systemic cancers. Recent research has provided insight into some important aspects of brain metastasis development, interaction of brain-metastatic tumor cells with resident cells of the CNS microenvironment and growth patterns within the brain parenchyma. Treatment choices have to consider clinical presentation, number, size and localisation of brain metastases, status of extracranial tumor burden, prior therapies, co-morbidities and histological and molecular tumor characteristics. Recent advances show that targeted therapy against glioblastoma, while established brain metastases and some targeted therapies are able to prevent brain metastasis development. Meningiomas are common and can be cured in 70–80% of cases by surgical resection. However, the rest of cases cannot be resected completely due to surgically inaccessibility (e.g. skull base) or show non-benign histopathological features that are associated with tumor recurrence. Meningiomas have been shown to be molecularly variable and carry distinct and recent genetic and epigenetic alterations that seem to enable targeted therapy and refined prognostication. Overall, significant advances in the biological understanding of brain metastasis and meningiomas drive clinical trial design and improvement of clinical management strategies for these common tumors.

**Key words:** brain metastasis, meningioma, targeted therapy, immunotherapy

**SDS2**

**CHALLENGES IN TREATMENT OF Glioblastoma: CURRENT CONCEPTS AND THERAPEUTIC PERSPECTIVES**

Wolfgang Wick; Neurology Clinic & Neurooncology Program at the National Center for Tumor Diseases

The natural disease course in glioblastoma is grim, in adults as well as in children. To date, there are no options for primary, secondary or tertiary prevention. However, unlike the fatalistic approach generally taken, there are subgroups of patients or individuals clearly benefiting over a variable time from current treatments, radiation and alkylating chemotherapy, as well as experimental precision or immune interventions. This heterogeneity in treatment response reflects the biological heterogeneity of the disease, which needs to be addressed in current preclinical and clinical investigations as well as this identifies primary and acquired treatment resistance as the key challenge in the field of glioblastoma. Importantly, even for most conventional treatments the basic molecular mechanisms for primary or secondary resistance are unknown or incompletely understood.

The present view is that progress will be made with a more precise classification and grouping of glioblastoma. The methylation subgroups clearly provide a first step, but further tumor bulk but potentially also subclinical or single-cell analyses might provide further insights and will be a prerequisite to meaningfully interpretable trials.

Novel preclinical and translational concepts of glioblastoma in adults reflecting the proposed network architecture of the glioma, but also the glioma-brain interface may for the first time separate options for trial interventions in glioblastoma form the usual mainstream in oncology.

Clinical trials of the past years have revealed the potential for further developments. Methylation/histone modifications in O6-methylguanine DNA-methyltransferase (MGMT) promoter hypermethylated glioblastomas and allow leaving out temozolomide for glioblastoma harboring an unmethylated MGMT promoter. The latter is not clinical standard, however we should at some point make sure we still understand, why temozolomide is provided in this clinical situation and how we make a next step.

The field of immuneoncology is rapidly growing with preclinical work and trial concepts, but whereas patients with brain metastases seem to benefit from this development, success in glioblastoma is restricted to uncontrolled early-phase developments.

**Key words:** Brain tumor networks, Molecular targeted Therapy, Neoantigens

**MS3-1**

**IMPLEMENTATION OF GENE PANEL TESTING USING NEXT-GENERATION SEQUENCING**

Kazuo Sakai; Department of Genome Biology, Kindai University, Faculty of Medicine

The advance of next-generation sequencers (NGS) has dramatically improved the performance of genomic analysis of clinical samples in cancer precision medicine. The practical use of gene panel testing for clinical applications has begun in Japan. At present, “OncomineTM Dx Target Test” is listed as a companion diagnostic system using NGS, and “FoundationOne CDs Cancer Genomic Profile” and “OncoGuide™ NCC Oncopanel System” are listed as gene panel testing under insurance coverage. Formalin-fixed paraffin-embedded specimen have been routinely used for molecular diagnosis testing, therefore quality control such as formalin fixation time and tumor contents is important to ensure validity of diagnostic results. In this presentation, the issue to obtain evaluable results of gene panel testing using formalin-fixed paraffin-embedded specimen will be discussed.

Due to evolution of detection technologies, we can detect gene mutation with high sensitivity. Detection of gene mutation in circulating tumor DNA is feasible approach for diagnostic testing in cancer treatment. Liquid biopsy has been approved as a companion diagnostic testing to detect EGFR mutations in NSCLC. Examples of the clinical utility of plasma testing in cancer treatment will be presented.

**MS3-2**

**TREATMENT STRATEGY BASED ON THE RESULTS OF GENE PANELS**

Masayuki Takeda; Department of Medical Oncology, Kindai University, Faculty of Medicine

The advance of next-generation sequencers (NGS) has dramatically improved the performance of genomic analysis of clinical samples in cancer precision medicine. The practical use of gene panel testing for clinical applications has begun in Japan. At present, “OncomineTM Dx Target Test” is listed as a companion diagnostic system using NGS, and “FoundationOne CDs Cancer Genomic Profile” and “OncoGuide™ NCC Oncopanel System” are listed as gene panel testing under insurance coverage. Formalin-fixed paraffin-embedded specimen have been routinely used for molecular diagnosis testing, therefore quality control such as formalin fixation time and tumor contents is important to ensure validity of diagnostic results. In this presentation, the issue to obtain evaluable results of gene panel testing using formalin-fixed paraffin-embedded specimen will be discussed.

Due to evolution of detection technologies, we can detect gene mutation with high sensitivity. Detection of gene mutation in circulating tumor DNA is feasible approach for diagnostic testing in cancer treatment. Liquid biopsy has been approved as a companion diagnostic testing to detect EGFR mutations in NSCLC. Examples of the clinical utility of plasma testing in cancer treatment will be presented.

**EL1**

**BUILDING A CAREER IN NEURO-ONCOLOGY RESEARCH**

Webster K. Cavenee; Ludwig Institute for Cancer Research, University of California San Diego

A young neurosurgeon has several interesting and important possible career paths: clinical care, clinical/translational research and more fundamental research. Each of these has its own requirements for training, talent and commitment. A closer inspection of each of these, however, reveals that they are basically quite similar. From this, several general conclusions can be gleaned and recommendations for optimizing the chances of long-term career success. In this short talk, I will review the aspects of our training program that has allowed each of our Japanese trainees to have remarkable success both while with us in the US and upon their return to Japan. My goal is to explicitly describe and state these as a roadmap for success, particularly in the rapidly developing field involving the application of molecular and genetic technologies to translational and basic neuro-oncology research— but also as more generally applicable principles.

**Key words:** career, research, training

**S4-KL-1**

**UPDATE OF WHO2016 CLASSIFICATION OF ADULT diffuse gliOMAS**

Takashi Komori; Department of Laboratory Medicine and Pathology, Tokyo Metropolitan Neurological Hospital

The World Health Organization (WHO) central nervous system (CNS) tumor classification has represented the primary source of diagnosis and grading criteria of brain tumors. Nonetheless, recent advances of studies on their molecular alterations require more rapid update of recommendations for clinical use. To accomplish this, cIMPACT-NOW (the Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy) was established in 2016 and has published four updates. For adult gliomas, update 1 clarified the use of the term NOS (Not Otherwise Specified) and proposed a new term NEC (Not Elsewhere Classifiable); update 2 revised EGF mutations, update 3 proposed molecular criteria for an IDH-wildtype diffuse or anaplastic glioma, update 4 removed IDH1, and update 5 revised clarifications regarding diffuse astrocytoma/anaplastic astrocytoma, IDH-mutant; update 6 proposed molecular criteria for an IDH-wildtype diffuse or anaplastic astrocytic glioma without histological features of glioblastoma, which would have been, at one time, categorized as grade IV glioblastoma. Nonetheless, no consensus on pathologic or molecular markers that could be incorporated into a more clinically relevant grading scheme for IDH-mutant gliomas has been reached. The molecular alterations previously studied using relatively large cohorts include CDKN2A/B homozygous deletion, CDK4 amplification, R1I mutation/homozygous deletion, PIK3CA or PIK3R1 mutations, PDGFRA amplification, NMYC amplification, global hypomethylation, genomic instability and chromosome 14 loss. The proliferative activity, based on the mitotic count or Ki67 indices, and other morphologic features typical of a high grade that
Abstracts

might stratify the risk better than the current criteria have also been evaluated. Despite the discordance among the results of previous studies, CDKN2A/2B homozygous deletions have been shown prognostic significance in high-grade IDH-mutant astrocytomas and microvascular proliferation straifies IDH-mutant gliomas lacking a CDKN2A homozygous deletion, suggesting that the integration of molecular information and traditional histological findings is still essential for achieving maximum risk stratification of adult cases of IDH-mutant diffuse gliomas. The grading scheme for adult IDH-mutant as well as wild-type gliomas should therefore be revised in the next WHO update.

SL3 PRIMARY CNS LYMPHOMA: CURRENT CONCEPTS AND THERAPEUTIC PERSPECTIVES
Christian Grommes; Department of Neurology, Memorial Sloan Kettering Cancer Center

The lecture will summarizes current standards of disease staging and treatment of Primary Central Nervous System Lymphoma (PCNSL). Concepts underlying the current first-line treatment regimen will be presented and current controversies in the treatment of PCNSL, including choice of induction regimen, choice of consolidation, and the roles of surgery/radiation/intrathecal therapy, will be discussed. In addition, the presentation will summarize novel insights into the pathophysiology of PCNSL, particularly the B-cell receptor signaling pathway (BCR). Results of completed and ongoing clinical trials testing the BCR will be presented. The treatment standards in the recurrent setting will be summarized and additional novel therapeutic avenues, eg, immune checkpoint inhibition will be discussed. Furthermore, novel combinational clinical trials in recurrent/refractory setting will be discussed. Moreover, the diagnostic and prognostic value of novel, genomic testing and their integration into clinical trial development and clinical decision making will be discussed.

Key words: -Primary Central Nervous System Lymphoma, chemotherapy regimen, salvage therapy, B-cell receptor signaling pathway

SS-KL-1 CURRENT TREATMENT FOR DLBCL AND PROPHYLAXIS AND TREATMENT FOR SECONDARY CNS Lymphoma.
Koji Izutsu; Department of Hematology, National Cancer Center Hospital

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of lymphoma, comprising 30% of all lymphoma cases. More than 60% of patients can be cured with current standard treatment, R-CHOP. On the other hand, prognosis of patients with relapsed or refractory DLBCL is disappointing with less than 10% being cured with salvage chemotherapy followed by high-dose chemotherapy with autologous stem cell transplantation. Prognosis of patients with central nervous system (CNS) relapse is especially poor because of a limited treatment option. Thus, evaluating risks of CNS relapse at diagnosis and administering prophylaxis including intrathecal methotrexate (MTX) or systemic high-dose MTX concurrently with R-CHOP or as consolidation therapy in high-risk patients are often-used approach. Clinically, higher risk according to the International Prognostic Index and extranodal involvement in organs such as kidney, adrenal gland, breast, testis, or bone marrow are considered to be high-risk for CNS relapse. Recently, CNS-International Prognostic Index has been proposed to integrate aforementioned risk factors. Moreover, patients with intravascular large B-cell lymphoma, CD5+ DLBCL, double hit lymphoma are reported as high-risk for CNS relapse. Further, the MYD88 L265P mutation, a common mutation in primary CNS DLBCL (PCNSL) is also common in DLBCL of testis or breast, which are the sites associated with CNS relapse.

Strategies for CNS prophylaxis have not established yet, and it is still unclear whether intrathecal MTX or high-dose MTX can prevent CNS relapse. Moreover, treatment for secondary CNS relapse have not been established. In particular, for those with both CNS and extra-CNS lesions, effective treatment options are very limited. The role of novel agents such as BTK inhibitors, lenalidomide, and immune check point inhibitors, whose efficacy have been shown for PCNSL, should be investigated further in the management of secondary CNS lymphoma.

Key words: Secondary CNS lymphoma, prophylaxis

SS-KL-1 CANCER GENOMIC MEDICINE: FROM BENCH TO CLINIC
Hiroiyo Aburatani; Genomescience Laboratory, Research Center for Advanced Science and Technology, The University of Tokyo

Over the last two decades, genomic technology such as microarray and next-generation sequencing (NGS) enabled comprehensive analysis of cancer genome. International cancer genome consortium, established in 2007, completed the analysis of 25,000 cases and has brought discovery of novel cancer driver genes and improved our understanding cancer biology. For example, discovery of IDH1/2 mutation in various cancers created a new concept, 2-hydroxyglutarate as Oncometabolite. The mutational signature patterns allow us to predict how the individual cancer was developed. Anti-cancer drugs, such as alkylating agents, occasionally modify the bases and introduce mutations through mispairing in replication.

Currently we are aware that cancer is a genetic disease, where accumulation of genetic and epigenetic alterations in the genome leads to cellular transformation, and that mutational landscape in each patient is unique. To realize the personalized oncology, clinical sequencing test was developed. This year a couple of NGS-based cancer panel tests have been approved for reimbursement by nation-wide healthcare system in Japan. In this seminar I will discuss the future improvement in genomic oncology.

Key words: cancer genome, genomic oncology, mutation signature

EI2 CHANGES IN JAPANESE ACADEMIC CLINICAL TRIALS AND FRAMEWORKS FOR PLANNING CLINICAL TRIALS
Kenichi Nakamura; JCOG Operations Office/Clinical Research Support Office, National Cancer Center Hospital

After the enforcement of the Japanese Clinical Trials Act, the number of investigator-initiated registration-directed trials (IRBDT, Chiken) is increasing while the number of non-registration academic trials is decreasing. Pharmaceutical companies tend to make an investment in IRBDT because the data derived from IRBDT can be utilized for registration for (Stup) when the goals and return are clear for industries. On the other hand, the reason of the decrease of non-registration academic trials is the burden of cost and procedures specified in the Clinical Trials Act. In order to start academic trials, certain amount of research budget is indispensable due to the cost for certified review board and clinical trial insurance. Also, even minor changes of specifications in jRCT should be submitted to certified review board and the hospital directors of all participating sites, which is one of the most serious burden for investigators. Confirmation of COI declaration in participating sites is another burden for investigators/sites. Under these circumstances, the number of non-registration academic trials will be decreasing for the time being.

In the Clinical Trials Act era, investigators must prepare some budget to start clinical trials. In order to obtain public funding, social/scientific value and scientific validity are substantially important. For expression the social value sufficiently, the purpose of the trial should focus not on the researcher's interest but on the contribution on patients. In terms of scientific validity, the framework of PICO is useful; PICO means Patient, Intervention, Control and Outcome.Utilization of this framework and the consistency of these four factors are essential to make the trial design sound.

Key words: Clinical Trials Act, Chiken, Clinical Trial Design

ANGIOGENESIS/INVASION (ANGI)

ANGI-01 ALTERATION IN IMMUNE REGULATORY CELLS BEFORE AND AFTER TREATMENT BY STUPP REGIMEN WITH OR WITHOUT BEVACIZUMAB FOR GLOBLASTOMA
Chihashi Tanaka1, Ryota Tamura, Yohs Yamamoto, Yukina Morimoto, Akihiko Tesigawa1, Satoru Tochigi1, Yuzuru Hasegawa1, Jun Takei, Yasuharu Akasaka, Hikaru Sasaki, Yuchi Murayama; 1Department of Neurosurgery, Jikei University School of Medicine, Kashawa Hospital, Chiba, Japan

BACKGROUND: In our previous study, bevacizumab (Bev), a humanized anti-vascular endothelial growth factor monoclonal antibody, downregulated the expression of programmed cell death-1 (PD-1)/programmed cell death ligand-1 (PD-L1) immune checkpoint molecules, suppressed the infiltration of immunosuppressing cells such as regulatory T cells (Tregs) and tumor-associated macrophages (TAMs), and induced cytotoxic T lymphocytes (CTL) infiltration. To explore the possibility that inhibition of immunosuppressive cell infiltration and induction of CTL were attributed to not only Bev alone but also radiation (RT) or temozolomide (TMZ), we re-evaluated those alterations in the tumor tissue obtained from patients before and after the treatment using Stupp regimen (RT concomitant with TMZ) without Bev therapy. MATERIALS & METHODS: We analyzed 10 tumor tissues from 5 patients with GBMs, which were paired patients before and after the treatment using Stupp regimen (RT concomitant with TMZ) without Bev therapy. We performed immunohistochemical analyses on formalin-fixed, paraffin-embedded tissue of 10 tumors. The sections were stained with anti-Ki-67, anti-VEGF-A, anti-VEGFR1, anti-VEGFR2, anti-CD34, anti-HF1 and anti-CD8, anti-nestin, anti-PD-1, anti-PD-L1, anti-CD4, anti-CD8, anti-FoxP3, and anti-CD163 antibodies. All expressions were assessed by authors with blinded clinical information. RESULTS: Immunohistochemical analyses demonstrated that the expres-