



# **THE INCIDENCE OF NON-HODGKIN'S LYMPHOMA IN THAI COMMERCIAL AIRLINE PILOTS BETWEEN 2015-2017**

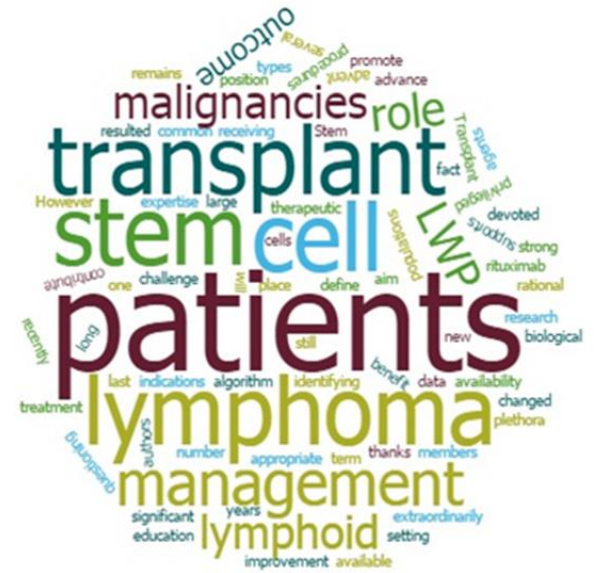
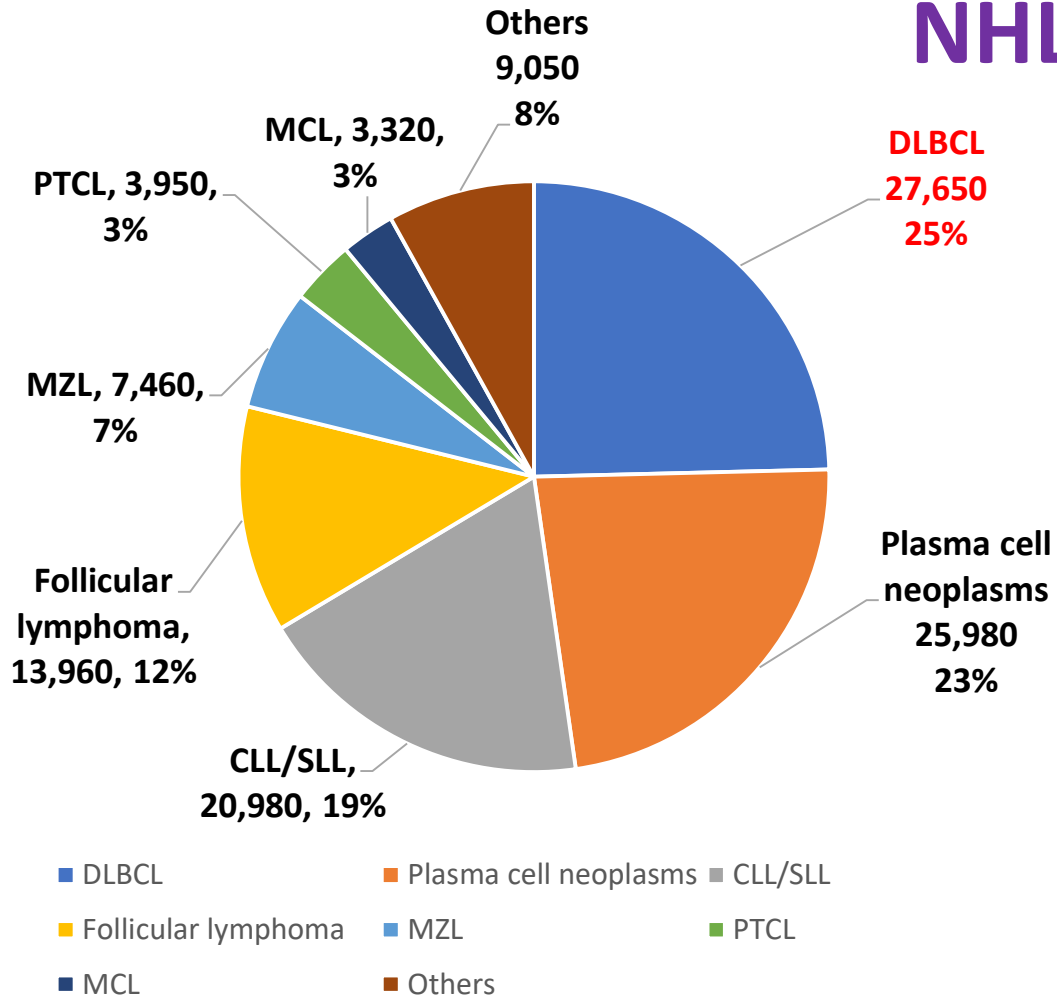
**Wg.Cdr.Hatairat Paowichan**

**Institute of Aviation Medicine Royal Thai Air Force**

# Disclosure

I have no actual or potential conflict of interest in relation to this presentation.

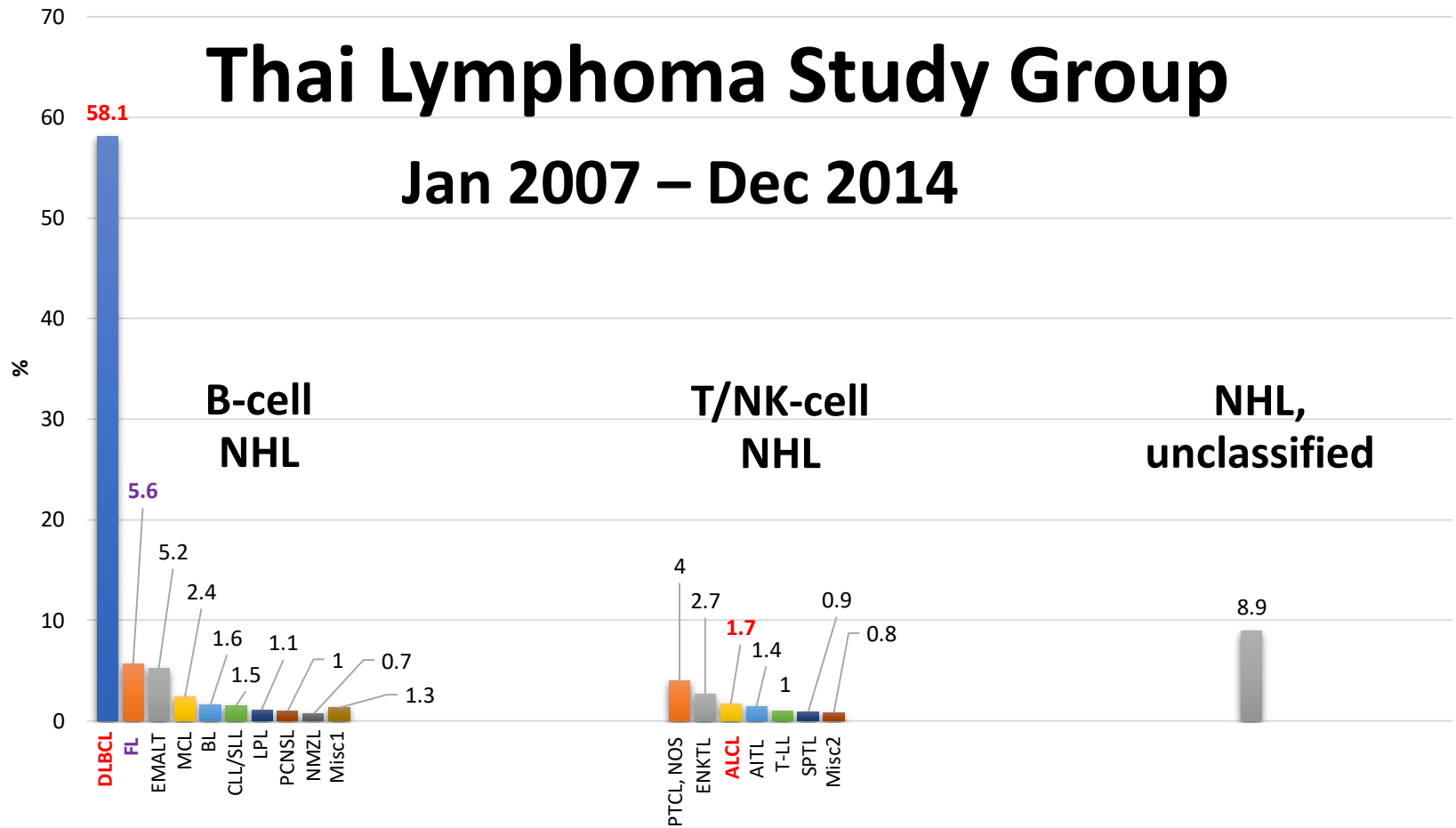
# NHL



2016 US lymphoid malignancy statistics by World Health Organization subtypes, Vol. 66, 6: 443-459

# Thai Lymphoma Study Group

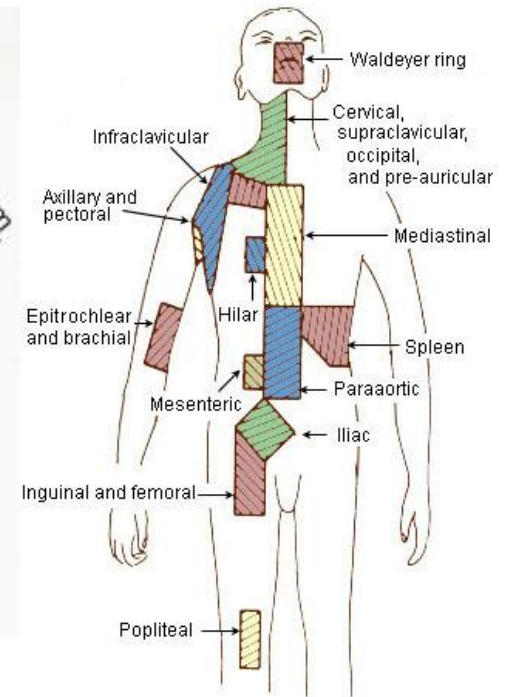
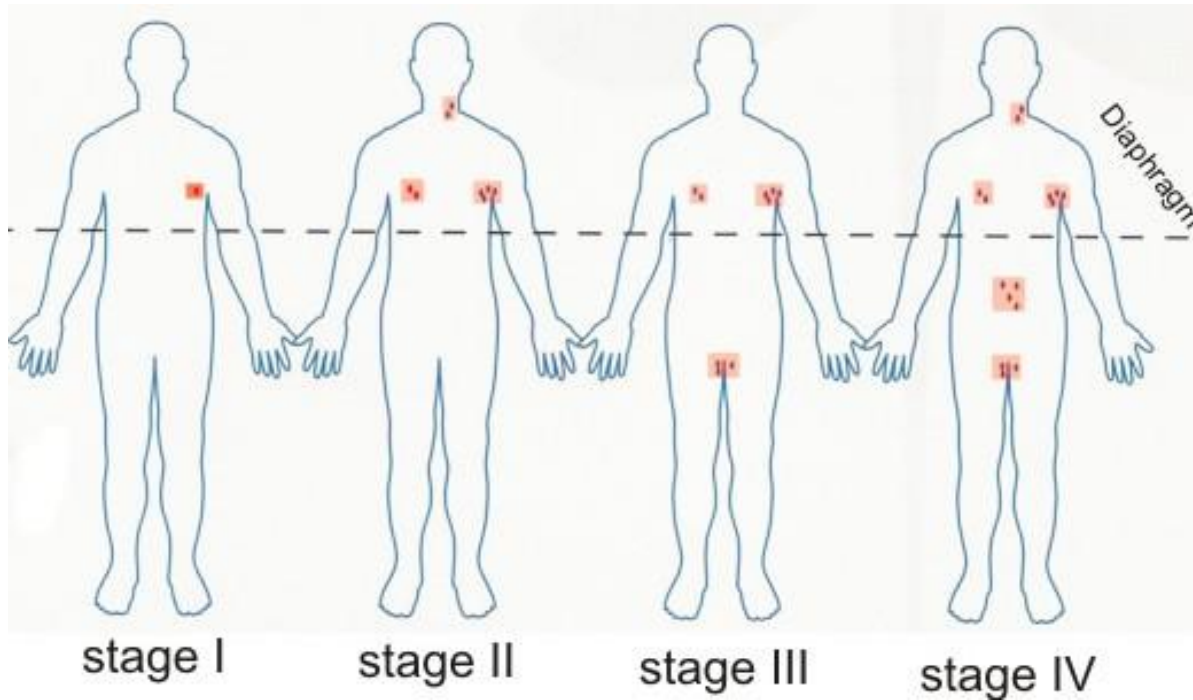
Jan 2007 – Dec 2014



Hematological Oncology.2018;36:28-36.



# Ann Arbor Staging



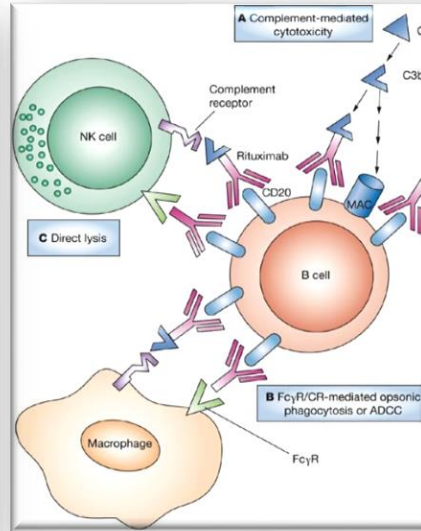
# Treatment



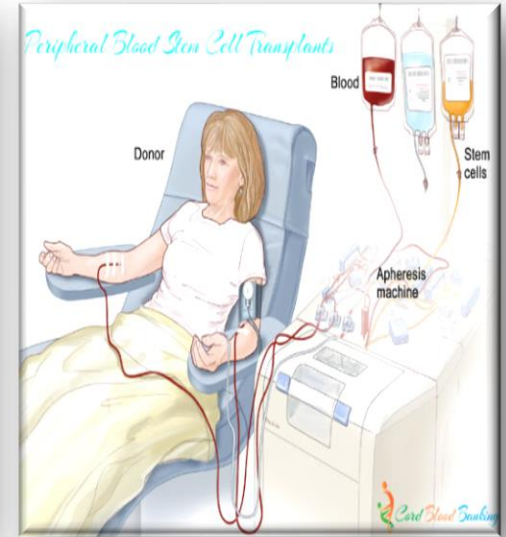
Chemotherapy



Radiation



Immunotherapy/  
Targeted therapy

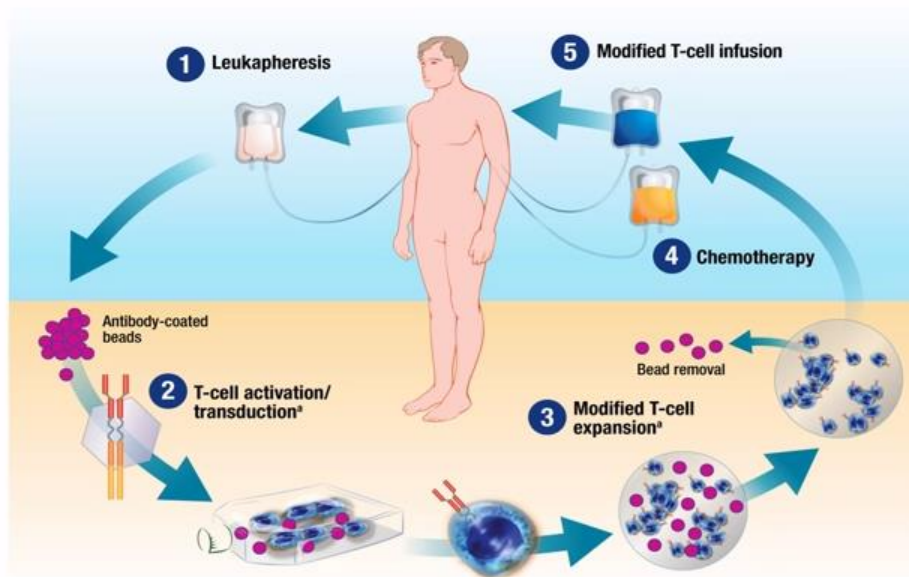


Stem cell  
transplantation

# Chimeric antigen receptor targeting CD19 therapy

The CAR T cell therapeutic approach involves the **adoptive transfer of autologous T cells** that have been **genetically modified** to express **anti-CD19 CARs** into patients

## CAR-T-cell production<sup>1</sup>



Cellular reprogramming and ex vivo expansion are conducted at a cell processing facility.

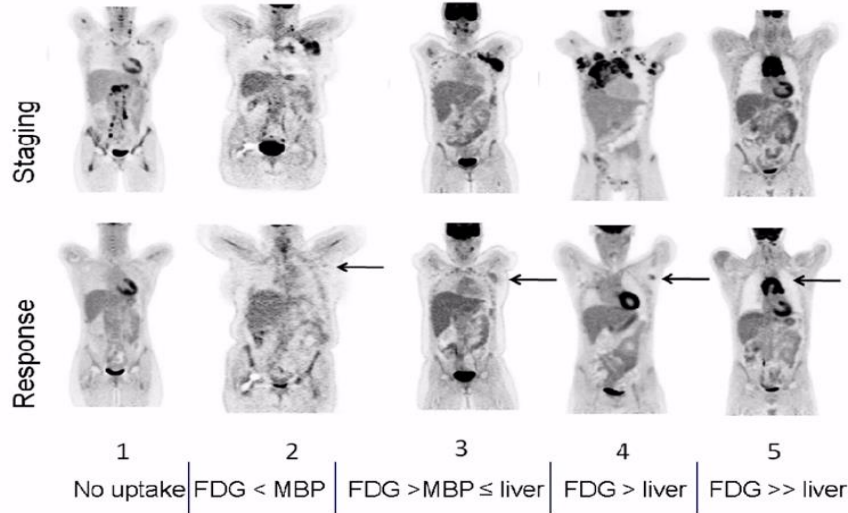
- 1. Leukapheresis:** patient's T cells are harvested<sup>2-4</sup>
2. Bridging chemotherapy
- 3. T cells are activated** on antibody-coated beads **and genetically transduced ex vivo** with a construct encoding the anti-CD19 CAR<sup>2-4</sup>
- 4. CAR T cells undergo ex vivo expansion** on antibody-coated beads<sup>2-4</sup>
- 5. Chemotherapy:** patient receives a preparative lymphodepleting regimen before T-cell infusion<sup>2-4</sup>
- 6. CAR T cells are reinfused** into the patient<sup>2-4</sup>

1. Levine BL. Cancer Gene Ther 2015;22:79-84; 2. Kalos M, et al. Sci Transl Med 2011;3(95):95ra73; 3. Porter DL, et al. J Cancer 2011;2:331-2; 4. Porter DL, et al. New Engl J Med 2011;365(8):725-33.



# PET/CT scan

## Deauville score 1-5 (visual)

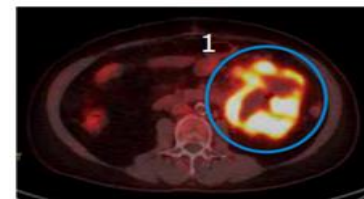
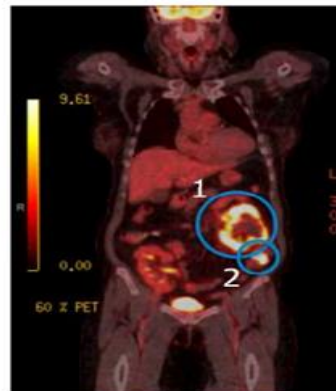
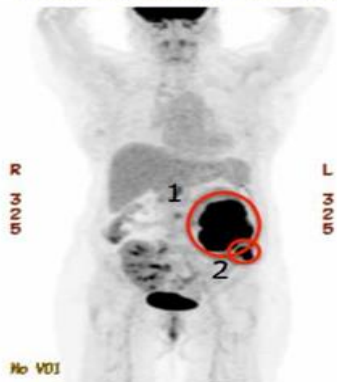


DS 1-3 : complete metabolic response

DS 4: partial metabolic response?

DS 5: stable disease/**progression**

Clinical Context: declined chemotherapy, suspicion of recurrence.  
 Findings: **Deauville 5. New FDG-avid foci.** Left-sided abdominal FDG-avid masses.  
<sup>1</sup>11.1x8.3x11cm, <sup>2</sup>2.3x2.1cm





# Evaluation

- Physical : Hematologist  
Cardiologist
- Mental : Psychiatric team  
Interview  
Psychological test

### Certification following treatment for Lymphoid Malignancy

| Group          | Potential Cure Rates                                    | Diagnosis  | Minimum time to certification after completion of treatment |   |
|----------------|---|--|---|---|
|                |   |  | Class 1 OML<br>Class 2 Unrestricted                         | Class 1 Unrestricted                              |
| <b>Group A</b> | >80%  | MZ MALT (stage I/II)<br>DLBC (stage I/II)<br>ALCL (stage I/II)<br>Solitary Plasmacytoma  | Once pre-requisites satisfied                               | 2-6 months<br>(dependent on type of chemotherapy) |
| <b>Group B</b> | 50%   | Primary Mediastinal Lymphoma   | 6 months  | 2 years   |
| <b>Group C</b> | 30%   | DLBC (stage III/IV)<br>ALCL (stage III/IV) including ALK negative<br>MZ MALT (stage III/IV)  | 1 year  | 2 years   |
| <b>Group D</b> | 30%   | Burkitt's/Burkitt-like Lymphoma<br>Pre-B Lymphoblastic Lymphoma/Leukaemia<br>B-cell Lymphoblastic Lymphoma/Leukaemia<br>Multiple myeloma (post BMT-csd)  | 2 years   | 3 years   |
| <b>Group E</b> | 10-20%  | Pre-T ALL<br>Pre-T LBL<br>Mantle cell lymphoma (2 years symptom free)  | 2 years   | 3 years   |
| <b>Group F</b> | <10% and moderately aggressive                          | Other Peripheral T-cell and NK Lymphoma/Leukaemia<br>Adult T-cell Lymphoma (HTLV+)<br>Mantle Cell Lymphoma<br>Multiple Myeloma (Other)<br>Subcutaneous panniculitis T-cell lymphoma                              | 5 years<br>See text   | N/A   |
| <b>Group G</b> | Considered incurable using current therapy but indolent | Follicular Lymphoma<br>SLL<br>B-cell CLL<br>Lymphoplasmacytic Lymphoma<br>T-cell Prolymphocytic Leukaemia<br>T-cell Granular Lymphocytic Leukaemia<br>Hairy Cell Leukaemia<br>MZ B-cell Lymphoma (nodal/splenic) | See text  | See text  |
| <b>Group H</b> | A miscellaneous group with a generally good prognosis   | Primary Cutaneous Lymphoma   | Once wound healed   | Once wound healed                                 |
| <b>Group I</b> | Poor prognosis  | Mycosis fungoides/Sezary syndrome  | See text  | See text  |
| <b>Group J</b> | > 60%   | Hodgkin's lymphoma   | 6 months  | 2 years   |

|               |           |  |
|---------------|-----------|--|
| <b>Legend</b> | ALCL      | Anaplastic Large Cell Lymphoma                         |
|               | ALK       | Anaplastic Lymphoma Kinase                             |
|               | BMT-csd   | Bone Marrow Transplantation – compatible sibling donor |
|               | CLL       | Chronic Lymphocytic Leukaemia                          |
|               | DLBC      | Diffuse Large B-cell Lymphoma                          |
|               | HTLV      | Human T-cell Lymphoma/Leukaemia Virus 1                |
|               | MZ        | Marginal Zone Lymphoma                                 |
|               | MALT      | Mucosa-Associated Lymphoid Tissue                      |
|               | N/A       | Not applicable   |
|               | NK        | Natural Killer   |
|               | Pre-T ALL | Precursor T-cell Lymphoblastic Leukaemia               |
|               | Pre-T LBL | Precursor T-cell Lymphoblastic Lymphoma                |
|               | SLL       | Small Lymphocytic (B-cell) Lymphoma                    |

## **Study design**

Retrospective

## **Objective**

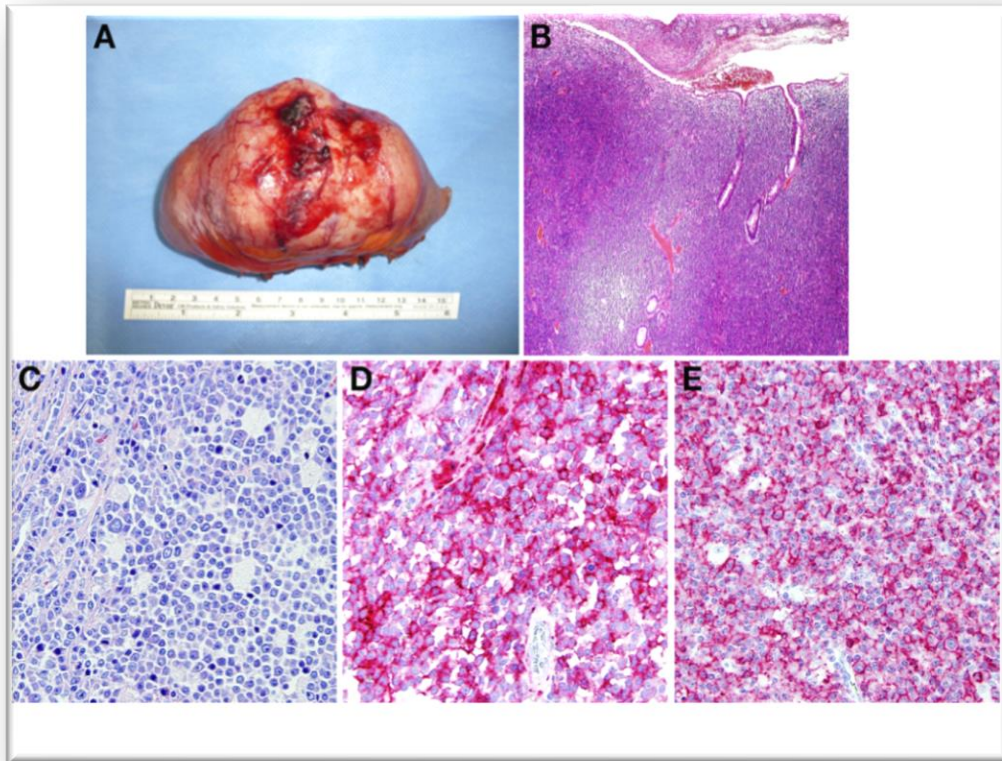
Know incidence of  
Non-Hodgkin's lymphoma  
in Thai commercial pilots

## **Method**

- Available medical documents
- Institute of Aviation Medicine  
Royal Thai Air Force
- 1 Jan 2015 - 31 Dec 2017

# Results

- 4 cases of NHL were found
- From 3,124 commercial airline pilots
- 1.28 : 1,000
- Males
- Thai



## Case 1

**Diffuse large  
B cell  
lymphoma  
at small  
intestine**


Clinical gastroenterology and hepatology 2012;10:e89-e90

# Case 1

- A 55 years old Thai male
- Microcytic anemia : Hb 9.1 g/dL Hct 29.8%  
WBC 10,020/mm<sup>3</sup> Plt. 454,000/mm<sup>3</sup> MCV 73.9
- Work up : antral gastritis , internal hemorrhoid
- Hematochezia → explore lap → small bowel resection
- Patho : Diffuse large B cell lymphoma
- CD 3 -, CD 20 + , CD 10 -, BCL6 + , MUM1 + , Ki67 : 40-60%

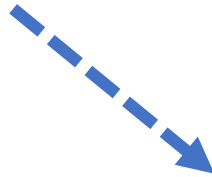


# Case 1

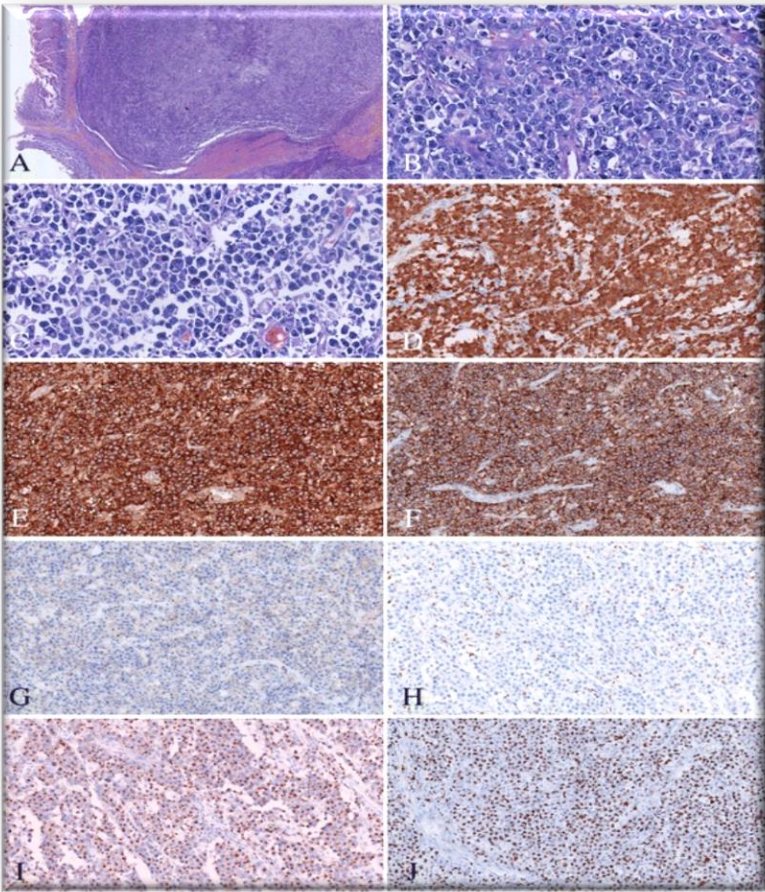
- Dx. Diffuse large B cell lymphoma (DLBCL) stage IIBE
  - Chemotherapy : R-CHOP-21 regimen x 6 cycles  
(Rituximab , Cyclophosphamide , Vincristine ,  
Doxorubicin , Prednisolone)
  - PET/CT (1 month after last chemotherapy) :  
multiple pulmonary nodules both lungs , lesion at cecum
- 
- Dx. **Refractory** diffuse large B cell lymphoma

# Case 1

- After diagnosed as refractory DLBCL
- Depression
- Suicidal idea



**Permanently  
grounded**



## Case 2

# Anaplastic large cell lymphoma

## Case 2

- A 54 years old Thai male , Prolong fever 1+ month
- CT whole abdomen : multiple paraaortic lymph nodes, retroperitoneal lymphadenopathy, Lt. diaphragm lymph nodes; 1 – 1.9 cms in diameter
- Intraabdominal CT guided biopsy :  
Patho → Anaplastic large cell lymphoma CD 30 + , ALK +
- CT chest : neg. , Bone marrow : neg. study

## Case 2

- Dx. Anaplastic large cell lymphoma stage IIB
- Chemotherapy : CHOP-21 regimen x 6 courses
- After 4<sup>th</sup> CHOP : resolved intraabdominal & retroperitoneal lymph nodes
- **Temporary** grounded 12 months after treatment
- PET/CT (before re-evaluation) : complete metabolic response at intraabdominal lymph nodes

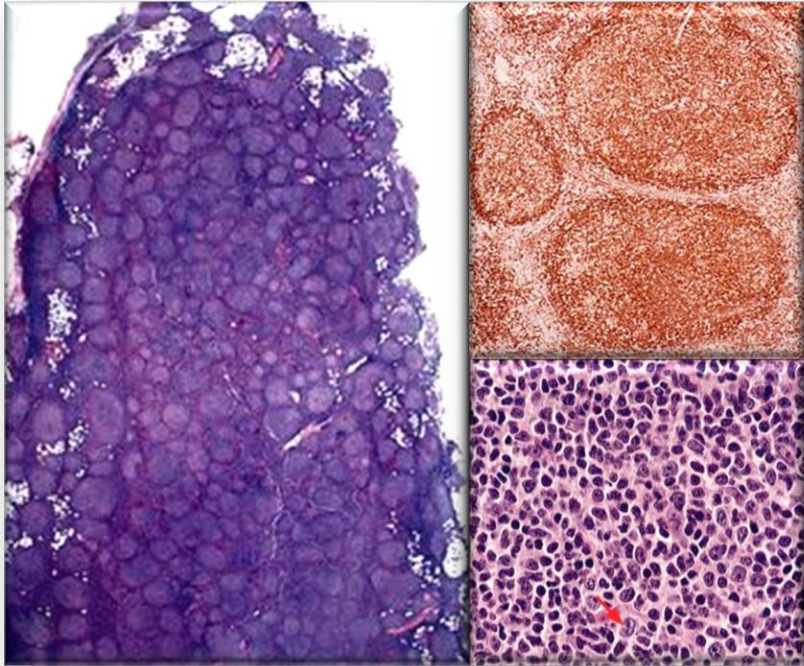
## Case 2

- Cardiac evaluation : LVEF 60%
- Psychological test : OK



- Class 1 OML every 6 months





## Case 3

# Follicular lymphoma stage II AE

Warnke et al, Clinical Rotation Talk;2007.

## Case 3

- A 43 years old Thai male
- Present with Rt. Submandibular mass 2 months
- FNA Rt. Submandibular mass : **Reactive** lymphoid hyperplasia
- Other PE : Rt. Tonsil 3+
- CT neck : Rt. Submandibular mass 3x1.6x2.2 cm ,  
Cervical LN 0.5-2 cm level IA,IB, II-IV bilateral,  
Mild bilateral palatine tonsil enlargement

## Case 3

- Rt. Submandibular mass excisional biopsy and bilateral tonsillectomy
- Patho : Follicular lymphoma grade1
- Hematologist → Dx. Follicular lymphoma stage IIAE
- Watch & wait , F/U every 3 months



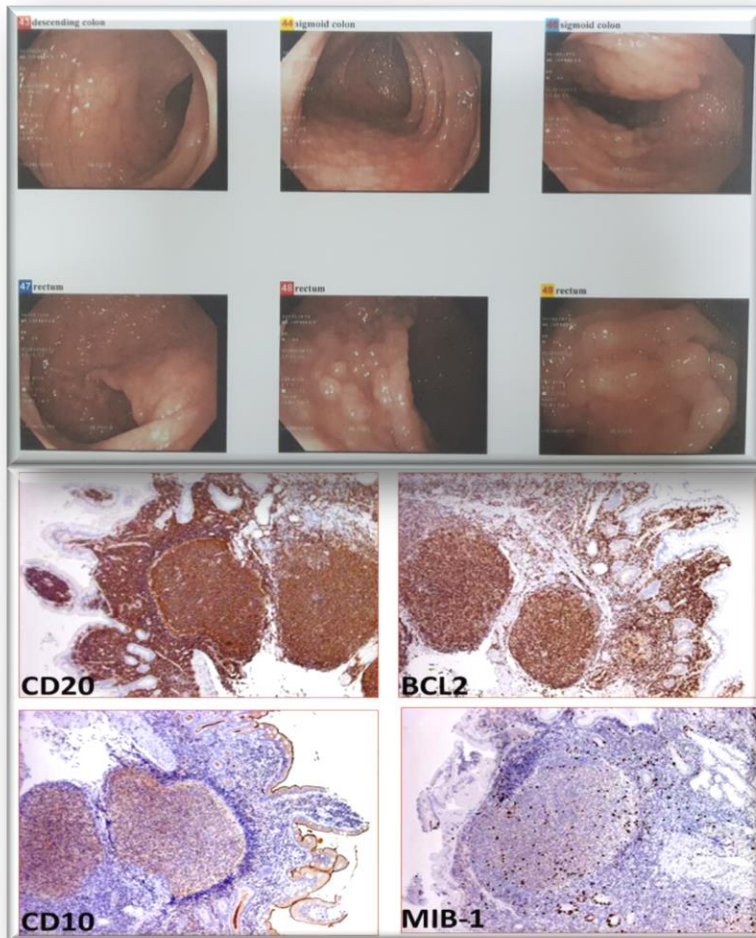
- **Temporary** grounded 3 months



- Class 1 OML every 3 , 6 months

## Case 4

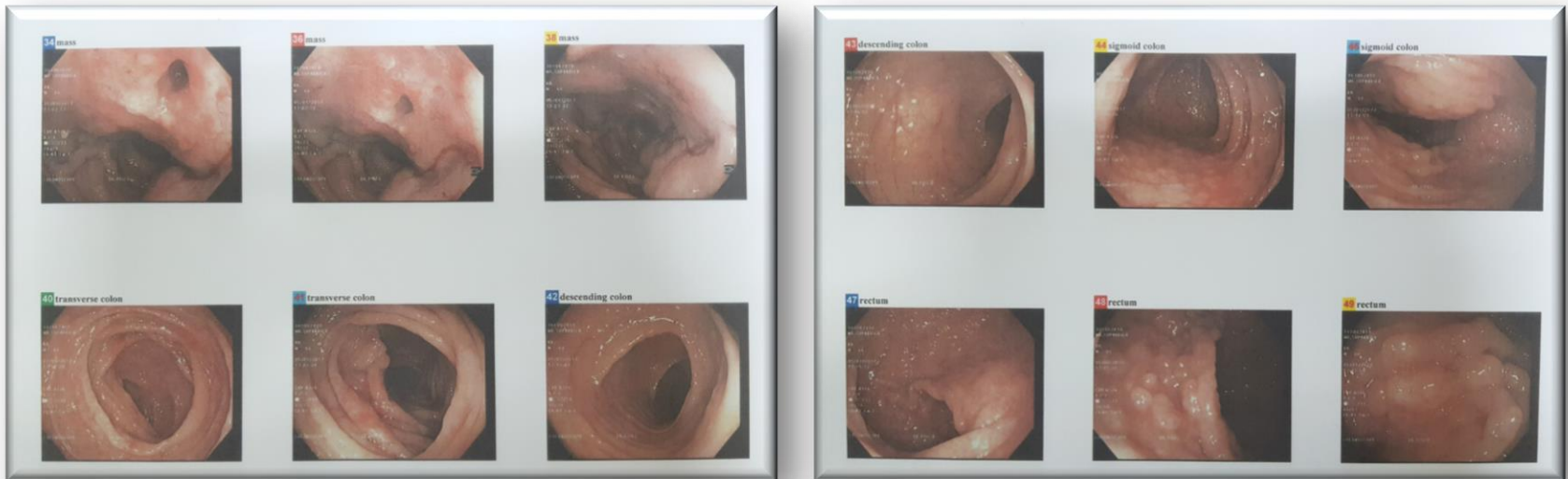
# Follicular lymphoma stage III AE



Mamessier E et al, Haematologica 2014;99:481

# Case 4

- A 44 years old Thai male
- Bilateral inguinal lymph nodes and bowel habit change 2 months



Extrinsic mass at AC , multiple ileal polyps , Diffuse mucosa nodularity ,  
markedly at SC and rectum

## Case 4

- Tissue Biopsy → Dx. Follicular lymphoma grade 1,2 Stage III AE ( Bone marrow : Neg.)
- CHOP \*1 , DA-EPOCH-R \* 5 last chemo May 2017 (Total chemo\*6) + Total body RT
- PET/CT 1 June 2017 : decrease size of mesenteric & intra abdominal LN, decrease size of bilateral supraclavicular & axillary LN, no lesion at intestine
- Complete remission : July 2017



# Case 4

- **Temporary** grounded 6 months after treatment
- Cardiac evaluation : LVEF 70%
- Psychological test : OK



- Class 1 OML every 6 months

## Group G

A remission of an indolent lymphoma may be complete or associated with the presence of small amounts of residual disease after treatment. Licence holders with a good partial remission (minor residual bone marrow involvement or a small amount of residual lymphadenopathy present on Computerised Tomography (CT) scan), which is not progressive, may be certificated. Persistent evidence of liver involvement or palpable enlargement of the spleen will disqualify.

### Follicular lymphoma

A 3 monthly full blood count to include a differential white cell count and biochemical profile to include liver function tests is required. Six-monthly follow up is acceptable after 5 years complete remission.

#### a) **Certification After Primary Treatment**

This may be possible if the International Prognostic Index (IPI) is low and there is no evidence of progressive disease.

Class 1      OML at 3 months  
                  Unrestricted at 1 year

Class 2      Unrestricted at 3 months

#### b) **Certification After Treatment for Relapse**

This may be possible if the relapse was only nodal, performance status was good and serum lactate dehydrogenase was normal at the time of relapse. Additionally for Class 1, if the relapse occurred within 3 years of previous treatment, an OML will be applied to the licence. Thereafter unrestricted certification is only possible if sustained remission is achieved (more than 3 years).

Class 1      OML at 3 months  
                  Unrestricted at 2 years (unless initial remission period < 3 years)

Class 2      Unrestricted at 3 months

# Data

| Case          | 1                    | 2                  | 3                  | 4                  |
|---------------|----------------------|--------------------|--------------------|--------------------|
| Disease       | DLBCL                | ALCL               | FL                 | FL                 |
| Presentation  | Microcytic anemia    | Prolong fever      | Submandibular mass | Inguinal LN        |
| Evaluation    | Refractory           | Complete remission | Stable Disease     | Complete remission |
| Flying status | Permanently grounded | Class I OML        | Class I OML        | Class I OML        |

# Conclusion

- Small amount of incidence
- Limited data
- Evaluation after complete remission
- Both physical and mental
- Patient - Doctor relationship



# Acknowledgements



**Thank you  
for  
Your  
attention**

