infect Dis J* 2001;20:635–637.

Kuijpers TW, Biezeveld M, Achterhuis A, et al. *Pediatrics* 2003;112:986-92.

Suzuki H, Terai M, Hamada H, et al. Pediatr Infect Dis J 2011;30:871-6

Tremoulet AH, Pancoast P, Franco A, et al. *J Pediatr* 2012;161:506-512.

## Hypothesis of CsA as a targeting drug

Patients with  $KD \rightarrow SNPs$  are found in *ITPKC and CASP3* 

 $\Rightarrow$ Function of *ITPKC*, *Caspase3* is down  $\rightarrow$  <u>excess inflammatory cytokines</u>



⇒Normal function of ITPKC, Caspase3 is to suppress excessive activation of immune cells

## Aim

## We examine result of the unified protocol using CsA as a third line therapy for IVIG non-responders between 2008-2014.

## Patients

KD patients who admitted in our hospital and received initial treatment were included for analysis.

Jan. 2008 - Apr. 2014

n= 441, male / female=252 / 189

Age; 1month to 11years, median= 2y3mo,



CsA; Cyclosporine A

## Result; IVIG response



## Case #1; 3ys old: CAL-



# Case#6; 1 y old: CAL-



## CsA for 14-21days as a third line therapy

#### ORIGINAL STUDIES

#### Cyclosporin A Treatment for Kawasaki Disease Refractory to Initial and Additional Intravenous Immunoglobulin

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#### n=28

(Suzuki H, et al. *Ped Infect Dis J* 2011)

Background: There are still no definite treatments for refractory Kawasaki

disease (CyA)

Metho

 $\mathbf{K}$ awasaki disease  $(\mathrm{KD})^1$  is an acute systemic vasculitis oc-

★ 78% of patients got afebrile within 5 days on CsA.

# There are no serious adverse effects by CsA in KD patients

## Modification of the protcol: short-term CsA treatment (2011-2014)



CsA; Cyclosporine A

11 patients received CsA treatment according this protocol

## Case #11: 1y old; CAL-



## Case #13: 3yrs old ; CAL+



### 11 cases with short-term CsA treatment Data before CsA treatment n=11



CsA: Cyclosporin A

## 11 cases with short-term CsA treatment Result 1



CAL: Coronary artery lesion CsA: Cyclosporine A Day: Day of illness

## 11 cases with short-term CsA treatment Result 2



## **Coronary complications**



## Summary

441 KD patients were treated on unified protocol with oral CsA following 3<sup>rd</sup> IVIG as the third line therapy.

There were no serious adverse events associated with CsA.

Occurrence of CAL was 1.1%. Maximum coronary diameter of the 5 patients with CAL was 5.5mm.

When patients did not get afebrile with CsA, 3<sup>rd</sup> IVIG was effective in these patients. CsA might affect on immune and inflammatory systems and modify IVIG responsiveness. 146: H.Suzuki; Tomorrow Poster



#### Aomori Honsh Akita Morioka Acknowledgement

Prof. Masaru Terai, MD

## **Clinical Reseach Team**

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## Pediatric Care Team

Character TYMC Greens!!

