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

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Disclosure

I have no actual or potential conflict of interest in relation to this presentation.
Thai Lymphoma Study Group

Jan 2007 – Dec 2014

B-cell NHL

T/NK-cell NHL

NHL, unclassified

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

1. **Leukapheresis:** patient's T cells are harvested
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
4. **CAR T cells undergo ex vivo expansion** on antibody-coated beads
5. **Chemotherapy:** patient receives a preparative lymphodepleting regimen before T-cell infusion
6. **CAR T cells are reinfused** into the patient

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

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. 11.1x8.3x11cm, 2.3x2.1cm
Evaluation

• Physical: Hematologist
  Cardiologist

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

Legend:
- ALC: Anaplastic Large Cell Lymphoma
- ALK: Anaplastic Lymphoma Kinase
- BMT-crd: Bone Marrow Transplantation – compatible sibling donor
- CLL: Chronic Lymphocytic Leukaemia
- DLBCL: Diffuse Large B-cell Lymphoma
- HTLV: Human T-cell Lymphoma/Leukaemia Virus
- 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

UK CAA Guidance on Lymphoid Malignancies 3 of 7 September 2012 v1.0

Civil Aviation Authority
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/mm³ Plt. 454,000/mm³ MCV 73.9
• Work up: anthral 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

Cao et al. Diagn Pathol(2016), Sep 9;11(1):83
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\textsuperscript{th} 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

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 grade 1
- 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
<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>DLBCL</td>
<td>ALCL</td>
<td>FL</td>
<td>FL</td>
</tr>
<tr>
<td>Presentation</td>
<td>Microcytic anemia</td>
<td>Prolong fever</td>
<td>Submandibular mass</td>
<td>Inguinal LN</td>
</tr>
<tr>
<td>Evaluation</td>
<td>Refractory</td>
<td>Complete remission</td>
<td>Stable Disease</td>
<td>Complete remission</td>
</tr>
<tr>
<td>Flying status</td>
<td>Permanently grounded</td>
<td>Class I OML</td>
<td>Class I OML</td>
<td>Class I OML</td>
</tr>
</tbody>
</table>
Conclusion

• Small amount of incidence

• Limited data

• Evaluation after complete remission

• Both physical and mental

• Patient - Doctor relationship
Acknowledgements
Thank you for Your attention