

MEETING ABSTRACTS

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A1

## Hope and despair in the current treatment of nasopharyngeal cancer

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Nasopharyngeal carcinoma (NPC) is a rare disease in the Western world, but it is endemic in certain parts of Southeast Asia and China. During the last decades, the outcome of the treatment has improved considerably. Concurrent chemo-radiation has become the treatment of choice in advanced NPC. Five years survival figures of 80-90 % for T1-T2 and 60-80 % for T3-T4 are not exceptional. The relation between NPC and the Epstein Barr virus (EBV), which is almost 100 % in endemic areas, has opened up several possibilities for early detection and monitoring of the disease using EBV based markers or to new treatment strategies based on this viral connection.

The main progress in the treatment of NPC is coming from the top end hospitals in the high endemic regions. Effective treatment schedules are applied and compliance with treatment and follow up are secured. The good news is the fact that the incidence of NPC is also declining in more prosperous cities like Hong Kong and Singapore and the big cities in Taiwan. So, apparently, preventive measures can be effective on the long term.

Unfortunately, NPC is correlated to hygiene and environmental circumstances like pollution in areas where those being treated live, the adding of carcinogens to food and even to candies and it is more common in developing countries where many patients are suffering from this disease. Furthermore, the treatment possibilities in these parts of the endemic regions are less favorable. Due to the shortness of radiotherapy capacity and the lack of adequate insurance systems, many patients do not have access to effective treatment for this disease.

In a recent study in a tertiary referral hospital in Yogyakarta, the treatment results appeared to be behind compared with the international literature. Waiting time for radiotherapy was during the years of the study (2009-2013) between 3 and 4 months, but has increased to over 1 year and 9 months in March 2015, probably due to the introduction of the National Healthcare program in Indonesia. The most obvious solutions would be to increase the number of RT devices.

However, the short supply is so serious that at least 10 to 20 years will pass before the capacity will be in line with the demand. In the meantime patients are suffering and dying of this treatable disease. Action is needed and preventive measures have to be taken.

Future research should focus on innovative treatment strategies like photodynamic therapy, which have been proven to be effective in residual or recurrent NPC. A combination with other novel treatments, like vaccination and immunotherapy is challenging.

I1

## NPC international incidence and risk factors

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The international geographic distribution of NPC is unique among malignancies. Incidence rates can exceed 20 per 100,000 person-years among males and 10 per 100,000 person-years among females in southern China. Intermediate rates are observed in Southeast Asia, North Africa, the Middle East, and the Arctic, as well as among Asian and Pacific Islander migrant populations, while rates generally remain below 1 per 100,000 throughout the rest of the world. The age-specific incidence rate peaks at around 45-59 years in high-incidence areas, whereas a small early incidence peak at ages 15-19 years is followed by a later peak at around 65-79 years in low-incidence areas. The male-to-female incidence ratio is consistently around 2-3 or greater. Much of the striking geographic variation may be attributable to certain risk factors, such as certain *HLA* alleles and consumption of Chinese-style salted fish, whose geographic distribution mirrors that of NPC. Other NPC risk factors, such as EBV infection, are ubiquitous, yet are almost certainly modified by geographically heterogeneous co-factors. Most established risk factors for NPC are associated with undifferentiated NPC, although tobacco smoking is more strongly associated with squamous cell NPC. The recent worldwide decline in NPC incidence, especially in high-incidence regions, points to an important role of modifiable environmental risk factors that could serve as targets for further disease prevention.

I2

## Familial nasopharyngeal carcinoma and the use of biomarkers

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Nasopharyngeal carcinoma (NPC) has a striking geographical variation with the highest incidence in South China, Southeast Asia, and East Africa; and the lowest incidence in Europe, West Africa, and Central America. As infection of Epstein-Barr virus (EBV), a well-documented cause of NPC, is ubiquitous; the geographical variation of NPC is likely attributable to ethnic and environmental cofactors. Chinese ethnicity in almost all cancer registries in the world has the highest incidence of NPC. Both case-control and cohort studies has

**Result and discussion** By using Chi-square it was found that there was a significant association between the type of mtDNA mutation and the distribution of those proteins. By ANOVA analysis it was found that there was significant association between the type of genes and the number of mutation between CO III gene as compared to CO I and CO II genes, ATPase 8 with ATPase 6, substitution with deletion and insertion. It was concluded that all EBV LMP-1 positive-NPC patients who experienced mtDNA mutation of coding region and types of mutation in those genes had a strong association toward the distribution of protein cytosol that induce apoptosis and ATP energy forming.

#### O16

##### Factors influencing treatment adherence of nasopharyngeal cancer and the clinical outcomes: a hospital-based study

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**Introduction** Adherence to treatment regimens offers both a better survival rate and lower recurrence in nasopharyngeal cancer (NPC) patients. Various factors influencing the adherence to long term therapy include socio economic and medical factors. Understanding those factors is essential to improve the patients' outcome.

**Aims** This study aims to define factors influencing adherence of NPC patients to their treatment regimens and the correlations between those factors and clinical outcomes.

**Methods** A retrospective cohort study was conducted in Dr. Sardjito Hospital based on medical record from 2007-2011. Factors examined were socio-demography, baseline characteristics, and survival. Adherence was defined as completion of the entire course of therapy and clinical follow-up. Data were described and analyzed with Kruskal-Wallis analysis. Kaplan-Maier survival analysis was done to observe its clinical outcome.

**Result and discussion** From 274 NPC cases, we found 184 (67.2 %) patients were adherent. Most of non-adherent patients (32.8 %) were due to lost to follow up (73.3 %), financial problems (9.9 %), adverse event (7.8 %), patient refusal (4.4 %), death (4.4 %), and empty stock of drugs (1.1 %). Patient adherence showed significant correlations with baseline staging ( $p=0.0001$ ), with stage III-IVA showed better adherence compared with those in stage IVB-IVC. Patients with nasal blockage ( $p=0.050$ ), epistaxis ( $p=0.320$ ), ringing ear ( $p=0.570$ ) had been more adherent compared with other complaints. The overall survival (OS) and clinical response were better in adherent than non-adherent patients ( $p=0.0001$ ) with median OS of 1.5 and 0.53 years, respectively. Moreover, adherent patients had more significant result in one, two, and three-year OS ( $p=0.0001$ ;  $p=0.0001$ ;  $p=0.040$ ). However, it declined in the following four and five year OS ( $p=0.993$ ;  $p=0.174$ ). The adherence showed poor correlations with sex ( $p=0.534$ ), first visit age ( $p=0.916$ ), education status ( $p=0.947$ ), occupation ( $p=0.752$ ), covering insurance ( $p=0.825$ ), neck mass complain ( $p=0.347$ ), faster diagnosis ( $p=0.592$ ), histopathology type ( $p=0.278$ ), and free-disease survival ( $p=0.341$ ). Further attention should be given to the factors influencing the adherence to treatment to finally improve patients outcome.

#### O17

##### Chromosomal breaks mediated by bile acid-induced apoptosis in nasopharyngeal epithelial cells: in relation to matrix association region/scaffold attachment region

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**Introduction** Chronic rhinosinusitis (CRS) has been recognised as a risk factor for nasopharyngeal carcinoma (NPC). CRS can be triggered by gastroesophageal reflux (GER) that may reach the nasopharynx. Bile acid (BA), the main component of refluxate, is a potential carcinogen. BA-induced apoptosis has been implicated in various malignancies. Chromosomal breakage is an early event in both apoptosis and chromosomal rearrangement. Matrix Attachment Region/Scaffold Attachment Region (MAR/SAR) appears to be a preferential site of chromosomal breakage. We hypothesised that BA-induced apoptosis may cause chromosomal breaks at MAR/SAR leading to NPC chromosomal rearrangements.

**Aims** To identify BA-induced chromosomal breaks within *AF9* (9p22) SAR and non-SAR regions.

**Methods** MAR/SAR sites in the *AF9* gene were predicted by MARS-CAN. NP69 cells were treated with BA at neutral and acidic pH. Flow cytometric analyses of phosphatidylserine (PS) externalization and mitochondrial membrane potential (MMP) disruption were performed. Inverse-PCR (IPCR) was employed to detect cleavages in SAR and non-SAR regions. IPCR bands were sequenced.

**Result and discussion** Treatment of NP69 cells with BA at neutral and acidic pH resulted in increased apoptosis and increased cleavage frequencies of the SAR region. No significant difference was detected in non-SAR cleavage frequency between untreated cells and cells treated with BA at neutral or acidic pH. A few breakpoints detected in the SAR region were mapped within the *AF9* region that was previously reported to be involved in the formation of *MLL* (Mixed Lineage Leukaemia)-*AF9* fusion gene in acute lymphoblastic leukaemia (ALL) patient. Our findings suggested that BA-induced apoptosis could be one of the mechanisms underlying NPC chromosomal rearrangements. MAR/SAR may play an important role in chromosomal breaks mediated by BA-induced apoptosis.

#### O18

##### Expression of p53 (wild type) on nasopharyngeal carcinoma stem cell that resistant to radiotherapy

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**Introduction** Recurrences remain frequent in nasopharyngeal carcinoma (NPC) patients, despite having received complete therapy. Recent studies have proven that recurrences were caused by NPC cancer stem cells that were resistant to radiotherapy. The mechanism of resistance in cancer stem cells to radiotherapy was assumed to be due to the blocking of apoptosis and/or proliferation induction. The blocking of apoptosis was caused by the decreased of p53 (wild type) expression.

**Aim** To describe the mechanism of NPC stem cells resistance to radiotherapy based on p53 (wild type) profiles.

**Methods** We used a experimental study with pre- and post-test control group design. The cultured NPC stem cells were divided into two